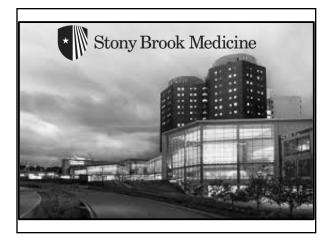
## **Question Everything** (Critical Common Sense)





#### Disclosures!

#### Publications:

- Rockwood and Green, Tornetta and Einhorn; Subspecialty series, Court-Brown, Tornetta; Trauma, AAOS; OKU Trauma, ICL Trauma 1,2, Tornetta; Op Techn in Ortho Surg, OTA Slide project,
- . Journals:; JOT; Deputy editor, CORR, JAAOS, JBJS; Reviewer

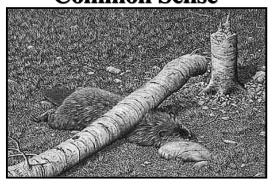
#### • Research:

- OTA, FOT, AIOD, DOD
- Consultant / Designer
  - Smith and Nephew, Exploramed

#### **Common Sense**



#### **Common Sense**

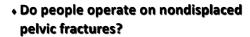


#### **Common Sense**



#### In Childhood

- Are we there yet?
- Why...
  - Is the sky blue?
  - Don't fish drown?
  - Do birds fly?





#### **School**

- Taught to accept
- Told that there are correct answers
- Conform to established thoughts

#### **Medicine**

- Overload of information
- Accept established theories
- Facts
- Textbooks

• Journals

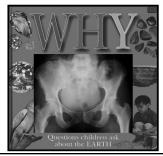



#### **Doubting Thomas**



#### **Healthy Skepticism**

- Challenge opinion
- Ask....



#### **Goals**

- Help patients
- Restore anatomy





#### Do the Right Thing

- Best choice for each patient
  - Available information
  - Surgical skill
  - Patient needs

#### **Common Sense**

- Available information
  - Standard Bertation per 0,000 points from Study Powel Representation
  - Evaluation
  - Flaws in what we think we know
- Surgical discipline
  - Art
  - Decision making



#### **Hippocrates**

"One must attend in medical practice not primarily to plausible theories, but to experience combined with reason"



#### How You Look at It



#### **Information**

- Is there any?
- Plantar sensation
- Syndesmotic fixation
- Cubitus varus
- Pilon fractures
- All of "sports medicine"

## 7



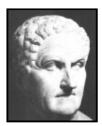
#### **Information**

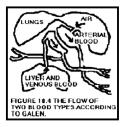
- Based on observation
- Hypothesis generation
- Hypothesis testing
- Objective evaluation of data
- Conclusions



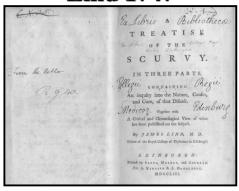
#### Galen

- Questioned how?
- Vivisections on primates





#### **Lind 1747**



#### **Others**

- Lister
  - Mortality after amputation

**+ 1864-86**: 46%

**◆ 1867-70**: 15%

- Hill
  - Treatment of Tb
  - Sealed envelopes, eligibility
  - Independent evaluation

#### **Evidence**

- Best available information
- Support clinical decisions
- "Evidence based medicine"
- Reality
  - Be able to critically analyze what we hear, read, and see
  - Apply to our patients' specific needs

# Level 1 Randor Trials Level 2 Prospect Studies Level 3 Car ies Level 4 Ratrospective Case Series Level 5 Opinion

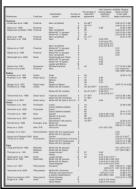
#### **All Studies**

- Classification used
- Evaluation of "union"
- Follow up percentage
- Outcome measures
- Clinical relevance



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#### Audige, et al



- 15% observer agreement
- Kappa = .23



#### Union

- Bhandari, et al
  - Nonunion 2 12 months
  - 45% always use criteria to evaluate



#### **Followup**



- Significant problem in traump00 Pts studies 80 Pts
  - 80 F
- 20% is significant!! =86 20 lost
- Case series =40
- Comparative studies



#### **Outcomes**

- We assign values to scoring
- Motion?



- Alignment?
- Functional assessment?
- What matters to the patient?

#### **Summed Scores**

- Floor and ceiling effects
- Multiple components



Subjective



- Objective
- Importance of all components?

