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Occam, Hickam, troponin and appropriate use - A commentary on the clinical efficacy of a frequently requested and useful lab test

recently attended on the cardiology consult service of an academic medical center. It involved working with a talented team of medicine interns, residents, and cardiology fellows in assisting colleagues caring for patients with a variety of cardiovascular issues. These consults were for patients not admitted to a cardiovascular service and came from essentially every medical and surgical specialty. At the presentation of each new patient, it was helpful to know the reason for the consult. For approximately 20% of the consults the reason was that the patient had an elevated troponin level. Most of these patients did not have an acute coronary syndrome. The focus of this commentary is appropriate use of current generation troponin tests. Acute coronary syndromes due to coronary plaque rupture and thrombotic occlusion are a major cause of morbidity and mortality and troponin assays are helpful in detecting them.1 Troponin is a protein in striated muscle that regulates excitation and contraction, and consists of three molecules (C, I, and T.) Troponin I and T are specific to cardiac tissue, and when released in the bloodstream are markers for myocardial injury or stress.1-3 For patients with signs and symptoms of myocardial ischemia, a troponin assay aids in early detection of acute coronary syndromes and saves lives.1-3 Per the Third Universal Definition of Myocardial Infarction global task force, troponin is now the biomarker of choice when evaluating for classic myocardial infarction (type 1) that is due to acute occlusion (partial or full) of a coronary artery.2 First generation troponin assays were highly predictive of acute coronary syndromes and clinicians were conditioned to make that diagnosis with any troponin elevation. This no longer holds true. Now in their fourth or fifth generation, troponin assays yield elevated levels for a number of conditions besides acute coronary syndrome.2-5 In a series of 12,553 hospitalized patients using a current assay, over 40% with an elevated troponin did not have a thrombotic coronary event, and the positive predictive value for diagnosing acute coronary

syndrome was 56%; with a troponin level of 1.0 ng/ml or lower it was 48% or less.4 When not due to decreased renal clearance, troponin elevations may be an indication of cardiac myocyte strain or injury without thrombotic coronary occlusion, when the heart is an "innocent bystander" during a severe noncardiac condition.3,5 This type of acute injury to the myocardial cells is designated as a type 2 myocardial infarction (myocardial necrosis where a condition other than coronary artery disease contributes to an imbalance between myocardial oxygen supply and/or demand 2); it is anticipated that type 2 myocardial infarction will be added as an ICD-10 code in October, 2017. Proposed mechanisms of cardiac injury in these patients include circulating inflammatory cytokines and elevated $cate cholamines. 5\,Conditions\,that\,may\,cause\,troponin\,detection$ with current assays include tachycardia (from essentially any cause), hypotension, hypertension, strenuous exercise (e.g. marathon runners), sepsis, renal failure, pulmonary embolus, heart failure, pericarditis, polymyositis, rhabdomyolysis, burns, cardiac trauma, respiratory failure, ventricular hypertrophy, drug toxicity (including cancer chemotherapy) and neurally-mediated sympathetic activation.2-5 Advanced age may be added to this list; one recent study found that 41% of patients over age 70 presenting to the ED in whom both acute coronary syndrome and other known non-thrombotic coronary syndrome causes were ruled out had troponin elevations.6

This relatively new phenomenon of elevated troponin levels in patients not having an acute coronary syndrome may lead to overlooking the appropriate diagnosis and thus inappropriate treatments, increased costs of tests and services, increased length of stay, and unindicated procedures. 7 For example, when patients with gastrointestinal bleeding or intracranial hemorrhage have elevated troponin results, treatment for acute coronary syndrome with antiplatelet or anticoagulant medication is antithetical to their primary diagnosis. Likewise, giving a beta blocker for a positive troponin to a hypotensive



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patient in septic shock may be detrimental. Clinicians dealing with an abnormal troponin result, even when the patient's presentation is not consistent with coronary thrombosis, often feel compelled to order additional cardiac tests and services, adding to the overall cost of care. Elevated troponin levels in such patients may lead to invasive cardiac procedures. In a study of patients with an elevated troponin and subsequent normal coronary angiograms, 28% had tachycardia, 10% pericarditis, 5% heart failure, 10% strenuous exercise, and 47% had no clear precipitating event.8

