Writing manuscripts

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Goals of the talk

- Purpose of writing
- Anatomy of a manuscript
- Mechanics of writing
  - style, language, tone
- Process of manuscript submission
- Difficult situations
Why write manuscripts?

- Why do we do science?
- Why do we ask questions?
Why write manuscripts?

- Why do we do science?
- Why do we ask questions?

- We form epistemic communities …”a global network of knowledge-based professionals in scientific and technological areas that often have an impact on policy decisions”…

Adapted from Wikipedia
Knowledge as a subset of that which is both true and believed
Why write manuscripts?

- the result of your effort - the fruit of your labor
- your product
Why write manuscripts?

• the result of your effort - the fruit of your labor
• your product
• part of your job
• required for promotion
Why write manuscripts?

- the result of your effort - the fruit of your labor
- your product
- part of your job
- required for promotion

- Ethical obligation to the study participants
- IRB’s can be your friend
Anatomy of a scientific manuscript

- Introduction
  - What’s known?
  - What’s unknown?
- Methods
  - How do we show it?
  - What are we showing now?
- Results
  - What did we show?
- Discussion
  - What’s known?

Introduction

1. Background/Statement of the issue
2. Gaps in current knowledge/Why your paper is needed
3. How you will provide the answer/test hypothesis

* Journals advice 2-3 paragraphs, not more
Methods

1. Subjects and Setting
2. Procedures/ Intervention
3. Laboratory Methods
4. Statistical methods: definitions, tests, modeling
5. Committee approval
Results

1. Demographic and clinical summary of study population
2. Results—simple first, then more sophisticated modeling
3. Table 1. Characteristics of study participants.
4. Table 2. Comparison between groups
5. Figures: Illustrate main results; for clinical trials, show the schema of the trial first, then survival curves.

- Remember tables and figures will be used for slides; Some people will look at tables and figures to decide if to read.
1. Re-cap your novel and important findings but do not repeat the numbers
2. Your interpretation of your findings
3. Comparison with others’ findings—how does your paper fit in the literature?
4. Strengths and Limitations – and why the latter are not that important
5. Clinical and/or public health implications
6. Summary and future directions
Be pithy! (def. Having substance and point: tersely cogent)

- “I have made this letter longer than usual, because I lack the time to make it short” *Pascal*
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- Publisher’s telegram to Mark Twain: NEED 2-PAGE SHORT STORY TWO DAYS
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- Publisher’s telegram to Mark Twain: NEED 2-PAGE SHORT STORY TWO DAYS

- Twain’s response: NO CAN DO 2 PAGES TWO DAYS. CAN DO 30 PAGES 2 DAYS. NEED 30 DAYS TO DO 2 PAGES.
• Fifteen years ago, medicine had little to offer HIV-infected women who desired to become pregnant. Since the widespread availability of Highly-Active Antiretroviral Therapy (HAART) in the US and the subsequent marked decrease in perinatal transmission of HIV, the emphasis of antenatal care for HIV-positive pregnant women has shifted. HAART has made it possible for pregnant women to have undetectable HIV viral loads at delivery making perinatal transmission of HIV a rare occurrence. Additional protection is afforded to the infant by administration of prophylactic zidovudine. These public health advances enabled healthcare practitioners to focus antenatal care for HIV-infected pregnant women on prevention of other comorbid infections in their infants.

• The rate of infant HIV infection in the U.S. has plummeted with the advent of routine HIV testing during pregnancy and the availability of potent antiretroviral therapy. These public health advances shift focus to prevention of other comorbid infections in HIV-infected women and their infants.
Examples

• Causally related to –
Examples

- Causally related to – caused by
- The presence of visceral KS involvement was not different among children of various ages
Examples

- Causally related to – caused by
- The presence of visceral KS involvement was not different among children of various ages – did not differ with age.
Clarity and brevity

- Causally related to – caused by
- The presence of visceral KS involvement was not different among children of various ages – did not differ with age.
- Treatment was not started less than 48 hours
Clarity and brevity

- Causally related to – caused by
- The presence of visceral KS involvement - was not different among children of various ages – did not differ with age.
- Treatment was not started less than 48 hours - was started more than 48 hrs
HIV seropositive women were 50% White, 21% Black and 29% other races.

Differences existed between subjects who developed clinical herpes zoster and those who did not.

Severe sepsis, defined as an individual with a documented infection, and resultant end organ dysfunction, persists as a common and concerning diagnosis.
Young epidemiologists….

- HHV-8 detection frequency decreased by 18% (IRR 0.82; p=0.012) on valacyclovir and 31% (IRR 0.694; p<0.001) on famciclovir.
- Few men are tested for syphilis or HIV during pregnancy.
- The group infected with subgenera D were significantly more likely to suffer from unresolved lid edema (HR 0.41, 95%CI 0.29-0.58, adj. p-value <0.009).
A better beginning?

