ELSEVIER

Vaccine

TIPS FROM A JOURNAL EDITOR FOR GETTING YOUR MANUSCRIPT ACCEPTED

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Workshop on Scientific Writing in Field Epidemiology
Hua Hin / Cha Am, Thailand, 4-8 February 2013

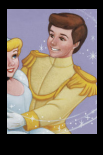
1

Planning a Manuscript

Ensure the study design adheres to fundamental principles of the scientific method.

- Successful publication determined by how well the experiment/study was designed and performed
- Editorial wizardry cannot turn the frog of a flawed, unscientific study into the prince of an outstanding publication





2

Planning a Manuscript - 2

- Before starting the study, consult a statistician
  - Ensure sample sizes suitable for comparisons, and study design is sound
  - Too many submissions with only 3-to-5 mice per arm
  - Unacceptable excuse: "too expensive or difficult to use larger numbers"
- Future manuscript will need to explain and justify your statistical model and its assumptions

3

Use Traditional Structure

Introduction, Methods, Results, and Discussion, except for good cause.

- Aids logical flow of ideas
- Easier to follow for readers (and reviewers)
- Special types of articles do not use this structure
  - Reviews of a subject
  - Editorials
  - Meeting report or conference proceeding
  - Case report

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Use Traditional Structure - 2

- Authors sometimes misallocate their phrases and sentences to the wrong section
  - Explains background/reasons for study? → **Introduction**
    - *"… little knowledge of this antibiotic in infants …"*
  - Describes what was done? → **Methods**
    - *"… determined mean inhibitory concentrations (MICs) …"*
  - Reports data generated? → **Results**
    - *"… 17 (68%) of 25 subjects had MICs greater than …"*
  - States implications, compares with others? → **Discussion**
    - *"… second study in this age group …" "… much higher MICs than reported by Somsak, et al via intravenous route."*

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The Introduction

The Introduction provides the why *of your study*

- Puts work into context
  - Educates reader in regard to the study
    - Particular field and area of the research
    - Current understanding and relevant issues
      - Cites key publications by others
      - Avoid extensive literature review!
  - Gaps in knowledge the study aimed to fill

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The Introduction - 2

The Introduction provides the why *of your study*

- Set readers' expectations
- Explain purpose of study
  - Why was study performed?
  - What is key research question to be answered?
  - Be precise
- Justify why it deserves space in print

The Methods

The Methods section details the who *and* how *and* when *of your study.*

- Establishes the study
- Details for others to replicate your work
  - Study design
    - Case-control, cohort, randomized, etc.
    - Observation or intervention integrity
      - E.g., blinding
  - Components
    - Subjects
      - Recruitment, eligibility, etc.
    - Experiment applied, assays performed, etc.

The Methods - 2

- Components (continued)
  - Materials used
    - Reagents, animals, software, sources, etc.
  - Statistics
    - Describe models used to test and claim "significance"
  - Ethical oversight for human or animal studies
    - Briefly mention the specific committees which approved the work, if relevant

The Methods - 3

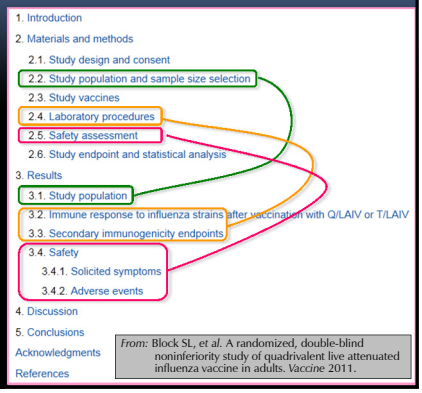
- Mention the *when* of study
  - May be relevant for secular trends
    - E.g., influenza seasons
  - Report dates work performed, to relevant detail
    - Start date to finish date of enrolled subjects
    - Start date to finish date of intervention
    - Month(s) and year(s), where season relevant
    - Year(s) alone may be sufficient
- Mention the *where* of study
  - Institution(s), city, country

The Methods - 4

- Describe study steps in some logical order
  - By importance:
    - most → least important
  - By perspective:
    - broad view → details
  - By chronology:
    - early → later
- Sequence should be as similar as practicable with order to be used in Results

The Methods - 5

- Use parallel structure
  - Follow similar order in Methods and Results



The Methods - 6

- Be quantitative in describing your sample
- Ensure numbers add up for "dropouts"
- Provide numerators/denominators so readers can do or check percentage calculations
- (Some report such subject numbers in Results)

Methods: " ... In recruiting our protocol-designated limit of 450 subjects for the study, we invited 517 to view the explanatory video, of which 482 did so and 461 were willing to have the consent form explained to them. The first 450 of these who volunteered and signed the consent form were thus formally recruited into the study. Of these, 4 (0.9%) subsequently withdrew their consent before any investigational doses were administered, 7 (1.6%) withdrew their consent after one or more doses were received but before followup serum could be collected, 6 (1.3%) failed to return before any post-vaccination serum could be collected and could not be found upon outreach by telephone or letter, and 2 (0.4%) were withdrawn before serum was obtained because of delayed discovery of contraindicating exclusion criterion (seizure disorder) and death (automobile trauma). Thus, sera from a total of 431 subjects were available for assay and analysis. ... "

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ANALOGY

- Methods = *"parents"*
  - *It takes parents to make children*
- Results = *"children"*
  - *It takes children to make grandchildren*
- Conclusion = *"grandchildren"*

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The Methods - 7

- Avoid "*childless methods*"
  - No mention in Results of finding or outcome of a procedure described in Methods
- Provide at least one finding in Results to justify every activity in Methods
  - E.g., if Methods says "We surveyed parent preferences for injection method."
    - Then, for example, add in Results:
      - "Parents preferred by two to one the jet injector over the needle-and-syringe (data not shown)."
- If no result to be reported, do not mention in Methods

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The Results

The Results section (+ tables and figures) reports what *you found*

- ***ORGANIZE AND FINISH TABLES AND FIGURES FIRST !***
  - Before writing a single word of outline or text
  - Allows significance of results to become clear
  - Helps "see" and comprehend one's findings

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The Results - 2

- Results text
  - Highlight general results and key findings from tables and figures
  - Point readers to location to prove the finding
    - E.g., "(Figure 1)" "(Tables 2 and 3)"
  - Do not put into words all data in tables/figures
  - Follow similar order as Methods
    - Most important → least important ?
    - Overview perspective → details ?
    - Chronologically ?