The practice of obtaining a troponin level before assessment of the patient deserves special mention. It runs counter to what most of us learned in our training, and contrary to good medical practice. It remains advisable to take a history, perform a physical examination, and then order appropriate studies. Indiscriminate troponin testing is an international finding: in a study from the U.K. at a National Health Service hospital, 28% of the troponin requests were deemed "completely irrelevant." 7 These were ascribed to "tick box" practice in the triage setting prior to a clinical assessment. When educational interventions were done on how to improve troponin requests and when to do so, this percentage decreased to 15%. In a busy emergency department, with its mandates to both turn patient census over quickly, and to not miss a patient having an acute myocardial infarction or unstable angina, it is understandable why indiscriminate ordering of a troponin level may be favoured. Also, in intensive care units a troponin may be requested for a sick patient who is poorly communicative.3 Yet in our pursuit of quickly recognizing acute coronary syndrome, giving patients that diagnosis when they do not have it is an undesired outcome. The routine practice of requesting a troponin as part of a bundled lab set should be re-examined.

A strategy for improved troponin use is to perform a history (with attention to cardiac risk factors), a physical exam, and a review of the ecg in order to put abnormal troponin results in the appropriate clinical context and avoid diagnostic confusion and malfeasance.2-5 In some cases an echocardiogram to detect left ventricular wall motion abnormalities adds additional value. I offer three examples of patients with positive troponin results due to non-thrombotic causes where this strategy was helpful: 1) a 55 year old man with colon cancer presented to the emergency department with dizziness after two days

of severe bleeding per rectum. He had sinus tachycardia, hypotension, and his hematocrit was 16%; 2) A 36 year old woman being treated for acute myelogenous leukemia on the oncology service developed atrial fibrillation with a fast ventricular response; her platelet count was severely low; the electrocardiogram did not suggest infarction or ischemia; 3) An 86 year old man was admitted to the intensive care unit with a temperature of 400 Celsius, septic shock, and renal failure. Cardiology consultation in such cases, if desired, may indeed aid the referring caregivers in sorting out the cause of the troponin elevation and can provide not only a clinical but also an educational service. It is recognized that an elevated troponin level in patients not having an acute coronary syndrome is an indication of illness severity and predicts mortality. This is an ongoing area of research.2-5

In clinical medicine we often like to refer to Occam's razor and the utility in finding one cause or diagnosis that accounts for the patient's presenting signs and symptoms. There will always be dynamic tension between Occam and Hickam, who stated "patients can have as many diseases as they.....please."9 The concern here is indiscriminant ordering of today's highly sensitive troponin assays dulls Occam's razor and renders it sorely in need of sharpening. We should avoid "check the box" or "click on the test" ordering of troponin levels without first doing an assessment of the patient. If however an indiscriminate troponin assay is abnormal it behooves us to put it in clinical context before ordering unnecessary tests, medicines, and procedures. When elevated troponin levels are present in patients admitted for non-cardiac reasons, and the probability of myocardial ischemia due to coronary thrombosis is low, evaluation and treatment should be directed towards the primary diagnosis. We, and our patients, can ill afford to do otherwise.

Speaker Biography

Gregory D. Chapman, MD, FACC is a Professor of Medicine/Cardiovascular Disease at the University of Alabama at Birmingham. He has published commentaries and research papers in The New England Journal of Medicine, Circulation, the American Journal of Cardiology, and the American Journal of Medicine. He is now in his third decade of practice as a cardiologist, with experience in academic and private practice settings. His interests include STEMI recognition and treatment, as well as the diagnosis of acute coronary syndromes and their mimics. In addition to an active clinical role, he enjoys teaching residents in internal medicine, emergency medicine, and cardiology.

