Conducting Clinical Research:

Identifying the Research Question - the Critical First Step

Laurie Twells PhD

Professor, Ltwells@mun.ca

Tuesday, Feb. 8, 12-1 p.m.

Presentation outline:

- The research process & where research ideas originate
- Why the research question is critically important
- Criteria to guide and develop research questions
- My experience with research ideas & questions
- Examples of research questions

Clinical Research

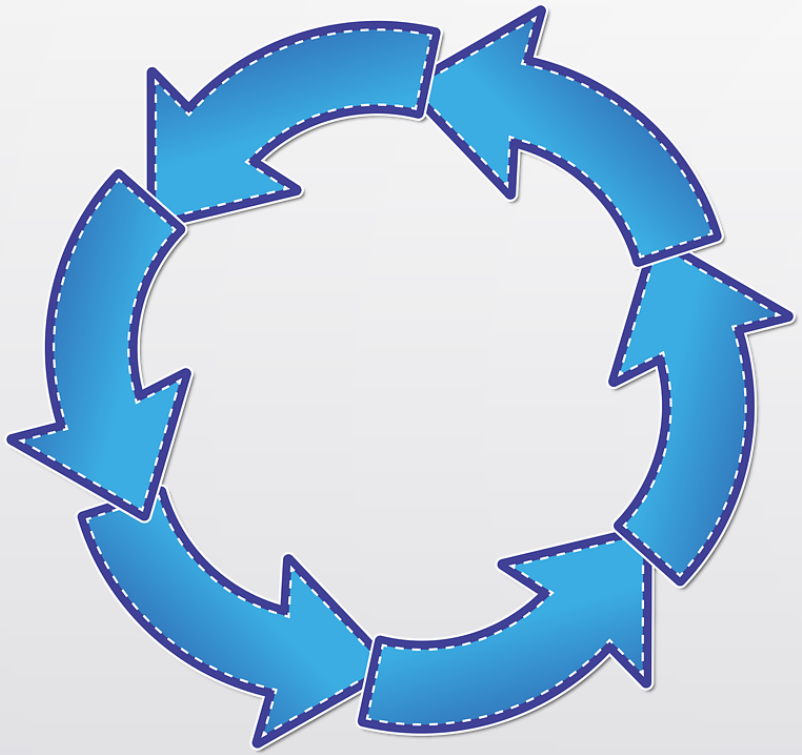
"The systematic investigation towards increasing the sum of knowledge"

(Chambers 20th Century Dictionary)

"The science of human disease investigation with a focus on diagnosis, prognosis and treatment"[1]

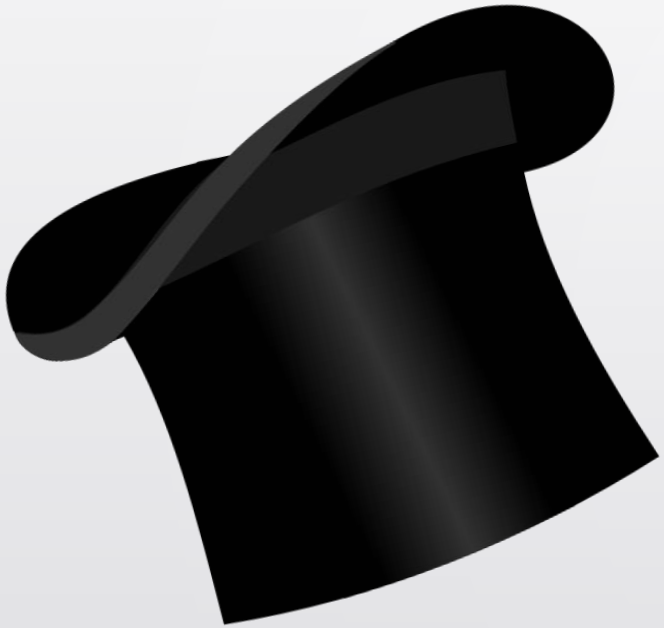
[1] Parfrey, Barrett (eds), Clinical Epidemiology: Practice and Methods 2020

Research Process: Iterative



1. **Ideas or Opportunities**
2. **Extensive literature search**
3. **Develop the research question/hypothesis**
4. Design study
5. Determine Sample Size
6. Collect Data
7. Conduct Analysis
8. Interpret Results
9. Answer research question
10. Draw Conclusion
11. Write up results and conduct KT
12. Apply results - e.g., inform clinical decision making, add to the body of knowledge
13. **Generate new ideas/research questions**
14. **Back to # 2**

Where do research ideas and questions come from?



Stop for 1 minute and think about the research you are involved in or have completed.

Where did the research question come from ?

Put it in the chat or just think about it

Where do research ideas come from?

Systematic Investigation

- Passion/interest
- Lived experience/family members
- Funding opportunities (CIHR, NSERC)
  - New industry e.g cannabis regulation
- Supervisors
- Colleagues (e.g., case reports/series)
- Clinical experience/observations
- New health policies (e.g. tax on SSB)
- Opportunities
- New Knowledge/Big Data
- New Discoveries: genetics
- Industry- public private partnerships

Ten most common reasons why journals reject articles:

1. **Unimportant or irrelevant topic (THE RESEARCH IDEA)**
2. **Insufficient or incomplete problem statement (THE RESEARCH QUESTION)**
3. **Inadequate review of literature (RATIONALE FOR THE RESEARCH QUESTION)**
4. Sample to small or biased
5. Inaccurate and inconsistent data reported
6. Insufficient data reported
7. Defective tables and figures
8. Overinterpretation of Results
9. Text difficult to follow/understand
10. Inappropriate or insufficient reporting of statistics

Bordage G. Academic Medicine

Criteria to Develop and Inform a Research Question

FINER CRITERIA	
F	Feasible
I	Interesting
N	Novel
E	Ethical Relevant
R	Relevant

Wolters Kluwer Health.

