Reproductive and Developmental Sciences (RDS) and The Women+ and Children's Health Sciences (WACH) program
Critical Appraisal of Research in Reproductive and Children's Health Sciences

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Course: OBST 509
Date: To be determined
Time: To be determined
Location: BC Children Hospital Research Institute

Course overview
A review of current scientific literature is the first step before formulating research questions and conducting medical research. Critical thinking and a basic knowledge of research terminology, types of study design, and principles of statistical inference is a prerequisite to proper understanding of the medical literature, and therefore essential not only to students conducting clinical research but also to students in the biomedical realm. The course will provide students with guidance to critically assess clinical and population studies in medical literature. The examples will include papers focusing on human reproduction, maternal and child health, and child development. Furthermore, class discussions will include topics on the ethics of medical research and publishing.

Rationale for adding this new course
A correct understanding of research methodology is essential in any scientific endeavor. In recent years, standard guidelines have been developed and required for reporting results of medical research, including, for instance, STROBE (STrengthening the Reporting of OBservational studies in Epidemiology), CONSORT (Consolidated Standards of Reporting Trials), and STREGA (STrengthening the REporting of Genetic Association studies) guidelines. These reporting standards rely on proper understanding of clinical and population research terminology and principles of statistical inference. The new course will address the need for such understanding by providing guidance to critically apprise the medical literature and fill an important gap in the curriculum of the current RDS/WACH program. Further, this course will differ from other currently available UBC courses in its focus on critical thinking and appraisal of literature that is particularly important in reproductive, maternal and child health research, the main thematic foci of the RDS/WACH program. The unique challenges and opportunities inherent in research in this substantive area will be highlighted. This course is not intended to

provide in-depth knowledge of epidemiology and/or biostatistics or any substantive area of reproductive sciences or maternal/child health. Rather, it will provide students with a guidance to evaluate scientific papers in medical literature, especially in the area of reproductive medicine, maternal-child health and women's health. The aim of the course is to facilitate improved communication between RDS/WACH students and other researchers regarding study designs, data analyses and statistical issues.

All classes will take place at the BC Children's Hospital Research Institute, allowing RDS/WACH students to incorporate this course into their schedule.

Learning Objectives
1.   Recognize clinical and epidemiological study designs and basic statistical tests commonly used in scientific papers published in medical journals.
2.   Apply critical thinking in evaluating medical literature describing clinical and epidemiological studies with respect to potential threats to validity of the study results and conclusions.

Course objectives

The objectives of the course are that students
1. Gain knowledge about basic terminology with respect to various study designs and statistical inference used in medical research.
2. Investigate good practices in reporting results of medical research in scientific journals.
3. Practice critical thinking using examples of medical research and statistical inference from scientific journals.

Course philosophy

Effective learning occurs through active interaction between the teacher and students, lively discussion, and the application of learned knowledge or skills in practice. The key components of my teaching philosophy are as follows:

1) A respectful learning environment at all times: This is a key condition for achieving the learning objectives and for a meaningful discussion between the teacher and the students (and between students themselves).

2) Promoting curiosity and critical thinking by encouraging students to ask questions and express their understanding of the new subject material or skill.

3) Freedom: Students should feel free to make mistakes as they learn and have the opportunity to correct and refine their knowledge and skills. Students should be free to respectfully express their disagreement with the subject being taught and provide a rationale for their opinion. However, the knowledge of the subject being taught, i.e., as reflected in the consensus of expert opinion and current evidence, will be the final criterion for assessing the student's performance in any learning activity.

4) Opportunity to communicate: Each student should be given the opportunity to communicate their newly acquired knowledge or practice the newly acquired skill.

Teaching goals and strategies

The goal of teaching is to facilitate learning. Whenever possible, I will employ an active learning approach, which includes the following:

1) Problem-based learning: based on the assumption that the student is the primary agent in learning.

2) The teacher's role is to uncover the question that the answer hides and to be a co-learner.

3) Primarily inductive method: the usual methods are discussion, dialogue, and problem solving.

4) Testing the truth of what is taught involves reason and evidence.

5) Integral part of learning is a resolution of any conflict of ideas: a thesis vs anti-thesis, and a synthesis that results in new knowledge.