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Stephen E Fry

Fry Laboratories, USA

Applied use of next gen sequencing for infectious disease

headvent of automated human genetic sequencing capability has allowed a crossover for sequencing infectious diseases. The same technologies that allow us to query the human genome for cancer mutations, SNP's, pharmacogenomics, and inborn genetic errors now allow more in-depth analysis of human samples for evidence of infectious disease. Next -Generation sequencing (NGS) for infectious disease has proven to be more accurate with greater sensitivity and specificity than culture, serologic and PCR methods. They also now allow better discrimination of species, detection of novel variants, new novel organisms, detection of an ever-growing array of uncultivable organisms, and the ability to detect eukaryotes that before were undetectable. NGS also may soon hold the ability to additionally provide drug resistance and sensitivity information. Here we describe the rapid infectious disease identification system, RIDI™, and its practical use. Application of the RIDI™ system is discussed in four case reports with

patients suffering from chronic malaise, rheumatoid arthritis, osteoarthritis, and chronic fatigue syndrome with discussion providing new insight..

Speaker Biography

Stephen E Fry has completed a BS in Microbiology, MS in Molecular Biology and Medical Degree all earned at the University of Arizona. He completed his Post-graduate training at Banner Health and St. Joseph's Medical Center in the Phoenix metropolitan area. He has been in general practice in the Scottsdale, Arizona since 1992 and has had a special clinical interest in CFS, autoimmune and vascular disease. He has lectured nationally and has numerous publications, abstracts, and patents. His science interests are in the microbial causation of chronic disease, biofilms, and their treatment. Because of these interests he has worked on new methods for disease detection which have culminated in the development of a next-gen sequencing system for microbial identification. He is the Founder of Fry Laboratories LLC, a CLIA clinical diagnostic laboratory that participates in CAP and API validation systems. The laboratory specializes in the vector borne diseases, molecular methods of detection of prokaryotes, archaea, protozoans, and fungi.

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Farah Ahmad

York University, Canada

Bringing interactive eHealth tools to community health centers for assessment of common mental disorders

Background: Access to timely care for common mental disorders is an on-going challenge, especially for vulnerable ethno-cultural and immigrant groups. With the aim to address such challenges for populations served by community health centres (CHCs), our team developed an interactive computer-assisted client assessment survey (iCCAS) tool for pre-consult assessment of common mental disorders of depression, anxiety, post-traumatic stress disorder and alcohol abuse (using PHQ9, GAD7, PTSD-PC and CAGE) along with questions on social determinants of health. Patients completed the assessment in their waiting time and the program generated point-of-care reports.

Methods: A pilot randomized controlled trial recruited (response rate 78%) adult patients, fluent in English or Spanish, and seeing a physician or nurse practitioner at the partnering CHC in Toronto. The trial objectives were to examine the interventions' efficacy in improving mental health discussion (primary) and symptom detection (secondary). The trial data were collected by a paper-pencil exit survey and chart review. We also conducted post-trial qualitative interviews with clinicians and with a subset of screen-positive patients.

Results: iCCAS (n=75) and usual care (n=72) groups were similar in socio-demographics; 98% were immigrants and 68% females. Mental health discussion occurred for 58.7% in iCCAS and 40.3% in the usual care group (p<0.05); the effect remained significant while controlling for potential covariates (language, gender, education, employment) in Generalized Linear Mixed Model, GLMM (Adj OR 2.2; 95% CI: 1.1-4.5). Mental health symptom detection occurred for 38.7% in iCCAS and 27.8% in usual care group (p>0.05); the effect was not significant beyond

potential covariates in GLMM (Adj OR 1.9; 95% CI: 0.9-4.1). Patients using the iCCAS reported its completion time was acceptable (94.5%), the touch-screen was easy to use (97.3%), and the instructions (93.2%) and questions (94.6%) were clear. The qualitative interviews with nine participating clinicians showed their positive experiences: tool's benefits (e.g., nonintrusive prompting of clients to discuss mental health, and facilitation of clinicians' assessment and care plans); tool's integration into everyday practice; and promoting integration effectively (e.g., settings readiness, language diversity, and EMR linkages). Further, the need for routine screening at the CHCs was supported by the high rates of CMDs found via iCCAS: 36% reported symptoms of moderate to severe depression (PHQ9 score>10); 17.7% reported moderate to severe symptoms for anxiety (GAD7 score >10); 28.4% had symptoms for posttraumatic stress (PTSD-PC>3). The follow-up qualitative interviews with a subset of screen-positive patients identified improved care quality of care via new detection of CMDs or comorbidity or possible relapse.

Interpretation: The studied intervention holds potential for CHCs to improve mental health discussion, detections and quality of care. Further research with larger sample and inclusion of multiple sites is needed to enhance generalizability..

