

How did HE get on this panel?

The Curious Case of the Casual Clinician Scientist

Dr. Tom Mutter MD, FRCPC, MSc

Assistant Professor

Medical Manager of
Quality Assurance



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À l'écoute de notre santé

Dept. of Anesthesia and Perioperative Medicine
Winnipeg, Manitoba, Canada

Disclosures

None



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Research career trajectories

Typical

The end goal:
"Success" ↓

Casual

Research chairs/ Professorships/ CIHR funding/ Fame/ Fortune

- Ever bigger studies
- Ever larger grants
- Ever thicker CV

- Research program development
- Small grants and publications

Research training

Residency

Clinical fraction

?

No formal
research
program

OSA

Regional
adjuvants

QA

HES

Research training

Clinical practice

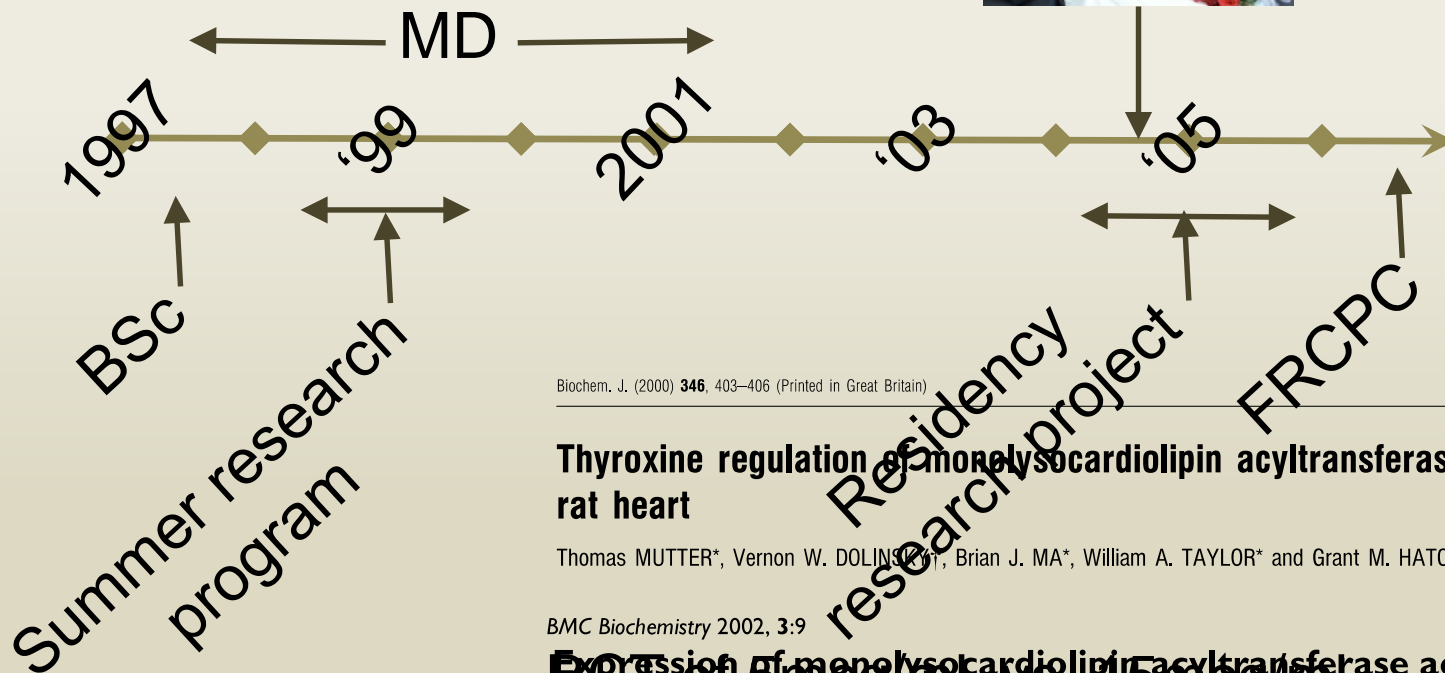
Residency

Objectives

The Curious Case of the Casual Clinician Scientist

- Describe how additional research training can be used to do more than get grants and publish papers.
- Appreciate the challenges and opportunities posed by maintaining a significant general practice and not having a formal program of research.
- List important requirements for completing successful clinical research with limited resources

Early research career timeline



Biochem. J. (2000) **346**, 403–406 (Printed in Great Britain)

Thyroxine regulation of monolysocardiolipin acyltransferase activity in rat heart

Thomas MUTTER*, Vernon W. DOLINSKY†, Brian J. MA*, William A. TAYLOR* and Grant M. HATCH*‡¹

