

# **SURG238: PRACTICAL INTRODUCTION TO CLINICAL RESEARCH**

**Welcome to Week 2!**

# Review

Publication = currency of academic medicine

Activity is not productivity: every research project should yield a peer-reviewed publication

Develop productive habits (don't multi-task, stay off phone/email while working)

Know how to structure an efficient research workflow

You need: time (make writing a habit), enthusiasm, skill, and the right team

Be super-organized

# Agenda

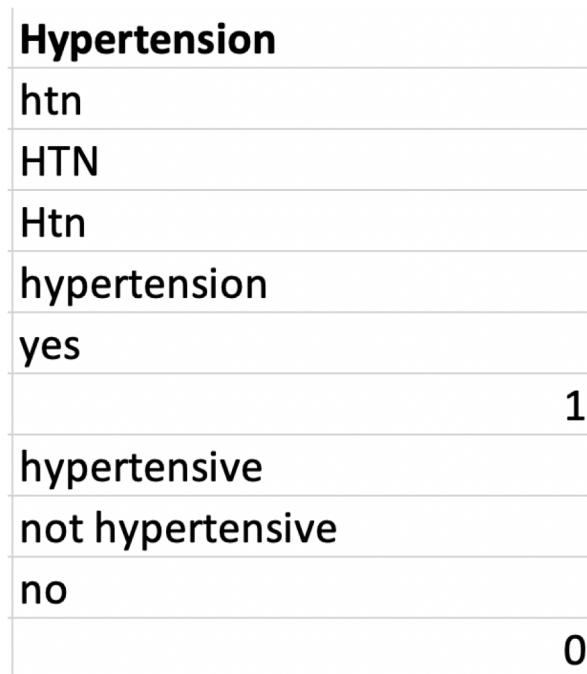
- 1) Practical overview of study designs
- 2) Designing the research question

# Retrospective chart reviews

- 1) Good & bad
  - 1) Good: lower barrier to get involved if not experienced (e.g. join as mid-author on ongoing project), important to learn by trial
  - 2) Bad: (in my opinion) high effort, low yield (not always) .
- 2) IRB, CITI-training, encryption
  - 1) eprotocol.stanford.edu
  - 2) Big consequences if not done properly
    - 1) Any PHI? email title: “SECURE:”
    - 2) Do NOT store PHI on your local machine long-term
    - 3) Use Stanford Medicine Box

# Retrospective chart reviews

**Most common mistake?** Not spending enough time upfront to create data collection table & dictionary



*“On second thought, we need to collect this variable too...let’s go through 500 charts again”*

# What is a data dictionary?

No spaces!

