Writing grant proposals and papers

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A friend of mine always says...

"Writing papers is just for those people with the *writing gene*"

Inspiration? Yes, it exists. But it usually appears while I am working.

Pablo Picasso

A reviewer received a paper on MRSA bacteraemia…

OK, another (OK, another (possibly boring) paper on MRSA bactareaemia…

The same data may produce different recommendations

- Difficult to read
- Not well organised
- Nothing new

RECOMMENDATION:
REJECT

- Data are clear
- Good discussion
- Some interesting points

LET'S GIV'EM AN OPPORTUNITY

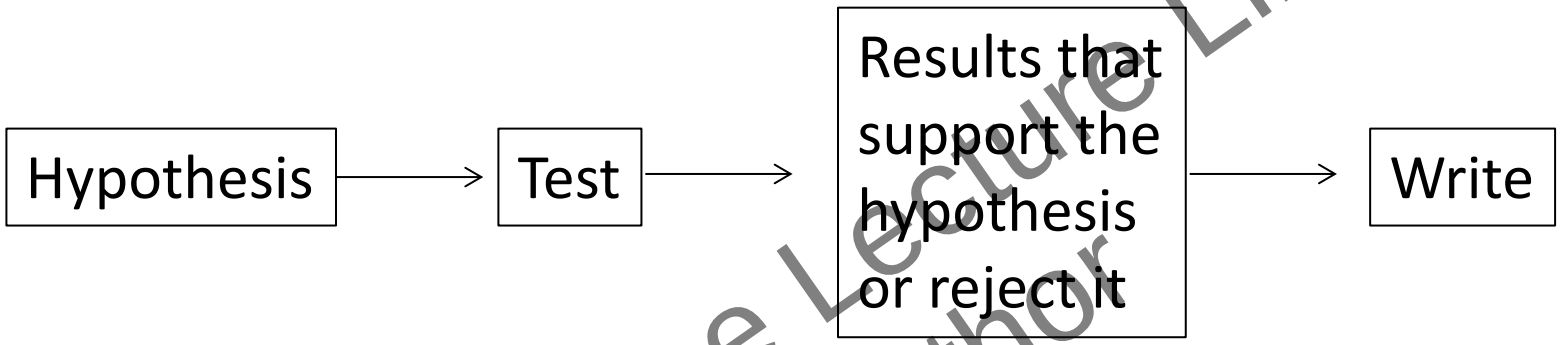
Your task…

- Convince the editor and reviewer that
  - … your study was necessary
  - … it was well performed
  - … your results are consistent, accurate and interesting
  - … that your data are original or at least open a new door for further research