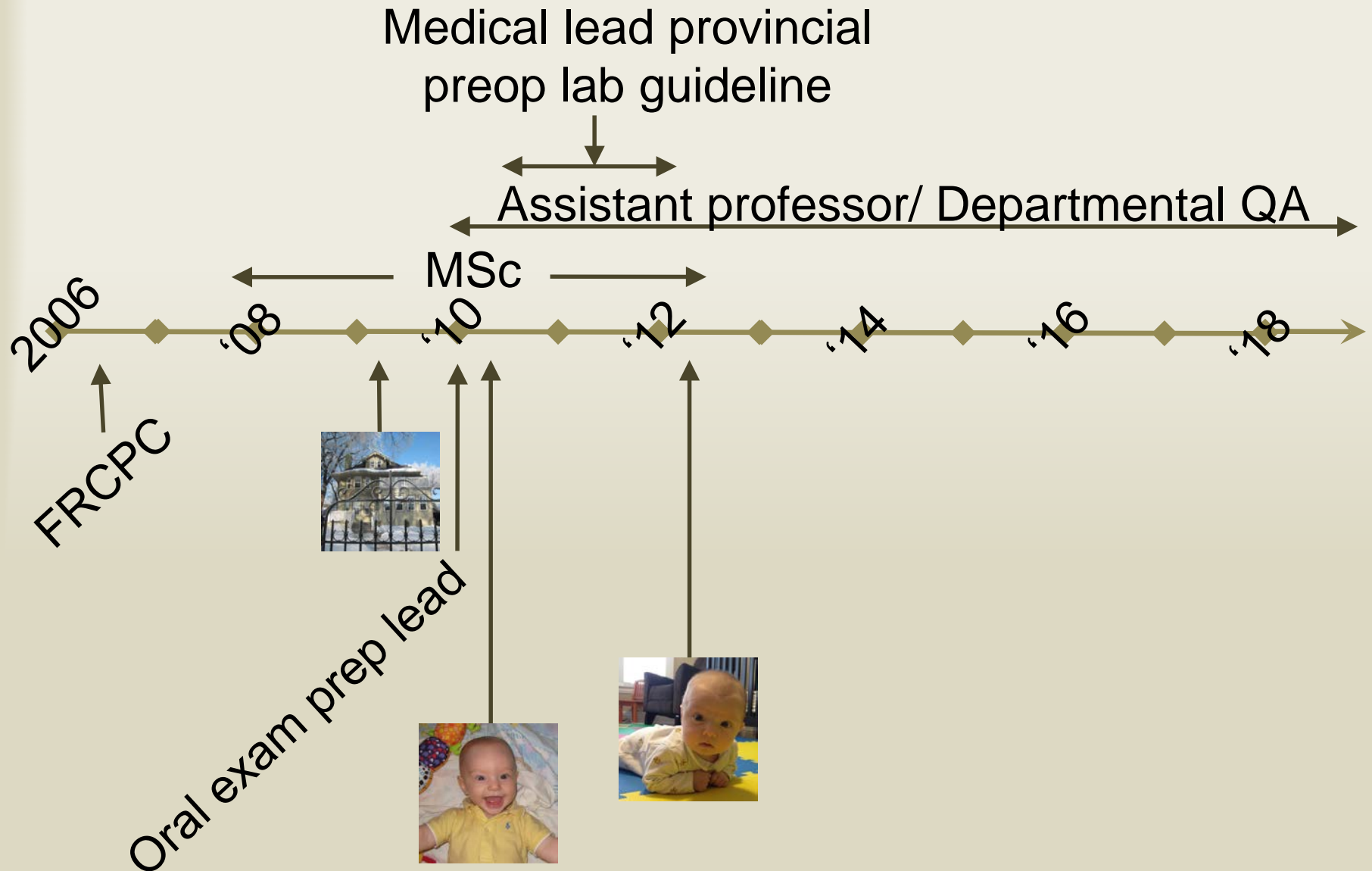
BMC Biochemistry 2002, **3**:9

Expression of monolysocardiolipin acyltransferase activity is regulated in concert with the level of cardiolipin and cardiolipin hydromorphone in the mammalian heart

William A Taylor¹, Fred Y Xu¹, Brian J Ma^{1,3}, Thomas C Mutter¹, Vernon W Dolinsky* and Grant M Hatch*†¹

ECT of 5mcg/mL vs 15mcg/mL hydromorphone in 0.2% ropivacaine for postoperative thoracic epidural analgesia

Research career timeline

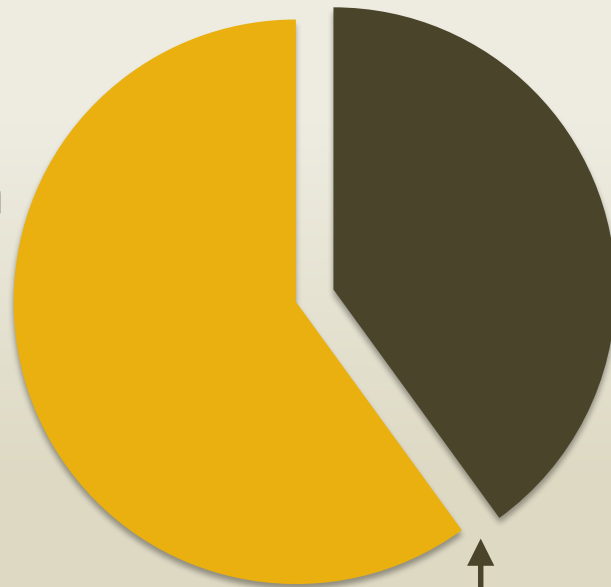


Time

CLINICAL FRACTION

= 0.6

- Adult Tertiary care
 - Level 1 Trauma
 - Neurosurgery
 - Thoracics
 - Vascular
 - Hepatobiliary
 - Acute pain
 - Obstetrics
- Free standing ambulatory surgical centre
 - Regional



