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Bench2Bedside 2022 Case Competition & Conference: Translational Research Proposals

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Abstract
The Bench2Bedside Case Competition & Conference is an undergraduate initiative which aims to further undergraduate student understanding of translational research. This initiative prompts students to examine clinical questions through a basic science lens while examining laboratory work from a clinical perspective. It promotes an understanding of how clinical research is conducted, effective ways of communicating cross-disciplinary research findings, how findings are critically evaluated, and productively applied to patient care. Students engage in a two round case competition involving an initial written research proposal stage, followed by an oral presentation stage. The case competition is based on a case study developed in conjunction with an authority in translational research. Experts with a rich understanding of translational research are also involved in judging the case competition, along with workshops conducted during the conference portion of the event. This year's case study focused on neurocognitive disorder and COVID-19 in an elderly patient. The research proposal abstracts for competition finalists are highlighted in this abstract book. For more information on the competition structure, and conference offerings please visit https://bench2bedside.club/.

Keywords: translational research; bench to bedside; neurocognitive disorder; bipolar disorder; dementia; elderly; older adult; COVID-19; undergraduate research; competition

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Conference Abstracts
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Senior Team Proposal Abstracts

Evaluating the efficacy of perindopril in preventing the onset of delirium in older adults hospitalized with COVID-19: A research study

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COVID-19 infection is known to present atypically in approximately 33% of older adults, with delirium being one of the most common symptoms.[1] The development of delirium is associated with a multitude of adverse outcomes including longer hospital stays, cardiopulmonary events, functional decline, and increased morbidity. Researchers predict that SARS-CoV-2 interferes with the renin-angiotensin system (RAS) through the binding of its spike protein to the ACE2 receptor in the lungs.

Ultimately, this restricts blood and oxygen supply to the brain, which is thought to contribute to delirium. Previous research has noted that centrally-active ACE inhibitors, such as perindopril, have neuroprotective properties and reduce the incidence of delirium post-surgery. However, the ability of ACE inhibitors to improve cerebrovascular blood flow to mitigate COVID-19-induced delirium in older adults has not yet been explored. We hypothesize that older adults with COVID-19 who are treated with perindopril will have a decreased incidence of delirium, improved cerebral blood flow, and higher levels of intracerebral oxygen saturation compared to a control group. This true-experimental, double-blinded, randomized controlled trial will have eligible patients allocated to either the treatment perindopril group or placebo control group. For the duration of their hospital stay, or until day 14 post-randomization, patients will receive 4mg of perindopril or the placebo. The onset of delirium will be evaluated using the standardized Confusion Assessment Method (CAM) twice daily throughout the study. Further, magnetic resonance imaging (MRI) and cerebral oximetry by near-infrared spectroscopy (NISR) will be conducted once every 72-hours to measure changes in cerebral blood flow and intracerebral oxygen saturation, respectively. A CAM, MRI, and NISR will also be conducted at a three-month follow-up visit. Future research should focus on the mechanisms by which ACE2 inhibitors prevent delirium to investigate the potential for perindopril to be used as prophylactic therapy for delirium in older adults.

Improving the quality of life of individuals with long COVID-exacerbated dementia: A research proposal