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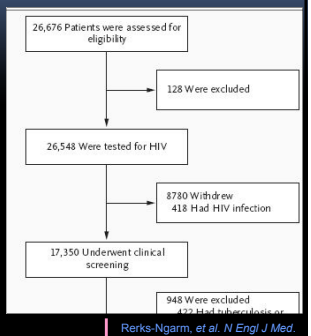
The Results - 3

- Accounting for subjects
  - Keep track of subjects like a bank does your money
  - Where did every *Baht* and *satang* go?
  - (Some put in Methods)
- Flow chart shows how subjects recruited and "dropped out" from analyses
  - Missing subjects raises suspicions of biased work



Rerks-Ngarm, *et al. N Engl J Med.* 2009;361;23:2209-2220

Continued

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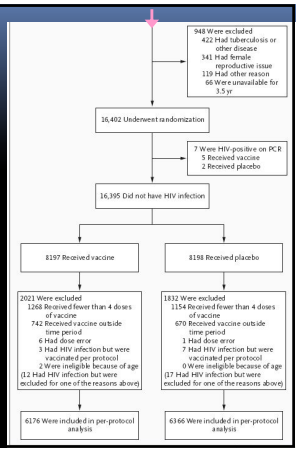
The Results - 4

- Flow charts required for clinical trials
  - See CONSORT rules
    - www.consort-statement.org
  - Useful for all studies, even if not submitted with manuscript



Rerks-Ngarm, *et al. N Engl J Med.* 2009;361;23:2209-2220

The Results - 5

- Most results are in the form of *probabilities*
  - Percentage, proportion, rate, ratio, prevalence, incidence (cases/events per some *population at risk*)
  - Provide numerators and denominators to allow readers to see how determined

Results: "... Among the 431 subjects from whom post-vaccination sera were available among 450 initially recruited, 141 (32.7%) had been allocated randomly to the investigational **ID-0.1mL** group, 146 (33.9%) to the investigational **IM-0.1mL** group, and the remaining 144 (33.4%) to the **IM-0.5mL** control group. The proportions of these groups which satisfied the criteria of the EMEA for influenza seroconversion [14] were 76% (107/141), 71% (104/146), and 79% (114/144), respectively, which demonstrated *non-inferiority* between both of the low-dose ID and IM groups and their comparator, the full-dose group. ..."

The Results - 6

- ANALOGY: Avoid "*orphan results*"
  - No mention in Methods of the process that yielded data reported in Results
- Include at least a brief "method" in Methods for even minor results reported
  - E.g., if Results say:
    - "Subtype B virus was identified in 10% (3) of 30 subjects"
  - Then add at least something to Methods, e.g.:
    - "Virus serotyping was performed by standard methods described elsewhere [23]."

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The Discussion

The Discussion section conveys the "so what?" and "who cares?" of the study

- Interpret results, explain significance, draw conclusions
  - May reiterate principal findings
    - But phrase differently from Results
- Relate to original research question(s) and formal hypothesis(es)
- Compare with work by others in this field
  - Partial reprise of Introduction and its citations
  - Corroborates prior work? Contradicts it?

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The Discussion - 2

- Point out weaknesses and limitations
  - (See later slide for details)
- With such caveats, you earn the privilege to speculate *modestly* on implications of study
  - How it may add to knowledge base of the field
  - How it may affect disease prevention, patient care, new diagnostics, technology development, etc.
  - Future followup studies

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The Discussion - 3

- Avoid a "virgin birth"
  - A *conclusion* in the Discussion …
    - … without any antecedent *conception* (*"grandparents"*) in Methods
    - … without any *gestation* of supportive evidence (*"parents"*) in Results

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The Discussion - 4

- Point out limitations of study to reviewers, editors, all the world
  - Often hardest aspect of writing a paper
  - Possible things wrong with conception, design, implementation, and analysis
  - Alternative explanations for findings
  - Other research with opposite results
- Reviewers are more comfortable accepting papers so "immunized" from possible error

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Four Steps to a First Draft

1. Select a Structure
2. Create an Outline
3. Identify *Key Terms*
4. Write for Flow

Give credit when due

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft"

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Four Steps to a First Draft
Step 1: Select a Structure at Two Levels

- 1st level determined by nature of writing
  - Original scientific manuscript
  - Narrative review
  - Commentary
  - Grant application
- 2nd level determined by target and content
  - Specific journal
  - Specific funding organization

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 27

Four Steps to a First Draft
Step 1: Select a Structure: Original Scientific Manuscript

I. Introduction
- *a.k.a.* "Background"

II. Methods
- *a.k.a.* "Materials and Methods"

III. Results

IV. Discussion
- *a.k.a.* "Conclusions"

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 28

Four Steps to a First Draft
Step 2: Create an Outline – The "Skeleton" Flesh Out *Future* Details

- Introduction
  - Explain field, issues, knowledge, and gaps
  - Limited citations to prior work
  - Nature and purpose of study
- Methods
  - List and detail all steps and processes
    - Organize in logical order, chronological order, etc.
    - Statistics, ethical oversight, when and where
- Results
  - Parallel order and structure as Methods
  - Describe the study population at baseline
  - Provide findings generated by the Methods

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 29

Four Steps to a First Draft
Step 2: Create an Outline – The "Skeleton" Flesh Out *Future* Details - 2

- Discussion
  - Major findings of this work
  - Limitations (in their proper place)
  - Its place among other work so far
  - Concluding paragraph
    - Puts the research in a positive light
    - Restate the major findings
    - Emphasize how this allows others to proceed
    - Describe future work

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Four Steps to a First Draft
Step 2: Create an Outline – Example

I. Introduction
II. Methods
- A. Study participants
- B. Vaccination and collection of blood samples
- C. Clinical assessment
- D. Antibody response assay
- E. Candidate genes and SNPs
- F. Statistical analysis

III. Results
- A. Demographic findings
- B. Safety
- C. Immune responses
- D. Genetic associations

IV. Discussion

Try to maintain parallel structure, same order, between Methods and Results

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Four Steps to a First Draft
Step 3: Identify Key Terms

- Key terms = words or phrases that name important ideas in the paper
  - Technical: e.g., *immunoglobulin, mutation, infarction*
  - Nontechnical: e.g., *increase, function, similarity*

Source: Mimi Zeiger, Essentials of Writing Biomedical Research Papers, 2000 32

Four Steps to a First Draft
Step 3: Identify Key Terms - 2

- Importance of key terms
  - Striving for reader comprehension
  - Use to form paper's title
  - Use to name concepts and components
  - Use to link sentences
    - Help reader follow your order of ideas
    - Help reader understand your writing

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 33

Four Steps to a First Draft
Step 3: Identify Key Terms - 3

- Repeat key terms nearly exactly (avoid synonyms)
  - Provides continuity between sentences and paragraphs
  - Avoids mental manipulation
    - Knowledgable readers may understand synonym
    - Unfamiliar readers may not know the synonym

Source: Mimi Zeiger, Essentials of Writing Biomedical Research Papers, 2000 34

Four Steps to a First Draft
Step 3: Identify Key Terms - 4

- Bad example

  "Digitalis increases the contractility of the mammalian heart. This change in inotropic state is a result of changes in calcium flux through the muscle cell membrane."
  - What is *inotropic state*? Ans.: Same as *contractility*
- Good revision for improved comprehension

  "Digitalis increases the contractility of the mammalian heart. This increased contractility is a result of changes in calcium flux through the muscle cell membrane."