NON-CLINICAL FRACTION = 0.4

- Clinical research
 - Principle Investigator
 - Collaborations
 - Resident projects
- Quality Assurance
- Peer review

PERSONAL
LIFE

Financial salary support

Publication as PI

(P)

P

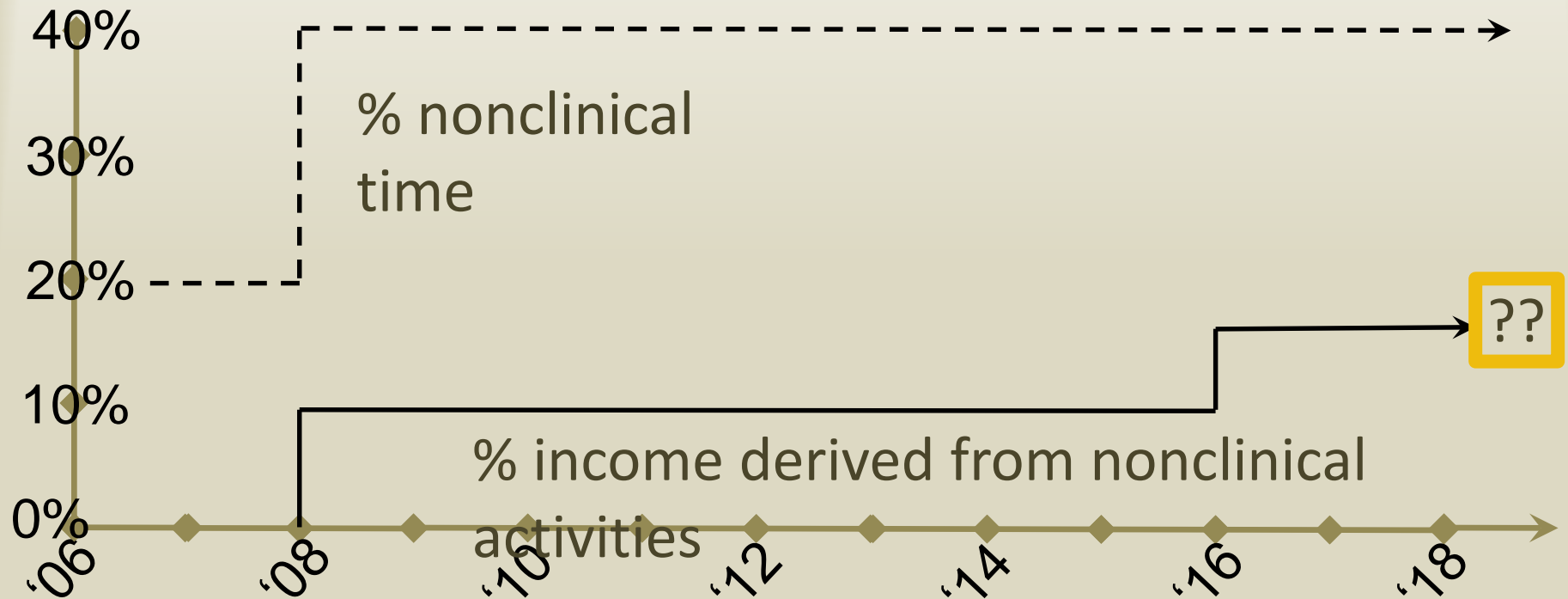
P

P

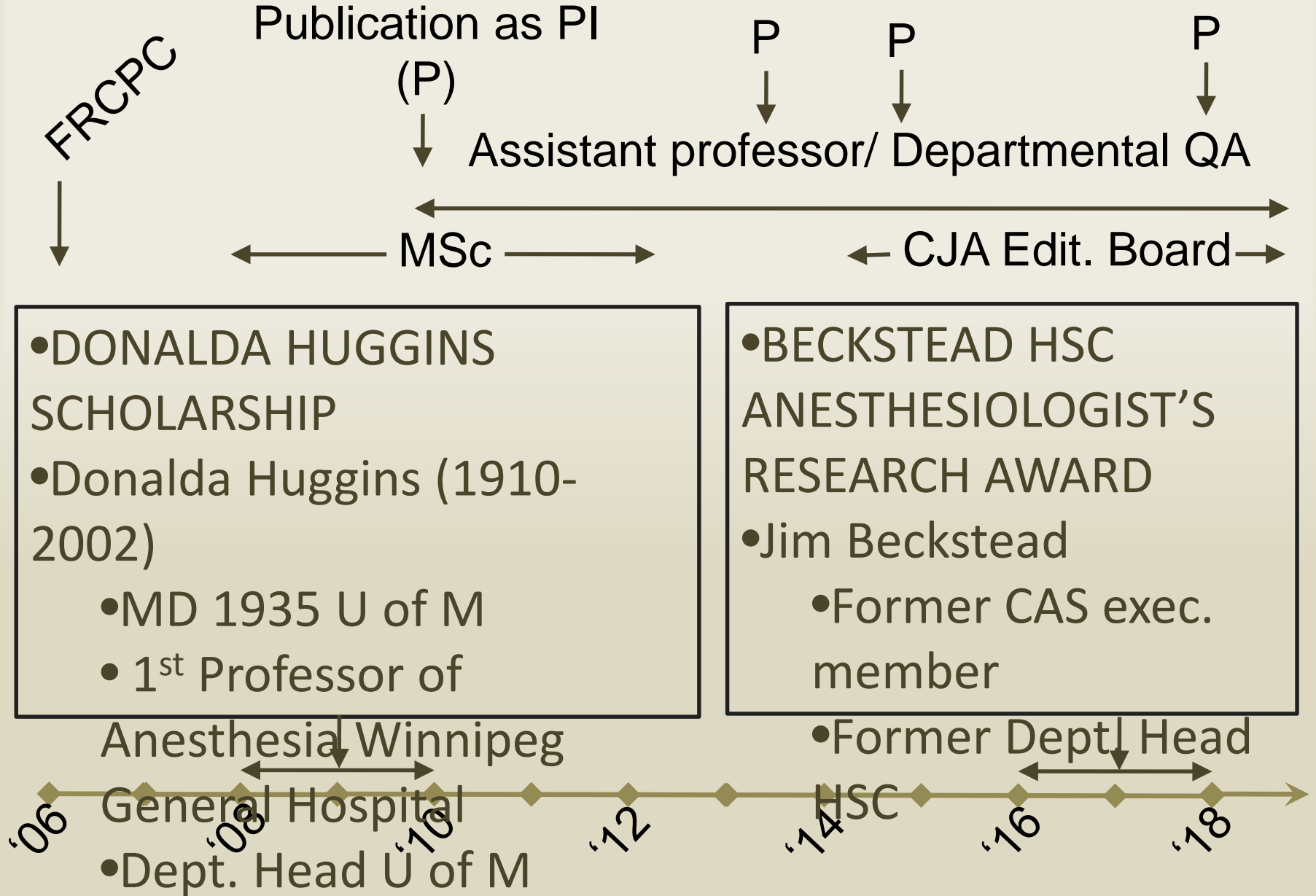
Assistant professor/ Departmental QA

MSc

CJA Edit. Board



Financial salary support



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Peer review

- Member of the Canadian Journal of Anesthesia Editorial Board
 - 2014 to present
 - 25 original submissions/ revisions per year
 - Broader perspectives on:
 - design and reporting of research
 - how journals, editorial boards and authors work together.
- Grant reviews
 - CAS research advisory committee
 - Trillium foundation
- Open peer reviewer
 - on the basis of experiences with peer review of my own work

Quality assurance activities: Standards/ Audits

- Medical lead
 - Disparities in postoperative deaths between facilities
- Advisory
 - Intraoperative hypothermia and surgical site infection

Quality assurance activities: Local guidelines

- Medical lead

- Provincial preoperative laboratory testing guideline
- Regional preoperative medication directive
- Regional difficult airway documentation and communication package

- Advisory

- Regional conscious sedation policy and learning package for advanced practice nurses
- Regional VTE and anticoagulant management



