View this email in your browser

Mission

The mission of the International Society for Evidence-Based Health Care is to develop and encourage research in evidence-based health care and to promote and provide professional and public education in the field.

Vision

The society is inspired by a vision to be a world-wide platform for interaction and collaboration among practitioners, teachers, researchers and the public to promote EBHC. The intent is to provide support to frontline clinicians making day-to-day decisions, and to those who have to develop curricula and teach EBHC.

Key objectives of the Society

- To develop and promote professional and public education regarding EBHC
- To develop, promote, and coordinate international programs through national/international collaboration
- To develop educational materials for facilitating workshops to promote EBHC
- To assist with and encourage EBHC-related programs when requested by an individual national/regional organization.
- To advise and guide on fundraising skills in order that national foundations and societies are enabled to finance a greater level and range of activities.

- To participate in, and promote programs for national, regional and international workshops regarding EBCP.
- To foster the development of an international communications system for individuals and organizations working in EBHC-related areas.
- To improve the evidence systems within which health care workers practice.

Help Spread EBM Teachings!

Forward to your colleagues who might like to read or contribute to future articles.

Click here to subscribe

Making Science Computable: Developing Code Systems for Evidence-Based Health Care (EBHC)

Brian S. Alper, Mario Tristan, Amir Qaseem, Amy Price, for the COVID-19 Knowledge Accelerator (COKA) Initiative

Edited by: Vahid Ashoorion

Processing the evidence to practice or support EBHC takes a lot of steps. This includes evidence identification, appraisal, synthesis, and dissemination, and each step requires several resources. Each transition is fraught with missteps, addressed by some duplication to confirm replication of effort. However, our current systems are uncoordinated, and excess duplication stretches our limited resources, so we do not reach as much evidence as quickly as we could to support current needs. This diverse collection of challenges was acutely demonstrated as COVID-19 emerged, and yet the COVID-19 challenge stimulated an unprecedented, multifaceted, multidisciplinary, multinational, multi-institutional collaboration to make things better.

A foundational solution to support many participants sharing evidence, in Findable, Accessible, Interoperable, and Re-usable (FAIR) ways, is to agree on common standards for data exchange – a universal shared form of expression of evidence in precise, unambiguous, coded, structured data suitable for computable expression. For

data to be machine-readable and transparent across systems we need common standard terminologies to allow systems to talk to each other without expensive and complex conversions that introduce a risk of bias and loss of accuracy. Such computable evidence will enable greater efficiency for all steps involving electronic data transfer. The COVID-19 Knowledge Accelerator (COKA) has assembled nearly 100 people from more than 25 countries across six continents to develop and advance such standards.[1]

Communicating evidence in coded, structured form requires controlled terminologies (or code systems) to uniquely and accurately express essential concepts. Code systems like SNOMED CT or ICD-10 may be used to describe conditions, but there are gaps. Multiple areas of EBHC do not have global code systems. When creating a standard for the computable expression of evidence (i.e., definition of the evidence variables, statistics, and certainty of the findings), we identified and prioritized four domains that did not have adequate code systems.

We created a Code System Development Protocol to provide an open, transparent, multifaceted method to develop such code systems.[2] We are currently developing Risk of Bias, Study Design, Statistic Type, and Statistic Model code systems. As of November 16, 2020, we have 61 people from 27 countries signed up for an Expert Working Group for one or more of these code systems. We have identified 23 commonly used tools and methods for what the code systems would support, such as the ROBINS-I tool for risk of bias assessment. There are 387 draft terms (174 for Risk of Bias, 56 for Study Design, 89 for Statistic Type, and 68 for Statistic Model) to support all recognized commonly used tools and systems. This system will enable clear, precise, unambiguous expression of the concepts. In turn, this will allow the data in evidence reports to be FAIR, ultimately resulting in much greater efficiency for identifying, processing, and communicating evidence.

You can participate in an Expert Working Group (https://tinyurl.com/InviteToEWG) or the COVID-19 Knowledge Accelerator (https://tinyurl.com/coka2020).

References

1. Alper BS, Richardson JE, Lehmann HP, Subbian V. It is time for computable evidence synthesis: The COVID-19 Knowledge Accelerator Initiative. J Am Med Inform Assoc 2020 Aug:27(8):1338-1339. Doi: 10.1093/jamia/ocaa114. https://academic.oup.com/jamia/article/27/8/1338/5842142
2. Alper BS, Dehnbostel J, Robinson K, Subbian V, Afzal M, Soares A, Kunnamo I, Shahin K, Lehmann H, Fedorowicz Z, McClure R, Thabane L. For the COVID-19 Knowledge Accelerator (COKA) Initiative. Code System Development Protocol. Created September 1, 2020. Last revised on September 17, 2020. Available at: https://tinyurl.com/CodeSystemDevelopmentProtocol. Also available at OSF: https://osf.io/3akjv/

Informing COVID-19 Optimal Practice: Living network Meta-analysis and Living WHO guidelines through MAGIC

Gordon Guyatt, Arnav Agarwal, Thomas Agoritsas, Romina Brignardello Petersen, Francois Lamontagne, Bram Rochwerg, Reed Siemieniuk, Per Olav Vandvik, Linan Zeng

Edited by: Jason Busse

Living systematic reviews are reviews that are constantly updated as new evidence becomes available. When conducted in a methodologically rigorous fashion, such reviews are ideal for informing living clinical practice guidelines: guidelines that are also constantly updated as new evidence that changes direction or strength of recommendations becomes available.

The extraordinary rapidity with which investigators such as the RECOVERY group in the UK and WHO's SOLIDARITY initiative are producing randomized trial evidence to inform a host of drug and immune interventions for COVID-19 demands living evidence summaries and living guidelines. The readiness with which clinicians, politicians and regulators have accepted preliminary but uncertain evidence as an indication for clinical use further highlights the need for trustworthy living reviews and living guidelines.

Our group, the MAGIC Evidence Ecosystem Foundation (MAGIC for "Making GRADE the Irresistible Choice") has taken on the challenge of producing both the evidence summaries and living guidelines. Australian national living guidelines is using our digital authoring and publication platform - the MAGICapp – to make actionable recommendations freely available for re-use and adaptation.