- “As expected…” vs.
- “This is the first study…”
Authorship credit should be based on

- 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
- 2) drafting the article or revising it critically for important intellectual content; and
- 3) final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.
Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship. All persons designated as authors should qualify for authorship, and all those who qualify should be listed. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
Other tips …

- Who writes—authorship and authors’ order
  - Policy vs. politics
- When you write
- Where you write
- Order that you write in (methods, results [tables and figures first], introduction, discussion, abstract)—from most concrete to most cognitive
- Options:
  - Outline
  - Writing Stream
  - Writing from slides
  - Dictating papers
After the initial draft

- Read it aloud
- Depending on the paper, often best for 2 (at most 3) people edit sequentially, then send to other authors at once. This makes incorporating the changes often easier and less confusing to you.
- Appreciate comments from other co-authors, but feel free to argue
- Date drafts instead of numbering—latter can be depressing.
- Have others in your field but not co-investigators read it—read it as if you would if you were reviewing it …
- After you are happy with content, edit for style
Writing Issues

- Typos
- Inappropriate spaces or lack of spaces.
  - For example, I think this is a good sentence. Is it not?
- Capitalization errors
  - I want to improve Childs health.
- Solution: pay attention to the red line under your words. Figure out why it is there – fix it or know that it should be there.
• Use Spell check but also read for spelling errors (eg, from – form; then – than)
• Read again for sentence structure
• Read again for flow and paragraph transition
• The end product should be an elegantly packaged message… you are selling your product …
specificity and low copy number cutoff maximized sensitivity. The threshold of virus
that may result in transmission is unknown. The probability of isolating HSV in tissue
culture rises linearly with the log copy number. However, even with low copy number,
such as $10^2$, a culture will be positive in small proportion, and the relevance of isolation
of HSV to transmission is speculative. Moreover, we have documented transmission of
HSV from maternal secretions to the neonate during birth at a time that culture was
negative and PCR positive.

A rapid test for HSV detection in labor should be combined with a serologic
test for HSV-2 antibodies. Those women who lack HSV-2 antibodies but are shedding
HSV at the time of labor are a very high risk – 30-50% – of transmitting the infection to
their neonate. In this situation, caesarean delivery is appropriate, and some experts would
also administer acyclovir to the neonate, especially if the membranes were ruptured. On
the other hand, the risk of HSV transmission is low if the woman has antibodies to HSV-2,
and a more conservative approach is warranted. In such women, perhaps a course of
intrapartum acyclovir may reduce further the already low risk of neonatal infection. His
approach would parallel the successful strategies for Group B strep prevention and HIV

There is no unanimity in managing such
women. Some would admit to C-section,
others Would

Rapid HSV PCR
For both bivalent and quadrivalent human papillomavirus (HPV) vaccines, come in a series of 3 injection three-dose regimens, impeding ease of administration and increasing cost. The investigators from an ongoing manufacturer-supported study of bivalent (HPV 16/18) vaccine vaccination in Costa Rican women asked whether 1 one or 2 two immunizations provide adequate protection against persistent HPV 16 or 18 infection (defined as infection that persisted for ≥10 months after the last vaccine dose), the precursor to cervical cancer and the endpoint of the trial.

Of 7466-7153 evaluable women who were randomized to receive HPV or control vaccine, 5967 received 3 doses, 929-802 received only 2 doses, of vaccine and 551-384 only received 1 dose. Vaccine efficacy was 80.9%. The most common reason for missing doses were pregnancy and colposcopy referral. Among women who received the standard 3 doses, 4.4% vs. 0.8% persistent HPV 16 or 18 infection in the control and vaccine arms, respectively), 84.1% among women who received 2 doses (4.5% vs 0.7%), and 100.0% among women who received 1 dose (5.3% vs 0.0%) had persistent HPV 16/18 infection compared with 0.9% in the vaccine arm, for 81% efficacy of the vaccine. Among women who received 2 doses, 4.4% vs 0.7% had HPV 16/18 (vaccine efficacy 84%), among women who received 1 dose, 5.3% vs 0 (vaccine efficacy 100%).

Comment: HPV vaccine vaccination is likely has the capacity to prevent most cervical cancers worldwide. However, coverage has been limited by low uptake in some countries (including the United States), low failure to completion of the vaccination 3-dose series, and high cost (resource-poor countries). Evidence that the vaccine immunization is effective when administered in only 1 or 2 doses may ease could facilitate implementation of HPV vaccine programs both logistically and economically, especially in regions where such need is greatest. Clinicians in developed countries can be reassured that even girls and women who do not complete the standard series of HPV 16/18 vaccine vaccination regimen have receive considerable protection. Further data from countries that are experimenting with fewer than 3 doses will be forthcoming.