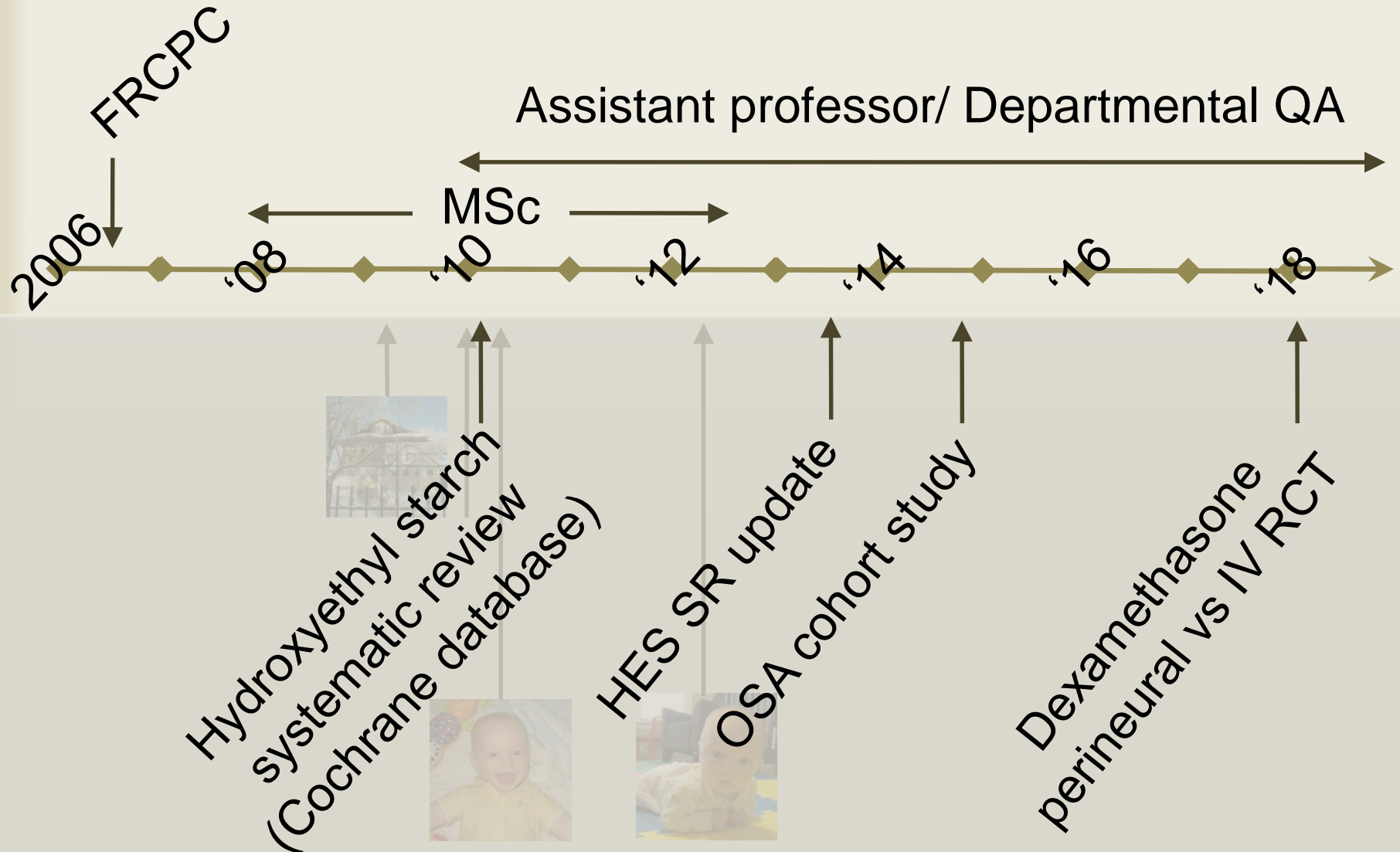
• Richard
Kgalin
towards
201315h

Objectives

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Original investigation Publication dates



Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function (Review)

Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD007594.

Mutter TC, Ruth CA, Dart AB

- Systematic review and meta-analysis of harm
- 2 publications arising out of MSc coursework
 - Original review (2010), Scopus: 127 citations
 - Scheduled update (2013), Scopus: 123 citations
- Altmetric = 21, 93%ile for same age articles
- Budget: \$4,500 Total cost: \$935



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Meta-analysis

The Young Investigator's friend

- Ethics exempt
- No data access permission/ No patient consent
- Low cost
- Go at your own pace
- Plenty of methodological resources available
 - i.e. Cochrane Handbook

Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function (Review)

Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD007594.

Mutter TC, Ruth CA, Dart AB

- Background:
 - HES were a commonly used synthetic colloid but concerns were mounting over adverse renal effects
- Strengths of our work:
 - Relatively early application of the RIFLE (AKIN) criteria for Acute Kidney injury (AKI).
 - Volume replacement in all settings (not just sepsis or “critically ill”)
 - Pre-specified clinically relevant sensitivity analyses
 - Previously unpublished data obtained from authors.

Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function (Review)

Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD007594.

Mutter TC Ruth CA Dart AB

Nephrologist	Anti starch
Neonatologist	Doesn't care
Anesthesiologist	Pro starch

- LESSON #1: Authorship team should be clinically knowledgeable on the subject
- LESSON #2: Authorship team's opinions should be balanced

Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function (Review)

Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD007594.

Mutter TC, Ruth CA, Dart AB

- Key findings:
 - Insufficient evidence (2010)
 - Increased risk of Dialysis and RIFLE stage F (2013), regardless of presence of sepsis

Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically ill Patients Requiring Volume Resuscitation

A Systematic Review and Meta-analysis

JAMA 2013; 309(7): 678-88.

- 318 citations

Ryan Zarychanski, MD, MSc

Ahmed M. Abou-Setta, MD, PhD

Alexis F. Turgeon, MD, MSc

Brett L. Houston, BSc

Lauralyn McIntyre, MD, MSc

John C. Marshall, MD

Dean A. Fergusson, PhD, MHA

- LESSON #3:
Choose your
outcomes
carefully

A Matched Cohort Study of Postoperative Outcomes in Obstructive Sleep Apnea

Could Preoperative Diagnosis and Treatment Prevent Complications?

Thomas C. Mutter, M.D., F.R.C.P.C., M.Sc., Dan Chateau, Ph.D., Michael Moffatt, M.D., F.R.C.P.C., M.Sc., Clare Ramsey, M.D., F.R.C.P.C., M.S., Leslie L. Roos, Ph.D., Meir Kryger, M.D., F.R.C.P.C.