Variable name	Variable label	Values	Examples
name	name of patient	full name	John Doe
ICN	intercostal nerve ablation	y=yes; n=no	y
mrn	Epic MRN number	number	111111
age	age of patient	number	46
sex	sex of patient	m=male; f=female	m
date_admit	date of admission	mm/dd/yyyy	9/25/2020
date_surgery	date of procedure	mm/dd/yyyy	9/26/2020
date_discharge	date of discharge	mm/dd/yyyy	9/27/2020
HLOS	length of stay in days	days	5
ICU	ICU admission?	y=yes; n=no (K4 or E2)	y
mortality	mortality inpatient?	y=yes; n=no	n
dispo	disposition of patient	home, home with home health, SNF, LTAC, acute care hospital	home
MOI	mechanism of injury	glf,fall_from_heigh, MVC,MCC,ped_vs_auto, bike, penetrating_stab, penetrating_gsw, other	glf
ISS	Injury severity score	0-75	5
AIS_chest	Abbreviated injury scale_chest	1 (minor) - 6 (maximum)	4
copy_CT_read	CT reading regarding rib fractures	copy and paste portion of CT radiologist report (not summary of findings, but usually under chest wall/	detailed description of rib fractures
id_fx	which rib was fractured (ie. 6th rib, 7th rib)	0,1,2,3,4,5,6,7,8,9,10,11,12	6,7
no_ribfx	Number of ribs fractured	0-12	3
location_fx	location of rib fracture	anterior; lateral; posterior	anterior 2, lateral 0, posterior 5
type_fx	type of rib fracture	undisplaced (>90% cortical contact); offset (<90% cortical contact); displaced (no cortical contact)	undisplaced 2, offset 0, displaced 5
character_fx	character of rib fracture	simple; wedge; complex	simple 3, wedge 0, complex 3
flail_chest	flail chest? (>3 consecutive ribs broken in ≥2 places)	y=yes; n=no	y
PTX	pneumothorax?	y=yes; n=no	y
HTX	hemothorax?	y=yes; n=no	y
pulm_contusion	pulmonary contusion?	y=yes; n=no	y
no_ribstable	number of ribs stabilized	0-24	3
id_ribstable	locations of stabilized ribs	L or R, rib #	L <sub>3</sub> , L <sub>4</sub> , L <sub>5</sub> , R <sub>5</sub> ,R <sub>6</sub>
no_nervecryo	number of intercostal nerves cryoablated	0-24	4
id_nervecryo	locations of cryoablated intercostal nerves	L or R, rib #	L <sub>4</sub> , R <sub>6</sub>
time_proc	procedure duration	minutes	120
postop_OMEm_daily_avg	Post-operative daily opioid requirement, oral morphine equivalents	OME number	20 OME/day
postop_painscore_daily_avg	Post-operative daily NRS pain scores	0-10	5
intubated_beforesurgery	intubated before surgery? (not periop)	y=yes; n=no	n
intubated_aftersurgery	required intubation after surgery? (not periop)	y=yes; n=no	y
chest_tube	tube thoracostomy?	n=no, pre-op= before surgery (i.e. in trauma bay), intra-op=during SSRF surgery	n
pneumonia	pneumonia?	y=yes; n=no	n
trach	tracheostomy?	y=yes; n=no	n

# Remember the efficient research work flow

- Come up with research idea
- Define research question. **Assemble team**
- Write IRB
- **While Waiting for IRB:** write manuscript (intro, methods, part of discussion), define analytic method, identify target journal, draft tables + figures
- Gain data access
- ~~Define analytic method~~
- **While someone Analyzes,** come up with next research idea
- Review results
- Write manuscript: intro, methods, results, discussion, conclusion
- ~~Define goal journal, pre-emptively plan for reviewer questions~~
- Submit

# Do NOT use Excel to make any changes. Learn R

1	patientID	age	sex	rce	moi	iss	injury_descrip	hlos	icu_los	vent_days	complications
2	1	30	F	W	MVC	12	T-SPINE FRACTURE W/O CORD CON	21	3	2	unplanned intubaion
3											UTI
4							THORACIC INJURY - HEMOPNEUMO				pneumonia
5							ONE RIB FRACTURE W/O FLAIL, [OIS				bleeding
6							ELBOW JOINT DISLOCATION - NFS				unexpected return to OR
7							RADIUS FRACTURE - NFS				
8							STERNUM FRACTURE - OIS GRADE II				
9							SCAPULA FRACTURE - NFS				
10							PELVIC RING FRACTURE - NFS				
11	2	23	F	A	GLF	20	PELVIC RING FRACTURE - NFS	15	5	4	pneumonia
12							THORACIC INJURY - PNEUMOTHOR				bleeding
13							SCAPULA FRACTURE - GLENOID W/				
14							>= THREE RIB FRACTURES W/O FLAI				
15							CLAVICLE FRACTURE - NFS				
16							C-SPINE FRACTURE W/O CORD CON				
17							L-SPINE CORD CONTUSION (COMPR				
18							T-SPINE FRACTURE W/O CORD CON				
19							OTHER NAMED LOWER EXTREMITY				
20							EXTERNAL CONTUSION - UNSPECIF				

```
data <- data %>%
  mutate_at(carry forward, na.locf)
```

Starting with original dataset & code file, should be able to replicate result perfectly, every time.