Source: Mimi Zeiger, Essentials of Writing Biomedical Research Papers, 2000 35

Four Steps to a First Draft
Step 3: Identify Key Terms - 5

- Abuses of key terms
  - Conversion in mid-stream to new term
    - "Viscerotropic adverse event" shows up later as "VAE" (without introducing the abbreviation)
    - Replaced by shorter synonym (even if good writing)
      - "Viscerotropic adverse event" later called "disease"
      - "17D virus" later called "vaccine virus"
  - Replacement with ambiguous pronouns
    - Too many words or phrases intervene between noun and pronoun "it" to make ambiguous

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Step 4. Write for Flow

- Gopen & Swan principles:
  - Sentence should begin with *Old Information*
    - Usually introduced in a prior sentence
    - Readers already familiar with it
  - Sentence provides *New Information* at its "*stress position*" at or near end of sentence
  - Next/nearby sentence/paragraph:
    - *New Information* becomes *Old Information*

Old Info. → *New Info.*
↘
Old Info. → *New Info.*
↘
Old Info. → *New Info.*

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Step 4. Write for Flow - 2

- At the beginning of sentence ("topic position"):
  - Place the person or thing whose "story" you are telling
  - Already known and familiar Old Information
  - Usually the grammatical "subject" of the sentence
  - Provides the important link to prior sentences
  -
- At the end of the sentence ("stress position"):
  - Place the New Information you want the reader to learn
  - This provides the important link to future sentences

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Step 4. Write for Flow - 3

- Sample sentence:
  - "When key regulatory pathways that control cell proliferation are subverted, genes with latent transforming potential (proto-oncogenes) can become oncogenes. … "
- Bad next sentence:
  - "… Several subfamilies of G-protein-coupled receptors, such as serotonin and muscarinic cholinergic receptors, can activate these proto-oncogenes"
- Why?

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft"
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Step 4. Write for Flow - 4

- Sample sentence:
  - "When key regulatory pathways that control cell proliferation are subverted, genes with latent transforming potential (proto-oncogenes) can become oncogenes. … "
- Bad next sentence:
  - "… Several subfamilies of G-protein-coupled receptors, such as serotonin and muscarinic cholinergic receptors, can activate these proto-oncogenes"
- Why? Old and New information in wrong positions

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Step 4. Write for Flow - 5

- Sample sentence:
  - "When key regulatory pathways that control cell proliferation are subverted, genes with latent transforming potential (proto-oncogenes) can become oncogenes. … "
- Bad next sentence:
  - "… Several subfamilies of G-protein-coupled receptors, such as serotonin and muscarinic cholinergic receptors, can activate these proto-oncogenes"
- Good next sentence:
  - "… These proto-oncogenes are activated by subfamilies of G-protein-coupled receptors, such as serotonin and muscarinic cholinergic receptors."

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Step 4. Write for Flow - 6

- Begin paragraphs with the *topic sentence*
  - Provides overview of what paragraph or next sentences will cover, e.g.:
    - "Prevention programs for AIDS involve a number of interacting components, including … ."
    - "A complex of proteins mediate transcriptional silencing at selected regions of the yeast genome."
  - Provides linkages
    - To preceding paragraph, if not preceding sentence
    - To next sentences, helping reader anticipate new material

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Step 4. Write for Flow - 7
Five Paragraph Progression Structures

1. Progression around a constant topic
   - Key term appears in each sentence
2. Progression through sub-categorization
   - Subsequent sentences address each subcategory
3. Chain progression
   - Key terms daisy chain sentence to sentence
4. Progression through time or order
5. Progression through shrinking Venn diagram enclosures

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 43

Step 4. Write for Flow - 8
1. Progression around Constant Topic

- _____ ➔ new **B**
- old-**B** ➔ new **C**
- old-**B** ➔ new **D**
- old-**B** ➔ etc.

"During the last decades, safe and effective live-attenuated **varicella vaccines** have been developed. The **vaccines** are used in **childhood immunization programs in many countries** [1]. All of the currently available **varicella vaccines** derive from a Japanese varicella-zoster virus (VZV) **wild-type strain** isolated from a **child** with typical varicella **named Oka** (parental Oka, pOka)."

Sauerbrei A, et al. Immune response of varicella vaccinees to different varicella-zoster virus genotypes. Vaccine 2011;29:3873-3877.

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 44

Step 4. Write for Flow - 9
2. Progression by Sub-Categorization

- old-**A** ➔ new **B+C**
- old-**B** ➔ new **D+E+F**
- old-**D** ➔ new **G+H**
- old-**C** ➔ new **I+J**

The **objective** was to determine the **immunogenicity** and **safety** of one or two injections of the XRX-001 vaccine at two dose levels. The **coprimary immunogenicity outcomes** were the **proportion of subjects with seroconversion** and the **geometric mean titer of neutralizing antibodies**. **Secondary outcomes** were the **distribution of titers** and **duration of antibody response**. Safety was assessed on the basis of **local and systemic reactions** and **clinical laboratory abnormalities**.

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Step 4. Write for Flow – 10
2. Progression by Sub-Categorization - 2

- old-**A** ➔ new **B+C**
- old-**B** ➔ new **D**
- old-**C** ➔ new **H**+old-**A**

A live attenuated **vaccine (17D)** developed in 1936 is widely used, with approximately **20 million doses** distributed annually.

Although remarkably immunogenic, the **17D vaccine** may cause serious **viscerotropic** and **neurotropic** adverse events and anaphylaxis.

Viscerotropic disease is a fulminant 17D virus **infection of the liver and visceral organs** resembling naturally acquired yellow fever.

Neurotropic disease typically follows **invasion of the brain** by the replicating **vaccine virus**.

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 46

Step 4. Write for Flow - 11
3. Progression by Chaining

- new-**A** ➔ **B**
- old-**B** ➔ **C**
- old-**C** ➔ **D**
- old-**D** ➔ …

The protein when it is first made exists in an extraordinarily large variety of shapes, resembling those accessible to a flexible strand of spaghetti. The Brownian motion of the protein strand will carry it willy-nilly between various shapes, somehow finally getting it to settle down into a much less diverse family of shapes, which we will call the native structure of the protein. The average native structures …

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft" 47

Step 4. Write for Flow - 12
4. Progression through Time or Order

- Ordered by chronological or logical steps
  - "First, …"
  - "Second, …"
  - "Third, …"
  - "Fourth, …"

In **step one** of the survey, we listed all villages in the province. The **second step** required listing each of their estimated populations from the 2000 census.[23] Using a random-number generator, in **step three** we selected a total of 20 villages, for whom cluster sampling was performed in **step four** by trained field teams. **Step five** involved assay of specimens and analysis of the data.