In parallel, our group at McMaster has put together a dedicated team of over 50 methodologists and clinicians to produce a living network meta-analysis (NMA) of randomized trials examining all drugs and immune agents for COVID-19. By organizing workflow into four independent teams that work in parallel, the group is able to produce updated evidence summaries within days of appearance of new evidence. The four teams are tasked with the following i) data identification; ii) data extraction and risk of bias assessment; iii) statistical analysis iv) evidence quality/certainty using GRADE's

approach for NMAs. Evidence summaries based on the NMA appear in the MAGICapp, a digitally structured interoperable platform that allows for efficient authoring, dynamic updating, immediate global dissemination of recommendations, interactive evidence summaries and decision aids. The publication of the living NMA in the BMJ has resulted in over 150,000 views; and its Altimetric score is in the 99.9th percentile.

Further, capitalizing on the rapidly available rigorous evidence summaries from the living NMA following the successful BMJ Rapid Recommendations (https://www.bmj.com/rapid-recommendations) the MAGIC Foundation has partnered with the WHO and the BMJ to produce living trustworthy guidelines. The guidelines follow all key elements for ensuring trustworthiness. These include an optimal panel (methodologists, clinical experts, frontline clinicians, patients and an ethicist, the composition meeting WHO standards for international and gender representation and freedom from problematic conflict of interest); the living NMA updated evidence summaries; and explicit and transparent consideration of patient and public values and preferences.

The first guideline from the group, offered as part of the MAGIC/BMJ Rapid Recommendation partnership before the arrangement with the WHO was finalized, addressed remdesivir (a weak recommendation in favour, noting the low quality/certainty of the evidence and need for continued trial enrolment: www.bmj.com/content/370/bmj.m2924). The second, which appeared as a formal WHO recommendation and a BMJ publication (as will be the case for all subsequent recommendations) included strong recommendations for use of corticosteroids in severe and critically ill COVID-19 patients (www.bmj.com/content/370/bmj.m3379).

At the time of writing, the living NMA has been updated to include the latest RCT results regarding remdesivir, hydroxychloroquine, lopinavir-ritonavir, and interferon from the WHO SOLIDARITY trial. The WHO living guideline panel has made its recommendations 10 days after the results were published as pre-print, and are planning for the guideline update to appear within 4 weeks after the trigger trial appeared.

These combined initiatives illustrate the extraordinary potential of the most recent advances in Evidence Based Medicine methods to take a key role in optimizing the management of patients with – or wanting to avoid – SARS-CoV-2 infection.

Fixed versus Random effects in Meta-analysis

Samuel A. Berkman

Edited by: Jeremy Ng

Meta-analysis, “a study of studies “is an evidence based methodology which involves combining similar trials in order to achieve greater power and precision than attainable from individual trials alone. Randomized trials are used to establish the standard of care in what is called a “pivotal” trial because only in a randomized trial will any outcome will be due to the intervention and not due to the fact that the groups may be of different composition to begin with. The process of randomization if it is sufficiently powered will insure that both groups are matched for both measurable and non-measurable covariates.

Consequently, a meta-analysis of randomized trials is perhaps the top of the hierarchy in evidence based medicine in realizing precision, power and freedom from bias. Meta-analyses, particularly of randomized trials, are often very influential, especially where a shift in standard of care is at stake. One example would be the meta-analysis involving anticoagulation in nonvalvular atrial fibrillation combining the Rocket, Rely, Aristotle and Engage trials[1-5] which shifted the standard of care from Warfarin to DOACs.[1]

The notion of fixed and random effects relates to how an investigator establishes relative weights of the component studies in a meta-analysis in calculating and demonstrating the result, which can be shown visually by Forest plot.
If all the studies in a meta- analysis were equally informative, one could just compute the mean of the effect sizes. However, if some studies are more contributory to the overall result than others on the basis of either size or methodology, one would assign more weight to those studies contributing more information.

Consequently rather than a simple mean of the effect sizes, one computes a weighted mean, with more power given to some studies and less to others. This variation in impact will be reflected on the Forest plot, a part of every meta-analysis, as the size of a square or circle on the plot being in proportion to the individual component trial’s impact on the overall meta-analysis result. Because the most influential study in the meta-analysis will have less influence in random effects than in a fixed effects model, the summary Forest plot box will frequently be shifted toward the line of unity in random effects. (See Figures)

Fixed-Effect Versus Random-Effects Models

Figure 1: Fixed effect model – forest plot showing relative weights

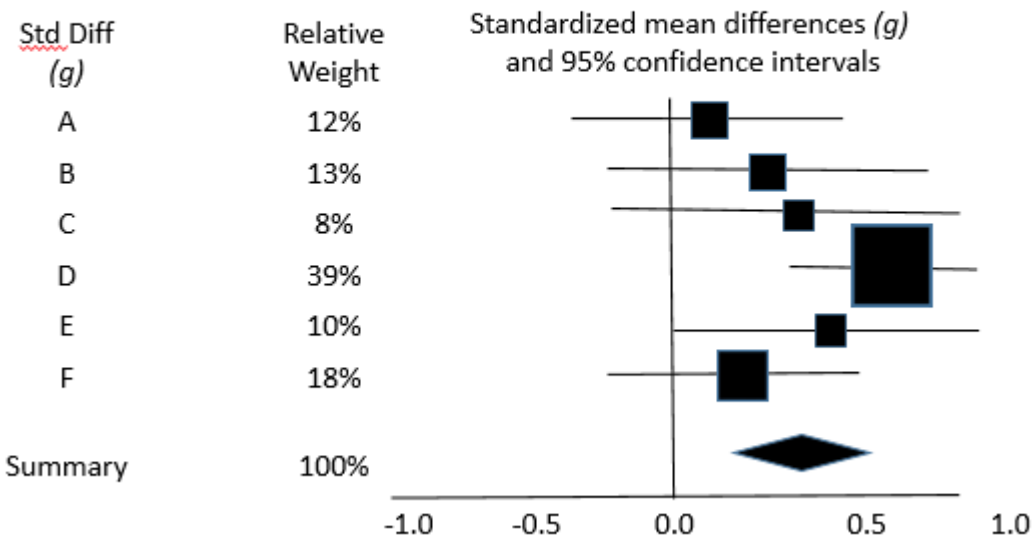
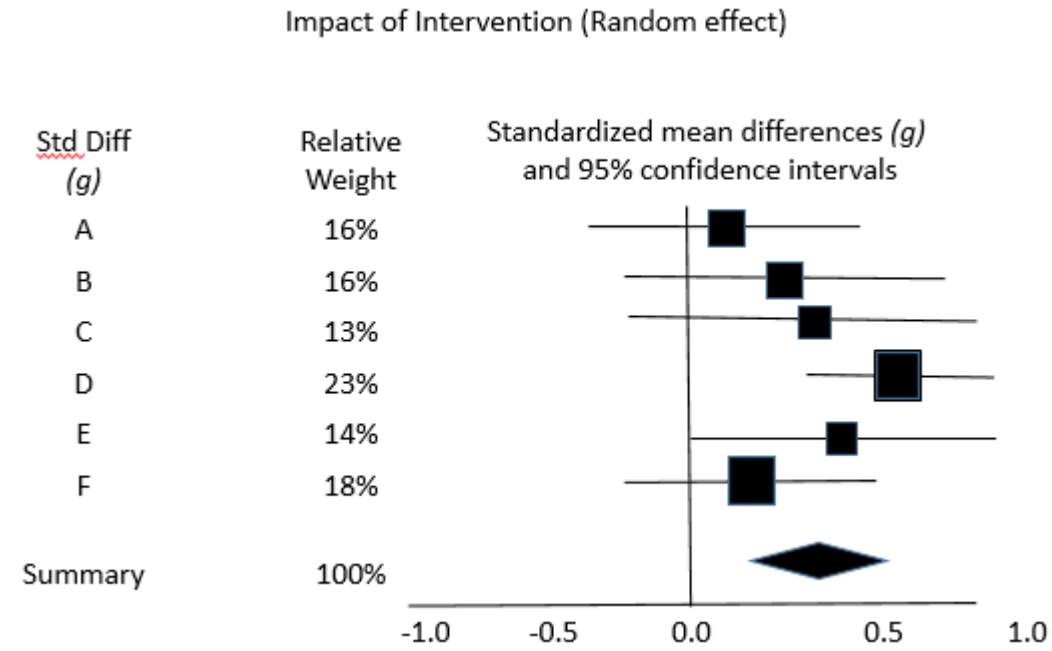


