INFORMED CHOICES - WHAT TO LOOK FOR IN A MED JOURNAL ARTICLE

Josh Epworth, ARNP – University of Washington/Seattle Cancer Care Alliance

AGENDA

Why do we write papers?

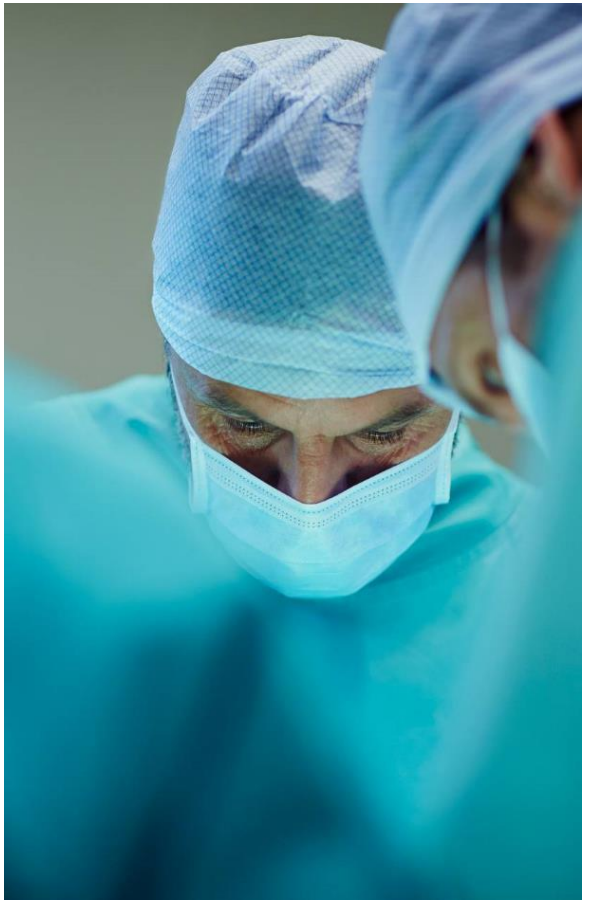
Types of study design

Different types of studies

Three questions

Hazards

Resources



In God we trust, all others must provide data

or

Facts often kill a good argument

Q: Why do we write papers?
A: They are a cornerstone of evidence-based medicine.

- Formulating answerable questions
- Identifying the best evidence
- Assessing the evidence with a critical eye
- Applying the evidence
- Integrating clinical acumen with patient values with this evidence.

Some Types of Study Design

- Meta-analysis: Combining data from many studies
- Systemic review: A summary of clinical literature
- Cohort study (Prospective Observational Study) - Groups with a condition are followed over time and compared to groups without the condition
- Clinical Trial: A research study that prospectively assigns human participants or groups of humans to one or more health related interventions to evaluate impact on outcomes.

Some Types of Study Design

- Meta-analysis: Combining data from many studies
- Systemic review: A summary of clinical literature
- Cohort study (Prospective Observational Study) - Groups with a condition are followed over time and compared to groups without the condition
- Clinical Trial: A research study that prospectively assigns human participants or groups of humans to one or more health related interventions to evaluate impact on outcomes.

Randomized Clinical Trials

- Often referred to as a Randomized Controlled Trial (RCT).
- RCT design should create groups of patients that are similar in all known prognostic factors except the intervention (for instance RVd vs. D-RVd – the intervention is the addition of D (Daratumumab)).
- Oncology RCTs of randomize to groups and follow them in parallel (exp - the control group *RVd* is getting treatment around the same period as the intervention group *D-RVd*)
- The most frequent goal is to determine *superiority (Is D-RVd a better treatment that RVd?)*