Recommended texts

Journal articles and reading material will be provided during the course (see below).

Pre-requisites: None.

Number of credits: 3

Course format

The class will start with a summary of the key points from the previous class, students will have the opportunity to ask questions. Two students will then present paper/s assigned for the current class in the form of a mini-debate, followed by a discussion. These papers will highlight relevant examples from obstetrics and gynaecology, pediatrics, reproductive sciences and women's health. Lecture-style teaching mixed with small-group discussions will further clarify and discuss this new topic. The class will end with questions from students or additional 'food-for-thought' suggestions related to the topic.

Method of evaluation

Grades will be based on:

- in-class engagement (25%) - learning objective 2;
- 1-2 presentation/s (debate format with 2 sides of the argument; 2-4 students presenting depending on the class size; 35%) – learning objective 2; and
- the end-of-term project (40%). The project will include a 5-page critical evaluation of a paper from a medical journal on a topic of reproductive medicine, maternal, fetal/infant or women's health demonstrating one or more principles learned in this course. The evaluation will include understanding of the terminology with respect to study design and biostatistics, critical thinking, and clarity of written communication - learning objective 1.

Further notes on grading:

- Grading criteria for in-class participation: equally weighted on a demonstrated ability to ask appropriate questions and/or provide appropriate comments at the end of the presentations/debates and throughout the lectures.
- Grading criteria for presentations and debates: equally weighted on clarity, understanding

of background, logic of presented arguments, ability to respond to the counter-arguments, and professional conduct.

- Grading criteria for the end-of-term project: equally weighted on understanding of the terminology with respect to study design and biostatistics, critical thinking, and clarity of written communication.
- Guest lecturers will provide scores for the student debates and discussions (an average will be used with the score by the course instructor).

Each grading component will be evaluated on a scale 0-100%, final grade will be based on the weighting scheme as outlined above (25% in-class participation, 35% presentation/debate, and 45% final project).

Generally, late assignments will not be accepted (grade = 0 on late/missing component).
A rotating schedule will be established to assign student presentation/debate dates. It is expected that each student will present 1-2 times over the term, this may be adjusted depending on the number of enrolled students. Changes in the presentation rotation schedule are permitted, however, it is the responsibility of the student to make these arrangements with classmates and inform the course instructor well in advance (before the start of the assigned module).

Course Schedule *(an example of 11 3-hour classes; readings are listed below)*
1. Course outline, evaluation criteria, discussion about the student projects
    Learning objectives: to list and describe basic terminology used in medical research (clinical medicine and population research), measures of association, research questions and hypotheses; examples of research questions and hypotheses from studies of maternal-infant health. Discussion of examples from the literature on how a scientific paper is structured. The assignment of readings for the next weeks.
2. Basic terminology and critical thinking in the assessment of study design in the context of obstetric and gynecologic research (Debate: What is more useful: experimental or observational research in studies of reproductive outcomes?)
    Learning objectives: to describe basic study designs, basic advantages and disadvantages of randomized controlled trials, cohort studies, case-control studies and ecological studies using examples from studies of maternal-child health.
3. Bias and confounding in reproductive medicine research: Introduction to the concept of validity of study results in medical research. (Debate: Are we able to control for confounding in studies of long-term health outcomes of children born to women with pre-pregnancy risk factors, e.g., obesity?)
    Learning objectives: this class will build on the previous class in discussing how bias can affect study results and how it can be minimized through the study design and analysis; how confounding can affect study results and how to asses and mitigate confounding. Examples from the literature in maternal-child health will be discussed.
4. P-values and reproductive health: what can researchers learn from the American

Statistical Association?. Introduction to basic terminology and critical thinking meaning of p-values, null hypotheses, and confidence intervals (Debate: should we always use p-values when we describe rare outcomes such as maternal death?)

> Learning objectives: to discuss basic terminology pertaining to statistical analysis, sampling, probability, hypothesis testing, p-values, and confidence intervals. Examples form the literature will be discussed with respect to interpretation of results and conclusions.

5. Prediction models in reproductive medicine: Introduction to basic terminology and basic concepts of multivariable analyses and regression models and critical thinking in their interpretation (Debate: Can we create statistical models for complex medical conditions such as preeclampsia?)