Figure 2: Random-effects model – forest plot showing relative weights



Legend: Note how the largest trial (D) has a bigger square in Fixed effects and the smallest trial € is larger in random effects. The summary in random effects is moved to the left but no major difference.[7]

So, then, how are the component weights assessed? This depends upon which of two models are used to calculate these numbers, either the fixed effects model or the random effects model. Each requires a separate rather complicated formula for making these calculations. Each model makes different assumptions about the nature of the

studies, and these assumptions lead to different definitions for the combined effect of the trials, and different mechanisms for assigning weights.

Under the fixed effect model it is assumed there is one effect size shared by all component trials. By contrast, under the random effects model, the true effect could vary from study to study. For example, the effect size might be a little higher if a given trial has more patients or had a longer course of the intervention or if the effect was measured more reliably. In other words, a larger trial or one carried on for longer would probably accumulate more information and have more to contribute to a meta-analysis than shorter or smaller trials. Precision would also be a factor, for example a study using an ultrasound to diagnosis deep venous thrombosis might add more accuracy than one based solely upon clinical examination.

Under the fixed effect model a large study would be given the majority of the weight, and a small study could be in large part ignored. For the most part as compared with the fixed effect model, the weights assigned under random effects model are more balanced. Large studies are less likely to dominate the analysis and small studies less likely to be trivialized.

The fixed effect model assumes that all studies in the meta-analysis share a common true effect size. In other words, all factors, which could influence the effect size, are comparable in all the study populations, and therefore the effect size is similar in all the study populations. By contrast, the random effects model assumes that the studies were drawn from populations that differ from each other in ways that could impact on the treatment effect.

Under the random effects model, while large studies may yield more precise estimates than small studies, each component trial is estimating a different effect size, and each of these effect sizes serve as a sample from the population whose mean we want to estimate. In other words, despite variations in component size in random effects, each component trial of the meta-analysis has its own unique information to contribute to the meta-analysis, which is why it deserves greater weight than it would receive in fixed effects even though smaller in size.

To give a few examples, if one performs a meta-analysis of the above mentioned pivotal atrial fibrillation studies comparing direct oral anticoagulants (DOACs) versus Warfarin[1-5], these 4 trials were all very highly powered having around 10.000 patients each, shared the same end points i.e. stroke and systemic embolism and major bleeding , and were performed in predominantly elderly patients over 70 with atrial fibrillation who all received warfarin as a comparator drug and all received the same category of interventional drug. (DOACs) Consequently some key opinion leaders and methodologists might feel that there is enough similarity between the studies to weight the meta-analysis in the fixed effects model. However since the Rocket trial[2] involving Rivaroxaban involved considerably sicker patients than those in the other trials, other experts may feel that, due to the heterogeneity introduced by Rocket, the meta-analysis

should be weighted in random effects. Often one uses both models and not infrequently there may not be that much difference in the result.

Another example would involve DVT prophylaxis in sick hospitalized medical patients post hospital discharge. A number of the trials such as the Apex, Magellan, Adopt or Mariner had different length of treatment and various criteria for being at high risk,thereby creating significant heterogeneity, so this meta-analysis might be best analyzed in random effects.[6] When one does a meta-analysis of real world trials there is usually significantly more heterogeneity, so these trials may be more likely to be weighted in terms of random effects.

So how would one choose to analyze the meta-analysis in fixed effects versus random effects? As per the above examples, many times both are used. However if trials seem to show more homogeneity they would be best analyzed in terms of fixed effects whereas those who show a lot of variation or heterogeneity would be best analyzed in terms of random effects.

When reading a medical article and scrutinizing a meta-analysis and Forest plot one should ascertain which model was used and reflect upon why it was chosen.

References

1. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomized trials. Lancet. 2014 Mar 15;383(9921):955-62. doi: 10.1016/S0140-6736(13)62343-0. Epub 2013 Dec 4. PMID: 24315724.

2. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Piccini JP, Becker RC, Nessel CC, Paolini JF, Berkowitz SD, Fox KA, Califf RM; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011 Sep 8;365(10):883-91. doi: 10.1056/NEJMoa1009638. Epub 2011 Aug 10. PMID: 21830957.

3. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, Waldo AL, Ezekowitz MD, Weitz JI, Špinar J, Ruzyllo W, Ruda M, Koretsune Y, Betcher J, Shi M, Grip LT, Patel SP, Patel I, Hanyok JJ, Mercuri M, Antman EM; ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013 Nov 28;369(22):2093-104. doi: 10.1056/NEJMoa1310907. Epub 2013 Nov 19. PMID: 24251359.

4. Connolly SJ, Ezekowitz MD, Yusuf S, Reilly PA, Wallentin L; Randomized Evaluation of Long-Term Anticoagulation Therapy Investigators. Newly identified

events in the RE-LY trial. N Engl J Med. 2010 Nov 4;363(19):1875-6. doi: 10.1056/NEJMc1007378. PMID: 21047252.

5. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz JA, Flaker G, Garcia D, Geraldes M, Gersh BJ, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky P, Lewis BS, Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin L; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011 Sep 15;365(11):981-92. doi: 10.1056/NEJMoa1107039. Epub 2011 Aug 27. PMID: 21870978.

6. Neumann I, Izcovich A, Zhang Y, et al. DOACS vs LMWH in hospitalized medical patients: a systemic review and meta analysis that informed 2018 guidelines. Blood Advances. 2020;14: 152-1517.

7. Borenstein M, Hedges, L.V., Higgins, J.P.T, Rothstein H.R, Introduction to Meta-Analysis , John Wiley and sons, chapter 13,ISBN 978-0-470-05724-7

The National Collaborating Centre for Methods and Tools: Supporting evidence-informed public health decision making for COVID-19

Claire Howarth, Sarah Neil-Sztramko, Heather Husson, Maureen Dobbins

Edited by: Vahid Ashoorion

The National Collaborating Centre for Methods and Tools (NCCMT) has been supporting public health professionals in the fight against COVID-19. The NCCMT envisions a public health system that is driven by the best available evidence leading to improved health and well-being for every person living in Canada. We work towards this vision by fostering evidence-informed decision making in public health through training, mentorship and by providing access to high quality resources.
When the COVID-19 global pandemic was declared in March 2020, the NCCMT team

immediately shifted priorities to take action to meet the needs of public health decision makers, under the leadership and direction of the center's Scientific Director, Dr. Maureen Dobbins, RN, PhD. An explosion of research on COVID-19 quickly overwhelmed the capacity of public health organizations to identify, appraise and interpret evidence to guide decision making. This led the NCCMT to participate in three key initiatives to support the Canadian and international community, reduce duplication of efforts and increase coordination of evidence generation and synthesis in response to COVID-19.

The NCCMT launched a Rapid Evidence Service to answer priority COVID-19 questions raised by Canadian public health decision makers at local, provincial/territorial, and federal levels; questions are received by email, nccmt@mcmaster.ca, and the service is widely promoted through the NCCMT's existing networks. Each week, the NCCMT selects relevant and timely questions to answer, develops an answerable question and appropriate search strategy, conducts searches, critically appraises the evidence, and synthesizes the findings into key messages and knowledge gaps, typically within five to ten days. Once completed, the reviews are posted on a unique webpage at the NCCMT (nccmt.ca/RES). These rapid reviews are then widely disseminated to key public health decision makers through social media and an email subscription list. As of November 6, 2020, the NCCMT has completed 44 full reviews or updates on 25 unique questions. Interest has been growing steadily since the launch of this service. Rapid reviews are downloaded an average of 550 times per week and have been accessed in 69 countries. Especially exciting is the living rapid review on the role of schools and daycares in COVID-19 transmission, which received nation-wide media attention, and pickup from more than 30 news outlets from August to October throughout the process of school re-opening. The NCCMT has also connected with a number of external organizations who are conducting their own rapid reviews, sharing our methodology and resources to build capacity for evidence-informed decision making worldwide, and have shared our process and impact with a variety of audiences through virtual presentations at academic conferences.

The NCCMT was one of the early members of the COVID-19 Evidence Network to support Decision-making (COVID-END), an international network of more than 50 evidence synthesis and knowledge translation organizations with the aim to support decision makers in finding and using evidence, and reducing duplication. This network has established seven key working groups; Dobbins co-leads the Engaging workgroup with Laurenz Langer from the African Centre for Evidence in South Africa. The engaging workgroup successfully launched the COVID-END community in July 2020, which is an online discussion group for those supporting decision makers. The Community has discussed a variety of topics thus far including methods for evidence synthesis during COVID-19.

The NCCMT also created a rapid review repository where organizations and individuals can submit public health related COVID-19 rapid reviews. This online repository is freely accessible, so all organizations and individuals can browse and search the available

rapid reviews by topic of interest. Contact information for rapid review authors is available, allowing users to access recently completed reviews or identify estimated timelines for completion with the aim to reduce duplication of efforts. As of November 6, 2020, over 50 organizations have contributed more than 215 rapid reviews. From March 30, 2020 (launch date) to November 6, 2020 the repository has received over 35,500 pageviews and been accessed in 105 countries.

Overall, the NCCMT's skills, expertise and resources were quickly and effectively mobilized to support public health professionals in their response to COVID-19. This work demonstrates that it is possible, albeit challenging to employ the best available evidence in practice during a rapidly evolving crisis. Evidence syntheses and repositories can be developed rapidly and put into use immediately to reduce duplication and disseminate evidence quickly to decision makers who need it. The NCCMT is funded by the Public Health Agency of Canada and hosted by McMaster University within the School of Nursing.

Flipped Classroom Learning versus Lecture-Based Approach in Health Education: A systematic review of randomized controlled trials

Nigar Sekercioglu

Edited by: Atefeh Noori and Jason Busse

Introduction

The passive methods of teaching, such as traditional lecture-based approaches (LBA) are employed in large-classroom settings when foundational knowledge needs to be provided in a synchronous manner[1]. Flipped classroom learning (FCL) is a pedagogical technique that is used in adult learners and has been linked to enhanced motivation, comprehension, long-term retention of the concepts and subsequent increased academic performance[1]. The core learning modules (videos, exercises, text) are delivered before the class and students enagege in participatory learning activities, such as discussion, problem-solving, peer-to-peer learning and experiments during the class time[1]. We conducted a systematic review of randomized controlled trials (RCT) comparing learning outcomes of FCL vs. LBA in higher health education.

Methods

We included studies: (1) among students who studied in the health-sciences undergraduate and graduate programs; (2) students randomized to FCL vs. LBA; (3) reported at least one of the learning outcomes related to engagement, performance, and perceptions of students. We excluded quasi-experimental designs, observational studies, narrative reviews, systematic reviews and editorials. We also excluded studies that compared text-based vs. multimedia pre-lectures for pre-class preparation. We checked the reference list of the previous systematic review for additional relevant studies[1].

We developed a database-specific search strategy without any language restrictions and searched the PubMed, Education Resources Information Centre (ERIC), Web of Science, Journals Scholar Portal, Google Scholar and World Cat databases from February 2016 up to February 2020. We screened titles, abstracts, and full-texts.
We used a modified version of the Cochrane risk of bias tool for RCTs with the following responses: ‘definitely or probably yes’ (considered as low risk of bias), or ‘definitely or probably no’ (considered as high risk of bias). Each eligible trial was assessed based on the random sequence generation, allocation concealment, incomplete outcome data (≥20% missing data were considered at high risk of bias), and selective reporting.