<u>This is the gold standard of oncology clinical research</u>

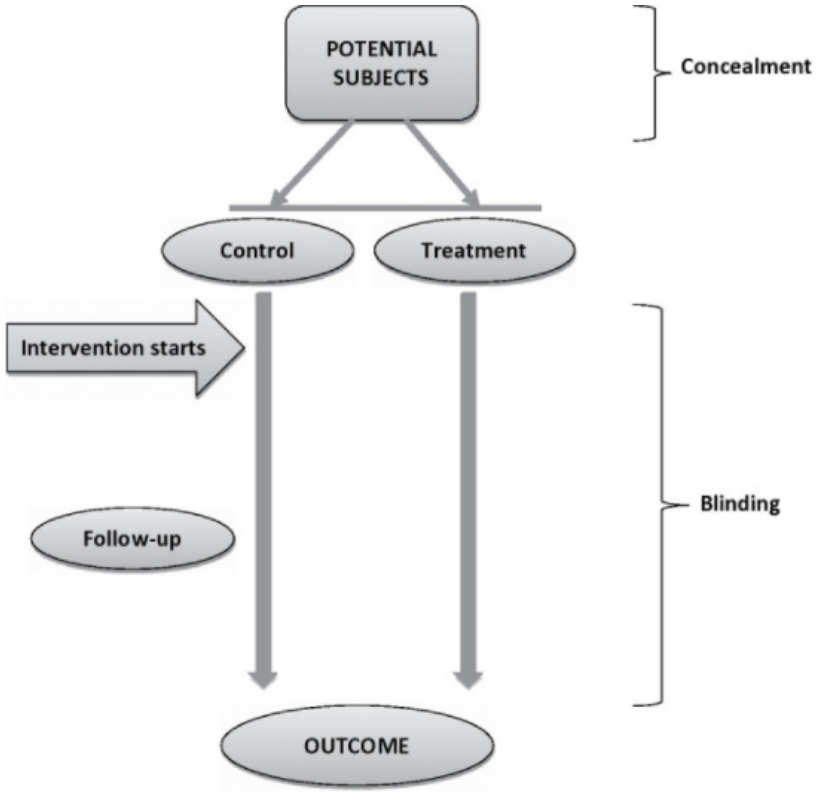
Peter M. Voorhees, Jonathan L. Kaufman, Jacob Laubach, Douglas W. Sborov, Brandi Reeves, Cesar Rodriguez, Ajai Chari, Rebecca Silbermann, Luciano J. Costa, Larry D. Anderson, Nitya Nathwani, Nina Shah, Yvonne A. Efebera, Sarah A. Holstein, Caitlin Costello, Andrzej Jakubowiak, Tanya M. Wildes, Robert Z. Orlowski, Kenneth H. Shain, Andrew J. Cowan, Sean Murphy, Yana Lutska, Huiling Pei, Jon Ukropec, Jessica Vermeulen, Carla de Boer, Daniela Hoehn, Thomas S. Lin, Paul G. Richardson; for the GRIFFIN Trial Investigators, Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood* 2020; 136 (8): 936–945. doi: https://doi.org/10.1182/blood.2020005288

Three Questions When Reviewing a Trial Paper

1. How valid are the results (or how much does the risk of bias affect the trustworthiness of the results)?
2. What are the results?
3. Are these results applicable in clinical medicine?

How valid are the results (or how much does the risk of *bias* affect the trustworthiness of the results)?

Bias: Systematic errors that encourage one outcome over others. The potential effect of bias is that investigators will come to the wrong conclusions about the beneficial and harmful effects of interventions.


POTENTIAL SUBJECTS
Concealment
Control
Treatment
Intervention starts
Follow-up
Blinding
OUTCOME

Are the Results Valid?

Study design
- Randomization
- Balance at baseline
- Allocation concealment

Was the trial well managed
- Blinding
- Adherence
- Absence of contamination

Was there good follow up following study completion?
- Intention to treat
- Follow up

What are the Results?

How profound was the result of the intervention?

Are the results precise

Applicability

Are the patients in the study reflective of real world patients?

Were all potential factors considered?

Did the benefit of the treatment outweigh the risks?

Once trial validity is established (i.e., risk of bias is low or unlikely to impact the conclusions) results need to be interpreted by asking about the magnitude of the effect and its precision.

What are the results and how do we measure them?

- Relative risk
- Odds ratio
- Risk difference
- Hazard ratio
- Confidence ratio: How often study results can be reproduced.
- Statistical significance: <0.05, the arbitrary cutoff for significance

Are these results applicable in clinical medicine?

- Do the inclusion and exclusion criteria for the RCT and compare them to the characteristics of the patient of interest? RCTs with a long list of exclusions are potentially doing just that, excluding a lot of real world patients.
- Were clinically relevant outcomes considered? Do trial goals match clinical goals?
- Do the benefits of the trial outweigh the risks?

HAZARDS

Not all clinical trials are created equal.

Not all science journals are created equal.

Objective data is in the eyes of the beholder.