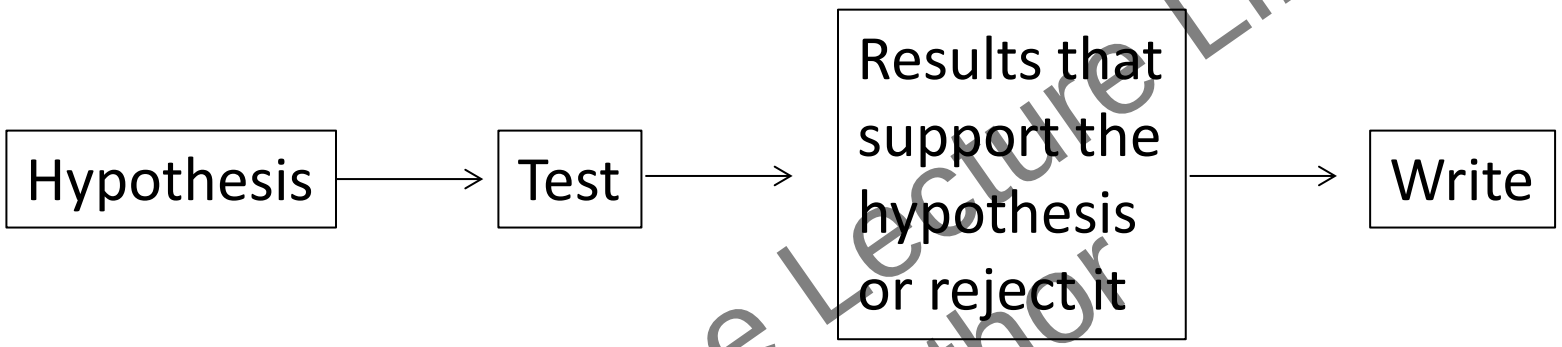
The most important tricks…

- Read
- Read
- Read
- Write
- Write
- Write

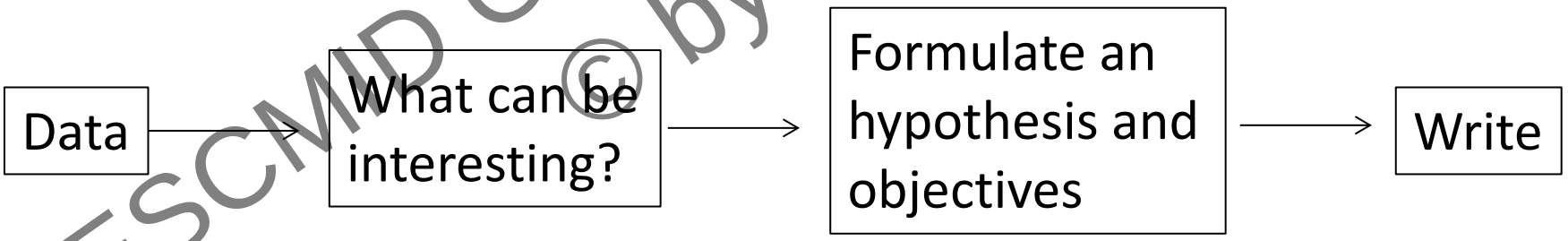
In theory….



In theory….



But too many times…



It should not be like this!!!

The Editor

- Usually just reads the letter, title and abstract
- (Sometimes also a very brief overview of the paper)
- Decides:
  - Sending to reviewers (you have an opportunity!!)
  - Directly reject it
- Formal aspects (authors' instructions) matter
- TITLE AND ABSTRACT ARE VERY IMPORTANT!!

The reviewers

- May be (or not) be experts
- (Might be competitors)
- Probably are busy people
- Remember: reviewing is for free
- They are probably tired of reviewing bad papers

- Do facilitate their work!!

A matter of strategy

How articles are read

- Title
- Abstract
- Introduction
- Methods
- Results
- Discussion

How I write articles*

- Results
- Methods
- Introduction
- Discussion
- Abstract
- Title

*Be careful, I might be wrong (but it works)

Results

- Select what would go for tables and figures
  - Tables: data that would need much text to explain and/or description would be confusing
  - Figures: flow charts, impact of imaging
- Remember: tables and figures should be understandable by themselves
- Clinical studies
  - Figure 1 usually a flow chart of patients included
  - Table 1: descriptive data of the series/cohorts/cases and control group