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The prevalence of COVID-19 infections in individuals over the age of 65 years is higher than in younger populations and is often associated with dementia, which is the most common COVID-19 comorbidity in older Canadian adults. Dementia seems to be associated with an enhanced risk of severity and mortality from COVID-19. This may be due to old age and previous underlying medical conditions that heighten the infection severity. A key physiological biomarker of dementia is low heart rate variability (HRV), which indicates dysregulation of the parasympathetic nervous system and is associated with a higher risk of all-cause mortality. Many older patients who develop Long COVID display exacerbated dementia symptoms following infection. However, there is no standard framework for dementia rehabilitation in Canada, despite studies showing the individual efficacy of therapies that can ameliorate dementia symptoms. We propose an in-patient rehabilitation program for these individuals using a multifaceted approach consisting of 60 minutes of daily occupational therapy, counseling, and music therapy. During counseling, participants will undergo 30 minutes of biofeedback therapy, which has been shown to improve HRV. 30 participants aged 65 years and older with Long COVID exacerbated dementia that has moderate to severe symptoms will be recruited through community outreach. Participant scores from 'The Activities of Daily Living Questionnaire' (ADLQ), a validated measure to assess functional ability in patients with dementia, will be assessed at baseline and following the intervention. HRV will be analyzed at baseline using blood volume pulse photoplethysmography and weekly throughout the intervention. Considering the absence of a standard framework to treat dementia symptoms, the findings from this study can be used to provide a framework to further develop existing dementia treatment programs and optimize older-adult quality of life.

Uncovering the underlying mechanisms in the bidirectional relationship between mood disorders and COVID-19: A research study

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Current research shows that pre-existing mental health conditions such as mood disorders increase COVID-19 severity, hospitalizations, and mortality. Higher levels of immune-inflammatory markers IL-6 and CRP were previously observed in both COVID-19 patients and patients with mood disorders, potentially explaining the appearance or worsening of neuropsychological symptoms due to COVID-19 infection. The underlying mechanism for this relationship is not yet understood. This research study aims to investigate how presence of mood disorders exacerbate the severity of COVID-19 infection. Patients 18 years and over diagnosed with mood disorders before 2020 and/or COVID-19 from psychiatrist rosters, hospitals, and support groups will complete a questionnaire corresponding to their experimental group: patients diagnosed with mood disorders, patients with mood disorders who have never contracted COVID-19, and patients with COVID-19 with no pre-existing mood disorders. The questionnaire will be sent at 3 time points, beginning, 7 months later, and 12-14 months later, and will contain two sections: COVID-19- and BPD-1-specific symptoms. Questions on symptoms are supported by

evidence on moderate and severe cases of COVID-19 in ICUs and consultation with individuals in support groups who have had long COVID-19. These questions will focus on neuropsychological symptoms, especially delirium. Participants diagnosed with COVID-19 that experience neuropsychological symptoms in the last survey period will receive a PET scan to check *in vivo* concentrations of IL-6 and CRP. Responses to the questionnaire will be collected via online forum or mail-in packages. Results from the questionnaire will be age-matched to account for confounding variables. The researchers predict that the concentrations of interleukin-6 and C-reactive protein will be significantly higher in individuals with COVID-19 that had pre-existing mood disorders than other experimental groups and manic/depressive episodes will intensify compared to baseline for BPD-1. Revealing this bidirectional relationship enables physicians to improve treatment plans for patients presenting both conditions.

Improving hospitalized QoL of UTIs with patient advocacy and value based care: A research study

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Treatment conferred to patients that is standard and resource extensive can be a non-sustainable approach and inadvertently lower patient's quality of life. Urinary tract infections (UTI), one of the most common bacterial infections are commonly treated using antibiotics. However, this there exist criteria to limit use of antibiotics, and determine when treatment is preferrable to no treatment of asymptomatic cases, as overtreatment can contribute to the rising problem of antibiotic resistance and put the patient at increased risk of re-infections. There exist patient advocates, a job that shows compassion and defends the stressed hospitalized patient. Our qualitative comparative study compares patient quality of life (QoL) before and after a patient advocate-based intervention in hospitalized UTI cases and hypothesise that a patient advocate aware of low-tech high value UTI treatment will improve patient and family QoL. The study revealed a significant increase in the mean QoL score following intervention and a decreased antibiotic prescription rate in the hospital. Patients describe improved communication with the hospital staff with the help of the advocates. A systemic problem that contributes to antibiotic over prescription needs a systemic solution, with advocates just the beginning of changing healthcare values to the human connection and be environmentally sustainable.