Anna Wald, MD, MPH
The graph shows the comparison of IP-10 (pg/mL) log₁₀ levels between HIV(+) and HIV(-) individuals. The p-value is 0.0016, indicating a statistically significant difference.
Vero Cell Transfections with Promotor>SEAP Fusion Reporters

SEAP Activity (Units)

100000

10000

1000

100

10

1

Pan>SEAP

RTA>SEAP

RTA>Tta +Tre>SEAP

Reporter Construct (Day 5)

Legend:
- w/o
- RTA
- XBP
Figure 2. Herpes Simplex Virus Detection and Viral Load by Study Group

A Genital HSV shedding

Study Participants Ordered by Frequency of Genital HSV Shedding During Valacyclovir Treatment

Swabs With HSV Detected, %

Pritelivir
Valacyclovir

Wald et al, JAMA, 2016
“As noted from our graphics editor, the bar graphs are per JAMA standards, including photocopying well in black-and-white.”

- Managing editor, Jama
Figure 2. Herpes Simplex Virus Detection and Viral Load by Study Group

A Genital HSV shedding

HSV DNA detection frequency by PCR

Study participant ordered by frequency on valacyclovir

Study participant ordered by frequency on valacyclovir
**Study design**

**Persistent Impairment of Quality of Life in Patients with Herpes Simplex Keratitis.**

Reynaud C¹, Rousseau A², Kaswin G¹, M'garrech M¹, Barreau E¹, Labetoulle M³.

**Abstract**

**PURPOSE:** To evaluate the quality of life (QoL) in patients with quiescent herpes simplex keratitis compared with control patients without ocular herpes.

**DESIGN:** Prospective, case-control study.

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**Rectus Extraocular Muscle Size and Pulley Location in Concomitant and Pattern Exotropia.**

Hao R¹, Suh SY², Le A³, Demer JL⁴.

**Abstract**

**PURPOSE:** To determine whether rectus extraocular muscle (EOM) sizes and pulley locations contribute to exotropia, we used magnetic resonance imaging (MRI) to measure these factors in normal control participants and in patients with concomitant and pattern exotropia.

**DESIGN:** Prospective case-control study.
Getting published

• Aim for the right journal in novelty and in audience
• Follow directions for format and length – use a published piece as a guide
• Letter to the editor: convince her that this is important, how does it change what we know, why would readers of her journal want to read it.
What happens to a submitted manuscript?

- Editor “reads” and decides to reject or send it for review
- Reviewers provide detailed critiques
- Editor makes a decision and mails you the response letter and critiques
- Whole process – 3 weeks to 3 months
Although association preferences documented in our study theoretically could be a consequence of either mating or shoaling preferences in the different female groups investigated (should we cite the crappy Gabor paper here?), shoaling preferences are unlikely drivers of the documented patterns both because of evidence from previous research and inconsistencies with *a priori* predictions. Our methods closely followed those of published mate choice experiments in this system (Tobler et al. 2009a,b; Plath et al. 2013),

Dave Harris
@davidjayharris

Not sure how this made it through proofreading, peer review, and copyediting. Via onlinelibrary.wiley.com/doi/10.1111/et...
#addedvalue

1:54 PM - 10 Nov 2014
How to review a paper – Ask your mentor to let you review manuscripts

- What is the manuscript about? Is it important?
- Does it add to existing literature on the subject? May need to do a literature review…
- Does the paper tell a story?
- How often does your mind wonder when you are reading it?
- Did the authors achieve what they did using the methods they provide?
- Could you replicate what they did using the methods they provide?
- Are there contradictions between the methods and the results?
- Do the results support the conclusions? Are the tables and figures helpful?
- Did the authors identify the flaws of their approach?
- Are they able to put it in context of prior data? How do these results change clinical practice/public policy or lead to further studies?
Remember the Golden Rule…

- What we wrote: Phase 1 dose-escalation study…”A heat shock protein vaccine with an HSV-2 peptide appears to be safe at the doses studied in healthy adults with or without HSV infection. Modifications of the dose, adjuvant, route, schedule, or HSV antigen may be required to improve responses.”

- What the reviewers saw: “There are no positive results from this study…We think this study reflects a waste of money, time, and volunteers”.