> Learning objectives: to describe basic concepts of statistical modelling and terminology used in the literature; interpretation of results will be discussed using examples of the most common regression models as reported in the medical literature pertaining to maternal and fetal/infant health.

6. Considerations in randomized clinical trials in reproductive medicine: Introduction to etiologic and prognostic research, and causal inference (Debate: Do we need prognostic research, in contrast with etiologic research, on congenital anomalies?)

> Learning objectives: to describe differences between prognostic and etiologic research; basic concepts of correlation, association, and causal inference; this class will bring together themes from the previous classes; examples of etiologic and prognostic studies will be discussed, including discussions about conclusions from clinical and population research in maternal-infant health.

7. Basic terminology and introduction to qualitative and mixed research methods (a guest lecture) (Debate: Can qualitative research inform maternal care?)

> Learning objectives: to describe basic fundamentals of qualitative research and its importance (a guest faculty researcher will describe an example of a qualitative study).

8. Screening for breast cancer: how effective are our tests? Basic terminology and introduction to the concept of diagnostic test, sensitivity and specificity, predictive values, and screening. (Debate: Should all women be screened for breast cancer?)

> Learning objectives: to explain basic principles of diagnosis and diagnostic tests including sensitivity, specificity, and predictive values; examples of screening tests. Examples will be discussed to encourage critical thinking in evaluating of medical studies with respect to diagnosis of diseases and medical conditions.

9. Non-publication and publication bias in reproductive medicine: Introduction to the concept of systematic review and meta-analysis, reporting standards in presentation of research results (Debate: Should we publish both statistically significant and non-significant results?)

> Learning objectives: to outline basic standards of reporting research, (e.g., STROBE guidelines) and how these relate to presentation and communication of research results in the literature and in conference presentations; the structure of research papers and the process of publishing, publishing bias.

10. Special topics: critical thinking and basic pitfalls in research using large datasets

(example: genetic research, the concept of DoHAD; a guest lecture) (Debate: Is our health determined in mother's womb?)

> Learning objectives: this lecture is reserved for a special topic, the students will learn about basic terminology and principles of large data analysis in genetics, gene-environment interactions and other basic concepts and pitfalls in research including large data.

11. Summary and overview: summary of key points from each class, ethics in critical thinking.

> Learning objectives: a summary lecture with further discussions, examples of research ethics considerations; Q&As about the students' projects, remaining students' presentations, if any.

Reading materials* for class No.:
1. No reading material.
2. Messerlian C, Basso O. Cohort studies in the context of obstetric and gynecologic research: a methodologic overview. Acta Obstetrica et Gynecologica Scandinavica 2018;97(4):371-379. doi:10.1111/aogs.13272
   Given JE, Loane M, Garne E, et al. Metformin exposure in first trimester of pregnancy and risk of all or specific congenital anomalies: exploratory case-control study. BMJ 2018; 361 :k2477
3. Correia KFB, Dodge LE, Farland LV, et al. Confounding and effect measure modification in reproductive medicine research, Human Reproduction 2020; 35(5):1013–1018, https://doi.org/10.1093/humrep/deaa051
   Radin RG, Rothman KJ, Hatch EE, et al. Recall error in time-to-pregnancy studies. Paediatr Perinat Epidemiol 2015;29:576-588. https://doi.org/10.1111/ppe.12245
4. Farland LV, Correia KF, Wise LA, Williams PL, Ginsburg ES, Missmer SA. P-values and reproductive health: what can clinical researchers learn from the American Statistical Association?. Hum Reprod. 2016;31(11):2406-2410. doi:10.1093/humrep/dew192
   Greenland S, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. European journal of epidemiology 2016;31(4):337-50. doi:10.1007/s10654-016-0149-3
   Makin TR, Orban de Xivry JJ. Science Forum: Ten common statistical mistakes to watch out for when writing or reviewing a manuscript. eLife 2019;8:e48175. DOI https://doi.org/10.7554/eLife.48175
5. Leushuis E, van der Steeg JW, Steures P et al. Prediction models in reproductive medicine: a critical appraisal. Human Reproduction Update 2009; 15(5):537–552.
   Tripepi G, Jager KJ, Dekker FW, Zoccali C. Linear and logistic regression analysis. Kidney International 2008;73(7):806–810. https://doi.org/10.1038/sj.ki.5002787
   Hoffman JIE. Logistic Regression. In Biostatistics for Medical and Biomedical Practitioners 2015: pp. 601–611. Elsevier. https://doi.org/10.1016/b978-0-12-802387-7.00033-0. Available online.
6. Venetis C, d'Hooghe T, Barnhart KT, et al. Methodologic considerations in randomized clinical trials in reproductive medicine, Fertility and Sterility 2020; 113(6):1107-1112 https://doi.org/10.1016/j.fertnstert.2020.04.038.