Junior Team Proposal Abstracts

Determining the efficacy of a multimodal treatment for COVID-19 associated delirium

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Recent evidence has linked COVID-19 to delirium, a neuropsychiatric syndrome characterized by an acute disturbance in cognition, attention, and awareness. Currently, no strong framework exists for assessing and managing COVID-19-associated delirium in elderly patients with complex health profiles. We propose an investigation to determine the efficacy of a multimodal treatment for COVID-19-induced hyperactive delirium in elderly patients, compared to that of unimodal pharmacological and non-pharmacological treatments. A three-week experimental cohort study will be conducted, involving 400 elderly Canadian patients presenting with hyperactive symptoms of delirium caused by hypoxemia, who will be recruited through purposive sampling. Four cohorts will be used, consisting of a control treatment, aripiprazole treatment (2-15 mg/day), the ABCDEF regimen, and a combination of aripiprazole and the ABCDEF regimen. The ABCDEF regimen involves A: assessment and treatment of cognitive pain, B: correcting breathing to monitor and correct hypoxemia, C: healthy choices of lifestyle, D: treating delirium through non pharmacological methods, E: exercise and mobility, and F: family engagement[8]. Based on results from Western blotting and a t-test, we expect to see improvements in delirium for all three treatment groups compared to the control group, measured using the Confusion Assessment Method (CAM) and S-100β biomarker. We hypothesize that a multimodal approach will be most effective at targeting the symptoms of delirium in elderly COVID-19 patients and result in a more significant decrease in S-100β protein abundance. The findings from this translational research proposal may be applied to address clinical uncertainty and improve patient outcomes in the treatment of COVID-19-associated delirium.

Biomarkers indicating delirium following SARS-CoV-2 infection in patients with bipolar disorder: A research study

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Delirium, which is linked to bipolar disorder, cerebrovascular disease, and more recently SARS-CoV-2 infection, has well-developed clinical practices to support patients during episodes, especially considering that one-third of hospitalized patients over the age of 70 present symptoms. However, research on biomarkers as a means of early intervention and preventative measures is lacking, which presents new uncertainties for COVID-19-infected patients (i.e., neurological deterioration; dementia). Our proposal addresses this shortcoming in translational medicine and aims to determine biomarkers that indicate delirium following SARS-CoV-2 infection in bipolar disorder patients to present a holistic understanding. By conducting a correlational and field study, quantitative data, such as hospital records, as well as qualitative data, in the form of semi-structured interviews and observations from a sample of 500 patients over the age of 60 with a history of bipolar disorder will be collected. Then, statistical analyses run by the one-way ANOVA test will be used to determine statistical significance; in other ways, the computation would extrapolate biomarkers. Additionally, ethics guidelines and approval will be followed to maintain patient anonymity, confidentiality, informed consent, and compassionate practices and ensure no harm. The indication of biomarkers with respect to delirium following SARS-CoV-2 infection in patients with a history of bipolar disorder can open a window of exploration into possible genetic risk factors and the influence of lifestyle choices for high-risk groups. Furthermore, it can allow for the development of preventative measures by raising awareness and educating the public.

Assessment of cognitive assistive technologies in elderly patients with dementia post-COVID-19 infection: A research proposal

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SARS-CoV-2 infection is thought to be implicated in an increased risk of various neurodegenerative diseases given its role in neuroinflammation. As a result, the regular implementation of practices designed to promote synaptic plasticity may decrease the risk of dementia in susceptible populations. It is hypothesized that incorporating 15 minutes of use of a mobile application designed to improve synaptic plasticity five times per week in the daily routines of patients aged 65+ who have survived a COVID-19 infection may decrease the prevalence of subsequent dementia. The goal of this application would be to (i) deliver interventions related to long-term potentiation as well as (ii) consolidate patient health data to improve ease of access for caregivers and medical staff. This may be investigated through a two-pronged randomized controlled trial aimed to compare neuronal functioning through repeat neuropsychological exams, magnetic resonance imaging and electroencephalogram tests over a 6-year timeframe between no-intervention and intervention groups while collecting caregiver and healthcare worker data regarding its efficacy in improving quality of life. It is expected that patients consistently using cognitive assistive technologies in long-term care facilities will experience lower incidence of cognitive decline compared to the control group due to improved maintenance of mental health and the learning of new skills. In addition, with the use of technology, patients may experience increased autonomy and independence, improving their quality of life while simultaneously providing relief to their families and caregivers. Some further considerations may include the degree of technological proficiency of the patients during the development process to ensure that patients reap the maximum benefits. Factors including rapid development and testing, funding, and strong technology support systems must be taken into consideration to ensure a seamless transition to increased reliance on technology in post-COVID-19 patients with dementia.