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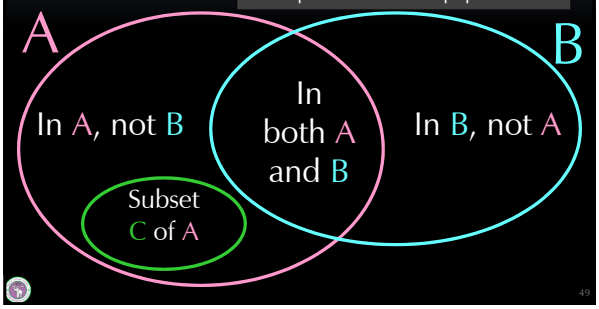
Step 4. Write for Flow - 13
5. Progression by Shrinking Venn Diagrams

Background: Venn diagrams Illustrate overlaps and subsets of populations



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Step 4. Write for Flow – 145.
Progression by Venn Diagram - 2

- Shrinking subsets reflected in flow chart

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Step 4. Write for Flow – 15
5. Progression by Venn Diagram - 2

- Population **A** ➔ shrinks into subset **B**
- Subset **B** ➔ shrinks into subset **C**
- Subset **C** ➔ shrinks into subset **D**
- Subset **D** ➔ shrinks into subset **E**

We invited all **127 married HIV-discordant couples** attending the university's HIV clinic to **view the explanatory video about the study, and 106 did so**. Of these, **101 were willing to listen to verbal explanation of the consent form**. Of these **57 volunteered** and after signing the consent form were **enrolled and vaccinated**. Of these, 6 couples (11%) withdrew their consent before followup serum could be collected. For another 3 (5%), insufficient serum was collected, leaving **48 specimens available for assay and analysis**.

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Step 4. Write for Flow - 16
How Important is This?

"In the end your writing is not what you mean it to be, but what the reader interprets it to be.

"Meeting your readers' expectations facilitates their interpretation.

*"When you fail to meet their expectations, they may insert interpretations to redress their expectations."**

* Gopen GD, Swan JA. The science of scientific writing. American Scientist (Nov-Dec) 1990;78:550-558.

With grateful acknowledgment to Robert M. Jacobson, Mayo Clinic "Writing a First Draft"

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Tables
Lay out tables to help interpretation

- Keep together results requiring direct comparison
  - Minimize required eye movements of the reader
  - Stratify to put research question results side-by-side

1.

A(H1N1)		A(H3N2)		B	
ID [a]	IM [b]	ID [a]	IM [b]	ID [a]	IM [b]
result	result	result	result	result	result

2.

ID			IM		
A(H1N1)	A(H3N2)	B	A(H1N1)	A(H3N2)	B
result	result	result	result	result	result

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Tables - 2
Titles, Footnotes, Appearance

- Use titles of tables that completely explain the content
  - Do not require reader to read text
  - Table should stand by itself
- Provide denominators for all proportions
- Use footnotes
  - To explain details of row and column labels
  - Define all abbreviations, even if defined in text
    - Subsequent tables (and figures) using same abbreviations may refer back to first table where defined

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Tables - 3

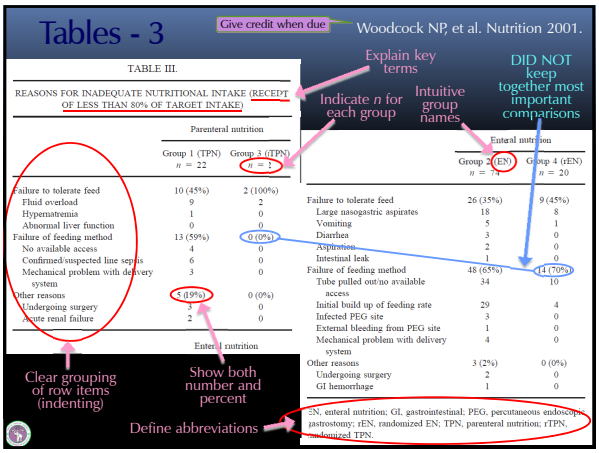


TABLE III.

REASONS FOR INADEQUATE NUTRITIONAL INTAKE (RECEIPT OF LESS THAN 80% OF TARGET INTAKE)

	Parenteral nutrition	
	Group 1 (TPN) $n = 22$	Group 3 (TPN) $n = 1$
Failure to tolerate feed	10 (45%)	2 (100%)
Fluid overload	9	2
Hypernatremia	1	0
Abnormal liver function	0	0
Failure of feeding method	13 (59%)	0 (0%)
No available access	4	0
Confirmed/suspected line sepsis	6	0
Mechanical problem with delivery system	3	0
Other reasons	3 (19%)	0 (0%)
Undergoing surgery	3	0
Acute renal failure	2	0

	Enteral nutrition	
	Group 2 (EN) $n = 74$	Group 4 (rEN) $n = 20$
Failure to tolerate feed	26 (35%)	9 (45%)
Large nasogastric aspirates	18	8
Vomiting	5	1
Diarrhea	3	0
Aspirations	2	0
Intestinal leak	1	0
Failure of feeding method	48 (65%)	14 (70%)
Tube pulled out/no available access	34	10
Initial build up of feeding rate	29	4
Infected PEG site	3	0
External bleeding from PEG site	1	0
Mechanical problem with delivery system	4	0
Other reasons	3 (2%)	0 (0%)
Undergoing surgery	2	0
GI hemorrhage	1	0

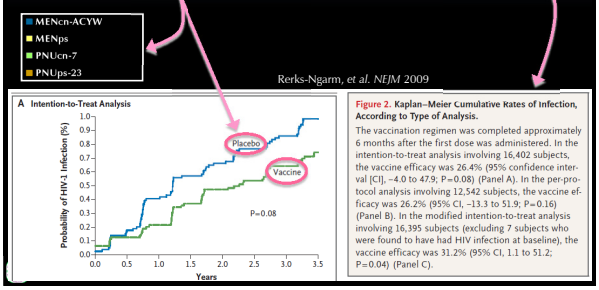
EN, enteral nutrition; GI, gastrointestinal; PEG, percutaneous endoscopic gastrostomy; rEN, randomized EN; TPN, parenteral nutrition; rTPN, randomized TPN.