Is your research question:

Feasible ?

Conducive Environment
Adequate Sample Size
Time Frame
Effect Size
Resources: expertise, consultation
Do we need to do a Pilot Study ?

Is your research question:

Interesting ?

Personal - passion/interest
Professional- promotion, reputation
Colleagues/peers
Funding call
Resources: expertise, consultation

Is your research question:

Novel ?

Confirms previous findings
Refutes previous findings
Extends knowledge of previous findings

Is your research question:

Ethical?

Amenable to ethics board approval	
Recruitment of participants	Where? How?
Consent	How will participants be consented?
Safety	How will you ensure safety?
Benefits versus Risks	Do not overstate benefits Do not underestimate risks
Confidentiality/Privacy	How will you ensure privacy? Remove identifiers, Unique respondent ID
Patient Data	Who has access? Where it is kept?

Is your research question:

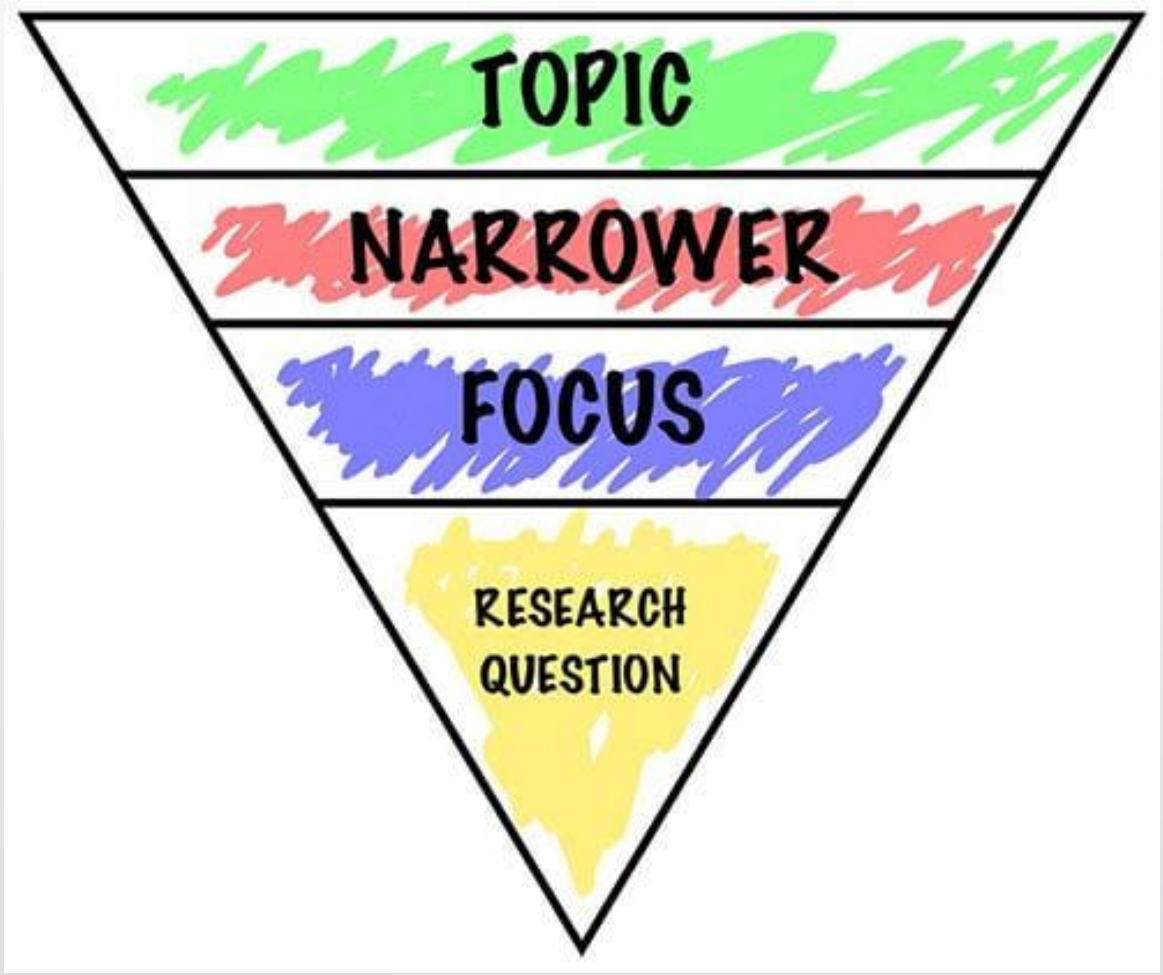
Relevant ?

Improve patient outcomes
Improve patient care
Improve patient safety
Guide recommendations/standards/protocols/practice guidelines
Generalizable? External validity?
Answering questions? Solving problems? Elucidating relationships?

Does your research question pass the most important question?

Is your research question clinically relevant & answerable?

Be aware of statistical significance versus clinical significance.



How do we develop a
focused
specific
clear
research question?