Results

Our search yielded 15 abstracts, of which 9 proved potentially eligible and underwent full review. Of these studies, six were excluded—five had an ineligible population (students from primary school and non-health science education studies) and one was a quasi-experimental design. We finally included three randomized trials enrolling 426 students. The overall risk of bias of the included RCTs was deemed low.

Boem et al. included exam scores and student satisfaction as learning outcomes in the study[2]. The exam scores was higher in the FCL arm; nevertheless, the study did not reach statistical significance as the p-value was greater than the alpha of 0.05[2].
Another study evaluated the effect of the FCL method on the students’ performance and perceptions for learning[3]. Those assigned to the FCL arms received higher test scores and student perceptions for learning were also positive in the FCL arm[3]. In the FCL arm, students spent more time before the class and less time after the class as compared to the LBA arm[3]. Moreover, students in the FCL arm demonstrated a more positive attitude and learning experience toward their teaching model than students in the LBA group[3].

Rui et al. employed a test for content knowledge in one week as well as a survey for students’ attitudes and learning experiences[4]. The study showed students in the FCL spent more time before the class while the time they spent after the class was not significantly different[4].

Conclusion

Our study summarized the existing evidence on the effectiveness of FCL as compared to LBA from the published RCTs. In the FCL approach, students have the opportunity to interact more in the class discussions, develop and utilize their problem-solving abilities, and enhance their motivation for active learning engagement[1]. Therefore, FCL has been associated with higher exam scores in health science education studies[1-4]. Further research is required to provide evidence about the effectiveness of FCL on other learning outcomes. Overall, FCL may be more effective in learning as compared to the traditional methods.

References

1. Chen KS, Monrouxe L, Lu YH, Jenq CC, Chang YJ, Chang YC, Chai PY. Academic outcomes of flipped classroom learning: a meta-analysis. Med Educ. 2018 Jun 25;52(9):910–24.

2. Beom JH, Kim JH, Chung HS, Kim SM, Ko DR, Cho J (2018) Flipped-classroom training in advanced cardiopulmonary life support. PLoS ONE 13(9): e0203114.

3. He Y, Lu J, Huang H, He S, Ma N, Sha Z, et al. (2019) The effects of flipped classrooms on undergraduate pharmaceutical marketing learning: A clustered randomized controlled study. PLoS ONE 14(4): e0214624-YES

4. Rui, Z., Lian-rui, X., Rong-zheng, Y. et al. Friend or Foe? Flipped Classroom for Undergraduate Electrocardiogram Learning: a Randomized Controlled Study. BMC Med Educ 17, 53 (2017)

The UpPriority tool helps with the prioritization of clinical guideline questions for updating

Andrea Juliana Sanabria, Pablo Alonso-Coello, Laura Martínez García

Edited by: Yasir Rehman

Clinical guidelines (CG) updating is very resource intensive and extremely time consuming. An updating strategy involves an iterative set of processes including the following: (1) identification of new evidence, (2) evaluation of the impact of the new

evidence, and (3) if necessary, modification of the current CG.

There is growing interest in approaches to streamline CG updating, including the prioritization of candidate CGs in need of updating or production of living guidelines (guidelines that are continuously being monitored and updated if needed). However, despite the publication of many prioritization criteria across systematic reviews, health technology assessments, and CGs, the methods used to develop and implement the processes suggested are generally inconsistently reported[1]. Our group has a long tradition in updating related research[2,3], and has now developed a pragmatic tool to prioritize clinical questions for updating within a CG, the UpPriority tool[4].

The UpPriority tool was based on a published methodological systematic review[1] and an explicit, structured multistep process involving a wide range of stakeholders, including CG methodological experts, developers, and users.[4]

The process included the following steps: (1) establishment of the working group, (2) generation of the initial version, (3) optimization of the tool (including an initial feasibility test, semi structured interviews, Delphi consensus survey, second feasibility test, external review, and pilot test), and (4) approval of the final version. A total of 87 participants including methodologists, clinicians, and other relevant stakeholders contributed to its development.

The tool consists of six items: (1) impact of out-dated recommendations on safety, (2) availability of new relevant evidence, (3) context relevance of the clinical question, (4) methodological applicability of the clinical question, (5) user's interest, and (6) impact on access to health care. UpPriority includes detailed guidance for using the tool and rating each item (using a 7-point Likert scale), for calculating and ranking the questions, and for summarizing results.

The UpPriority tool was developed to guide the prioritization of clinical guideline questions for updating. It is our hope that CG developers benefit now from this prioritization tool to determine which clinical questions within a CG could benefit most from being updated. The tool could be useful for standardizing prioritization processes when updating CGs and for fostering more efficient use of resources in the CG field.

References

1. Martínez García L, Pardo-Hernandez H, Superchi C, Nino de Guzman E, Ballesteros M, Ibargoyen Roteta N, et al. Methodological systematic review identifies major limitations in prioritization processes for updating. J Clin Epidemiol. 2017; 86:11-24.

2. Martínez García L, Sanabria AJ, García Alvarez E, Trujillo-Martín MM, Etxeandia-Ikobaltzeta I, Kotzeva A, Rigau D, Louro-González A, Barajas-Nava L, Díaz Del

Campo P, Estrada MD, Solà I, Gracia J, Salcedo-Fernandez F, Lawson J, Haynes RB, Alonso-Coello P; Updating Guidelines Working Group. The validity of recommendations from clinical guidelines: a survival analysis. CMAJ. 2014 Nov 4;186(16):1211-9.

3. Vernooij RW, Alonso-Coello P, Brouwers M, Martínez García L; CheckUp Panel. Reporting Items for Updated Clinical Guidelines: Checklist for the Reporting of Updated Guidelines (CheckUp). PLoS Med. 2017 Jan 10;14(1):e1002207.

4. Sanabria AJ, Pardo-Hernandez H, Ballesteros M, Canelo-Aybar C, McFarlane E, Niño de Guzman E, Penman K, Posso M, Roqué I Figuls M, Selva A, Vernooij RWM, Alonso-Coello P, Martínez García L; G-I-N Updating Guidelines Working Group and Collaborators. The UpPriority tool was developed to guide the prioritization of clinical guideline questions for updating. J Clin Epidemiol. 2020 Oct;126:80-92.