Anesthesiology (2014) 121:707-18. PMID: 25247853

- Publication arising out of MSc thesis
- Altmetric = 61, 97thile for same age articles
- Scopus: 82 citations, 99thile for same age and discipline
- One of the top 20 cited articles published in *Anesthesiology* for the year 2016
- Budget: \$10,200 Total cost: \$1,470**



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Anesthesiology (2014) 121:707-18. PMID: 25247853

- **Background:**
 - Large studies of important postoperative outcomes in OSA patients were lacking.
 - Difficult to assemble large cohorts of patients diagnosed by gold standard (PSG)
 - OSA administrative data codes and questionnaires have limited sensitivity/ specificity

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• ~~LESSON~~ ~~data~~ ~~Take~~ ~~a~~ ~~4,500~~ ~~OSA~~ ~~patients~~ ~~diagnosed~~ ~~by~~ ~~POLYSOMNOGRAPHY~~ between 1990 and 2006, previously linked to administrative data.

- Healthcare utilization in the 10 years prior to diagnosis in obstructive sleep apnea syndrome patients. *SLEEP* 1999.
- Utilization of Healthcare Resources in Obstructive Sleep Apnea Syndrome: a 5 Year Follow-Up Study in Men using CPAP. *SLEEP* 2005.
- Expenditure on health care in obese women with and without sleep apnea. *SLEEP* 2009.

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- Manitoba Centre for Health Policy (MCHP) administrative data repository-- Equivalent to ICES in

- Ontario LINKAGE of OSA patient Clinical database with MCHP data

- Longitudinal tracking of surgical exposures and outcomes for OSA patients in clinical database
 - before and after OSA diagnosis
- Validated ICD code definitions of common comorbidities and important postoperative outcomes
- Matching (by surgery) to population controls at low risk of OSA

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Anesthesiology (2014) 121:707-18. PMID: 25247853

- Key features:
 - Quantification of OSA risk for important outcomes, not surrogates
 - Characterization of effect of OSA severity,
 - Inferences about effect of diagnosis and prescription of CPAP therapy

A Matched Cohort Study of Postoperative Outcomes in Obstructive Sleep Apnea

Could Preoperative Diagnosis and Treatment Prevent Complications?

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- LESSON #2: Do the dirty work yourself
- Inexperienced programmer with outstanding clinical knowledge, works for FREE**

A Matched Cohort Study of Postoperative Outcomes in Obstructive Sleep Apnea

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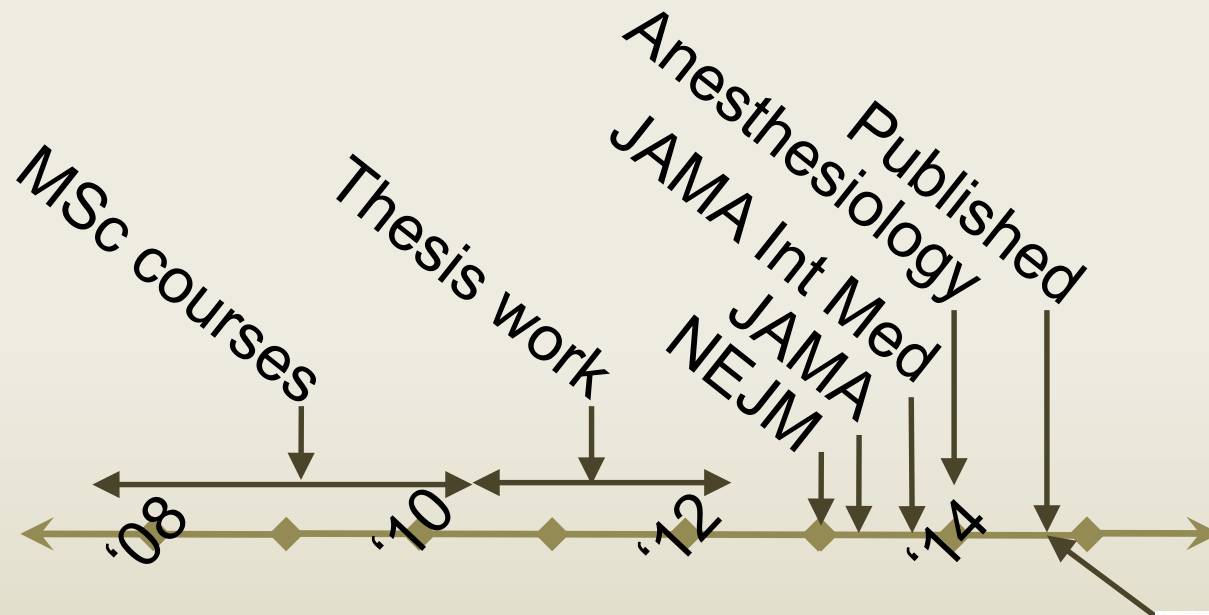
Anesthesiology (2014) 121:707-18. PMID: 25247853