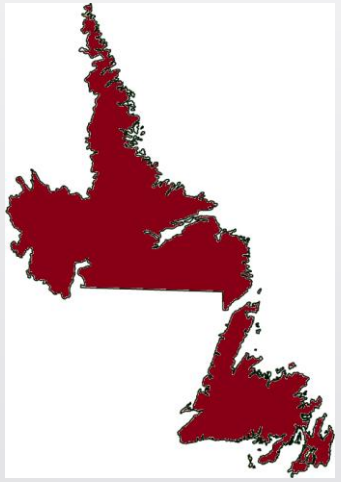
Formulate your research question using the PICOT format

P	Population (patients)	What specific population are you interested in?
I/E	Intervention	What is your intervention? What is your exposure?
C	Control group/exposure	What is the alternative to your intervention?
O	Primary Outcome	What will you measure, improve, affect, accomplish?
T	Time	What is the appropriate follow up time to assess the outcome?

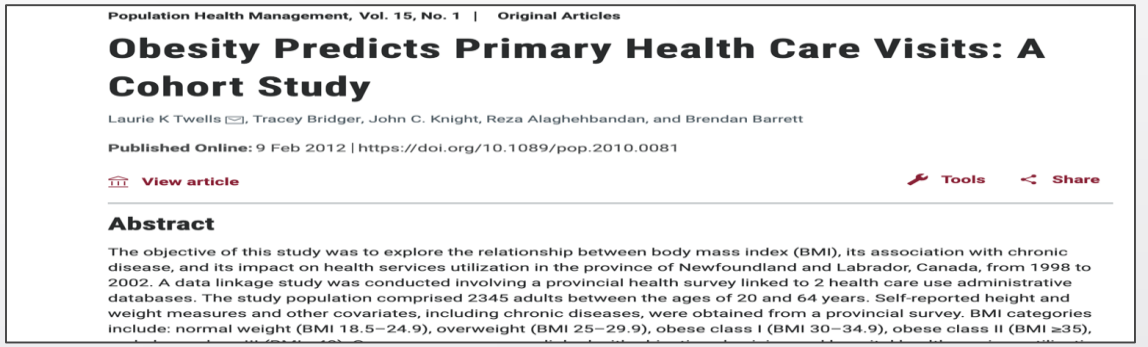
Brian Haynes R. Forming research questions. J Clin Epidemiol 2006; 59:881-6.


Opportunity

My experience with research ideas & questions



- NL had the highest prevalence of obesity in Canada
  ~25 - 35% or 1/3 adults is obese
- 8% of NL's adult population 18+ have
  BMI ≥35 kg/m^2
  - **~29,800 people**
  - ~ 75% of individuals living with severe obesity report > 3 chronic conditions



Population Health Management, Vol. 15, No. 1 | Original Articles

Obesity Predicts Primary Health Care Visits: A Cohort Study

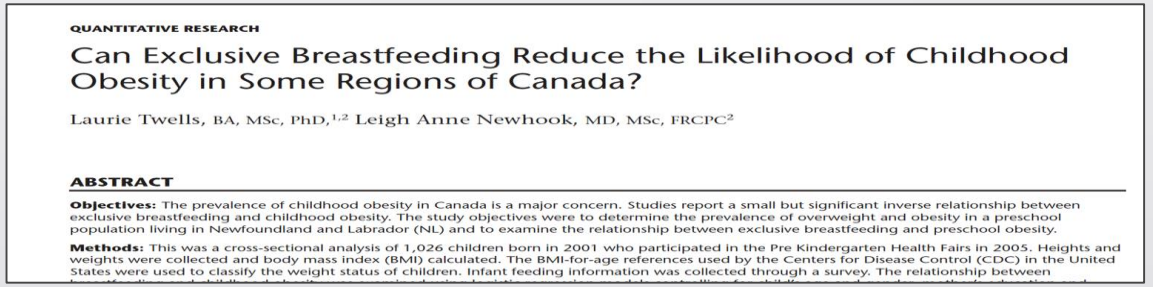
Laurie K Twells, Tracey Bridger, John C. Knight, Reza Alaghehbandan, and Brendan Barrett

Published Online: 9 Feb 2012 | https://doi.org/10.1089/pop.2010.0081

View article Tools Share

Abstract

The objective of this study was to explore the relationship between body mass index (BMI), its association with chronic disease, and its impact on health services utilization in the province of Newfoundland and Labrador, Canada, from 1998 to 2002. A data linkage study was conducted involving a provincial health survey linked to 2 health care use administrative databases. The study population comprised 2345 adults between the ages of 20 and 64 years. Self-reported height and weight measures and other covariates, including chronic diseases, were obtained from a provincial survey. BMI categories include: normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), obese class I (BMI 30–34.9), obese class II (BMI ≥35),



QUANTITATIVE RESEARCH

Can Exclusive Breastfeeding Reduce the Likelihood of Childhood Obesity in Some Regions of Canada?