Inverting The 'Telos-scope':

Why we should study, promote and be passionate about evidence-based medicine when 'everyone' has already been trained in it

Larry Birger

Edited by: Mahmood AminiLari

The whole wide world, an endless universe. Yet we keep looking through the eyeglass in reverse….
– Neil Peart (Rush), "Territories"

One of the surprises I encountered when recruiting attendees for our first-ever Evidence-Based Medicine (EBM) workshop in rural central Washington was a sentiment of diminutive need for such a workshop. Among some, there seemed to be the sense that their skill level was already sufficient.

Recruitment for our subsequent workshop suggested that others regarded one go-round as enough – at least for now. And all of us laboring under the demands of clinical practice, as well as those still in training, are faced with justifying time to focus on what seems to be perhaps more academic or abstract than practical.

So why should we study, promote and be passionate about EBM, when 'everyone' has already been trained it?

EBM, at heart, is the pursuit of truth, a pursuit employing certain *tools*. But even more fundamentally, it is about truth with a *telos*: the application of truth for the good of individual patients first and foremost, and then for the benefit of society and of science. Inimitable wordsmith, Neil Peart, provides us with insight in the quote above as to a cause for under-appreciation of the need for ongoing study of EBM, and a corresponding solution. Modifying this a bit, I suggest the neologism, 'Telos-scope', and its inversion, as a diagnosis and an efficacious remedy.

Telos is the Greek term indicating end, ultimate goal or aim, while *skopos* originates from the Greek word meaning 'look at.' I submit that the *tools* of EBM are often emphasized above the *telos*, and that reversing this – inverting the 'telos-scope' – helps us see EBM for what it is, why its active study is never passe, and why the need to pursue it passionately is as great or greater than it's ever been.

More specifically, holding the eyeglass correctly – inverting the 'telos-scope' – underscores the importance of a vigorous pursuit of EBM by viewing what it provides the patient, what it gives the practitioner, and what forces are at play that are inimical to both.

In my own practice, I explain to patients that an evidence-based approach involves the same principles we use in our day-to-day lives to solve problems and make shopping decisions. I illustrate diagnostics with examples like how one would go about figuring out why the ice cubes in the freezer are melted: pre- and post-test probabilities of 'tests' like checking to see if the fridge is plugged in and whether other appliances on the same circuit are working, leading to potential expert consultation (the repairman or electrician) or a simple home remedy (resetting the circuit breaker). Therapeutics are elaborated with the coupon metaphor: a coupon promising 50% off might be great or it might be trivial – it all depends on whether you can use it to buy a car, or a candy bar. With this groundwork laid, we discuss why we would or wouldn't want to order a given test, calculate approximated individualized risk differences, etc.

Why bother? Because I've found that it greatly fosters the quintessential quality for patient care: trust.

We went into medicine to help others, serve as their advocates, help them navigate the bewildering and stressful terrain of medical problems and medical claims. Strengthening

the connection with our patients and their families, empowering them by demystifying frightening and confusing concepts and claims, teaching and modeling these for our students and residents: these and other benefits of an evidence-based approach feed the soul of the practitioner. They resonate with and reinforce our core values, and energize us in a milieu that increasingly sucks the life and joy out of what we love, and to which we have devoted our lives. And, importantly, they foster collegiality and even solidarity among healthcare providers.

The pursuit of truth implies and leads to accountability. This idea was conveyed to me early in my formal study of EBM, when Dr. Gordon Guyatt explained to me that “at its heart, EBM is about challenging authority.” We need this accountability now more than ever, especially as we see the term ‘evidence-based’ commandeered and perverted to promote systems, metrics, and agendas that are abusive to providers and detrimental to patients.

Further, I have found this accountability applied to self leads to a more balanced approach. Rather than a binary, “there is/isn’t evidence for X,” I find myself looking at the strength of the evidence and approaching patients in a more nuanced and humble way. For instance, therapeutics supported by weak evidence can sometimes be life-changing in their benefits, but the binary approach (which some wrongly attribute to EBM) could pass by such opportunities.

The *telos* of EBM is the good of the patients for whom we care. Subservient to this end, we develop and apply the *tools* of EBM. Inverting the ‘telos-scope’ fixes before us this *telos*, or ultimate goal or aim, in clarity and magnitude. It shows us that the better we are at practicing, modeling and teaching EBM, the greater good we do for our patients, society, and science. Patients, practitioners, society, and science need this. They always will. That makes EBM perennially relevant. And *that* is why we should study, promote and be passionate about EBM.

EBHC Teaching Point: Going back to the roots of the scientific method

Pierre La Rochelle

Edited by:Atefeh Noori and Vahid Ashoorion

In the province of Québec, Canada, the Code of Ethics of Physicians requires that: “a physician must practice in accordance with scientific principles”[1], without providing

definition of this fundamental concept. The scientific method is overlooked and taken for granted somewhere after high school during clinician formation that started from medical school and continues through the life. Nevertheless, this basic approach worth considering in the general clinical approach.

At the foundation of the scientific method in clinical area, we essentially have two elements: the first part, refers to the mechanism or model that can vary in details and complexity and supported with pathophysiologic rationale (e.g. antiarrhythmic drug will prevent death caused by malignant arrhythmia after acute myocardial infarction); and, on the other hand, the evidence, facts or phenomenon that can vary in precision and quality (e.g. sudden death observed within a randomized controlled trial where anti-arrhythmic drugs were compared to a placebo during the treatment of acute myocardial infarction). In this specific case[2], the model predicted a mortality reduction, but the trial, in of spite the widespread adoption of this therapy, demonstrated an unexpected increase in mortality. To develop our ability to discover the truth, these two elements, that seems to be closely related, must be analysed completely independently otherwise the link between these two basic elements will lead to a spurious and dangerous circular reasoning. If the model does not explain all the relevant facts, the model has to be replaced by a more adapted (appropriate) or powerful one; conversely, the facts that were historically considered of high quality, that are not explained by a new model capable to predict previously unknown facts, may force re-examination of the facts for their quality. This is the process to make any sensible progress in our knowledge. Dissecting of the models and evidence in a day to day practice may seem counter intuitive and/or time consuming for clinicians, nonetheless this approach serves as the cornerstone of the scientific method and constitute the shortest path leading to the truth.

Mechanism and evidence represent two confronting poles of tension where user of science may prefer one more. Researchers of basic science may focus their attention on new models rather than trying to explain every known fact, considering their variable quality. This way, new promising models will not be discarded too early if some facts are revealed to be of poor quality later. On the other hand, users of applied sciences, as clinicians, may devote their attention primarily on facts rather than models, to get more details on the outcomes and ensure more reliable results. A clinician enthusiastic on mechanism, which can be very legitimate if understood as such, may neglect to look at good evidence and impact negatively the expected outcomes as the example cited above. This is where EBHC expresses all its strength and value. This approach is the primary task expected from any clinician focusing on the patients' important outcomes, looking at the best chances of success, minimising known risks. To develop these skills, practitioners must develop the ability to build an efficient black box where all its scientific beliefs, prejudices, enthusiasm, fears, … are sealed, and focus its attention only on the input and the output where we can get the best opportunities to deliver real patient-centered care. These competences are not innate and require a minimum of discussion, thought and training.