Opportunistic Journals in the Clinical Pharmacology Space:

A Policy Statement From the Publications and Public Policy Committees of the American College of Clinical Pharmacology

American Journal of Therapeutics

Outline
Images

THERAPEUTIC ADVANCES

Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines

Conclusions:

Moderate-certainty evidence finds that large reductions in COVID-19 deaths are possible using ivermectin. Using ivermectin early in the clinical course may reduce numbers progressing to severe disease. The apparent safety and low cost suggest that ivermectin is likely to have a significant impact on the SARS-CoV-2 pandemic globally.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Early Treatment with Ivermectin among Patients with Covid-19

Gilmar Reis, M.D., Ph.D., Eduardo A.S.M. Silva, M.D., Ph.D., Daniela C.M. Silva, M.D., Ph.D., Lehana Thabane, Ph.D., Aline C. Milagres, R.N., Thiago S. Ferreira, M.D., Castilho V.Q. dos Santos, Vitoria H.S. Campos, Ana M.R. Nogueira, M.D., Ana P.F.G. de Almeida, M.D., Eduardo D. Callegari, M.D., Adhemar D.F. Neto, M.D., Ph.D., et al., for the TOGETHER Investigators*

A large collaboration of clinical trialists working on ivermectin treatment for Covid-19 has conducted a meta-analysis of trials and has concluded that ivermectin did not offer a treatment benefit when trials that were considered to be of moderate or better quality were examined.[6]

How do we separate the predatory from the professional?

SIFT

CRAP

How do we separate the predatory from the professional?

Stop
Investigate
Find better coverage
Trace claims, quotes, media to the original source

Currency/Credibility
Reliability
Authority
Purpose/point of view

RESOURCES

Clinical Practice Guidelines We Can Trust. This 2011 Institute of Medicine consensus report made recommendations for identifying high-quality clinical practice guidelines (CPGs) among the nearly 27,000 then contained in the National Guideline Clearinghouse. The report committee concluded that certifying organizations with trustworthy CPG development procedures, rather than evaluating the content each individual CPG, was a reasonable (although not the only) approach to the challenge.

The CRAP Test. Developed by librarian Molly Beestrum, the CRAP Test is a system for evaluating the credibility of a website according to four major attributes: **C**urrency/**C**redibility, **R**eliability, **A**uthority, and **P**urpose/**P**oint of View. Embedded within each of these attributes are questions such as, *How recent is the information? Does the website include citations? What are the author's credentials? Does the author seem to be trying to push an agenda or sell you something?* Educator Mike Caulfield has developed an alternative to the CRAP model called SIFT (**S**top. **I**nvestigate the Source. **F**ind Better Coverage. **T**race claims, quotes, and media to the original context), which is designed to help "students get better at sorting truth from fiction from everything in between" [a].

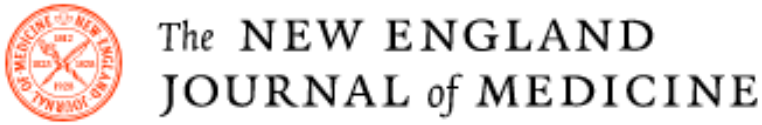
Health on the Net (HON) Foundation Certification. HON is an international nonprofit organization based in Switzerland. HON certification holds health and medical websites accountable to basic ethical standards in the presentation of information, including sharing information from only trained and qualified professionals, respecting patient and consumer privacy, providing evidence in support claims, and disclosing financial interests, among others. Websites with HON certification earn the right to display a visual seal as an indication of their integrity.

MEDLINE and MedlinePlus (National Library of Medicine [NLM]). MEDLINE is an NLM database with over 27 million references to journal articles in the life sciences. To decide which journals (i.e., article sources) to include, MEDLINE applies a set of criteria including scope and coverage, editorial policies and processes, scientific and methodological rigor, production and administration, and impact. MEDLINE selection also depends on the judgment of an independent Literature Selection Technical Review Committee, a Federal Advisory Committee.

MedlinePlus is an NLM website designed to share health information with the public. MedlinePlus primarily links to other government websites but will consider inclusion of nongovernment websites (i.e., information sources) if they demonstrate a mission to share high-quality health information; display transparency and trustworthiness; provide unbiased content for the purpose of education; and ensure the accessibility of information, among other criteria. MedlinePlus also gives preference to websites that do not host advertisements.

URAC Certification for Health Content Providers and Health Websites. URAC is an accreditor that offers certifications for health information sources that meet standards for disclosures, editorial and content review processes, privacy and security, external linking policies, consumer complaint processes, and more.

CONSIDER THE SOURCE (BUT RECOGNIZE THEY'RE NOT PERFECT EITHER)



THANK YOU