OSA diagnosis/ treatment associated with reduced risk of

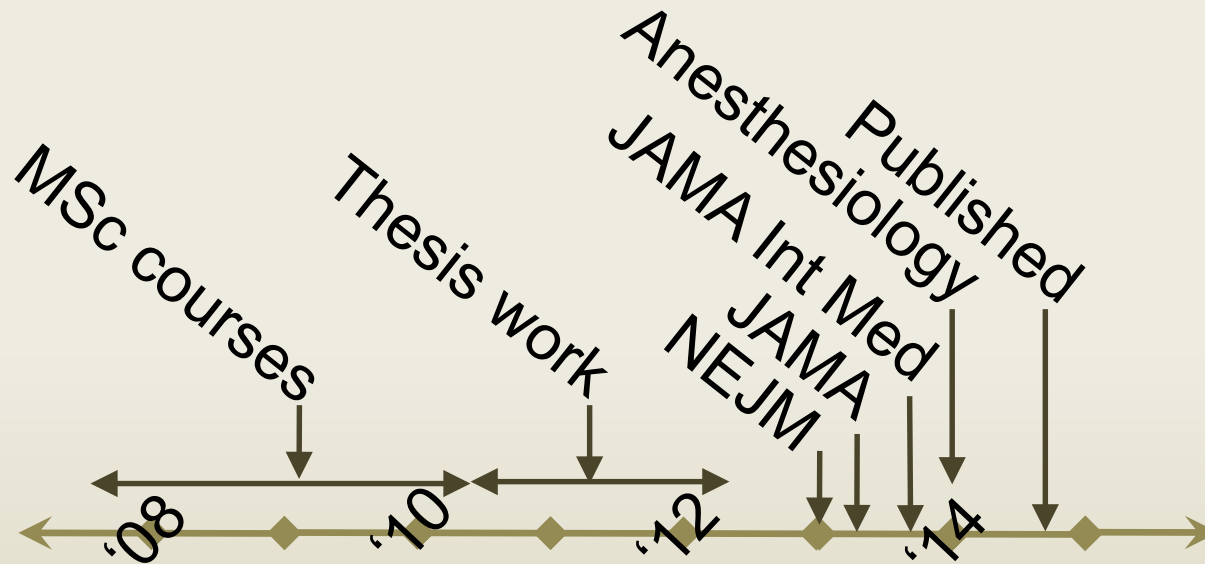
postoperative cardiovascular complications

Complication type	Odds ratio (95% CI)	p
Respiratory	0.68 (0.27-1.71)	0.4
Cardiovascular	0.34 (0.15-0.77)	0.009

Publication timeline




Publication timeline



- LESSON #3: Be persistent.
- LESSON #4: Pitch your work to the right journal the first time.
- LESSON #5: Take reviewer comments seriously.

Effect of dexamethasone dose and route on the duration of interscalene brachial plexus block for outpatient arthroscopic shoulder surgery: a randomized controlled trial

**Darren Holland, MD · Ryan J. J. Amadeo, MD, FRCPC · Scott Wolfe, MD, FRCPC ·
Linda Girling, BScHons · Faylene Funk, RRT · Mark Collister, MSc · Emily Czaplinski, BSc ·
Celeste Ferguson, BSc · Jeff Leiter, PhD · Jason Old, MD, FRCSC · Peter MacDonald, MD, FRCSC ·
Brenden Dufault, MSc · Thomas C. Mutter, MD, FRCPC, MSc **

Can J Anesth (2018) 65:34-45. PMID:
29127558

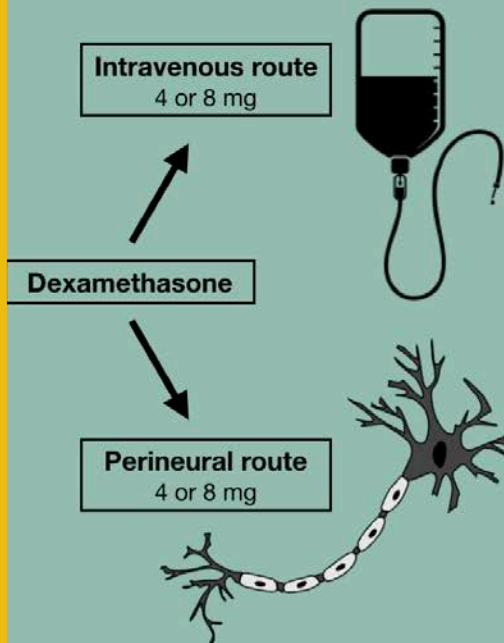
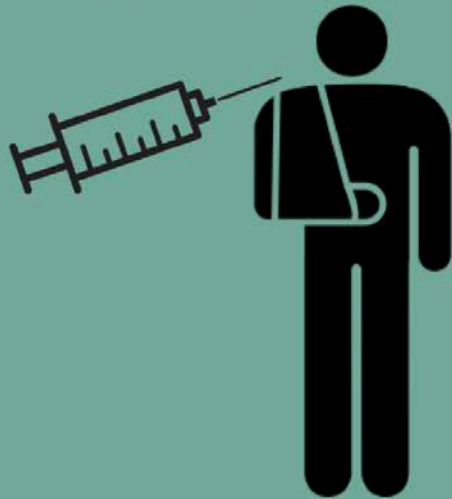
- My first significant prospective work
 - 2*2 factorial RCT, n = 280