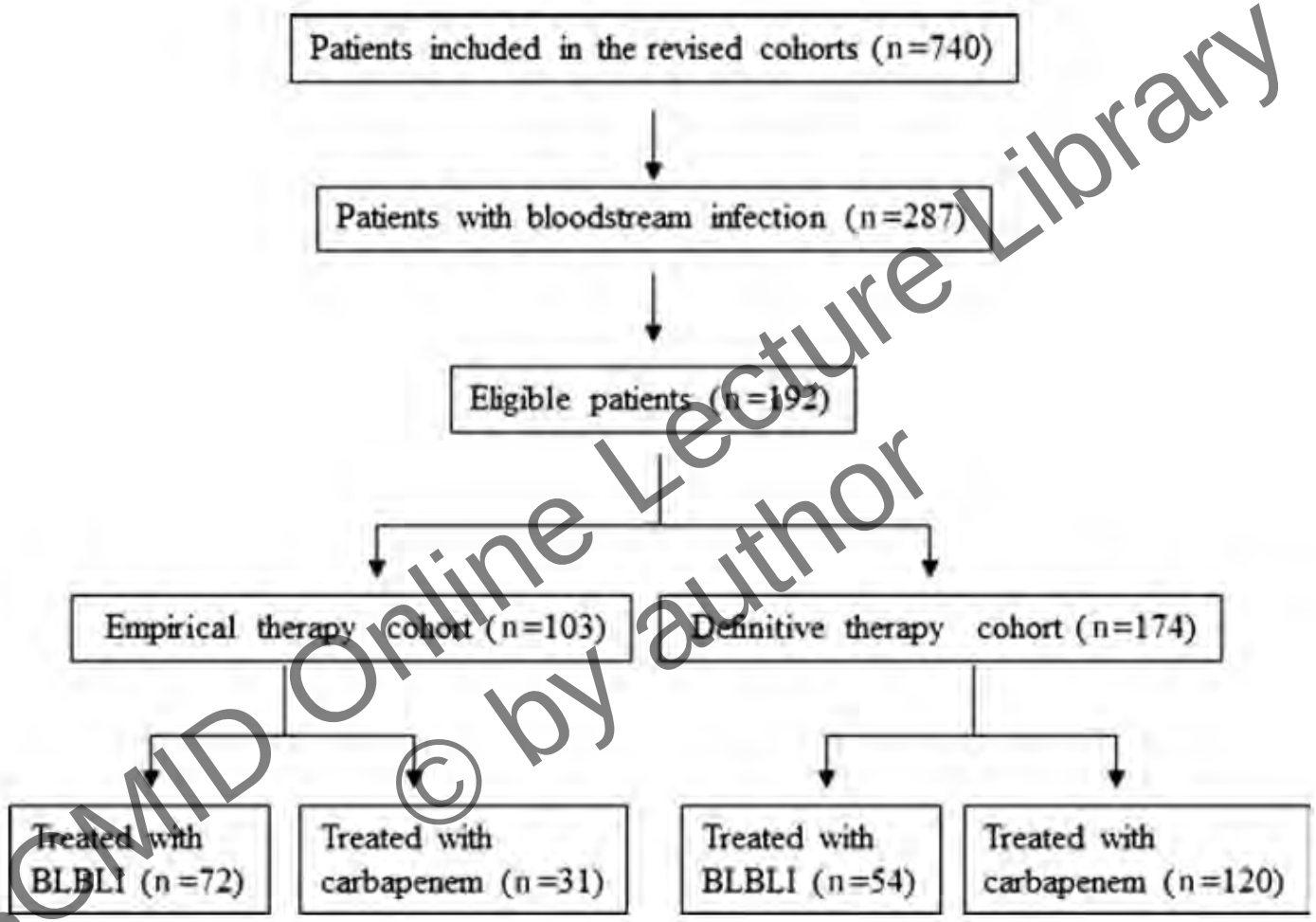


Figure 1. Flow chart of patients included in the study. BLBLI, β-lactam/β-lactamase inhibitor.

Rodríguez-Baño et al. Clin Infect Dis 2012; 54: 167-174

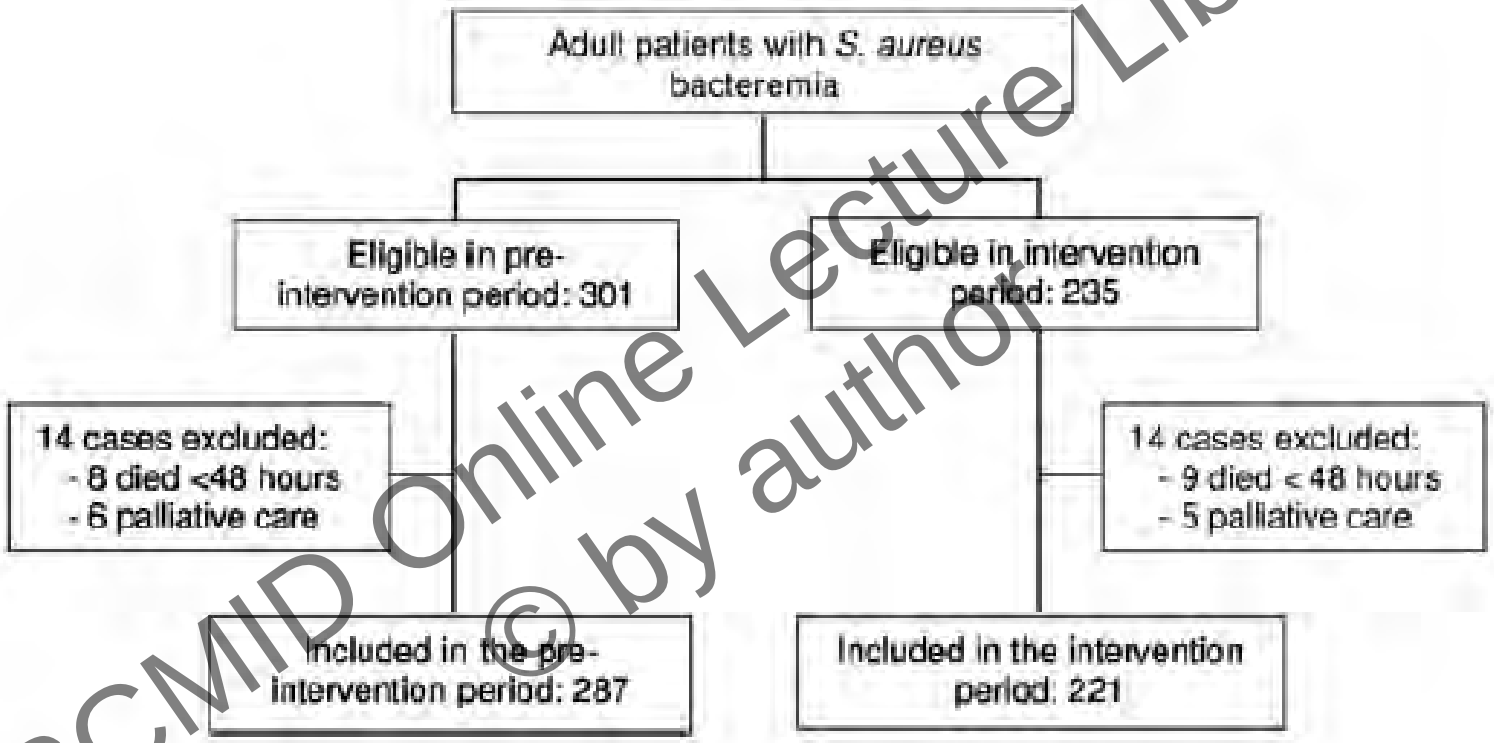


Figure 1. Flow chart of patients included in the multicenter quasi-experimental study.