## 47

#### **Materials**

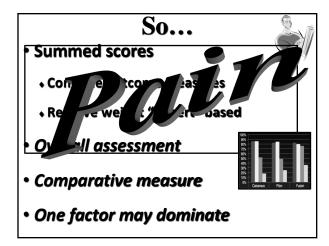




55

Followup 51 mos (> 2 yr) AOFAS, Maryland, SF36

Pain		
AOFAS	83% - 86%	
Maryland	80% - 86%	
SF36 PCS	52% - 76%	
SF36 MCS	18% - 36%	



#### **Error**

- All studies have error
- Critical analysis necessary
  - Appropriate question
  - Appropriate population
  - Selection bias
  - Technique bias
  - Outcomes measure



#### **Standard Evaluation**

- Just like an x-ray
- Same method each time
- Systematic approach

#### **Standard Evaluation**

- Study design (RCT, series)
- Methodology
  - Hypothesis (if there is one!)
  - Population
  - Intervention
- Outcomes assessed
- Results

#### **Highest "levels"**

- Comparative studies
- Specific types of error
  - Beta
  - Alpha



#### **Statistics**

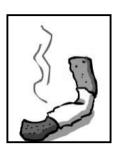
- Boring
- Facilitate lies!



Data can be manipulated to say anything!

#### Randomization

- Balance
  - Known
  - Unknown



#### **Hypothesis**

- Basic element of any comparison study
- Clearly stated
  - Usually a "null" hypothesis
  - Assumption of NO difference
- Evaluated with as little bias as possible

#### **Example: Tibia Fx**

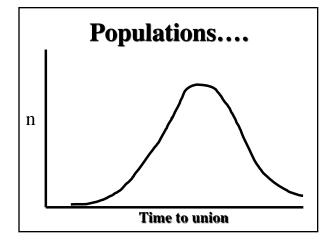
- Reamed vs unreamed nailing
  - Union (%)
  - Time to union (weeks)
- Null hypothesis:
- There is no difference in the union rate or time between the groups

#### The "p" Value

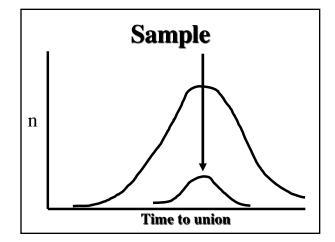
- Probability
- Coin toss

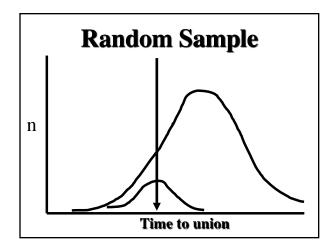


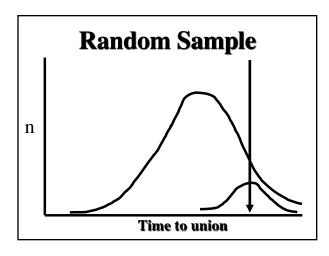
- + Heads twice 25% (p = .25)
- Heads ten times < 1/1000 (p<.001)</li>

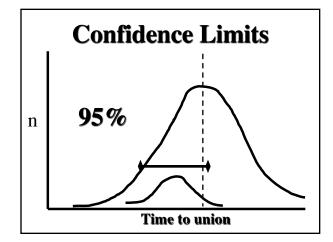


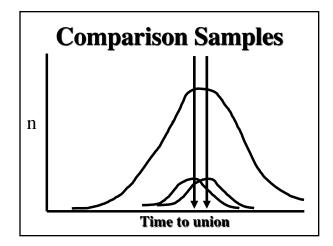
•		

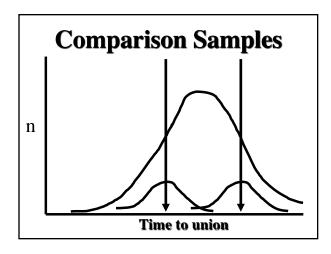






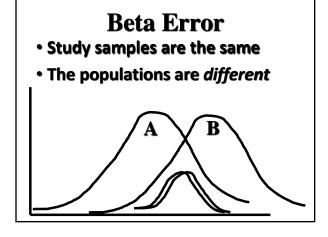






#### **Conclusions of RCT's Truth** No Difference Difference Study **Hypothesis False Hypothesis True** Difference **False Positive** Correct **Reject Hypothesis** α error $(1-\beta)$ No Difference Correct **False Negative Accept Hypothesis** $(1-\alpha)$ βerror

