

# Confidence Interval and p-values

- **Confidence interval**- the range within which the true effect is likely to lie
- **p-value** whether trial results are likely to have occurred simply through chance
- Confidence intervals are preferable to p-values, as they tell us the **range of possible effect sizes** compatible with the data.
- p-values simply provide a cut-off beyond which we assert that the findings are 'statistically significant' (by convention, this is  $p < 0.05$ ).
- A confidence interval that **embraces the value of no difference between treatments (Null or 1.0)** indicates that the treatment under investigation is not significantly different from the control.

# Example OPH Review

Topic: ASTDR Mortality Study of Marines at Camp Lejeune and Camp Pendleton

Review of: Bove FJ, Ruckart PZ, Maslia M, et.al. Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC base camp LeJeune: a retrospective cohort study. Environmental Health 2014, 13:10.

- The authors state “We did not use statistical significance testing to interpret findings”. It is methodologically suspect that in a study sample this large (N=20,000), statistical testing was not performed, since statistical significance (p-values) is largely a function of sample size.
- All non-significant results. All p-values are not significant, and all 95% confidence intervals include 1 (which means no association).
- Data on major confounders was not collected.
- ATSDR Assessment: “This study makes an important contribution to the body of evidence about harm caused by these chemicals. However, due to its limitations it does not provide definitive evidence for causality nor can it answer the question whether an individual has been affected by these exposures at Camp Lejeune.”

**Table 5 Camp Lejeune vs Camp Pendleton: Hazard ratios and 95% confidence intervals, adjusted by sex, race, rank and education, 10-year lag**

| Underlying cause of death           | Hazard ratio | 95% LCL | 95% UCL | p-value |
|-------------------------------------|--------------|---------|---------|---------|
| All Cancers                         | 1.10         | 1.00    | 1.20    | 0.02    |
| <b>Diseases of primary interest</b> |              |         |         |         |
| Kidney Cancer                       | 1.35         | 0.84    | 2.16    | 0.19    |
| Bladder Cancer                      | 0.76         | 0.34    | 1.71    | 0.50    |
| Liver* Cancer                       | 1.42         | 0.92    | 2.20    | 0.11    |
| Esophageal Cancer                   | 1.43         | 0.85    | 2.38    | 0.17    |
| Hematopoietic Cancers               | 1.05         | 0.82    | 1.33    | 0.57    |
| Hodgkin                             | 1.47         | 0.71    | 3.06    | 0.26    |
| NHL**                               | 0.81         | 0.56    | 1.18    | 0.43    |
| Multiple Myeloma                    | 1.68         | 0.76    | 3.72    | 0.21    |
| Leukemias                           | 1.11         | 0.75    | 1.62    | 0.63    |
| Cervical Cancer                     | 1.33         | 0.24    | 7.32    | 0.74    |

# Report Format

Consistent formatting makes MO easier to read and understand

- Use font large enough to read easily
- Topic headings should be used and bolded to identify sections
- Short, concise paragraphs are most effective
- Number pages

# Report Format

- Claimed condition-on first page for VBA
- Actual diagnosis and how established-on first page for VBA
- Medical Opinion-on first page for VBA
- Case discussion – individual case specific aka “Executive Summary”
  - Disease; current status; risk factors-mention all contaminants pertinent, if not why not; address all nexus; rationale and summary
- Disease discussion
  - Standard
  - Modify for your case
- Literature review
- Record review documentation

Date:  
Date of Birth:  
Sex:  
Dates of military service:  
Dates of service at Camp Lejeune:  
The following report was based on record review.

Reviewer: [REDACTED]  
**Member, Subject Matter Expert Panel**  
Camp Lejeune Contaminated Water Project  
Time Dedicated to this review:

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Contention, the veteran claims the following condition as secondary to exposure to CLCW:

**Contention 1:** esophageal cancer

**Diagnosis 1:** esophageal adenocarcinoma

**Nexus:** The diagnosis above is caused by or a result of exposure to CLCW

**Case Specific Discussion:**

**Disease Specific Discussion:**

**References:**

# Medical and Other Records Reviewed

The thoroughness of the evaluation is directly related to which medical records and other documents were reviewed and the diligence of that review.