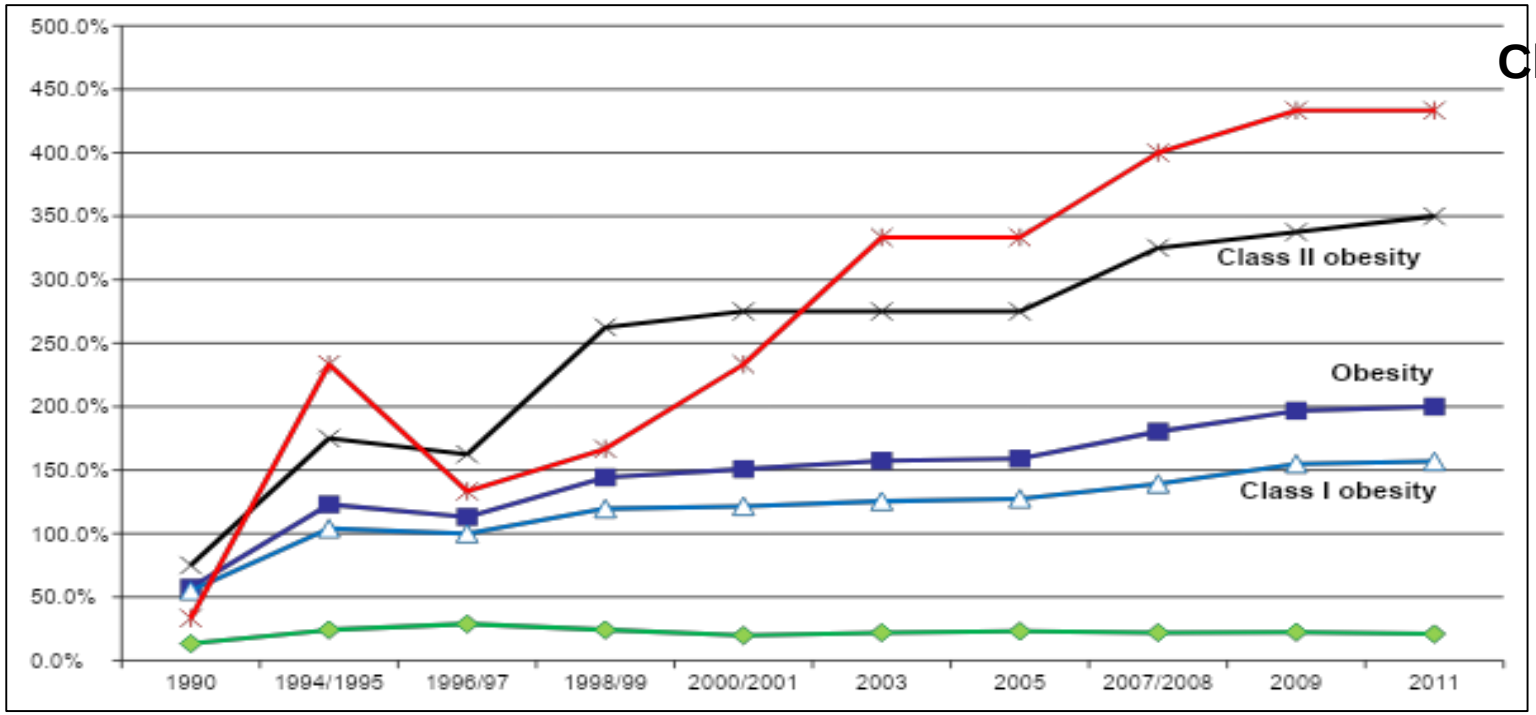
Laurie Twells, BA, MSc, PhD,[1,2] Leigh Anne Newhook, MD, MSc, FRCPC[2]

ABSTRACT

Objectives: The prevalence of childhood obesity in Canada is a major concern. Studies report a small but significant inverse relationship between exclusive breastfeeding and childhood obesity. The study objectives were to determine the prevalence of overweight and obesity in a preschool population living in Newfoundland and Labrador (NL) and to examine the relationship between exclusive breastfeeding and preschool obesity.

Methods: This was a cross-sectional analysis of 1,026 children born in 2001 who participated in the Pre Kindergarten Health Fairs in 2005. Heights and weights were collected and body mass index (BMI) calculated. The BMI-for-age references used by the Centers for Disease Control (CDC) in the United States were used to classify the weight status of children. Infant feeding information was collected through a survey. The relationship between