Speaker Biography

Farah Ahmad, MBBS, MPH, PhD is an Associate Professor at the School of Health Policy and Management, York University and affiliate Research Scientist at the North York General Hospital. Her training includes family medicine and public health sciences. She conducts health services research with a focus on psychosocial health vulnerable communities, primary care and eHealth innovations. She has extensively published in the areas of underserved populations, mental health and partner violence.

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Salim Sohani

Director Global Health Unit (GHU), International Operations, Canada

Sustaining essential maternal, newborn, and child health (mnch) services during the ebola outbreak: Evidence from Liberia

Background: Despite a substantial reduction in child mortality over the last decade, 5.9 million children under the age of five died in 2015; 16, 000 every day 1. Early detection and timely treatment of pneumonia, diarrhea, and malaria can save lives, but the timely access to effective treatment continues to be a challenge in resource poor settings. To broaden access to lifesaving treatment for children for the leading causes of child mortality, integrated community case management (iCCM) has been promoted by global agencies and adopted by the ministry of health in many countries, including Liberia. In a Red Cross project in Liberia before the outbreak, community health workers (CHWs) were trained in iCCM. These CHWs improved access to essential primary health care services, where the health system lacked capacity to adequately deliver them. During the Ebola outbreak in Liberia, the limited health system experienced further disruption. The objective of this study was to examine the value of a trained community health workforce in ensuring continued service delivery at the community level during the Ebola outbreak.

Methods: A descriptive observational study design was used, integrating mixed methods to collect data from CHWs (structured survey, n = 60; focus group discussions, n = 16), government health facility workers, and project staff. Monthly data on child diarrhea and pneumonia treatment was collected from Outpatient Department or Child Health Registers from government health facilities in the project catchment areas for the period of January 2013 to February 2015, and monitoring data from CHW registers (n=92). This data was used to assess

trends in the delivery of iCCM by CHWs before, during, and after the outbreak.

Results: Throughout the project areas, CHWs continued to treat child diarrhea and pneumonia before, during, and after the Ebola outbreak, with a slight decrease from September to October 2014 at the height of the outbreak. CHWs and project staff outlined the government circulated a "No Touch iCCM" policy during the outbreak. Training on this policy, CHWs reported, provided them with guidance and confidence to assess and treat sick children. During the outbreak, the primary activity of CHWs was to communicate Ebola awareness and prevention messages: 78% of CHWs surveyed conducted house-to-house visits and 50% used community meetings to disseminate messages. In a climate of distrust, where health workers were reluctant to treat patients, and the sick afraid to visit facilities, these findings affirm CHWs as a trusted source of treatment for childhood illnesses.

Discussion: Community-based health service delivery by CHWs during the Ebola outbreak in Liberia helped buffer the negative impact of the crisis. Investing in community health systems by providing training, essential medicines and equipment to community-based health workers can help build community resilience. Locally trained and available health workers understand cultural and social complexities, and are trusted by the community. During the Ebola crisis, this trust resulted in the ability of CHWs to quickly disseminate Ebola prevention messages, and provide continued access to basic health services to some extent.



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Conclusions: Investments in community-based health service delivery contributed to continued access to lifesaving treatment for child pneumonia and diarrhea during the Ebola outbreak; making communities more resilient when facility-based health services were impacted by the crisis. To maximize the effectiveness of these interventions during a crisis, proactive training of CHWs in infection prevention and "No Touch iCCM" guidelines, strengthening drug supply chain management, and finding alternative ways to provide supportive supervision when movements are restricted are recommended

Speaker Biography

Dr. Salim Sohani has a medical degree from the University of Karachi and Masters in Public Health from Harvard School of Public Health. He has over 25 years' experience working in Africa, Asia and the Americas with a major focus on health systems strengthening. His specific area of interest has been reproductive, maternal, newborn,