- Documents should be listed chronologically or by some natural logical grouping (imaging, laboratory, etc.; STRs, MPRs)
- Consider brief summary of records reviewed
- Do not list documents which were not reviewed
- Illegibility should not be used an excuse for wholesale ignoring of records
- Document inconsistencies

# Medical and Other Records Reviewed

## Good

### Records Reviewed:

1. John Smith, M.D. 03/07/2005-04/08/2007 (51 pgs)
2. MRI, TSA Imaging LLC. 05/07/2008
3. VA 21-526 EZ 10/01/2010
4. Jane Doe, M.D. 05/19/1995-07/01/2000 hand written and illegible

## Better

### Records Reviewed:

1. 04/08/05 Smith, MD...Rt breast tumor (benign) no further treatment required...
2. 05/07/08 MRI, TSA Imaging...IMP: normal MRI of the head and neck-no metastatic disease...
3. 10/01/2010 VA 21-526EZ...veteran claims breast cancer a result of serving from Camp Lejeune from 05/01/1977-05/02/1978.

# Veteran's History

Thorough review of records:

- Past medical history: Diabetes since 2007 treated with Actos for 5 years; Oil refinery maintenance treated in 2002, 2004 and 2006 for recurrent solvent related dermatitis of hands bilaterally
- Social/socioeconomic history: Smokes 2-3 ppd x 21 years
- Family history: Mother-deceased, lung cancer-past smoker; Brother-CaP dx at 50
- Occupational history post service: Oil refinery maintenance 1992-2007 (National Occupational Exposure Survey 1981-1983 or HazMap)

<https://web.archive.org/web/20110717195714/http://www.cdc.gov:80/noes/noes2/occs0000.html> or <https://hazmap.nlm.nih.gov/>

- History of condition(s) claimed and current treatment, residuals, active, remission, etc.

# Establish Diagnosis

- Pathology – confirms oncological condition claimed (NHL vs HL)
- Primary source treatment records
- Treatment records – report “history of”
- Imaging
- Death Certificate – legal not medical document
  - If insufficient records to establish diagnosis, state that.
  - Give opinion on the correct diagnosis not 2507 claim (AML vs CML)
  - No medical opinion warranted for wrong condition unless associated with CLCW

# Determine Causation

- Identify evidence of disease (is the dx correct, does the history, imaging, laboratory testing etc. support dx?-it's not cancer until pathology reveals cancer vs tumor/neoplasm hx)
- Review and assess the available epidemiological evidence for a causal relationship (does the data support a relationship with disease?)
- Obtain and assess the evidence of exposure (ATSDR Water modeling; 2507, MPRs, or STRs)
- Consider other relevant factors (forensic review of records for other risk factors-post service occupation, Shx, FHx, etc.)
- Judge the validity of testimony (veteran statement, Nexus letter – are there conflicting dates, Nexus predicated solely on profession?)
- Evaluation and conclusions (individualized case-by-case basis)

# Medical Rationale

- Your opinion must be state clearly, explicitly and with confidence
- Define all medical/technical terms (VBA not medically trained)
- Use “more likely-than-not basis...” etc. (>50/50)
- Avoid hedge words: “I believe”, “I think” or absolutes “always” and “never”, avoid inflammatory words or characterizations
- Document a concise and reliable reasoning for opinion(s) that supports findings and conclusions
- Discuss relevant history and risk factors and how they were factored
- Citations should be detailed and precise, literature should be up-to-date
- Avoid general statements “the weight of the literature” or “studies”
- Final report needs to be internally consistent and consistent with other opinions for similar conditions previously provided

# When to Say “NO”

- Being asked to opine without being provided crucial records or documents resulting in the inability to reasonably confirm claimed condition or stratify risk:

\*Cannot resort to mere speculation- "There are no notes which allow a proper forensic evaluation which include past medical, social, family and occupational histories. Therefore a proper forensic review cannot be done and the claimed condition cannot be found to be related to service absent any definitive diagnosis and a timeline of diagnosis. An additional medical opinion may be requested when supporting medical records are made available for review."

# Putting it All Together

- Know your audience (written for VBA-RVSR, veteran, legal, BVA, public interest groups, etc.).
- Requires meticulous attention (SME seen as expert, MO will be viewed potentially by many).
- Proof MO for mistakes, each and every mistake made will lessen the report's value and credibility of the SME.
- The report is not for a "patient"-no doctor/patient relationship; use the term Veteran, Mr. or Ms. XXXX.
- Must be thorough (no stone unturned).
- A complete explanation must be given for conclusion.
- Conclusion must be predicated on valid scientific methods.
- Consider reports of colleagues and adapt best features.