# Retrospective cohort study (database)

# Read this article!

## Box 2. Checklist to Elevate the Science of Surgical Database Research

1. Have a solid research question and clear hypothesis. Consider using the FINER (Feasible, Interesting, Novel, Ethical, Relevant) or PICO (Patient, Population, or Problem; Intervention, Prognostic Factor, or Exposure; Comparison or Intervention; Outcome) criteria to develop these.
2. Ensure compliance with the institutional review board and data use agreements.
3. Conduct a thorough literature review. Use a reference management program for ease in manuscript development.
4. Make sure this is the best data set available and that it has the appropriate variables to answer your research question.
5. Clearly define the inclusion criteria, exclusion criteria, and outcome variables. Use a flow diagram to describe final patient selection.
6. Identify potential confounders and use risk adjustment to minimize bias. Consider using a directed acyclic graph to represent potential associations. Avoid use of causal language in reporting results of these observational studies.
7. Ensure that the data variables have not changed over time. If so, account for this.
8. Ensure that competing risks are identified and addressed.
9. Ensure that data issues, such as missing data, are discussed and that any sensitivity analyses or imputations performed are reported in a clear and cohesive way.
10. Ensure that your article has a clear take-home message that addresses how your research advances current knowledge and has important policy or clinical implications.

**Editorial**

June 2018

FREE

## A Checklist to Elevate the Science of Surgical Database Research

Adil H. Haider, MD, MPH<sup>1,2</sup>; Karl Y. Bilimoria, MD, MS<sup>3</sup>; Melina R. Kibbe, MD<sup>4,5</sup>

Usually IRB exempt

Read articles that used same database

Excellent resource for practical guide to popular datasets, reporting guidelines, etc.

<https://www.surgicaloutcomesclub.com/resources/jama-surgery-1>

# Understand limitations of database research

In general:

hypothesis-generating research. Causal inference requires very thoughtful study design (e.g. more than the vanilla multivariable egression analysis)

Do NOT use causal language

~~Leads to~~ → associated with

# Follow STROBE/RECORD guidelines

**The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies**

<https://www.equator-network.org/reporting-guidelines/strobe/>

**The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement**

<https://www.equator-network.org/reporting-guidelines/record/>

# Include STROBE checklist as supplement for every submission

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
<b>Title and abstract</b>					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.  RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.  RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	
<b>Introduction</b>					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses			
<b>Methods</b>					
Study Design	4	Present key elements of study design early in the paper			
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			

If reviewers see this they will likely have a favorable bias:  
 “these authors probably knew what they were talking about.”

But this should really be a requirement, not a plus.

# “Review article”

“Do you want to write a quick review article?”

Good & bad

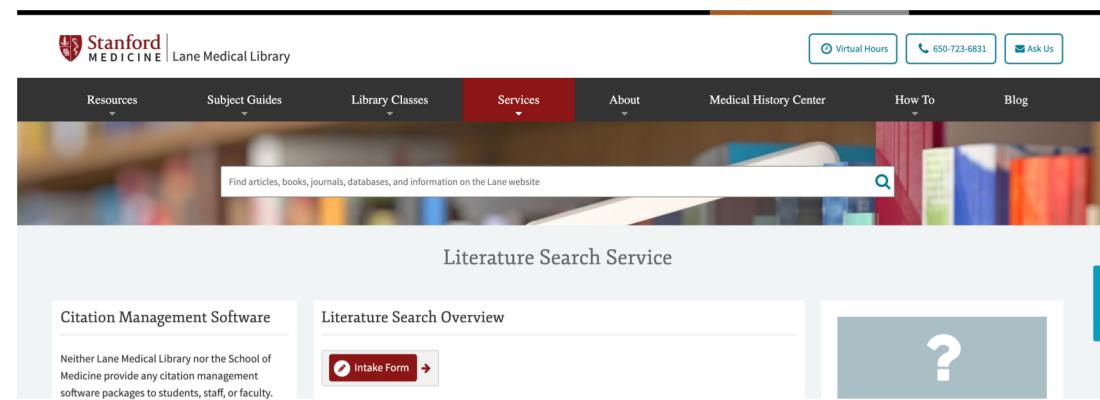
- Good: (IF done well) journals like them (highly-cited)
- Bad: takes considerable effort to perform evidence synthesis properly (systematic review/scoping review/meta analysis).  
“Narrative reviews” (in my opinion) are low-yield (unless invited reviews from a reputable journal)