## No True Difference • Study samples are the same • Study finds no difference



#### Beta Error (type 2)

 Concluding no difference when one does exist

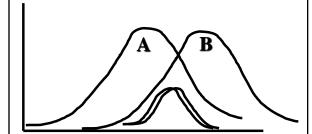
20% A B

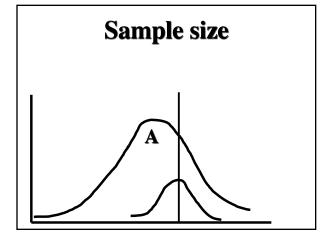
#### **Power**

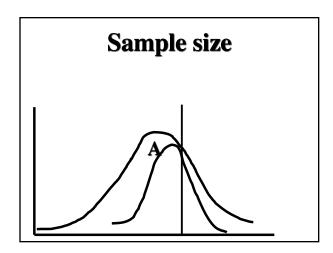
- Power (1-β)
  - Strength of study
  - Desire > 80%
  - Determined by
    - Effect size (difference / SD)
    - Type 1 error rate
    - Sample size

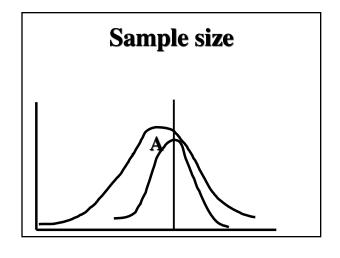
#### **Power**

• Related to "n"



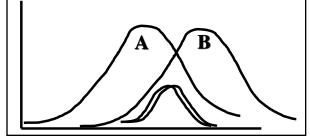






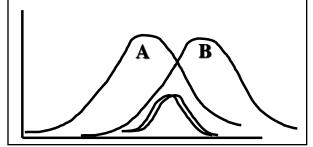
#### **Small Sample size**

Related to "n"



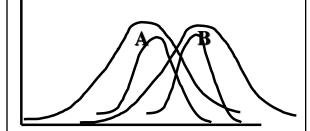
#### **Increase Sample size**

Related to "n"



#### **Increase Sample size**

• Related to "n"



#### **Power**

- Should be built in at the beginning
- Can be evaluated post-hoc

#### **Calculation of Power**

- For continuous variables:
  - N= {[  $(Z\alpha Z\beta) \sigma]/\Delta$ }
    - N=sample size
    - Zα=1.96, and
    - Δ= difference b/n treatments.
    - Standard deviation (σ)

 $\sigma^2$ = [ (Ntreatment-1)(  $\sigma$ treatment)<sup>2</sup> + (Ncontrol-1)(  $\sigma$ control)<sup>2</sup>]/ Ntreatment-Ncontrol

- For dichotomous variables:

#### **Power**

- Very important concept!
- "No statistically significant difference"
- Need to demonstrate pover there!



#### Lochner, et al

J Ball S

- 196 Studies
  - 79 Eliminated
  - 43 Reported positive result
- 117 Studies underwent power analysis
  - "No statistically significant difference"

β Error Rates				
	Power (1- β) Type II Er Rate (β			
Outcome Type	Average	SD	Range	Total
Primary n=213	24.65%	27.21%	2.24%-99.9%	90.61%
Secondary n=127	19.66%	21.31%	2.24%-99.9%	96.85%

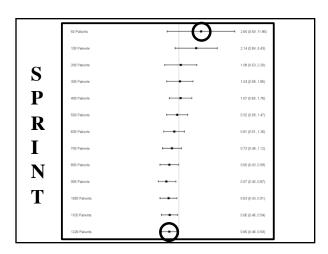
## **Example: Tibia Healing**

Time To Healing Control Group	Time to Healing Treatment group	% Reduction in Time to healing	Number of patients needed per group
150 days	120	20%	16
150 days	135	10%	63
150 days	143	5%	289

	<b>Example: DVT</b>				
PE Rate Control Group	PE Rate Treatment group	% Reduction in PE Risk	Number of patients needed / group		
10%	8%	20%	3213		
1%	0.8%	20%	35,001		
0.1%	0.08%	20%	352,881		