Graphs

- Principles
  - Appropriateness:
    - Show data not easily understandable in text or table
  - Efficiency:
    - Convey maximum data using minimal ink
  - Independence:
    - Figure and its legend should stand by itself without reference to text
    - Use titles and legends that explain the content

Graphs - 2

- Legends
  - Caveat: there are two common uses of term "legend"
    - The explanation text that accompanies the figure
    - The code to explain colors or icons in the figure
      - Sometimes known as the *"key"*



Graphs - 3

- Legends should:
  - Indicate clearly number of subjects (mice or men) in each study arm (investigational or control)
  - Provide both high and low sampling error bars, if relevant
    - Define their nature
      - 95% C.L., Standard Error (of mean), Standard Deviation
      - In general, avoid SD as it does not reflect sample size

Graphs - 4

Complete text explanation
Show both high-low sampling error bars
Bar shadings that work in black-white.
No solid blacks to hide lower error bar

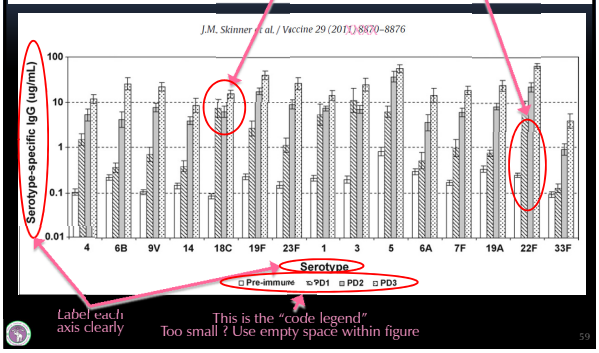


Fig. 4. PRE, PD1, PD2, and PD3 IgG concentrations of infant rhesus monkeys immunized with PCV-15. Data are represented as the geometric mean concentration with the error bars representing one standard error from the geometric mean (n = 8 infants/group).

Graphs - 5

- Dot plots preferable than bar graphs
- "Jitter" to see all datapoints
- Twin lines can show central tendency and high-low error
- Show sample size, skew
  - Hidden by bar graphs

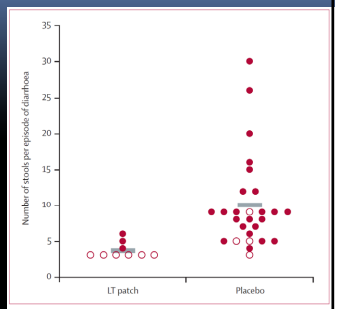


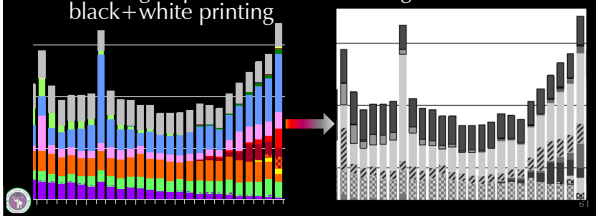
Figure 2: **Severity of diarrhoeal episodes and number of stools by treatment group**
Cumulative stools from individual episodes in LT-patch recipients versus placebo recipients, including analysis population as well as two individuals who had more than one episode (two and three episodes, respectively). Solid spot=moderate to severe episode. White spot=mild episode. Solid bar=mean number of diarrhoea stools per group. Note that placebo-to-vaccine rate

Frech, et al. Lancet 2008

Graphs - 6

Do not rely on color alone in graphs and charts to distinguish data points, lines, and shapes

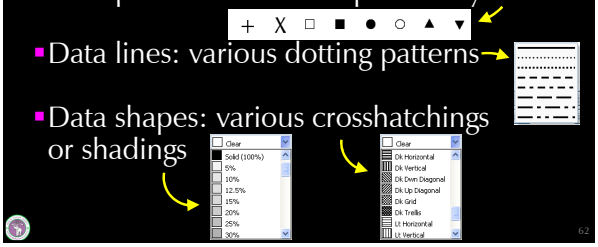
- Consider readers without color printers; color blind
- Ensure groups and series are distinguishable in black+white printing



Graphs - 7

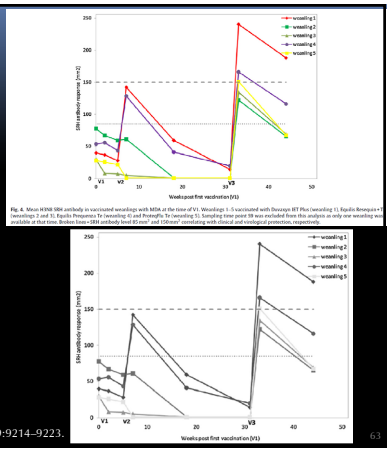
Do not rely on color alone in graphs and charts to distinguish data points, lines, and shapes

- Data points: various shapes and symbols
- Data lines: various dotting patterns
- Data shapes: various crosshatchings or shadings



Graphs - 8

- Example of color problem
  - Indistinguishable in black-white printout
  - Various datapoint symbols are too small to help
- Be kind to reviewers and readers



Gildea S, et al. Vaccine 2011;29:9214–9223.

Graphs - 9

Flow Chart Examples

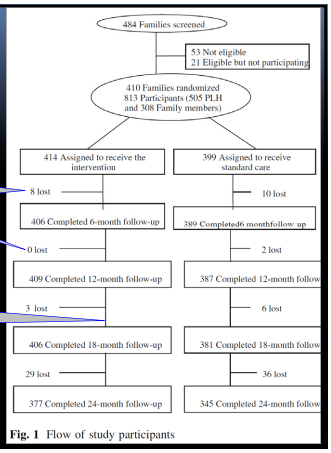
- Flow charts required only for intervention and cohort trials
  - But useful, even if never published
  - Helps keep track of your subjects
- Top to bottom vertical flow
  - Chronological sequence
- Right or left flow
  - Exclusions and losses to followup

Graphs – 10

Flow Chart Bad Examples

CRITIQUE: Place all subjects in boxes, not loose in the table

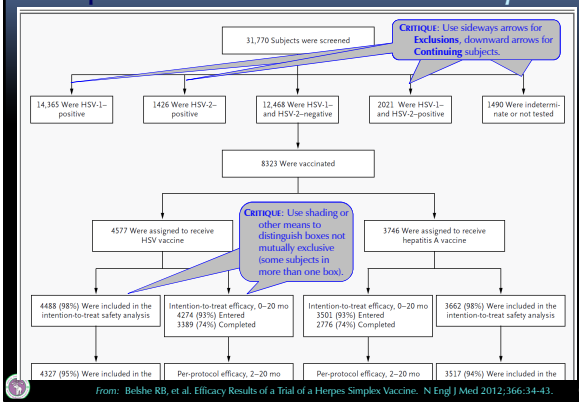
CRITIQUE: Use arrows to connect boxes to make flow clear, not just lines



From: Li L, Liang L-J, Lee S-J, Iamsirithaworn S, Wan D, Rotheram-Borus MJ. Efficacy of an intervention for families living with HIV in Thailand: A randomized controlled trial. AIDS Behav 2011.

Fig. 1 Flow of study participants

Graphs – 12 *Flow Chart Bad Examples*



From: Belshe RB, et al. Efficacy Results of a Trial of a Herpes Simplex Vaccine. N Engl J Med 2012;366:34-43.

Abstracts

Compose the Abstract last, not first; ensure it contains quantitative content, not promises.