# “Review article”

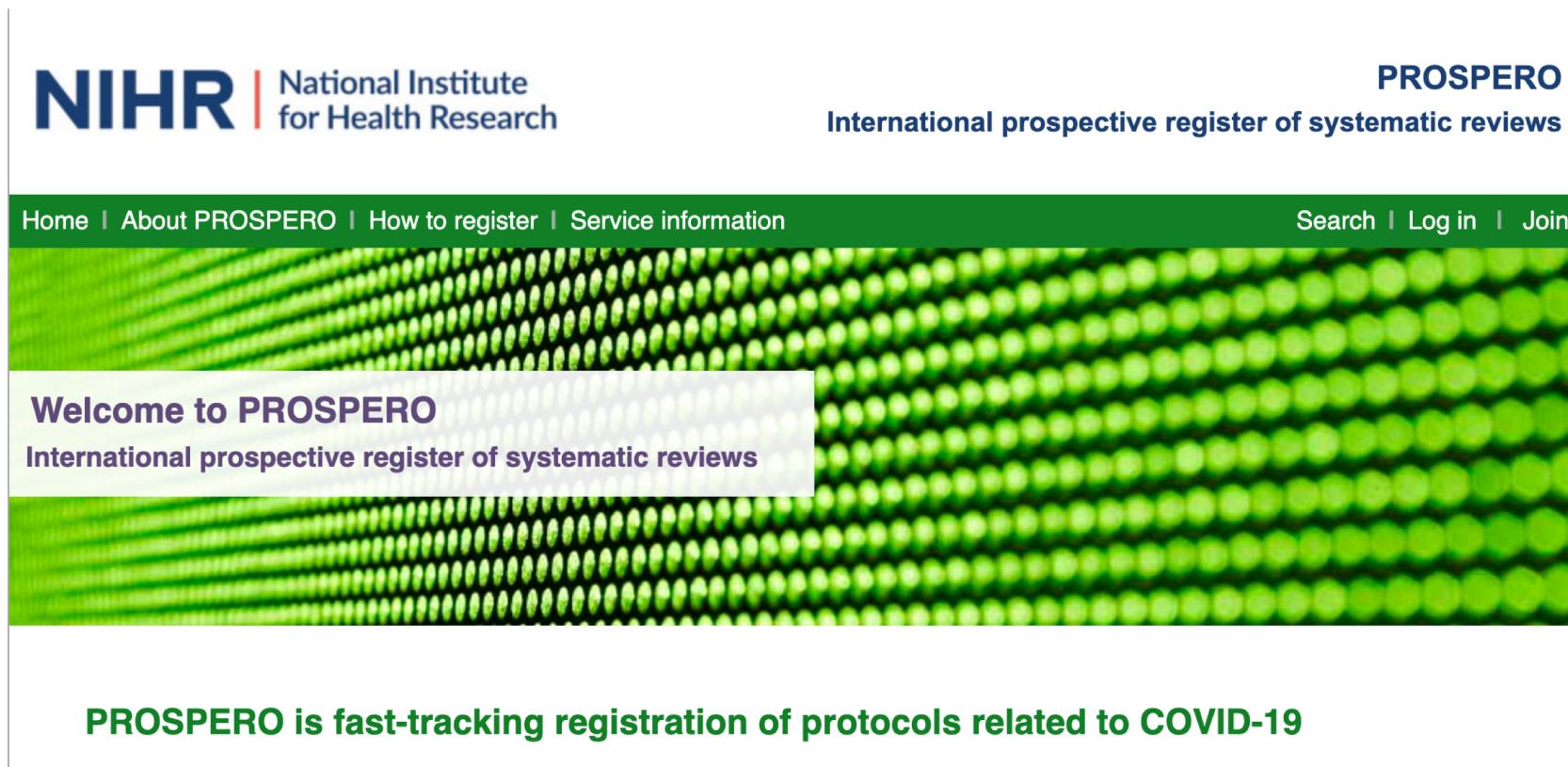
How large of a team do you need? minimum 3 (for scoping/systematic review/meta analysis)

Literature review must be performed SYSTEMATICALLY (i.e. not searching “non-operative management of appendicitis” on PubMed or Google Scholar)

- You MUST get librarian's help to design search terms across multiple databases



Register study on PROSPERO: <https://www.crd.york.ac.uk/prospero/>



MUST write in *Methods*, something like: “We registered this study on PROSPERO prior to abstract screening...”