#### **Example: planning**

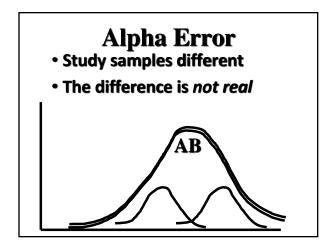
- Mortality in elderly trauma patients
  - 423 Patients...4 centers
  - Early fixation = 11%
  - Late fixation = 18%
  - To prove it.... >1500
  - Can use this to plan future work



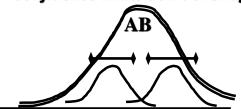


#### **Conclusions of RCT's Truth** No Difference Difference Study **Hypothesis False Hypothesis True** Difference **False Positive** Correct **Reject Hypothesis** α error $(1-\beta)$ No Difference Correct **False Negative Accept Hypothesis** $(1-\alpha)$ βerror

# True Difference • Study samples different • P = 0.05 • 95% the difference is real A B

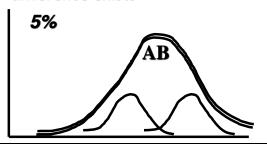


- Alpha Error
   Study samples different
- The difference is not real
- Confidence limits don't overlap



#### **Alpha Error**

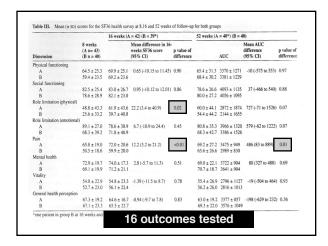
• Chance of incorrectly concluding a difference exists

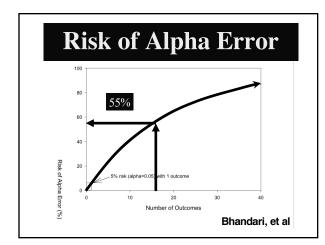


#### **Alpha Error Rates**

- 60 Orthopaedic journals
- 37% at risk for type 1 error
  - Conclusion that there is a difference when there is not
  - Primarily due to multiple evaluations
    - 20 endpoints
    - 1 / 20 chance.....
  - Fishing expedition







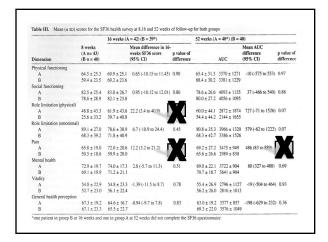
#### **Multiple Testing**

- Set p = 0.05 (alpha level)
  - Assumes one outcome!
  - 16 = 55% risk of alpha error



Bonferroni Correction= 0.05/16=0.003

New level of statistical significance!

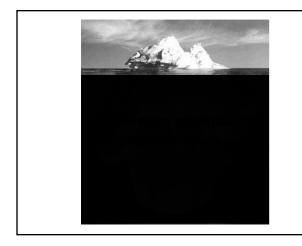


#### **Assume the Best...**

- Randomized
- Well powered



- True differences found
- Single outcome



#### Even When "Significant"

- Can we trust the p value?
- Discreet outcomes
  - Infection



- Union
- Number of Events

RECOMBINANT HUMAN BONE
Morphogenetic Protein-2
for Treatment of

		rhBl	MP-2	
Invasiveness†	Standard Care (N = 139†)	0.75 mg/mL (N = 130†)	1.50 mg/mL (N = 135†)	P Value
Most invasive	29 (43)	26 (39)	12 (18)	0.02648
ess invasive	29 (43)	21 (31)	18 (26)	0.3074
Noninvasive	0	0	2 (100)	
Total	58 (42)	47 (34)	32 (23)	0.03269

The values are given as the number of procedures with the percentage of the total number of procedures of the specified degree of invisioness in parentheses. Twost invasive = bone graft, exchange nalling, plate fixation, floular osteolomy, or bone traisport, less invasive and dynamization or exchange from internal fluidation for functional bancs; and noninvasive = utrassound, electrical simulation, or magnet leld stimulation. Evaluable patient population who received treatment as randomized. §Chi-square test for goodness of fit.