Lopez-Cortés et al. Clin Infect Dis 2013

TABLE 1 Features of 801 episodes of bloodstream infections, according to adequate or inadequate empirical therapy

Characteristic	Value[a]		
	Inadequate empirical therapy (n = 199)	Adequate empirical therapy (n = 602)	P value[b]
Hospital-acquired infection	142 (71.4)	318 (52.8)	<0.001
Male gender	116 (58.3)	357 (59.3)	0.8
Median age (yr) (interquartile range)	67 (56–76)	66 (51–75)	0.3
Tertiary hospital	154 (77.4)	483 (80.2)	0.3
ICU admission	43 (21.6)	1112 (18.6)	0.3
Median Charlson index (interquartile range)	2 (1–4)	2 (1–3)	0.2
Median Pitt score (interquartile range)	1 (0–3)	1 (0–3)	0.9
Cancer	67 (33.7)	160 (26.6)	0.05
Diabetes mellitus	48 (24.1)	159 (26.4)	0.5
Chronic pulmonary disease	25 (12.6)	80 (13.3)	0.7
Chronic renal insufficiency	20 (10.1)	70 (11.6)	0.5
Chronic liver disease	18 (9)	55 (9.1)	0.9
Neutropenia	9 (4.5)	37 (6.1)	0.3
Central venous catheter	77 (38.7)	168 (27.9)	0.004
Urinary catheter	81 (40.7)	195 (32.4)	0.03
Mechanical ventilation	28 (14.1)	66 (11)	0.2
Parenteral hyperalimentation	18 (9)	26 (4.3)	0.01
Previous antimicrobial use	98 (49.2)	231 (38.5)	0.008
Surgery	39 (19.6)	75 (12.5)	0.01
Source of bacteremia			0.002
Unknown	55 (27.6)	135 (22.4)	
Urinary tract	23 (11.6)	137 (22.8)	
Intra-abdominal infection	29 (14.5)	110 (18.2)	
Vascular catheter	51 (25.6)	82 (13.6)	
Respiratory tract	25 (12.6)	77 (12.8)	
Other source	16 (8)	61 (10.1)	

Retamar et al. Antimicrob Agents Chemother 2012; 56: 472

Tables case-control studies

Risk factor	Case patients (n = 95)	Control group A (n = 190)	OR (95% CI)	P
Age >65 years	69 (73)	96 (51)	2.5 (1.5–4.3)	<.001
Female gender	42 (44)	80 (42)	1.0 (0.6–1.7)	.7
Health care–associated bacteremia	72 (76)	102 (54)	2.6 (1.5–4.6)	<.001
Previous admission	45 (47)	63 (33)	1.8 (1.0–2.9)	0.02
Nursing home residency	10 (11)	3 (2)	7.2 (1.9–27.1)	.001
Hemodialysis	4 (4)	4 (2)	2.0 (0.4–8.3)	.3
Day hospital	37 (39)	59 (31)	1.4 (0.8–2.4)	.1
Home care	2 (2)	2 (1)	2.0 (0.2–14.5)	.4
Transplant	0 (0)	1 (1)	…	.4
Charlson index >2	46 (48)	71 (38)	1.5 (0.9–2.5)	.08
Diabetes mellitus	24 (25)	36 (19)	1.4 (0.7–2.5)	.2
Chronic pulmonary disease	18 (19)	33 (18)	1.1 (0.5–2.0)	.7
Heart failure	11 (12)	19 (10)	1.1 (0.5–2.5)	.6
Neoplasia	24 (25)	35 (19)	1.4 (0.8–2.6)	.1
Cirrhosis of liver	10 (11)	6 (3)	3.5 (1.2–10.1)	.01
Chronic renal insufficiency	10 (11)	14 (7)	1.4 (0.6–3.4)	.3
Use of immunosuppressive drugs	7 (7)	25 (13)	0.5 (0.2–1.2)	.1
Obstructive urinary disease	26 (27)	16 (9)	4.0 (2.0–8.0)	<.001
Obstructive biliary disease	8 (8)	7 (4)	2.3 (0.8–6.8)	.09
Neutropenia	4 (4)	7 (4)	1.1 (0.3–4.0)	.8
Venous catheter use	8 (8)	10 (5)	1.6 (0.6–4.3)	.3
Urinary catheter use	23 (24)	17 (9)	3.2 (1.6–6.4)	.001
Surgery	12 (13)	10 (5)	2.5 (1.0–6.2)	.02
Previous antimicrobial use	39 (41)	44 (23)	2.2 (1.3–3.8)	.002
Aminopenicillins	7 (7)	22 (12)	0.6 (0.2–1.4)	.2
Cephalosporins	12 (13)	17 (9)	1.4 (0.6–3.2)	.3
Fluoroquinolones	23 (24)	15 (8)	3.7 (1.8–7.5)	<.001