# Use Covidence (free)

Review Summary

Import references 665 total duplicates removed Import

Title and abstract screening 2200 irrelevant 0 studies to screen

TEAM PROGRESS

2534 • DONE 0 • CONFLICTS  
0 • ONE VOTE 0 • NO VOTES

Jeff,  
you have screened **2553** studies

Full text review 157 excluded 0 studies to screen

TEAM PROGRESS

317 • DONE 0 • CONFLICTS  
17 • ONE VOTE 0 • NO VOTES

Jeff,  
you have screened **21** studies

Extraction 0 extracted 153 studies to extract

Get Stanford institutional account (unlimited # of reviews)

<https://support.covidence.org/help/stanford-university>

# What figures/tables do you need?

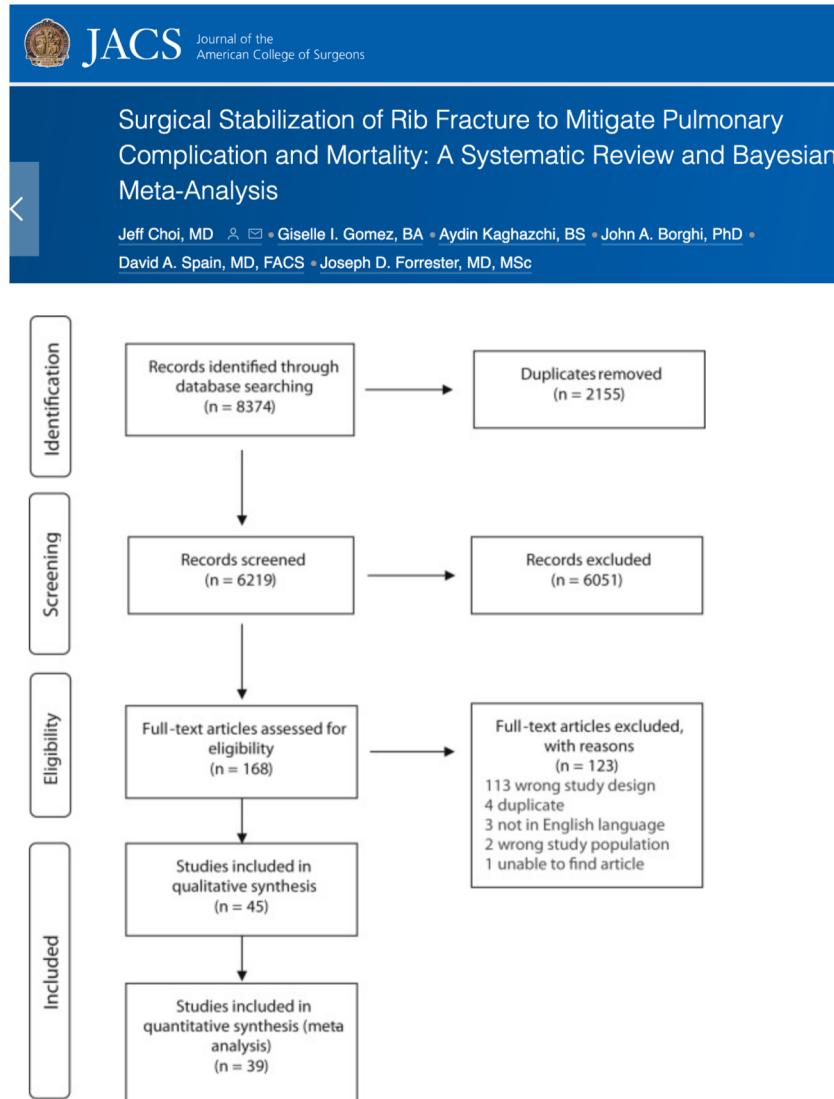


Table 1 Characteristics of Studies Undergoing Evidence Synthesis

Study author and year (reference no.)	RCT	Study population: flail chest only	SSRF indication
Ahmed 1995 <sup>35</sup>	No	Yes	Undergoing thoracotomy for another thoracic injury
Ali-Osman 2018 <sup>36</sup>	No	No	≥2 displaced rib fractures, severe pain, subcutaneous emphysema
Althausen 2011 <sup>37</sup>	No	Yes	Flail chest with persistent respiratory failure, progressive displacement of rib fracture, or undergoing thoracotomy for another thoracic injury
Balci 2004 <sup>38</sup>	No	Yes	Flail chest with respiratory impairment/poor general condition, and arterial blood gas abnormalities
Buyukkaraback 2015 <sup>39</sup>	No	Yes	Flail chest
de Moya 2011 <sup>40</sup>	No	No	Pain, ≥2 severely displaced rib fractures, worsening respiratory status
DeFreest 2016 <sup>41</sup>	No	Yes	Flail chest with persistent pain, respiratory failure, or failure to wean from ventilator

Figure 1= PRISMA Flow diagram

Table (can be supplement) detailing study characteristics