Increases in Severe Obesity in Canada

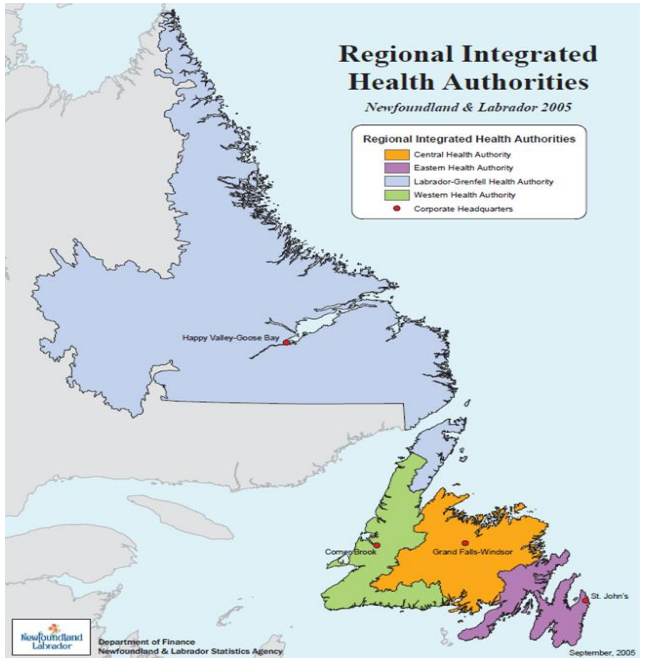


Twells et al., ***CMAJ Open***

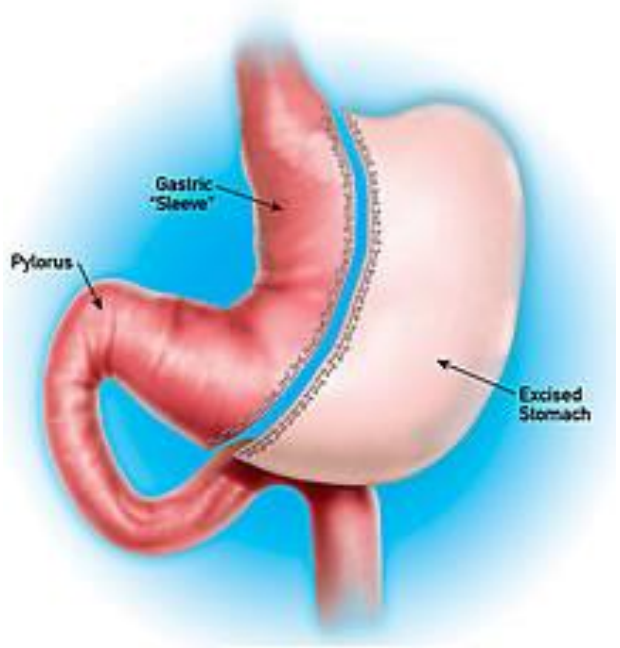
December 2010:
Eastern Health approves bariatric surgery - treatment for severe obesity

2006 Clinical Practice Guidelines: recommended Bariatric Surgery as a treatment for Canadians living with severe obesity

- **Eligible patients:**
  - BMI ≥ 35kg/m^2 + a comorbidity OR a BMI ≥ 40 kg/m^2
- **Agreed to fund between 100-150 procedures per year**
  - Surgical Option/laparoscopic sleeve gastrectomy (LSG)
- **Eastern Health established a multi-disciplinary team**
  - Two surgeons (now three/four)
  - Nurse practitioner
  - Dietician

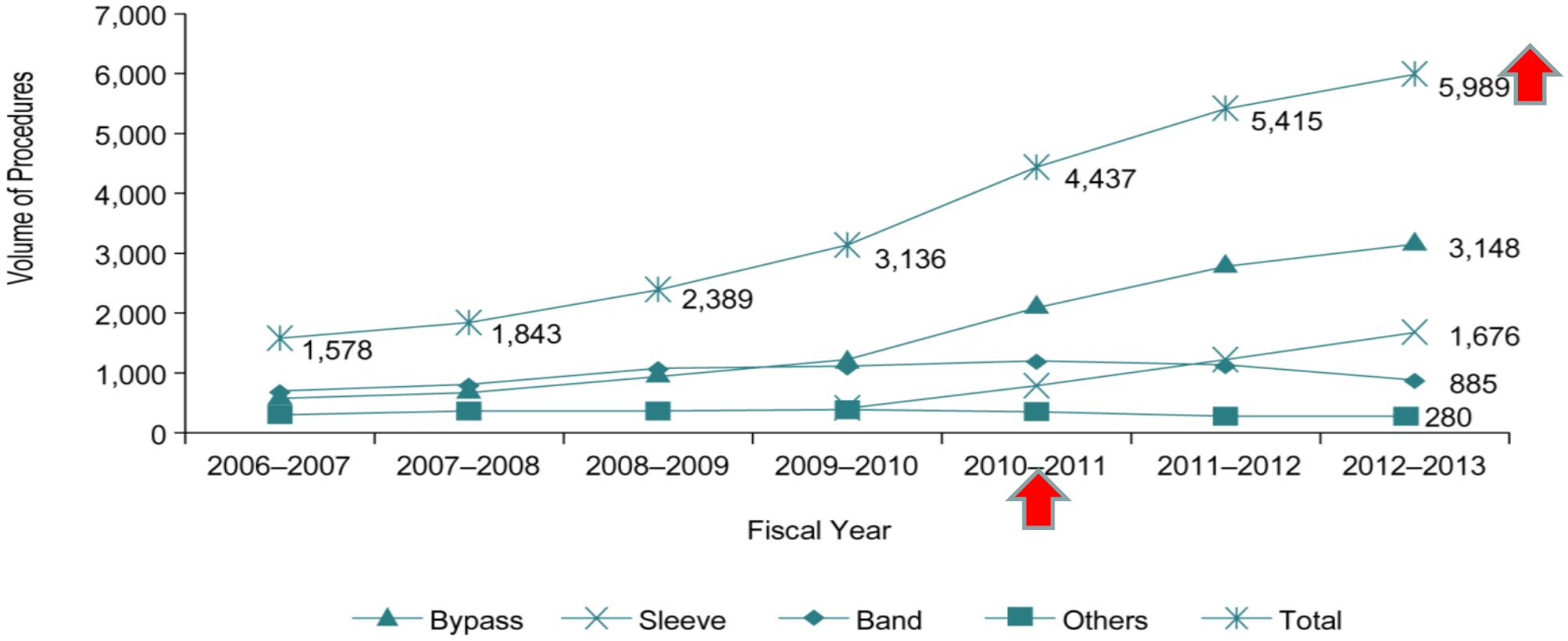


Laparoscopic Sleeve Gastrectomy (LSG)



- Removes ~80% of the stomach laparoscopically so that the stomach takes the shape of a tube or "sleeve"
- Restricts the stomach to a volume of 60-100mL
- Accounts for ~5% of bariatric surgeries
- Impacts weight and metabolic parameters
  - **In 2010, LSG was considered an investigational procedure**