INFOGRAPHIC CREDIT: Dr. R George

@CJA_Journal

Effect of dexamethasone dose and route on the duration of interscalene brachial plexus block for outpatient arthroscopic shoulder surgery: a randomized controlled trial

280 patients
Ambulatory arthroscopic shoulder surgery with ultrasound-guided interscalene block
(30 mL 0.5% bupivacaine)



First shoulder pain after surgery reported to a blinded observer



Perineural

4mg	25.4 hr (95% CI, 23.8 to 27.0)
8mg	27.2 hr (95% CI, 25.2 to 29.3)


Intravenous

4mg	24.0 hr (95% CI, 22.9 to 25.1)
8mg	24.8 hr (95% CI, 23.2 to 26.3)

Perineural > Intravenous
2.0 hr (95% CI, 0.4 to 3.5; $P = 0.01$)

- Dexamethasone prolongs block duration with PERINEURAL ROUTE
- Dose and Route (IV vs perineural) unclear
- DOSE no significant effect

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Can J Anesth (2018) 65:34-45. PMID: 29127558

- 1 citation (Up to Date)
- Altmetric attention score = 29.
 - 92nd %ile for outputs of a similar age
- Cost: ~\$25,000




Canadian Anesthesia Research Foundation
La Fondation canadienne de recherche en anesthésie



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Brenden Dufault, MSc · Thomas C. Mutter, MD, FRCPC, MSc 

- LESSON #1: Broader team engagement needed




Canadian Anesthesia Research Foundation
La Fondation canadienne de recherche en anesthésie

- CARF New Investigator Research Award 2015
- EXTERNAL FUNDING =
LEGITIMACY

Can J Anesth (2018) 65:34-45. PMID: 29127558

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- LESSON #2: Reliable participant volumes needed

- 700 eligible surgeries per year
- n = 280 patients recruited in 13 months
 - only 95 eligible patients declined to participate
- Resident screens for interest in the study by

Cap Anesth (2018) 65:34-45. PMID: 29127558

- Research assistant completes consent day of surgery

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- LESSON #3: Make it as easy for staff and patients as possible


- PATIENTS: Phone follow up instead of diaries
 - complete follow up for primary outcome and almost all secondary outcomes

- STAFF: Only deviation from routine care is the intervention, and the ACA closely supervises this.

- 1 protocol violation

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- LESSON #4: Know the literature and design the research question carefully.
- 2*2 factorial RCT of dexamethasone DOSE & ROUTE
 - n = 280

		ROUTE	
DOSE		IV	Perineural
	4mg	n = 70	n = 70
	8mg	n = 70	n = 70

Effect of dexamethasone dose and route on the duration of interscalene brachial plexus block for outpatient arthroscopic shoulder surgery: a randomized controlled trial

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Brenden Dufault, MSc • Thomas C. Mutter, MD, FRCPC, MSc

Can J Anesth (2018) 65:34-45. PM

- Peer review purgatory:

- “This isn’t a factorial trial. Reana

- “You need a control arm with no c

- “The 30ml local anesthetic dose

- “Waste of resources! Dexametha

- “uncommon

- “consistently superior to placebo

- “You should have standardized th

- “It’s actually the most common do

- “dexamethasone regimens” study in all pre

- “Not standardizing them makes th

- “applicable to real clinical practice



Keeping a good thing going. . .

- Intravenous Dexmedetomidine, Dexamethasone and Interscalene block duration after Arthroscopic Shoulder Surgery (NCT: 03270033)
- n = 189 RCT with 3 groups:
 - dexamethasone
 - dexmedetomidine
 - dexamethasone + dexmedetomidine
- Recruitment completed Sep 2017 to April 2018
- Budget: \$15,000



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How to complete successful clinical research with limited resources

- Access to small internal operating grants
 - They can go a long way!
 - Access to external funding when needed
- Willingness to do the heavy lifting on your own
- Flexibility: tailor areas of investigation to unique patient populations or data resources
- Carefully choose team members and their roles
- Good understanding of clinical epidemiology
- Both patience and persistence through peer review
- A little bit of good luck/ Don't give up

Challenges and Opportunities of the Casual Clinician Scientist

- Research output limited
- Expect credibility issues at peer review
- There is a fine line between being good at everything and good at nothing

- Flexibility: Not constrained by a program of research.
- Avoid the grant pursuit rat race (to a certain extent).
- Keep research fun.
- Still do valuable work(?)

*Favours high research
FTE and formal
research program*

*Favours Casual Clinician
Scientist*

Acknowledgements



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Donalda Huggins
Scholarship

Beckstead HSC
Anesthesiologist's
Research Award



Canadian Anesthesia Research Foundation
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