Choi J, Gomez GI, Kaghazchi A, Borghi JA, Spain DA, Forrester JD. Surgical Stabilization of Rib Fracture to Mitigate Pulmonary Complication and Mortality: A Systematic Review and Bayesian Meta-Analysis. *J Am Coll Surg.* 2021;232(2):211-219.e2. doi:[10.1016/j.jamcollsurg.2020.10.022](https://doi.org/10.1016/j.jamcollsurg.2020.10.022)

# What figures/tables do you need?

**Table 2 Summary of Findings Comparing Surgical Stabilization vs Non-operative Management of Rib Fracture Using Random-Effects Bayesian Meta-Analysis**

Variable	Ventilator	ICU length of stay	Hospital length of stay	Pneumonia	Tracheostomy	Mortality
SSRF participants, n	369	669	804	1,050	642	1,247
Non-operative participants, n (studies)	13,217 (13)	13,683 (16)	13,827 (16)	2,617 (23)	1,801 (18)	4,461 (27)
Quality of the evidence (GRADE)	LOW	LOW	LOW	LOW	LOW	LOW
Relative effect, d						
Mean difference (95% CrI)*	-4.86 (-7.43 – -2.28)	-5.96 (-7.05– -4.86)	-9.90 (-11.79– -7.99)	–	–	–
Odds ratio (95% CrI)*	–	–	–	0.37 (0.18– 0.73)	0.41 (0.16– 0.83)	0.33 (0.15– 0.63)
Probability SSRF is associated with better outcome, %	100	100	100	100	99.97	100

GRADE, grading of recommendations, assessment, development, and evaluation; SSRF, surgical stabilization of rib fracture.

\* 95% CrI (credible interval) for ventilator would be interpreted as: there is 95% probability SSRF is associated with 2 to 7 fewer ventilator days compared with non-operative management.

## Summary of findings table

**Table 1. GRADE certainty ratings**

### Certainty    What it means

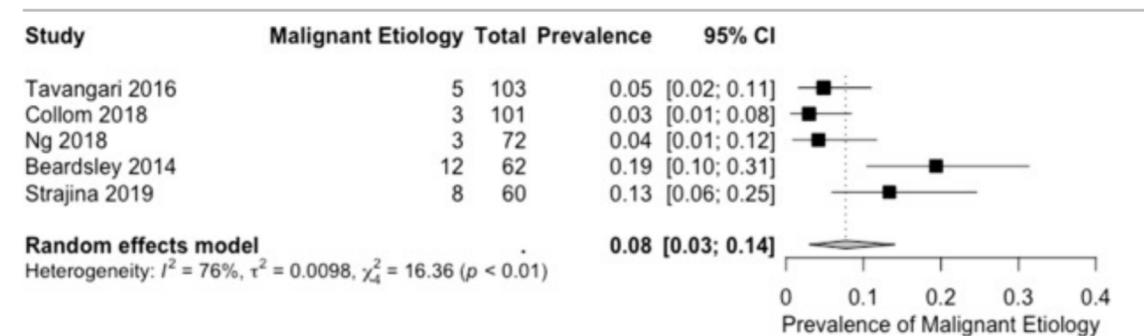
Very low	The true effect is probably markedly different from the estimated effect
Low	The true effect might be markedly different from the estimated effect
Moderate	The authors believe that the true effect is probably close to the estimated effect
High	The authors have a lot of confidence that the true effect is similar to the estimated effect