Rodríguez-Baño et al. Clin Infect Dis 2010; 50: 40-48

Tables cohort studies

TABLE 2 Univariate analysis of associations between exposure to different variables and 14-day mortality in 801 episodes of bloodstream infection

Variable	Mortality at 14 days (no. of deaths/no. of infections [%])	RR (95% CI)	P value[c]
Gender			
Male	96/473 (20.3)	Reference	
Female	52/318 (15.9)	0.71 (0.57–1.06)	0.1
Age (yr)			
≤55	25/204 (12.3)	Reference	
>55	123/597 (20.6)	1.68 (1.13–2.51)	0.007
Type of acquisition			
Community	22/149 (14.8)	Reference	
Health care associated	34/192 (17.7)	1.20 (0.73–1.96)	0.4
Hospital	92/560 (20)	1.35 (0.88–2.08)	0.1
Type of hospital			
Tertiary	112/637 (17.6)	Reference	
Community	36/164 (22.0)	1.25 (0.89–1.74)	0.1
Charlson index			
0–1	42/334 (12.6)	Reference	
2	41/212 (19.3)	1.54 (1.04–2.28)	0.03
≥3	65/255 (25.5)	2.03 (1.52–3.74)	<0.001
Neutropenia			
No	133/755 (17.6)	Reference	
Yes	15/46 (32.6)	1.85 (1.19–2.88)	0.01
Pitt score			
0-1	47/491 (9.6)	Reference	
2	15/92 (16.3)	1.70 (1.00–2.91)	0.05
≥3	86/218 (39.4)	4.12 (3.00–5.66)	<0.001

Retamar et al Antimicrob Agents Chemother 2012; 56: 472

Tables in quasiexperimental or RCT

Table 3. Features of the Patients With *Staphylococcus aureus* Bacteremia

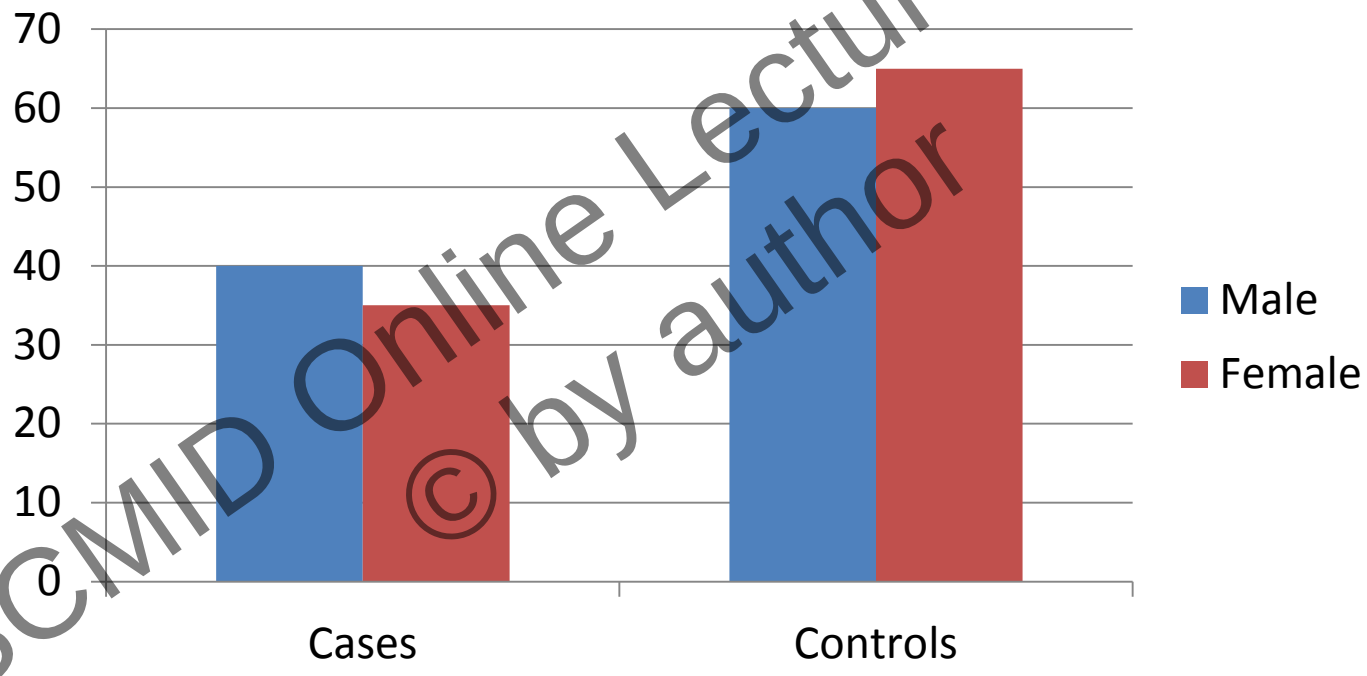
Variable	All Patients (n = 508)	Preintervention (n = 287)	Intervention (n = 221)	*P* Value
Median age, y, (IQR)	67 (55–76)	67 (55–75)	66 (56–77)	.63
Female sex	170 (33.5)	89 (31)	81 (36.7)	.18
Comorbidities				
Diabetes mellitus	148 (29.1)	83 (28.9)	65 (29.4)	.90
Chronic pulmonary disease	69 (13.6)	39 (13.6)	30 (13.6)	.99
Hemodialysis	46 (9.1)	21 (7.3)	25 (11.3)	.12
Malignancy	122 (24)	73 (25.4)	49 (22.2)	.39
Chronic liver disease	60 (11.8)	32 (11.1)	28 (12.7)	.59
Immunosuppression	73 (14.4)	42 (14.6)	31 (14)	.84
Intravenous drug abuse	9 (1.8)	7 (2.4)	2 (0.9)	.19
Endocarditis-predisposing condition	72 (14.2)	42 (14.6)	30 (13.6)	.73
Charlson index ≥2	331 (65.3)	191 (66.8)	140 (63.3)	.42
Pitt score >2	110 (21.7)	64 (22.3)	46 (22.2)	.79
Acquisition				
Hospital-acquired infection	292 (57.5)	165 (57.5)	127 (57.5)	.99
Healthcare-related bacteremia	132 (26)	73 (25.4)	59 (26.7)	.74
Source of bacteremia				
Vascular catheter	197 (38.8)	100 (34.8)	97 (43.9)	.04
Unknown source	172 (33.9)	95 (33.1)	77 (34.8)	.68
Skin and/or soft tissue	53 (10.4)	38 (13.2)	15 (6.8)	.02
Respiratory tract	25 (4.9)	13 (4.5)	12 (5.4)	.22
Osteoarticular	31 (6.1)	21 (7.3)	10 (4.5)	.19
High-risk source[a]	32 (6.3)	18 (6.3)	14 (6.3)	.97
Complicated bacteremia	238 (46.9)	140 (48.8)	98 (44.3)	.32
MRSA	102 (20.1)	57 (19.9)	45 (20.4)	.89
Endocarditis (primary and secondary)[b]	22/180 (12.2)	11/83 (13.3)	11/97 (11.3)	.69
Appropriate empirical therapy	125 (80.1)	65 (75.6)	60 (85.7)	.12
Severe sepsis or septic shock	120 (22.4)	71 (24.2)	46 (20.9)	.51
Unfavorable course[c]	179 (35.2)	96 (33.4)	83 (37.6)	.33