- Only after
  - Finishing the Discussion …
  - … which was based on evidence in Results …
  - … which was produced by Methods …
  - … which was envisioned by Introduction …
  - … do you really know for sure what the Abstract should say
- Select and summarize the major highlights of each section to comprise the Abstract
- Every section merits at least a phrase or sentence in the Abstract.

67

Abstracts - 2

- Give busy readers specific, hard numbers and facts from your work
  - The abstract may be all they have the time to read
  - If interested in details, they will read the main parts
- Do not "advertise" what the full paper will say, teasing readers so they "buy the product" to learn its findings
- Even complex research can be generalized for summary in the Abstract

68

Abstracts - 3

- Unsatisfying Abstract (**Vaccine** 2006;24/S3:S178-186)
  - Economic model of vaccine usage (**HPV**)
  - Hard to discern surrogate phrases/sentence standing in for each section of paper
  - No data
  - Promises the paper will "highlight" things
    - What "different models" were "explored"?
    - What "model results are consistent" in predicting utility?

Abstract

The impact of human papillomavirus (HPV)-16/18 vaccination on the incidence of infection and disease can be explored in a range of different models. Here we explore the epidemiological and economic impact of vaccination where screening is absent and where it is well established. The importance for epidemiology of assumptions about naturally-acquired immunity and heterogeneity in risk behaviours are highlighted, as are the importance for health economic outcomes of vaccine costs and the ability to modify screening strategies. To date, model results are consistent in predicting a useful role for vaccine, but further epidemiological data are required to help test the validity of models.

69

Abstracts - 4

- Excellent Abstract example (**Vaccine** 2010;28:3856-3864)
  - Each section of paper represented, in order
  - Has quantitative data!

I.
M.
R.
D.

ABSTRACT

A complete economic study was carried out to assess the economical impact of two rotavirus vaccine in Colombia. A Markov decision model was built to assess the health outcomes from birth to 24 months of age for three hypothetical cohorts: one unvaccinated, one vaccinated with 2 doses of Rotarix™ and the third, with 3 doses of Rotateq™. Without vaccination, the annual number of medical visits by diarrhea in children under 2 years would be 1,293,159 cases, with 105,378 medical visits and 470 deaths (IC95% 295–560) related to rotavirus. Without vaccination, rotavirus disease would cost around USD$8 millions including direct and indirect costs. Assuming a cost per dose of USD$7.5, average cost-effectiveness ratio would be USD$663/DALY with Rotarix and USD$1391 with Rotateq. When price per dose falls below USD$7 both vaccines yield a similar average cost-effectiveness ratio (USD$1063/DALY). Incremental cost-effectiveness ratio of Rotateq versus Rotarix was USD$7787/DALY. Cost-effectiveness ratio was influenced mainly by vaccine cost and cost per case hospitalized. Other programmatic aspects such as number of doses to be applied, likelihood of completing vaccination schedule with shorter versus longer schedules, and storage space within the chain cold should be considered to make decisions on which vaccine should be introduced. In conclusion, vaccinating against rotavirus in Colombia with either vaccine would be very cost effective. If cost per vaccinated children falls below USD$3 per dose vaccination would be cost saving.

70

Peer Review

Sympathize with reviewers.

Harper's Magazine, May 2011

[Critiques]

JEER REVIEW

From comments appended to manuscripts under consideration by reviewers for the journal Environmental Microbiology. *The journal publishes a selection of reviewer comments each year in its December issue.*

The biggest problem with this manuscript, which has nearly sucked the will to live out of me, is the terrible writing style.
More explanation is required; most readers will not know what "krigged" means.
The trees are crap, but, besides this, excellent work.
The Abstract describes results that I could not find in the Results section.
This is an interesting manuscript, not because of its results, but because of its complete ignorance of due scientific process.

"Hijacked" is a very dramatic word; maybe the bacteria are more polite with their biosynthesis.
I felt like I was teaching my grandmother to suck eggs. Accept with minor revision.
"Gentile" stream of nitrogen. It is not clear why this stream needs to be non-Jewish.
I like lipids, but they have their limitations, which appear to have been overlooked.
I recommend that this manuscript be rejected because I can't figure out what they did.
This was a possible candidate for the "worst use of statistics to substantiate a falsehood" award.
I'm not convinced that they know what they're talking about.
I nearly said reject, but then I recalled that I have a hangover and am feeling grumpy.
For the sake of time I have listed only a few (thirteen!) of the most glaring errors.
Alfachetoglutarate
The finding is not novel and the solution induces despair.

Peer Review - 2

- Volunteers
  - Hurried, tired, busy
  - Unconscious factors in play
    - Time of day, hunger, interruptions
- Make their work as easy as possible
  - Write for generalists (reviewers and readers)
    - Not necessarily familiar with your field's jargon
  - Label clearly
    - Pages, lines, figures, tables
  - Define clearly
    - Terms, abbreviations

72

Follow Journal Instructions

Follow instructions of the journal's Information for Authors section.

- Found at journal's website
  - E.g., http://www.elsevier.com/locate/inca/30521/authorinstructions
  - Or in printed issue of journal
- Provides details on structuring your manuscript
  - Labeling and numbering sections
  - Preparing tables and figures
  - Citing references
- Examine recent articles in journal as examples

73

Follow Journal Instructions - 2

- For example, if journal specifies following symbols as data points of curves in graphs ... :

  \+ X □ ■ ● ○ ▲ ▼

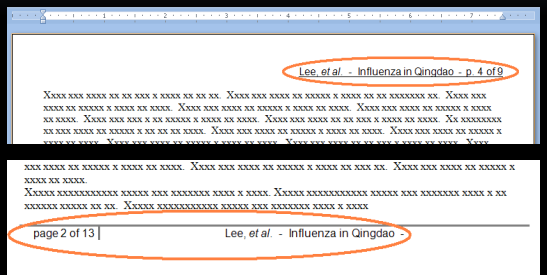
  ... Use them.