Conclusion

Clinicians must develop awareness of their inborn clinical perception skill limitations, whichever they are appreciating outcomes alone or part within a group. Somewhere, somehow, our senses, intelligence, knowledge cannot reach the required scope of perception to ensure efficacy and safety. Practitioners must be very familiar with clinical study appraisal which remains our primary perception tool and be informed of the best evidence, otherwise claiming using the scientific method, as required in certain jurisdictions, or taking advantage of its presumed use, in regard to patients, make disrespectful, hazardous and inefficient decisions.

References

1. Code of Ethics of Physician, CQLR c M-9, r 17, s 6(2020).

2. Cardiac Arrhythmia Suppression Trial I. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. N Engl J Med. 1989;321(6):406-12.

Concepts of risk, conditional risk, hazard rate and hazard ratio

Kameshwar Prasad

Edited by: Jason Busse

Suppose you followed 100 patients for a fixed period of 3 months. The numbers of deaths in the first, second and third month are 40, 20 and 10, respectively. The risk of death during the three periods, is as follows:

- 40% in the first month, 40/100 = 0.4
- 20% in the second month, 20/100 = 0.2
- 10% in the third month, 10/100 = 0.1

The risk of death in a time interval conditional upon a subject surviving to the beginning of that interval (conditional risk), is:

- 40% in the first month, 40/100 = 0.4
- 33% in the second month, 20/60 = 0.33
- 25% in the third month, 10/40 = 0.25

For a large sample size, as the measurement unit for time becomes small, e.g. one quarter of a month instead of one month or even smaller, so that it approaches zero, the conditional risk divided by the width of time interval will approach a smooth curve, and in case of the risk remaining constant, a straight line. This curve or line represents the hazard rate (also called simply hazard, or hazard function). A hazard rate is the conditional risk of failure in an extremely small time interval divided by the width of the time interval. It is, in other words, the conditional, instantaneous risk. A formal definition may be as follows: The **hazard rate** is the **limit** of the number of events per unit time divided by the number at risk at the beginning of the time-interval, as the time interval approaches 0. The concepts of hazard and proportional hazard are particularly important in survival analysis. Some authors use the term average hazard rate, therefore, it may be wise to use the term 'instantaneous hazard rate' to distinguish it from average hazard rate, which is the same as incidence rate, or incidence density. Obviously, it is easier to calculate average rate than instantaneous rate. Calculating the average speed of a car is something all of us can do: divide the distance the car travelled by time.
Consider the example of a car covering a distance from point A to B. Suppose there are speed bumps (also called 'speed breakers') on the road. The car has to slow down and accelerate, each time it faces a speed bump. The reading on the car speedometer changes, but eventually the car reaches point B. The instantaneous speed, which is given by the speedometer changes as many times as the car crosses a speed bump. Average speed is given by (distance between point A and B) divided by time taken to cover the distance. Here average speed is NOT equal to instantaneous speed. Now suppose there was no speed bump on the road between point A and B, and the car travelled at constant speed smoothly so that the reading on the speedometer remained the same. In this case, average speed will be equal to instantaneous speed. Similarly, average hazard rate is equal to the instantaneous hazard rate when the hazard is constant. This is why in some calculations the underlying assumption is of a 'constant hazard'.

Hazard ratio

Hazard ratio (HR) is the ratio of two hazard rates, conventionally one for an exposed/treated group and one for an unexposed/untreated group. In a treatment trial, hazard ratio is usually the hazard rate in the treated group divided by the hazard rate in the control group. When a study reports one hazard ratio, it is assumed that difference between groups was proportional over time. Hazard ratios become meaningless when this assumption of proportionality is not met.

Interpretation of hazard ratio

In simple terms, you can interpret is as a risk ratio averaged over time. Thus, in a treatment trial, a HR of '1' means no difference in the effects of the two treatments. If it is < 1 (and the outcome in unfavourable and authors follow the convention of putting treatment hazard rate in the numerator), then treatment is associated greater benefit versus the control. When it is > 1, then the treatment increases the hazard and is harmful.

Treatment outcomes may be influenced by several variables, aside from treatment. We can adjust the hazard ratio for the effects of these other variables by Cox regression, also called proportional hazards regression.

Patient Values: An EBM guideline for the Big data era

Ramón Puchades

Edited by: Yaad Shergill

The past decade has seen major developments in Big data and Artificial intelligence (AI), creating a new paradigm in clinical research.[1, 2] The number of peer-reviewed medical research papers published on Big data and AI is increasing exponentially, and this trend is likely to continue in the foreseeable future.[3, 4, 5] Big data and AI innovations can be categorized as either machine learning or deep learning. Machine learning makes use of algorithms to learn from data and applies this data to make informed decisions. Deep learning is a subcategory of machine learning, layering algorithms to create an "artificial neural networks" helping inform most human-like AI developments. Machine learning and deep learning methods can lead to significant improvements in precision medicine, particularly for diagnosis and prognosis accuracy. Thus, in this changing era, the role of evidence-based medicine (EBM) remains crucial in guiding and maintaining proper methodological and scientific integrity in daily clinical practice while integrating Big data and AI. To highlight this, a recent article published in the Journal of the American Medical Association (JAMA) titled "How to Read Articles That Use Machine Learning Users' Guides to the Medical Literature",[6] the authors present a systematic approach focusing on three major components: validity, results and real world application. These methods have been informed by critical appraisal methods derived from EBM, demonstrating an influence on Big data and AI.

With respect to Dr. Sackett's definition of EBM[7] as the "integration of clinical expertise, patient values, and the best research evidence into the decision making process for patient care," the paradigm shift created by Big data and AI could influence two of the three components of EBM practice: clinical expertise, facilitating human & machine collaboration and best evidence, and advancing diagnosis and prognosis accuracy.

Patient values are the most difficult to measure and define objectively as these values can change over time and are influenced by variable psychosocial factors. This fact currently stands as a limitation for the Big data and AI clinical application. Both Big data and AI, constitute a clear advance in medicine, however the filter of EBM during the integration process into clinical practice is crucial to keep a high scientific standard. Furthermore, there is a need for Big data and AI to incorporate patient values in the clinical decision-making process.