child and adolescent health (RMNCAH) throughout the continuum of emergency response to recovery and development. In his capacity as Director of the Global Health Unit, he is currently leading a multidisciplinary team of health experts who are responsible for providing technical advice and support to all Canadian Red Cross health programming, initiatives which are being implemented in diverse and challenging contexts. The team provides the technical leadership in developing, maintaining and disseminating the operational frameworks for the CRC's global health programming. In addition, the team leads the CRC's health policy dialogue with the International Red Cross and Red Crescent Movement, and engages on key health policy initiatives with the Government of Canada and global health institutions. Under his leadership the GHU team is also providing technical support to CRC programs through evidence-based monitoring and evaluation and in using the findings to strengthen programs through quality assurance. Salim has worked with and / or provided consultancy support to organizations such as the Canadian Coalition for Global Health Research, Aga Khan Health Services in East Africa, the Asian Development Bank, World Bank, Agri team and the Aga Khan University, and has authored and co-authored several publications, among them publications with a focus on equity based interventions for mothers and

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Xin Wang

The 4th Center Hospital, China

A new method to predict hospital mortality in severe community acquired pneumonia

Background & Aims: The aim of this study is to develop a new method that is able to accurately predicate the 28 day hospital mortality in patients with severe community acquired pneumonia (SCAP) at an early stage.

Methods: We selected 37348 SCAP patients in ICU from 173 hospitals during 2011.1-2013.12. The predictive factors for 28 day hospital mortality was evaluated retrospectively. All cases underwent intensive care, blood routine, blood biochemical tests and arterial blood gas analysis. Under the classification and regression tree (CART) analysis, a new clinical scoring system was developed for early prediction in SCAP patients. The receiver-operating characteristic (ROC) curve was plotted to calculate the area under the receiver operating characteristic curve (AUC).

Results: A novel clinical model named CLCGH scoring system, including serum creatinine (Cr)>259.5 umol/L, leukocyte (WBC)>17.35×109/L, C-reactive protein (CRP)>189.4 ug/ml, GCS<=9 and serum HCO3-<=17.65 mmol/L, was carried out and each index was an independent factor for hospital mortality in

SCAP. In validation cohort, the AUC of the new scoring system was 0.889 for prediction of hospital mortality, which was similar to SOFA score 0.877, APACHE score 0.864, and was better than the PSI score 0.761 and CURB-65 score 0.767.

Conclusions: The new scoring system CLCGH is an efficient, accurate and objective method to predicate the early hospital mortality among SCAP patients.

Speaker Biography

Xin Wang has his expertise in evaluation and passion in improving the health and well-being. His open and contextual evaluation based on responsive constructivists creates new pathways for improving healthcare. He and his staff have built this CLCGH scoring system model after years of experience and practice in research, evaluation, teaching and administration both in hospital and education institutions. Also, he has abundant clinical experience in clinical field especially in the area of acute abdominal disease and physical medicine disorder. The new scoring system CLCGH is an efficient, accurate and objective method to predicate the early hospital mortality among SCAP patients. The CART analysis is a methodology that utilizes the previous generations of evaluation, measurement, description and judgment. His research allows for value-pluralism. His approach and study achievement is responsive to all stakeholders and has a different way of focusing.

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Roxana Behruzi

McGill University, Canada

Probiotics effect on group B *Streptococcus* (GBS) recto-vaginal colonization in pregnant and non-pregnant women: A systematic review of published randomized controlled trials

Background & Aims: Probiotics have been suggested as a safe strategy to prevent or reduce the prevalence of GBS rectovaginal colonization in pregnant and non-pregnant women. Probiotics are not yet part of the clinical practice for prevention of GBS recto-vaginal colonization in women and less physicians recommend probiotics in prenatal to maintain urogenital health. The aim of this study was to systematically review the published controlled randomized trials (RCTs) on the effects of probiotics on Group B *Streptococcus* recto-vaginal colonization.

Methods: Literature searches were made up to September 2017. This systematic review included the published randomized, double-blind or open label, and placebo-controlled trials on the effects of probiotics on Group B *Streptococcus* (GBS) rectovaginal colonization in pregnant and non-pregnant women. The PubMed, Medline, HEN, Google Scholar and Cochrane Central Register of Controlled Trials were searched for keywords.