Herpes simplex virus (HSV) is one of the most common, yet frequently overlooked, sexually transmitted infections. **Since the type of HSV infection affects prognosis and subsequent counseling, type-specific testing to distinguish HSV-1 from HSV-2 is recommended.** Although PCR has been the diagnostic standard for HSV infections of the central nervous system, until now viral culture has been the test of choice for HSV genital infection. However, HSV PCR, with its consistently and substantially higher rate of HSV detection, will likely replace viral culture as the gold standard for the diagnosis of genital herpes in people with active mucocutaneous lesions, regardless of anatomic location or viral type. Alternatively, **type-specific serologic tests based on glycoprotein G should be** the test of choice to establish the diagnosis of HSV infection when no active lesion is present. **Given the difficulty in making the clinical diagnosis of HSV, the growing worldwide prevalence of genital herpes and the availability of effective antiviral therapy,** there is an increased demand for **rapid, accurate laboratory diagnosis** of patients with HSV.


Since the type of herpes simplex virus (HSV) infection affects prognosis and subsequent counseling, type-specific testing to distinguish HSV-1 from HSV-2 is **always recommended.** Although PCR has been the diagnostic standard method for HSV infections of the central nervous system, until now viral culture has been the test of choice for HSV genital infection. However, HSV PCR, with its consistently and substantially higher rate of HSV detection, could replace viral culture as the gold standard for the diagnosis of genital herpes in people with active mucocutaneous lesions, regardless of anatomic location or viral type. Alternatively, antigen detection—an immunofluorescence test or enzyme immunoassay from samples from symptomatic patients—could be employed, but HSV type determination is of importance. **Type-specific serology based on glycoprotein G should be** used for detecting asymptomatic individuals but widespread screening for HSV antibodies is not recommended. In conclusion, rapid and accurate laboratory diagnosis of HSV is now become a necessity, given the difficulty in making the clinical diagnosis of HSV, the growing worldwide prevalence of genital herpes and the availability of effective antiviral therapy.

*Strick & Wald Mol Diag Ther 2006; 10 (1): 17-28*
Plagiarism?

- ... values: that you work hard for what you want in life; that your word is your bond and you do what you say you're going to do; that you treat people with dignity and respect …

- ... Because we want our children — and all children in this nation — to know that the only limit to the height of your achievements is the reach of your dreams and your willingness to work for them.

- ...values that you work hard for what you want in life, that your word is your bond and you do what you say and keep your promise, that you treat people with respect…

- ... Because we want our children in this nation to know that the only limit to your achievements is the strength of your dreams and your willingness to work for them.
Plagiarism

- Cite appropriately
- Re-word, including your own work
- Ask permission
- Ask opinion
Dear Dr. Doctor,

I am aware that you recently admitted to wrongly publishing, as your own, a scientific research paper that I had submitted to *Annals of Internal Medicine*. After serving as an external peer reviewer on our manuscript, you published that same manuscript in a different medical journal a few months later. You removed the names of the authors and the research site, replacing them with the names of your coauthors and your institution.

It took 5 years from conceptualization of the study to publication of the primary analysis (1). This study was my fellowship project and required a lot of work. It took effort to find the right research team, design the study, and many research papers. It just doesn't make sense. Whether the pressure to publish is so intense, or whether the culture where you work is relatively permissive such that plagiarism is not taken as seriously, or whether getting caught seemed unlikely—it is hard to imagine why you would take this chance.

I hope you will not steal anyone else's research in the future. Instead, perhaps there is some way you can assist the scientific community's efforts to reverse the growing epidemic of plagiarism and scientific fraud. Helping to raise awareness of the problem and identifying potential solutions would be positive steps in the right direction.

Michael Dansinger, MD
Salami publication
Safety of pertussis vaccination in pregnant women in UK: observational study

Katherine Donegan *pharmacoepidemiologist*, Bridget King *scientific assessor*, Phil Bryan *scientific assessor*

Effectiveness of maternal pertussis vaccination in England: an observational study

Gayatri Amirthalingam, Nick Andrews, Helen Campbell, Sonia Ribeiro, Edna Kara, Katherine Donegan, Norman K Fry, Elizabeth Miller, Mary Ramsay

**Summary**

**Background** In October, 2012, a pertussis vaccination programme for pregnant women was introduced in response to an outbreak across England. We aimed to assess the vaccine effectiveness and the overall effect of the vaccine programme in preventing pertussis in infants.
• Everything is vague to a degree you do not realize till you have tried to make it precise
  
  Bertrand Russell

• I was working on the proof of one of my poems all the morning, and I took out a comma. In the afternoon I put it back again.

  Oscar Wilde
• Reading maketh a full man, conference a ready man, and writing an exact man
  Sir Francis Bacon

• A writer is a person for whom writing is more difficult than it is for other people
  Thomas Mann
The pages are still blank but there is a miraculous feeling of the words being there, written in invisible ink and clamoring to become visible.

Vladimir Nabokov
THE PAST,
THE PRESENT,
AND THE FUTURE
WALKED INTO A BAR.
IT WAS TENSE.