Zemek R, Barrowman N, Freedman SB, et al; Pediatric Emergency Research Canada (PERC) Concussion Team. Clinical risk score for persistent postconcussion symptoms among children with acute concussion in the ED. JAMA 2016;315(10):1014-1025.

Tolles J, Meurer WJ. Logistic regression: relating patient characteristics to outcomes. JAMA 2016;316(5):533-534.

Meurer WJ, Tolles J. Logistic Regression Diagnostics: Understanding How Well a Model Predicts Outcomes. JAMA 2017;317(10):1068–1069. doi:10.1001/jama.2016.20441

7. Reading will be selected by the guest lecturer in advance.
8. Moskowitz M. Screening for breast cancer: how effective are our tests? A critical review. CA Cancer J Clin. 1983;33(1):26-39. doi:10.3322/canjclin.33.1.2

   BMJ Best Practices: Diagnostic test studies: assessment and critical appraisal. https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/diagnostic-test-studies-assessment-and-critical-appraisal/
9. Lensen S, Jordan V, Showell M, et al. Non-publication and publication bias in reproductive medicine: a cohort analysis. Hum Reprod. 2017;32(8):1658-1666. doi:10.1093/humrep/dex236

   Optional readings:

   Hopewell S, Loudon K, Clarke MJ, Oxman AD, Dickersin K. Publication bias in clinical trials due to statistical significance or direction of trial results. Cochrane Database of Systematic Reviews 2009. Summary. John Wiley and Sons Ltd. https://doi.org/10.1002/14651858.MR000006.pub3

   Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials BMJ 2011; 343:d4002

   Li G, Zeng J, Tian J, Levine MAH, Thabane L. Multiple uses of forest plots in presenting analysis results in health research: A Tutorial. J Clin Epidemiol. 2020 Jan;117:89-98. doi: 10.1016/j.jclinepi.2019.09.021. Epub 2019 Oct 4. PMID: 31589955.
10. Reading will be selected by the guest lecturer in advance.
11. Emanuel EJ, Wendler D, Grady C. What Makes Clinical Research Ethical? JAMA. 2000;283(20):2701–2711. doi:10.1001/jama.283.20.2701

    Montori VM, Jaeschke R, Schünemann HJ, Bhandari M, Brozek JL, Devereaux PJ et al. Users' guide to detecting misleading claims in clinical research reports BMJ 2004; 329:1093

* Additional readings will be assigned to students to prepare presentation debates. These will involve 2-4 students, debating 2 sides of the argument; presentations will take 40-60 minutes for 2 rounds (15 minutes of arguments for each side and 10 minutes of a rebuttal each), followed by a class discussion.

Course instructor qualifications:
Dr. Sarka Lisonkova is an Associate Professor in the Department of Obstetrics and Gynaecology and the Children's and Women's Hospital of British Columbia in Vancouver, and an adjunct faculty at the School of Population and Public Health, UBC. Her medical training was in the Czech Republic and she obtained her MSc in Epidemiology from the State University of New

York, USA, and PhD in Epidemiology and PhD in Epidemiology and Biostatistics at UBC. She holds a Michael Smith Foundation for Health Research Scholar Award for her research in maternal and perinatal health, and the Sick Kids Foundation and CIHR New Investigator Awards. Dr. Lisonkova is a perinatal epidemiologist working in the area of maternal, fetal, and neonatal health and health services research, and her research focuses on adverse perinatal outcomes among high-risk and vulnerable women. She has published numerous papers on this topic in high-impact medical journals including JAMA and PloS Medicine.

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