**RRR= 59%** 

12/135 vs 29/139 events



P=0.02

#### **Study Stability**

• 12/135 vs 29/139 events

**JUST 3 EVENTS** 

• 15/135 vs 26/139 events

RRR=40%, P=0.08

March 2011

Recombinant Human Bone Morphogenetic Protein-2: A Randomized Trial in Open Tibial Fractures Treated with Reamed Nail Fixation

By Hannu T. Ano, MD, PhD, Shunmugam Govender, MBRS, MD, FBCS, Amratial D. Patel, FRCS, Philippe Hemigsu, MD, Arturo Penera de Gregorio, MD, Gheorghe Ion Ropescu, MD, Jane Davis Golden, MHP, Jared Christensen, PhD, and Alexandre Valentin, MD

"The healing of open fractures treated with reamed IM nails <u>was not significantly improved</u> by BMP-2"

and routine soft tissue management (the SOC good) or the standard of care plus an absorbable collagen ponge implicacortaining 1.5 mg/mL of hBMP-2 (total, 12.0 mg) (the rhBMP-2/ACS group). Randomization was stratified by fracture

Total Events: 23 BMP vs 21 Controls (44 events)

60% and 40% at week 13 p = 0.0041) and 00% and 07% at week 20 in the mBMP 2/KCS and 500 groups, respectively. These percent of the subjects understant secrotage procedures in each group, one heasies procedures is q. exchanges on the major procedures in each group. The major procedures is q. exchanges in each group and 57% in the 500 group p = 0.1271, in fection point p = 0.0045, and the medium 2/KCS group and 57% in the 500 group = 0.0045, and the medium 2/KCS group = 0.0045, and the medium

Conclusions: The healing of open tibial fractures treated with reamed intramedullary rail fixation was not significant accelerated by the addition of an absorbable collagen sponge containing mBMP2.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.

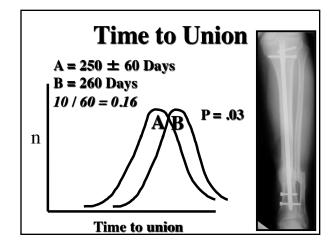
#### **Study Stability**

- Parisien, et al
- 198 Studies 769 outcomes
- <0.05 <del>→</del> ≥0.05
  - + 4 events, 6.8% of one arm
- · >0.05 <del>→</del> ≤0.05
  - 5 events, 9% of one arm



#### Clinical 'Significance'

- Reaching statistical significance is not all!
- Must ask...does it matter?
- Clinically important
- Effect Size..



#### **Clinically Relevant**

- Effect size
  - **4 > 0.8**
- Relative risk reduction
  - > 50%
- 76 RCT's; 185 outcomes
  - Effect size: 30%
  - RRR: 47%

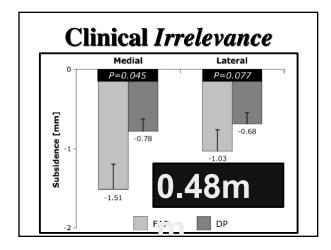
Sung, Siegel, et al

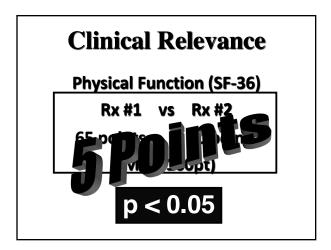
#### Clinical Irrelevance

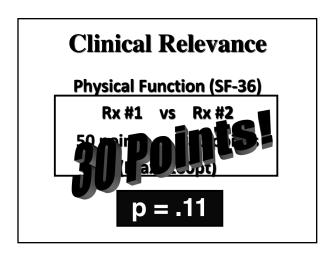
Biomechanical Analysis of Bicondylar Tibial Plateau Fixation: How Does Lateral Locking Plate Fixation Compare to Dual Plate Fixation?

Thomas F. Higgins, MD, Joshua Klatt, MD, and Kent N. Bachus, PhD

Conclusions: The results of this study demonstrate that dual-plate fixation allows less subsidence in this bicondylar tibial plateau cadaveric model when compared to isolated locked lateral plates. This may raise concerns about the widespread use of isolated lateral locked plate constructs in bicondylar tibial plateau fractures.