- Follow guidance for endnotes and footnotes within text, tables, and figures
  - E.g.: [a, b, c, d] or [1, 5, 7-9] or [1,5,9] or (1,5,7-9)

74

Make the Reviewer's Work Easier

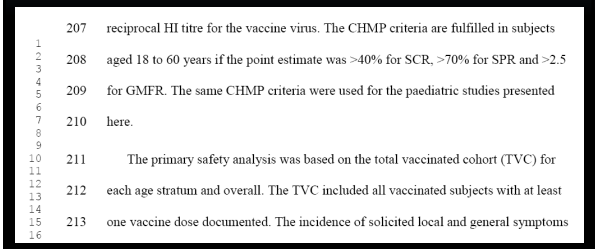
- Headers or footers help find places and assemble printouts



75

Make the Reviewer's Work Easier - 2

- Use continuous line numbering
  - Avoids having to specify page number in reviews



207 reciprocal HI titre for the vaccine virus. The CHMP criteria are fulfilled in subjects
208 aged 18 to 60 years if the point estimate was >40% for SCR, >70% for SPR and >2.5
209 for GMFR. The same CHMP criteria were used for the paediatric studies presented
210 here.
211 The primary safety analysis was based on the total vaccinated cohort (TVC) for
212 each age stratum and overall. The TVC included all vaccinated subjects with at least
213 one vaccine dose documented. The incidence of solicited local and general symptoms

76

Follow Journal Instructions - 5

- Following journal style demonstrates authors pay attention to detail
  - Increases credibility for underlying research
    - Protocol followed correctly?
- Not following style may raise doubts about quality
  - Borderline manuscripts may be tipped into "reject"

77

Write Well
Titles should describe the work clearly

- Article titles
  - Title should orient reader to the entire work
  - Convey key finding:
    - Poor: "Study of mobile telephone use and brain cancer"
    - Good: "Lack of association between mobile telephone use and brain cancer"
    - Good: "Mobile telephone use increases the risk of automobile collisions"
- Figure and table titles
  - Each fully-titled to explain their context without reference to Intro, Methods, or Results sections.

CREDIT FOR SOME TIPS AND EXAMPLES:
Michael Alley, Pennsylvania State University, (http://www.writing.engr.psu.edu)
Nicole Kelley, Mass. Institute of Technology, (web.mit.edu/me-ugoffice/communication/)

78

Write Well - 2
Connect sentences with variety

- Boring bad example (11 sentences):
  - *"Mount St. Helens erupted on May 18, 1980.*
  - *A cloud of hot rock and gas surged northward from its collapsing slope.*
  - *The cloud devastated more than 500 square kilometers of forests and lakes.*
  - *The effects of Mount St. Helens were well documented with geophysical instruments.*
  - *The origin of the eruption is not well understood.*
  - *Volcanic explosions are driven by a rapid expansion of steam.*
  - *Some scientists believe the steam comes from groundwater heated by the magma.*
  - *Other scientists believe the steam comes from water originally dissolved in the magma.*
  - *We need to understand the source of steam in volcanic eruptions.*
  - *We need to determine how much water the magma contains."*

CREDIT: Michael Alley, Pennsylvania State University 79

Write Well - 3
Connect sentences with variety

- Pleasing, interesting example (10 sentences):
  - *"Mount St. Helens erupted on May 18, 1980.*
  - *Its slope collapsing, the mountain emitted a cloud of hot rock and gas.*
  - *In minutes, the cloud devastated more than 500 square kilometers of forests and lakes.*
  - *Although the effects of the eruption were well documented, the origin is not well understood.*
  - *Volcanic explosions are driven by a rapid expansion of steam.*
  - *Recently, debate has arisen over the source for the steam.*
  - *Is it groundwater heated by magma or water originally dissolved in the magma itself?*
  - *To understand the source of steam in volcanic eruptions, we have to determine how much water the magma contains."*

CREDIT: Michael Alley, Pennsylvania State University 80

Write Well - 4
Define unfamiliar terms

- At first mention, *italicize* and define new terms
- Define directly or indirectly
  - Directly
    - "For purposes of this review, we defined *cutaneous vaccination* as delivery of antigen by all methods anywhere into or onto the skin."
  - Indirectly
    - "Fertility in Thailand started to decline in the late 1960s, reaching as early as the late 1980s the *replacement rate* of 2.1, the average number of births to women of child-bearing age needed to maintain a steady population (Hirschman, *et al*. 1994)."

81

Write Well - 5
Use intuitive and consistent abbreviations

- Always define abbreviations, even common ones
  - "Human immunodeficiency virus (HIV)"
  - "Hemagglutination inhibition assay (HAI)"
- Define abbreviations at first use in (1) abstract, (2) text, and (3) in each table/figure footnote
  - Then provide abbreviation only for remainder of uses
  - When definitions extensive, footnotes of first table or first figure can provide them
    - Footnote in later table(s)/figure(s) refers back to prior one for definitions

82

Write Well – 6
Use descriptive labels for study groups

- Avoid generic labels
  - "**Group A**", "**Group B**", "**Group C**"
  - Forces forgetful, busy readers back again to Methods
- Use intuitive names that convey group identity
  - "**0.1mL ID**", "**0.1mL IM**", "**0.5mL IM**"
  - "**5-yr Boost**", "**10-yr Boost**", "**15-yr Boost**"
  - "**anti-rAlp3/1:2000**", "**anti-rAlp3/1:10000**", "**anti-rBCPAIgA/1:2000**"

83

Write Well – 7
Avoid or minimize jargon

- Informal, short-hand, technical terms and abbreviations
- Used in a workplace or narrow field
- Often unknown by many outside the field
- Sometimes have general meaning understood differently by general population
- Examples
  - "Internalizing and externalizing scales"
  - "iPrEx participants"
  - "Neuts"
  - "Open-label"

84

Write Well – 8
Avoid or minimize jargon

- Example with jargon
  - *"For the first year, the links with SDPC and the HAC were not connected, and all required OCS input data that were artificially loaded. Thus CATCH22 and MERWIN were not available."*
- Example without jargon
  - *"Because some of links in the computer system were not connected the first year, we could not run all the software codes."*

CREDIT: Nicole Kelley, Massachusetts Institute of Technology

85

Write Well - 9
Avoid needlessly complex language

Category	Example	Substitute
nouns	utilization functionality	use feature
verbs	facilitate finalize	cause end
adjectives	aforementioned individualized	mentioned individual
adverbs	firstly, secondly, heretofore	first, second previous

CREDIT: Nicole Kelley, Massachusetts Institute of Technology

86

Write Well - 10
Remove redundancy

- Three sentences
  - *"Water quality in the Hawk River declined in July. This decline occurred because of the unusually heavy rainfall in July. All the extra rain water overloaded the Tomlin County water treatment plant."*
- One sentence
  - *"Water quality in the Hawk River declined in July because heavy rainfall overloaded the Tomlin County water treatment plant."*

CREDIT: Nicole Kelley, Massachusetts Institute of Technology

87

Write Well - 11
Seek both technical review and editing assistance before submission.

- Many submissions are surprising
  - Lack simple editing for grammar, spelling, style
  - Lack technical review by knowledgeable experts
- Share your drafts with colleagues, supervisors, others in same institution and elsewhere
  - Request critical comments and candid feedback
- For non-English speakers, get help editing for good English by a native speaker
  - Ideally someone familiar with science
  - Commercial, internet services available for a fee

88

Write Well - 12
Proofread. Proofread. Proofread.