References:

1. Jiang F, Jiang Y, Zhi H, et al. Artificial intelligence in healthcare: past, present and future. Stroke and Vascular Neurology 2017;2: doi: 10.1136/svn-2017-000101

2. Yu, KH., Beam, A.L. & Kohane, I.S. Artificial intelligence in healthcare. Nat Biomed Eng 2, 719–731 (2018).

3. Mehta N, Pandit A. Concurrence of big data analytics and healthcare: A systematic review. Int J Med Inform. 2018 Jun;114:57-65.

4. Economic evaluations of big data analytics for clinical decision-making: a scoping review. J Am Med Inform Assoc. 2020 Jul 1;27(9):1466-1475.

5. Pashazadeh A, Navimipour NJ. Big data handling mechanisms in the healthcare applications: A comprehensive and systematic literature review. J Biomed Inform. 2018 Jun;82:47-62.

6. Yun Liu, Po-Hsuan Cameron Chen, Jonathan Krause et al. How to Read Articles That Use Machine Learning. Users' Guides to the Medical Literature. JAMA. 2019;322(18):1806-1816.

7. Sackett, D. Evidence-based Medicine - What it is and what it isn't. BMJ. 1996; 312:71-72.

The McMaster Evidence-based Health Care Workshops: A last hurrah

Gordon Guyatt, Deborah Cook, Sheri Kietz

Edited by: Jason Busse

In 1992, David Sackett launched the first “How to teach evidence-based medicine” workshop at McMaster University. In 1993, a team that included two of us (Deborah Cook and Gordon Guyatt), along with administrator Deborah Maddock, assumed organizational leadership of the workshop. The broad interest from a wide variety of health professionals led to a rapid evolution into the “How to teach evidence-based health care” workshop.

Those who started the workshop had a somewhat ironic vision of a standard for its success: we would know when we have achieved our goal when we were no longer needed. For almost a decade, that achievement has appeared imminent. For many years, the workshop was sold out months before it began. Applications gradually decreased, and when the conduct of the workshop was in jeopardy, we expanded to a new audience, and the workshop became “How to teach and practice evidence-based health care”. With that transition, the leadership again evolved, with Sheri Kietz joining Gordon Guyatt in the primary organizational role, and Laurel Grainger in 2000 and in later years Jennifer Ayres and Gail Clark joining the administrative team.

Still, the workshop could not escape the consequences of its success. Having trained well over 1,000 EBM educators, and with the widespread publication and dissemination of EBM teaching materials, institutions all over the world now have the EBM educators they need. These individuals now run their own programs in undergraduate and post-graduate health professional education, and indeed, a number have organized their own workshops, some of which continue to thrive.

Concluding that our job was almost complete, we decided to organize a final celebratory workshop to be held in June 2020. That effort became one of the casualties of the COVID-19 pandemic. The original cancellation included a plan for the final workshop in 2021.

The evolution of COVID-19 has now put even that plan in jeopardy. How the world will look in terms of the pandemic, and the implications for an in-person McMaster EBHC workshop, appears perilously uncertain. In the face of that uncertainty, we have decided to delay the final face-to-face event until 2022. We look forward to an energized event, reflecting on an approach to teaching and practice, and a grand celebration of the impact of over 35 years of workshops!

GUEST CONTRIBUTORS

Arnav Agarwal

arnav.agarwal@mail.utoronto.ca

Thomas Agoritsas

thomas.agoritsas@gmail.com

Pablo Alonso-Coello

palonso@santpau.cat

Brian S. Alper

balper@computablepublishing.com

Samuel A. Berkman

sberkman@ucla.edu

Larry Birger

lbirger@kvhealthcare.org

Romina Brignardello Petersen

brignarr@mcmaster.ca

Deborah Cook

debcook@mcmaster.ca

Maureen Dobbins

dobbinsm@mcmaster.ca

Gordon Guyatt

guyatt@mcmaster.ca

Claire Howarth

howartce@mcmaster.ca

Heather Husson

hhusson@mcmaster.ca

Sheri Keitz

sheri.a.keitz@lahey.org

Pierre La Rochelle

pierre.la.rochelle@videotron.ca

Francois Lamontagne

Francois.Lamontagne@usherbrooke.ca

Laura Martinez Carcia

laura.martinez.garcia@cochrane.es

Sarah Neil-Sztramko

neilszts@mcmaster.ca

Per Olav Vandvik

per.vandvik@gmail.com

Kameshwar Prasad

drkameshwarprasad@gmail.com

Amy Price

amyprice@stanford.edu

Ramón Puchades

rpuchades@gmail.com

Amir Qaseem

aqaseem@acponline.org

Bram Rochwerg

bram.rochwerg@gmail.com

Andrea Juliana Sanabria

ajsanabria@cochrane.es

Nigar Sekercioglu

sekercn@mcmaster.ca

Reed Siemieniuk

reed.siemieniuk@medportal.ca

Mario Tristan

mtristan@ihcai.org

Linan Zeng

zengl15@mcmaster.ca

EDITORS

Jason W. Busse

Associate Professor, Dept of Anesthesia
McMaster University, Faculty of Health Sciences
(HEI) Health Research Methods, Evidence & Impact
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
bussejw@mcmaster.ca

Paul Glasziou

Professor of Evidence-Based Medicine
Director of the Centre for Research in Evidence-Based Health Care,
Bond University
Queensland, Australia 4229
pglaszio@bond.edu.au

Gordon H. Guyatt

Distinguished Professor, Clinical Epidemiology & Biostatistics

McMaster University, Faculty of Health Sciences
(HEI) Health Research Methods, Evidence & Impact
1280 Main Street West, HSC-2C12
Hamilton, ON L8S 4K1
Canada
guyatt@mcmaster.ca

GUEST EDITORS

Mahmood AminiLari

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
aminilam@mcmaster.ca

Vahid Ashoorion

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
ashoorion@gmail.com

Jeremy Ng

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
ngjy2@mcmaster.ca

Atefeh Noori

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
atefeh.noori@gmail.com

Yasir Rahman

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1
Canada
dry_rehman@yahoo.ca

Yaad Shargill

McMaster University, Faculty of Health Sciences
1280 Main Street West, HSC-2U1
Hamilton, ON L8S 4K1

Canada
yaad.shergill@gmail.com

EDITORIAL ASSISTANT

Jennifer Ayres
McMaster University, Faculty of Health Sciences
Clinical Epidemiology & Biostatistics
1280 Main Street West, HSC-2C9
Hamilton, ON L8S 4K1
Canada
ayres@mcmaster.ca