Bariatric Procedures Performed in Canadian Hospitals: Changes in Volume



CIHI, Bariatric Surgery in Canada, May 2014

Development of a research team & program of research

- Established a research team & determined research needs (dynamic)
- Connected with mentors/expertise (Researchers in Alberta, CIHR Planning Meeting)
- **Identified gaps in the research literature**
- Decided research questions and data collection **BEFORE** any data was collected
- Planned a prospective study (before and after within subject)
- Wrote research grants & sought funding
- Established a program of research

Bariatric Care: Gaps in Research

MEMORIAL UNIVERSITY

Report published in 2010

"*Developing a Research Agenda to Support Bariatric Care in Canada*"

a joint report by CIHR & Obesity Canada

Research Questions around Sleeve Gastrectomy: an investigational procedure

The patient will have many questions:

1. What is sleeve gastrectomy? Are there other options?
2. How does LSG compare to other surgical and non surgical weight loss options?
3. How much weight might I lose?
4. Will it improve my quality of life ?
5. Will this help with my T2DM, HTN or sleep apnea?
6. What are the risks of surgery?
7. Are there long term complications ?
8. Will I need to take vitamins for the rest of my life?

Researchers, decision makers will have questions too:

1. Does LSG impact patients use of the health care system?

1. Is the procedure cost effective?

1. Do the benefits outweigh any risks?

1. Can we make the process more efficient?

Overarching Research Question in PICOT Format (Met FINER Criteria)

In eligible patients (19-70yrs) who undergo bariatric surgery (n=200), does LSG impact the following outcomes post-surgery compared to pre-surgery:

-weight loss, comorbid conditions, HRQoL, nutrient deficiencies, health services use and costs.

Study design: Population-based prospective cohort study with assessments pre-surgery and at 6,12,18, 24 months and mid to long term post surgery (5-10 yrs).

The NL Translational Research Program in Bariatric Care

Pre-surgical Studies

- Waiting for Bariatric Surgery Qualitative Study (3)
- Patient Goals and Weight Loss Expectations Post Surgery Quantitative Study (3)
- Weight bias, stigma and discrimination in the healthcare system (1)
- Health Professionals' Practices and Attitudes towards Patient with obesity
- Ghrelin and Weight loss

Surgical Cohort Study

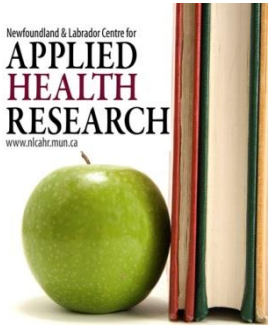
- Inception Cohort Protocol (1)
- Mid-Term Health Outcomes Weight, Comorbid Improvement Quality of Life (1)
- Impact on Macro/Micro Nutrient deficiencies (1)
- Impact on medication use(1)
- 30 day Complications of Surgery (1)
- Longer Term Clinical Outcomes(2) (in progress)

Post Surgical Studies

- "Patient Reported" Outcomes and "Definitions of Success" 12 Months Post Bariatric Surgery (1)
- Long term impact of bariatric surgery on health related quality of life (1)
- Prioritization of bariatric surgery in Canada: a Discrete Choice Experiment (1)
- Non Surgical Weight Loss Options: a meta analysis (1)
- Are Canadians Willing to Pay for Bariatric Surgery: A Discrete Choice Experiment (1) (ready to submit)

Research Funding

Newfoundland Labrador



HEALTH CARE FOUNDATION

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

MEMORIAL UNIVERSITY
Faculty of Medicine

MEMORIAL UNIVERSITY
School of Pharmacy

In-kind Support

Centre for Health Information
Newfoundland & Labrador

NEWFOUNDLAND AND LABRADOR
SUPPORT
Support for People and Patient Oriented Research and Trials

Examples of Research Objectives and Research Questions

Young *et al. BMC Family Practice* 2011, **12**:88
http://www.biomedcentral.com/1471-2296/12/88

BMC Family Practice

RESEARCH ARTICLE **Open Access**

Comparison of pharmacist managed anticoagulation with usual medical care in a family medicine clinic

Stephanie Young[1*], Lisa Bishop[1,2], Laurie Twells[1,2], Carla Dillon[1,2], John Hawboldt[1,2] and Patrick O'Shea[2,3]

Abstract

Background: The beneficial outcomes of oral anticoagulation therapy are dependent upon achieving and maintaining an optimal INR therapeutic range. There is growing evidence that better outcomes are achieved when anticoagulation is managed by a pharmacist with expertise in anticoagulation management rather than usual care by family physicians. This study compared a pharmacist managed anticoagulation program (PC) to usual physician care (UC) in a family medicine clinic.

Methods: A retrospective cohort study was carried out in a family medicine clinic which included a clinical pharmacist. In 2006, the pharmacist assumed anticoagulation management. For a 17-month period, the PC group (n = 112) of patients on warfarin were compared to the UC patients (n = 81) for a similar period prior to 2006. The primary outcome was the percentage of time patients' INR was in the therapeutic range (TTR). Secondary outcomes were the percentage of time in therapeutic range within ± 0.3 units of the recommended range (expanded TTR) and percentage of time the INR was >5.0 or <1.5.

ABSTRACT

The study compared a pharmacist managed anticoagulation program (PC) to usual physician care (UC) in a family medicine clinic [Abstract].

PICOT

In patients on warfarin attending a family medicine clinic, does PC compared to UC result in differences in the % of time patients' INR was in the therapeutic range over a 17 month period?