Results: A total of four studies, incorporating two pilot RCTs, were identified as eligible for analysis. Three studies were conducted in low risk pregnancies. Two of the studies examined the efficacy of probiotics in pregnant women who presented as GBS positive at 35-37 weeks of gestation. One of the RCTs showed significant (GBS) culture change from positive to negative in 21 women in the probiotic group (42.9%) and in nine women (18.0%) in the placebo (p=0.007). The sample size in the two pilot RCTs that aimed to examine the effect of an oral prenatal probiotic on (GBS) colonization in pregnancy were too small to draw meaningful conclusions. The randomized controlled trial in non-pregnant and healthy fertile women showed a significant reduction of GBS recto-vaginal colonization

in intervention group compare placebo group (p=0.036). Overall, heterogeneity in choice and dose of probiotics, and lack of enough statistical information made it impossible to do a meta-analysis. The Cochrane Collaboration's tool for assessing risk of bias showed 3 of 4 reviewed randomized controlled trials had poor quality.

Conclusion: There is inadequate evidence relatied to the use of probiotics for either prevention or treatment of GBS rectovaginal colonization in pregnancy. The reviewed studies have provided suggestion of benefit of probiotics in prevention of GBS recto-vaginal colonization, nevertheless, available evidence is not sufficient to support the routine administration of probiotics to reduce GBS colonization in pregnancy. Further investigation with better design and larger studies are needed regarding the efficacy and safety of specific probiotics strains in pregnancy.

Speaker Biography

Roksana (Roxana) Behruzi is working as an Assistant Professor at McGill University, Department of Family Medicine, and a Clinician Researcher in the Research Center at CISSS in Outaouais. She has more than 20 years of experience in both teaching and clinical research. She has a Master's degree (MSc) in Midwifery and she completed a PhD in Public Health at the University of Montreal, during which she obtained many awards and bursary from CIHR, STIRRHS, Bourse Étude Supériour en Santé Publique, and Japan Society for the Promotion of Science (JSPS) Fellowship. In 2008, she accomplished a Fellowship in Japan on maternity care services. She also accomplished three years Post-doctoral fellowship at the Department of Family Medicine at McGill University, for which, she was awarded two times the Fond de Recherche en Santé du Québec (FRSQ). She collaborates with GCP Trials Center in Montreal, in where, she provide workshops in good clinical practice for clinical research staff. Her latest research interest is working on the safety and efficacy of probiotics on Group *Streptococcus* (GBS) recto-vaginal colonization in pregnancy.

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Helen Senderovich

University of Toronto, Canada

The role of exercises in osteoporotic fracture prevention and current care gaps, where are we now? Recent updates

Introduction: The primary non-pharmacological management recommended for patients with osteoporosis (OP) is exercise, but whether it should be high force, resistive, or other means can be obscure.

Objective: To describe the role of exercises in osteoporotic fracture prevention, identify effects and potential risks of high-force exercises, detect the optimal exercises to combat OP, and explore the challenges that might arise.

Methods: A MEDLINE, and a Cochrane databases search was conducted on the role of exercises in preventing osteoporotic fractures from 1989 onwards, leading to 40 results, including op-ed pieces, qualitative studies, randomized clinical trials (RCTs) (n = 5), and RCT follow up studies (n = 1). Articles deemed relevant to the objective hands were analyzed and summarized. Data on effects of vitamin D and calcium supplementation was later gathered from different sources as well.

Results: High-intensity, resistive strength training provided the maximum benefit in Bone Mineral Density (BMD) levels, muscle mass and reduction in fracture, while posture and balance exercises only improved mobility. High force exercises did not increase fractures, and were associated with increases in BMD. Interventions including exercises, vitamin D and calcium intake had limited effect when used as single interventions, while the latter may potentially cause increases of cardiovascular events.

Conclusion: A long term regular exercise program designed to improve postural stability, mobility, and mechanical efficiency, alongside vitamin D and dietary calcium intake is most effective in preventing OP and reducing osteoporotic fractures

Speaker Biography

Senderovich is a Physician at Baycrest Health Science System with practice focused on Palliative Care, Pain Medicine and Geriatrics. She is a Lecturer at the Department of Family and Community Medicine, and Division of Palliative Care at the University of Toronto who are actively involved in teaching medical students and residents. She has a broad international experience and a solid research background. Her research was accepted nationally and internationally. She is an Author of multiple manuscripts focused on geriatrics, patient's centered care, ethical and legal aspect of doctor patient relationship, palliative and end-of-life care.

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