Lopez-Cortés et al. Clin Infect Dis 2013

This does not need a table…

	Mean change in CFU /mL (SD)
Treated	-3.4 (1.2)
Controls	-0.5 (0.7)

This does not need a figure…



What's wrong?

	Cases	Controls	P
Male	71 (51%)	145 (53%)	0.2
Female	69 (49%)	138 (47%)	0.2

Results: frequent mistakes

- Inconsistency with objectives
- Messy order
- Methods repeated
- Inconsistency with methods: use of undefined variable or procedure, or not use of variables defined
- Repeating data already in tables
- Comments or opinions
- Inclusion of not relevant data

Methods

- Should allow someone else to reproduce the study and evaluate the validity of your results

- Boring to write BUT reviewers take them very seriously

Methods: clinical and epi studies

- Design, site and population
- Method for detecting, selecting and following participants
- State and define the variables
  - Main and secondary outcome variables
  - Independent variables
- Ethical aspects
- Statistical analysis

Methods: lab studies

- Materials used
- Procedures (detailed)

Introduction

- Critical for
  - Convince the reader that the topic is important and your study is necessary
  - To state the objectives
- 2-3 paragraphs
  - Background – importance of the topic, where we are
  - Gap in knowledge
  - What are your (hypothesis and) objectives
- Write according to the journal type
  - General vs. specialized journals

Discussion

- Key message of your results
- Interpretation
- Generalisability
- Limitations and strengths

- Outline first!!

Discussion

- Don´t be too hypothetical…
- But do go beyond the data!!