A retrospective cohort study

Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

Long-Term Health-Related Quality of Life in Bariatric Surgery Patients: A Systematic Review and Meta-Analysis

Shannon Driscoll[1], Deborah M. Gregory[1], John M. Fardy[1], and Laurie K. Twells[1,2]

Objective: Bariatric surgery results in significant weight loss in the majority of patients. Improvement in health-related quality of life (HRQoL) is an equally important outcome; however, there are few studies reporting long-term (≥5 years) HRQoL outcomes. This study assesses the quality of evidence and effectiveness of surgery on HRQoL ≥ 5 years.

ABSTRACT

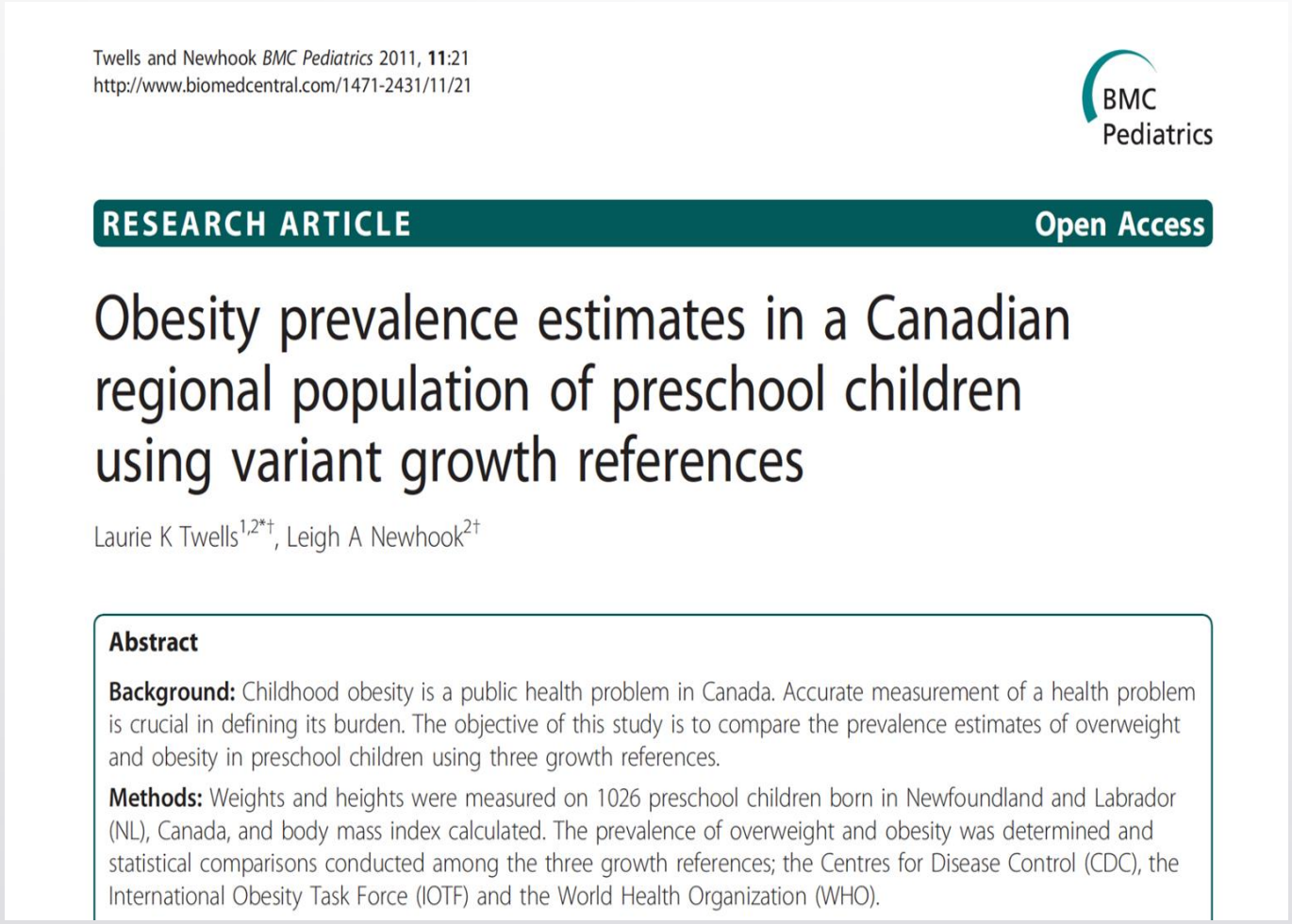
This study assesses the quality of evidence and the effectiveness of bariatric surgery on Health Related Quality of Life >= 5 years.

PICOT

In patients living with severe obesity, does bariatric surgery compared to a control improve health related quality of life 5 years or more after surgery?

Primary outcome: Patient Reported Outcome Measure (PROM)

A systematic review and meta-analysis



Twells and Newhook *BMC Pediatrics* 2011, **11**:21
http://www.biomedcentral.com/1471-2431/11/21

BMC Pediatrics

RESEARCH ARTICLE Open Access

Obesity prevalence estimates in a Canadian regional population of preschool children using variant growth references

Laurie K Twells[1,2*†], Leigh A Newhook[2†]

Abstract

Background: Childhood obesity is a public health problem in Canada. Accurate measurement of a health problem is crucial in defining its burden. The objective of this study is to compare the prevalence estimates of overweight and obesity in preschool children using three growth references.

Methods: Weights and heights were measured on 1026 preschool children born in Newfoundland and Labrador (NL), Canada, and body mass index calculated. The prevalence of overweight and obesity was determined and statistical comparisons conducted among the three growth references; the Centres for Disease Control (CDC), the International Obesity Task Force (IOTF) and the World Health Organization (WHO).