Prevention of long-term neurological effects of COVID-19 in elderly patients

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COVID-19 has detrimental effects on human health, one of those include a neurological problem due to hypoxemia (lack of oxygen in blood). This might eventually lead to the signs of delirium in the patients and therefore is essential to be prevented with a specific treatment. This study aims to determine long term neurological consequences of COVID-19 to provide better patient care. Specifically, it investigates delirium as a symptom of COVID-19 in elderly patients with and without a history of previous mental health disorders. In this context, those with existing mental health issues might be more likely to develop dementia. To test the hypothesis, potential experiments involving the prevention of delirium in the elderly COVID-19 patients could be conducted. The participants (elderly covid patients) are randomly divided into two groups, one of which received standard care, while the other received extra care in addition to the standard care. The difference in delirium symptoms may be analyzed via Pearson's r calculation or ANOVA test comparing the symptoms or blood oxygen levels. The other factor that could be accounted for during another analysis was the mental health records. The potential results showed that there was a higher degree of delirium symptoms in people with lower oxygen levels. In addition, the data supported the idea that patients experiencing delirium are more prone to dementia in the future. The second set of the experiment suggested that post-COVID-19 patients with existing mental health issues were more likely to show the signs of delirium. These results suggest that potential extra care for the elderly patients recovering from COVID-19 is crucial for prevention of delirium symptoms, especially if they have a history of mental health disorders. On this basis, the concept of special treatment should be considered to improve patient well-being since it might lower risks of developing dementia in the future.

Exploring the effects of SARS-CoV-2 infection in those with pre-existing mental disorders

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COVID-19 has had a major effect on the world, leading to one of the world's biggest pandemics the world has experienced, while also affecting many mentally ill patients. In fact, due to COVID-19, many mentally ill patients, specifically patients with bipolar disorder, have been negatively affected by COVID-19 and even some patients had a relapse of bipolar disorder or even increase in severity or occurrence of depressive symptoms and manic episodes, which are associated with bipolar disorder. Additionally, in recent case studies, it has been observed that COVID-19 would lead to increased manic episodes and increased severity of depressive symptoms. This may not be a direct cause of COVID-19, but also due to how COVID-19 is treated through the general clinical protocol (i.e., medication given to the patient) or even the environment the patient is experiencing. We propose a clinical trial on four different groups of people: patients with COVID-19 and bipolar disorder, patients without COVID-19 and but have bipolar disorder, patients with COVID-19 and without bipolar disorder, and a control group with neither COVID-19 nor bipolar disorder. This clinical trial would observe the different physiological and behavioral differences between these patient groups. This research would be a great indication of why these patients experience these increased manic episodes or depressive symptoms. It may also lead to future research into other mental illnesses, and even a change to the modern protocol to increase patient health outcomes with mental illnesses.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Authors' Contributions

RA: Served as Co-head of the conference planning committee, drafted the conference abstract booklet, and gave final approval of the version to be published.
DP: Served as Co-head of the conference planning committee, assisted authors in submitting abstracts, and gave final approval of the version to be published.
AQ: Served as consultant for the conference planning committee and gave final approval of the version to be published.
DD: Served as consultant for the conference planning committee and gave final approval of the version to be published.

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