DECIPHERING ACADEMESE

YES, ACADEMIC LANGUAGE CAN BE OBTUSE, ABSTRUSE AND DOWNRIGHT DAEDAL. FOR YOUR CONVENIENCE, WE PRESENT A SHORT THESAURUS OF COMMON ACADEMIC PHRASES

"To the best of the author's knowledge..."	=	"WE WERE TOO LAZY TO DO A REAL LITERATURE SEARCH."
"Results were found through direct experimentation."	=	"WE PLAYED AROUND WITH IT UNTIL IT WORKED."
"The data agreed quite well with the predicted model."	=	"IF YOU TURN THE PAGE UPSIDE DOWN AND SQUINT, IT DOESN'T LOOK TOO DIFFERENT."
"It should be noted that..."	=	"OK, SO MY EXPERIMENTS WEREN'T PERFECT. ARE YOU HAPPY NOW??"
"These results suggest that..."	=	"IF WE TAKE A HUGE LEAP IN REASONING, WE CAN GET MORE MILEAGE OUT OF OUR DATA..."
"Future work will focus on..."	=	"YES, WE KNOW THERE IS A BIG FLAW, BUT WE PROMISE WE'LL GET TO IT SOMEDAY."
"...remains an open question."	=	"WE HAVE NO CLUE EITHER."

www.phdcomics.com

Discussion (1)

- What your paper found (key results)
  - Results: Clinical cure was achieved in 15% with drug A and in 2% with drug B (absolute difference, 13%, 95% CI, 8%-22%). … … … Multivariate analysis showed that treatment with B was independently associated with clinical cure when controlling for confounders (OR=2.3, 95% 1.7-2.9)
  - Discussion: A sentence for that??

Discussion

- What your paper found (key results)
  - Results: Clinical cure was achieved in 15% with drug A and in 2% with drug B (absolute difference, 13%, 95% CI, 8%-22%). … … … Multivariate analysis showed that treatment with B was independently associated with clinical cure when controlling for confounders (OR=2.3, 95% 1.7-2.9)
  - Discussion:

Our results consistently showed that B was more effective than A in the treatment of…

Discussion (2)

- Interpretation
  - Put your data in context
  - Compare and comment previous data
  - Meaning for clinical practice or future research
- Generalisability
  - To which situations may your data be extrapolated

Discussion (3)

- Limitations
  - Do not try to hide!!
  - Briefly comment if they are important or how they may change the interpretation
- Conclusion

Abstract

- Non-structured or structured

- Write at the end
- Yes, it's boring but CRITICAL
- Do not just simply copy-paste from the text
- Read your paper and take notes → write the abstract from the beginning

Title

- As short as possible but
- Informative of the topic and methods
- Attractive, tempting (not too much…)

Epidemiology and Clinical Features of Infections Caused by Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* in Nonhospitalized Patients

Rodríguez-Baño et al. J Clin Microbiol 2004; 42: 1089-1094

Now my title would be more like:

Emerging multidrug resistant *Escherichia coli* in the community: risk factors and clinical features

Feel free to criticize…

Bacteremia Due to Extended-Spectrum β-Lactamase–Producing *Escherichia coli* in the CTX-M Era: A New Clinical Challenge

Rodríguez-Baño et al. Clin Infect Dis 2006

Long-term control of hospital-wide, endemic multidrug-resistant *Acinetobacter baumannii* through a comprehensive "bundle" approach

Rodríguez-Baño et al. Am J Infect Control 2009

Impact of an Evidence-Based Bundle Intervention in the Quality-of-Care Management and Outcome of *Staphylococcus aureus* Bacteremia

López-Cortés et al. Clin Infect Dis 2013

References

- Relevant, recent
- (Consider including some from the reviewers you are recommending…)

Look at the checklists from…

OPEN ACCESS Freely available online

PLoS MEDICINE

Guidelines and Guidance

CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials

Kenneth F. Schulz[1]*, Douglas G. Altman[2], David Moher[3], for the CONSORT Group[¶]

The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection

Sheldon P Stone, Ben S Cooper, Chris C K Kibbler, Barry D Cookson, Jenny A Roberts, Graham F Medley, Georgia Duckworth, Rosalind Lai, Sarah Ebrahim, Erwin M Brown, Phil J Wiffen, Peter G Davey

Annals of Internal Medicine | ACADEMIA AND CLINIC

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies

Erik von Elm, MD; Douglas G. Altman, DSc; Matthias Egger, MD; Stuart J. Pocock, PhD; Peter C. Gøtzsche, MD; and Jan P. Vandenbroucke, MD, for the STROBE Initiative

Rebound letter

- Be grateful and polite to reviewers (although it maybe you would like to kill them)
- Answer ALL their questions and comments
- Mostly do as suggested. Only reject doing so if:
  - They ask for the impossible
  - You can convincingly argue against

- “The reviewer raise a very important question…”
- “… Although we agree that…, we are afraid we cannot follow the reviewer’s suggestion because the data are unavailable. However, we think that…”
- “We are afraid that was beyond the objective of our study.”