ABSTRACT

The objective of the study is to determine the prevalence estimates of overweight and obesity in preschool children using different growth references.

PI/ECO

In preschool children in NL, are there differences in the prevalence of overweight and obesity using 3 growth references (CDC, IOTF, WHO)?

A cross sectional study analysis

RESEARCH • RECHERCHE

The usefulness and costs of routine contrast studies after laparoscopic sleeve gastrectomy for detecting staple line leaks

Dimitry Terterov, MD
Philemon Ho-Yan Leung, MD
Laurie K. Twells, PhD
Deborah M. Gregory, BN, PhD
Chris Smith, MD
Darrell Boone, MD
David Pace, MD, MBA

This work was presented at the 2015 Canadian Surgery Forum in Québec, Que.

Background: Although laparoscopic sleeve gastrectomy (LSG) has been shown to be a safe and effective treatment for severe obesity (body mass index ≥ 35), staple line leaks remain a major complication and account for a substantial portion of the procedure's morbidity and mortality. Many centres performing LSG routinely obtain contrast studies on postoperative day 1 for early detection of staple line leaks. We examined the usefulness of Gastrografin swallow as an early detection test for staple line leaks on postoperative day 1 after LSG as well as the associated costs.

Methods: We conducted a retrospective review of a prospectively collected database that included 200 patients who underwent LSG for severe obesity between 2011 and 2014. Primary outcome measures were the incidence of staple line leaks and the results of Gastrografin swallow tests. We obtained imaging costs from appropriate hospital departments.

ABSTRACT

We examined the usefulness of gastrograffin swallow as a an early detection test for staple line leaks on post surgery day after LSG.

PICO

In eligible patients who underwent LSG surgery between 2010 -2014, was the gastrograffin swallow test sensitive and specific in the early detection of staple line leaks?

A retrospective cohort study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 2, 2015 VOL. 373 NO. 1

A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management

Xavier Pi-Sunyer, M.D., Arne Astrup, M.D., D.M.Sc., Ken Fujioka, M.D., Frank Greenway, M.D., Alfredo Halpern, M.D., Michel Krempf, M.D., Ph.D., David C.W. Lau, M.D., Ph.D., Carel W. le Roux, F.R.C.P., Ph.D., Rafael Violante Ortiz, M.D., Christine Bjørn Jensen, M.D., Ph.D., and John P.H. Wilding, D.M., for the SCALE Obesity and Prediabetes NN8022-1839 Study Group*

ABSTRACT

BACKGROUND

Obesity is a chronic disease with serious health consequences, but weight loss is difficult to maintain through lifestyle intervention alone. Liraglutide, a glucagon-like peptide-1 analogue, has been shown to have potential benefit for weight management at a once-daily dose of 3.0 mg, injected subcutaneously.

METHODS

We conducted a 56-week, double-blind trial involving 3731 patients who did not have type 2 diabetes and who had a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of at least 30 or a BMI of at least 27 if they had treated or untreated dyslipidemia or hypertension. We ran-

From the Division of Endocrinology and Obesity Research Center, Columbia University, New York (X.P.-S.); Department of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg (A.A.), and Novo Nordisk, Søborg (C.B.J.) — both in Denmark; Department of Nutrition and Metabolic Research, Division of Endocrinology, Scripps Clinic, La Jolla, CA (K.F.); Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge (F.G.); Obesity and Metabolic Syndrome Unit, Division of En-

ABSTRACT

Aim or objective not specifically stated

PICOT

In patients without T2DM who were overweight/obese, did 3.0 mg of liraglutide compared to placebo result in significant weight loss?

A double blind randomized controlled trial

Where do you find the research question?

Young *et al. BMC Family Practice* 2011, **12**:88
http://www.biomedcentral.com/1471-2296/12/88

BMC Family Practice

RESEARCH ARTICLE **Open Access**

Comparison of pharmacist managed anticoagulation with usual medical care in a family medicine clinic

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- Should be in the abstract - helps editor forward to reviewers
  - Often stated as an objective or study aim
- **In the Introduction Section it should be the last sentence.**

Clinical Area, type of question and types of research study- typical

Table 3
The relationship between clinical area/type of question and research study

Clinical area	Type of question	Type of research study
Diagnosis	What disease is responsible for the abnormal findings?	Prospective, blind comparison to a gold standard Cross-sectional study
Therapy	What therapy is appropriate for a disease?	RCT Prospective cohort
Prognosis	What are the expected outcomes of a disease?	Longitudinal studies Retrospective/prospective cohort studies
Prevention	How can a disease be prevented or delayed?	RCT Cohort Case–control Case series
Harm	What intervention or other factor may be contributing to a disease?	RCT Cohort Case–control/case series

Clinical Epidemiology 3rd Edition, TWells LK, Chapter 21 EB Decision Making

A poorly devised research question:

- Affects the choice of study design;
- Decreases the chance of determining anything of clinical relevance or significance; and
- Impacts the potential for publication.

Without time spent upfront developing the research question, the quality of your study and subsequent results may be compromised.

FINAL THOUGHTS

Did your study answer your research question?

- The **Results** provide evidence for the answer- be clear & precise
  NO SUBJECTIVE INTERPRETATION HERE

- The **Discussion** builds the bridge to the **Introduction** where the question was first formulated.
  - Did you find an answer?
  - Is it confirmed or contradicted by others?

- The **Conclusion** answers your research questions in one or two sentences.

- For your research should be relevant, provide new understanding, expand knowledge and **inform new research questions.**

THANK YOU FOR LISTENING