## What is GRADE?

<https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/>

# What figures/tables do you need?

## Forest plot



[Download](#) : Download high-res image (163KB)

[Download](#) : Download full-size image

Figure 2. Forest plot of pooled prevalence of malignant etiologies among patients presenting with small bowel obstruction in the virgin abdomen.

# Follow PRISMA and MOOSE guidelines

**Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement**

<https://www.equator-network.org/reporting-guidelines/prisma/>

**Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group**

<https://www.equator-network.org/reporting-guidelines/meta-analysis-of-observational-studies-in-epidemiology-a-proposal-for-reporting-meta-analysis-of-observational-studies-in-epidemiology-moose-group/>

# Part 2: Designing the research question

# First, some habits

Observe

Question (challenge dogma)

Keep running list of questions

Where to find “good” questions?

- Ask experienced faculty
- Read “limitations”/ “future directions” sections
- Read “classical” literature

# What will your reviewer/editor be looking for?



Tips for authors of surgical manuscripts from senior reviewers

**Table V**  
Specific annoyances for reviewers categorized by themes

Theme	n	Selected comments
Manuscript construction	5	Unacceptable grammar and sentence structure  Incomplete reference list Reference list fails to reference major contributions to the field
		Overstated or over-interpreted results Incorrect or inconsistent data presentation Invalid conclusions Unsubstantiated conclusion that a prospective, randomized clinical trial is needed
Importance/relevance	3	If you are 100% sure, could say, "to our knowledge,..."
	2	Claim that this is the first observation of this phenomenon  Recommendation for management changes based on a single institutional experience
	1	Poorly designed study
Study design		

Malangoni MA, Evans DB, Prinz RA, Hodin RA, Rege R, Harken AH. Tips for authors of surgical manuscripts from senior reviewers. *Surgery*. Published online January 22, 2021. doi:[10.1016/j.surg.2020.12.020](https://doi.org/10.1016/j.surg.2020.12.020)

**Table II**  
Themes noted in making recommendations to initially accept a manuscript

Theme	n	Selected comments
Importance/relevance	6	High interest to the readership Answers a clinically relevant question Adds new knowledge Improves understanding of a disease process Improves patient outcomes Conclusions are useful and important
Data analysis	5	Conclusions are supported by the results Data analysis is appropriate Supports or challenges a hypothesis in a valid evidence-based manner
Study design	3	Study is well designed and appropriate Hypothesis-driven Mechanistically based
Manuscript construction	3	Well written and organized

**Table III**  
Themes noted in making recommendations to initially reject a manuscript

Theme	n	Selected comments
Importance/relevance	6	Purpose of the study is unclear Importance and relevance of the study are unclear Topic is not relevant or important Absence of new information
Data analysis	6	Results do not support the conclusions Conclusions are not valid Sample size is inadequate for analysis Statistical analysis is inappropriate
Study design	5	Poor methodology Inadequate sample size Flawed design
Manuscript construction	2	Poorly written Poor grammar and/or sentence structure

# To design a good research question

Strive to be a content expert

- know research landscape inside out
- know burning Qs vs beating a dead horse
- how? Ask. Read. Read. Read.

Ask a meaningful, actionable question that adds new knowledge & has potential to improve patient outcomes

Have a CRYSTAL-CLEAR (usually singular) hypothesis: “**We hypothesized...**”

These phrases should be in last paragraph of intro, verbatim

Have a CRYSTAL-CLEAR aim: “**We aimed to...**”

# For MedScholars proposal: write out “White Paper” ASAP

Title

Background

Justification of importance

Hypothesis

Aim

Study design

- Inclusion criteria
- Exclusion criteria
- List of variables

Key tables & figures