After finishing…

- Leave it there and read again 3 days later
- Show to your colleges for review

Writing grant proposals: the call

- Read the call carefully
- Read it again
- Read it once more

- Try to understand what the funders are looking for and what they are expecting
- Write an outline with the key aspects of the call
- Decide if this is your call

- Translational vs. on the edge
- Clinical vs. basic
- Small vs big projects
- Targeted vs. open calls
- Specialised vs. generalistic review
- National vs. international

State of the art

- Objective: convince the reviewers that
  - The topic is within the scope of the call
  - The topic is scientifically relevant
  - Your research is needed in this area (gaps) for future development / patients

- Explain the idea to a college/friend/relative not related to the area
  - Not your mother/father – they would probably fund it!!

- WRITE: CLEAR, STRUCTURED, BRIEF BUT COMPREHENSIVE

Hypothesis and objectives

- State clearly
- Coherent
- Be sure that can be answered with your proposed methods

Methods

- Design, etc etc.
- Ethical issues
- Bias, limitations and solutions
- Contingency plan

Workplan

- Sort in work packages with specific tasks
- Include milestones and deliverables for each
- Include time to complete
- Leaders and collaborators for each task

Added value and expected impact

- Explain which is the added value of your consortium / team for this project and beyond
- What is the expected impact if successful? What if not?

Budget

- Read the call again – what expenses may be included?
- Explain what you need and why. Any alternative?
- Elaborate on number of patients/isolates/experiments
- Be specific
- Do not overestimate too much…

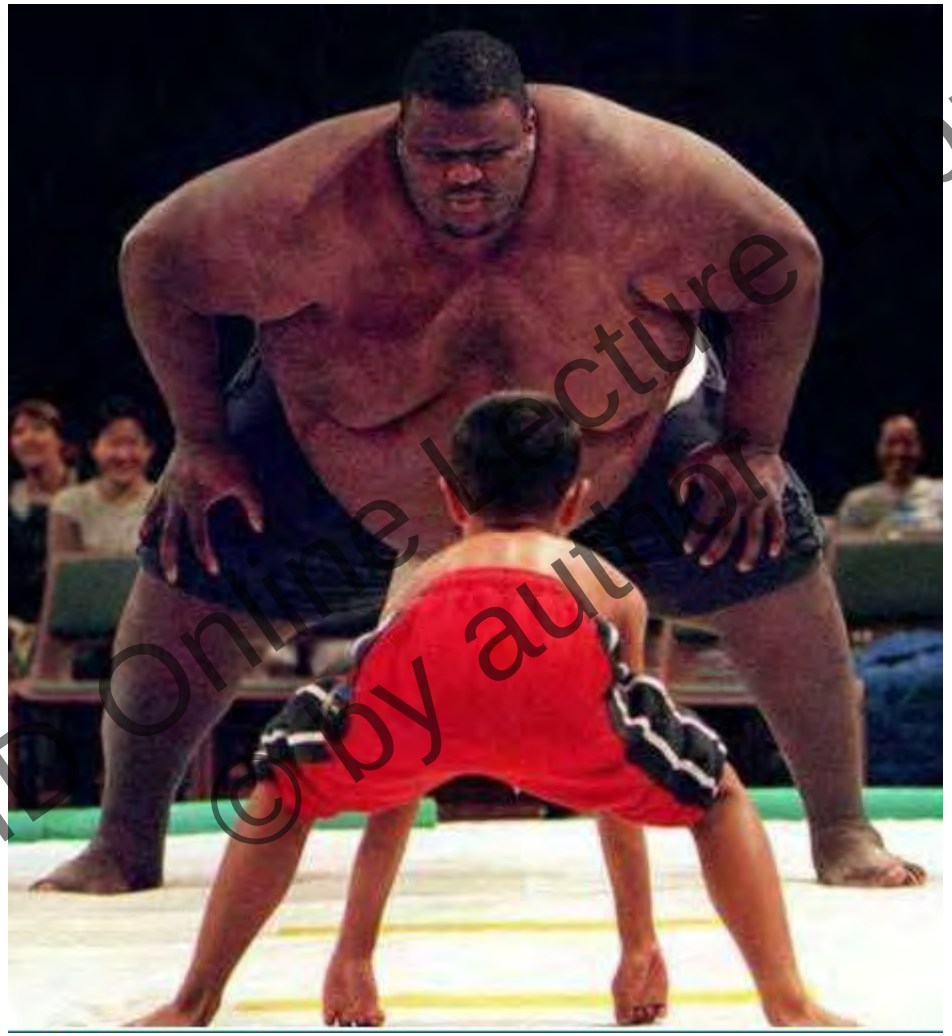
Two-stage calls (H2020)

- Expression of interest (EoI)
- Full project proposal (FPP)

EoI (H2020)

- 7 pages
- Excellence
  - Objectives
  - Relation to the work programme
  - Concept and approach
  - Ambition
- Impact
  - Expected impact
- References

- First lesson
  - Do not start an investigation if you haven't written a project
- Second lesson
  - Do not write a project before clearly setting your hypothesis and objectives
- So begin from the beginning…



Yes, you can!!

Thank you

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