- Simple mistakes …
  - Arithmetic
    - E.g., numerators and denominators do not add up
  - Formulas
    - E.g., ">" instead of "<" or vice versa
  - Spelling
  - References
    - Wrong order or missing authors, incorrect title, year, issue, pages
- Mistakes raise doubts in reviewers minds
  - Scientific quality of underlying research?
  - Sloppy implementation of study?
  - Flawed analysis?
- Cannot always judge quality from the paper; reviewers use intuition
  - Mistakes may undermine credibility, leading to rejection

89

Reviewer Nominations
Suggest potential reviewers who are knowledgeable but do not have real or perceived conflicts of interest

- Many journals welcome nominations
  - Should know the subject matter
- Avoid financial conflicts in nominees
  - Own stock or receive money from manufacturers of products studied in the reported research
- Avoid emotional conflicts in nominees
  - Current or former colleagues at same institution
  - Co-authors of past papers
  - Good friends or relatives

90

Submission

Submit the paper to one journal, selected for its scope, mission, and usual content

- Does this journal often publish such reports?
- Does this work fall within the stated subjects of interest for the journal?
- How often do you find similar studies as yours in the journal?
- Use MEDLINE's journal search and the journal's website to examine article titles and abstracts for issues over prior year

91

Submission - 2

Be patient; proper peer review takes time

- Many steps required
  - Receiving and processing
  - Assigning editor
  - Identifying subject matter experts to review
    - In addition to those nominated by authors
  - **Vaccine** allows 14 days for reviews; some late needing reminders
- Good experts are busy
- Must sometimes invite 6 – 12 to obtain 2 - 3 willing to accept task

92

Invitation to Revise

In *cover letter, respond in detail to every reviewer comment*

- Prepare cover letter for revised manuscript (ms.)
  - Copy word-for-word each reviewer's comments
  - Explain point-by-point how paper changed in response to each comment or criticism
    - Set off by indenting, font, color to ease readability
  - Show a quote of the changed sentence or item
  - If disagreeing with reviewer, provide a polite rebuttal
- Revised manuscript
  - Highlight the changed items
    - Avoid *italics*, **boldfacing**, underlining to avoid accidental publication
  - Use continuous line numbering, not resetting each page

93

Invitation to Revise - 2

In cover letter, respond in detail to every reviewer comment.

- Use formatting to set off comment from response
- Provide page and line numbers to find changes

3. The authors may wish to cite the paper listed below which showed differences in stability of measles vaccines after reconstitution for nebulization.

Dilraj A, Cutts FT, Bennett JV, Fernandez de Castro J, Cohen B, Coovadia HM. Persistence of measles antibody two years after revaccination by aerosol or subcutaneous routes.
Pediatr Infect Dis J. 2000 Dec;19(12):1211-3.
Thank you for the reference (now #38 in the manuscript, line 358) of which were not previously aware.

Specific comments

Page 2, line 9 and page 4, line 16, of former manuscript. Responder cells were PBMCs, not T lymphocytes; PBMCs also contain B cells. PBMCs contain B and T cells, so there is no evidence that T cell proliferation is enhanced.
We consider our assay is generally accepted as one for measuring T cell specific proliferation, but following the reviewer comment we have changed "T cell" for "PBMC" (page 2, line 8 and page 4, line 16).

94

Invitation to Revise - 3

In cover letter, respond in detail to every reviewer comment.

- Examples
  - Quote the actual changed text or citation

7. Either in the introduction or the discussion, the authors should review the (supportable) hypothesis that NIDs tend to have a leveling influence on coverage across economic quintiles.

We have added the following sentence to the second paragraph of section 1:
"Supplementary immunization activities may serve to reduce these disparities, but they are limited to polio and measles vaccines and therefore have no benefit for other target diseases."

2. The IGA levels were surprisingly low. I wonder if there is a positive control for this or how well the assay has been worked up or validated. The authors should comment on this as I couldn't find a reference to this assay in their lab.
- Both IgG and IgA assays have been previously validated in plasma and mucosal samples. Specificity of the isotype-specific anti-monkey IgG and IgA reagents were addressed in *Miller CJ, et al. J Virol. 1997, 71(3) p. 1911-21.* This reference is now included in the antibody section of the material and methods.

95

Invitation to Revise - 4

In cover letter, respond in detail to every reviewer comment.

- One need not agree with every reviewer suggestion
  - Politely explain disagreement

1. Inclusion of the obtained titers from the vaccinated hamsters in an ELISA format would be informative. The immunoblots show the presence of reactivity, but do not show the level of reactivity. The possibility exists that the observed lack of protection is a function of relatively minor antibody titers being achieved from one primary immunization and one boost.
Titers by, e.g., ELISA would actually not be informative because they would be totally arbitrary, there being no correlate of immunity with which to compare them. We have used doses and regimes similar to those reported by others, as now emphasised (lines 188-190).

96

Invitation to Revise - 5

In cover letter, respond in detail to every reviewer comment.

- Examples
  - Highlight new text in revised manuscript

393 vaccine. However, the rates of grade 3 local and general symptoms (including fever
394 >39°C) remained low in all groups and only one grade 3 unsolicited AE considered as
395 related to vaccination (transient inflammation of the armpit) was reported. Moreover,
396 neither pIMDs nor SAEs related to vaccination were reported. The clinical impact of
397 these observations remained limited and both vaccine dosages had clinically
398 acceptable reactogenicity and safety profiles.

97

Invitation to Revise - 6

Include every answer to reviewer question in revised manuscript

- Readers of the publication may have the same questions as reviewers did
  - Ensure revision averts future questions by clarifying the matter

P18. Were there any CD8+ T cells induced in the mice?

Using flow cytometry assay we were unable to detect any CSP-specific CD8+ T cell responses in mice.

They answered the reviewer's question, but was the ms. changed to ensure readers will not have the same question?

98

Manuscript Offences

Avoid offences in scientific publishing such as plagiarism and falsification

- *Plagiarism* = Using another's words and claiming them as ones own
- *Falsification* = Providing fake or fictional data
- *Duplicate submission* = Sending the same work to a second publisher before first has declined it
- *Redundant Publication* = Submitting the same body of work to multiple journals with only minor differences

- See *Uniform Requirement for Manuscripts* (http://www.icmje.org)
- No excuses such as "not an issue in my country"
- Offenders subject to banishment from journal(s)

99

Handling Rejections

Rejection is not necessarily a negative judgment on your work; if it is, use it as a learning experience

- Many journals try to maintain focus on their narrow subject matter
  - Your paper may be outside that scope
- Your paper may be duplicative
  - The 10th paper reporting a finding adds little to first nine
- If rejection was based on poor quality, take advantage of the reviewers' criticisms before submitting elsewhere

100

Wishing your success

To receive many clicks of …

Thank you!

Bruce G. Weniger, MD, MPH
International Professor, Research Institute of Health Sciences, Chiang Mai University
Associate Editor, *Vaccine*
bgweniger@siamlotus.com

Workshop on Scientific Writing in Field Epidemiology
Hua Hin / Cha Am, Thailand, 4-8 February 2013

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