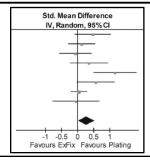






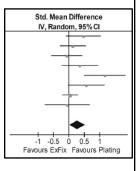
External Fixation Versus Internal Fixation for Unstable Distal Radius Fractures: A Systematic Review and Meta-Analysis of Comparative Clinical Trials

David H. Wei, MD, MS.\* Rudolf W. Poolman, MD, PhD,† Mohit Bhandari, MD, MSc.‡ Valerie M. Wolfe, MD,\* and Melvin P. Rosenwasser, MD\*



#### **But...Important?**

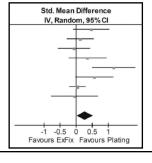
- No report of the actual difference
- Only statistical
- Need the real #'s to decide importance



External Fixation Versus Internal Fixation for Unstable Distal Radius Fractures: A Systematic Review and Meta-Analysis of Comparative Clinical Trials

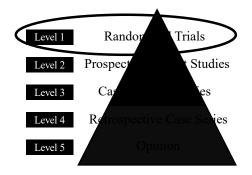
David H. Wei, MD, MS,\* Rudolf W. Poolman, MD, PhD,† Mohit Bhandari, MD, MSc,‡ Valerie M. Wolfe, MD,\* and Melvin P. Rosenwasser, MD\*

14.8



12.1

#### **Hierarchy of Evidence**



#### So...Do We Believe??

**The Effect of Level I Evidence** on Surgical Decision Making

#### Methods

- 2 Multicenter level one RCT's
- Operative vs nonoperative
- > 2 years since publication
- Equal in quality
- Survey
  - Knowledge of the article
  - Practice modification
  - Examples of patients



#### **Operative**

Nonoperative Treatment Compared with Plate Fixation of Displaced Midshaft Clavicular Fractures

A Multicenter, Randomized Clinical Trial

By the Canadian Orthopaedic Trauma Society



#### Non-Operative

Operative versus Nonoperative Treatment of Acute Achilles Tendon Ruptures

A Multicenter Randomized Trial Using Accelerated Functional Rehabilitation

By Kevin Willits, MA, MD, FRCSC, Annunziato Amendola, MD, FRCSC, Dianne Bryant, MSc, PhD, Nicholas G. Mohtadi, MD, MSc, FRCSC, J. Robert Giffin, MD, FRCSC, Peter Fowler, MD, FRCSC, Crystal O. Kean, MSc, PhD, and Alexandra Kirkley, MD, MSc, FRCSC



#### Survey

- 19,574 Orthopaedic Surgeons
  - + 18,843 in U.S.
  - 731 in Canada
- 1 of 2 Surveys
  - Practice demographics
  - Familiarity with RCT
  - Change in practice
  - 5 patient scenarios (fit into studies)



#### **Patients**

- 20 male Division I athlete
- 35 male day laborer
- 50 male Orthopaedic Surgeon
- 40 male (BMI 35)



• 65 female (lives alone)

#### **Clavicle Survey**



- Of the 1,546 respondents
  - Majority (64.8%) Non-academic
  - +72.3% familiar with RCT
  - Majority fixed 3 of 5 patients
  - 64.6% increased operative treatment

#### **Achilles Survey**



- Of the 1,128 respondents
  - Majority (64.2%) Non-academic
  - 78% familiar with RCT
  - Majority fixed 4 of 5 patients
  - 32.4% increased non-op treatment

### **Only Nonop**

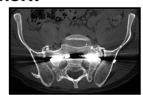


#### **Influence?**

Clavicle	Achilles
58%	42%

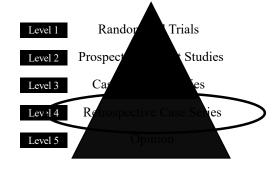
#### **Surgical Discipline**

- Not all questions can be answered with RCT!!
  - Surgical skill
  - Learning curve
  - Unethical



• Best available information

### **Hierarchy of Evidence**

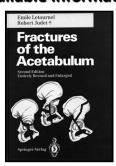


#### **Case Series**

- Very valuable if....
  - Same population
  - Reproducible intervention
  - High percentage f/u
  - Outcome measures important
- Arthritis after acetabular ORIF

#### **Acetabulum Fractures**

• Best available information



4	100	6		6	
1					
		1	1		
1			8	1	

#### **Prognosis**



Type of fracture	Clinical result					Total	Percentage of excellent results
	Excellent	Very good	Good	Fair	Poor		excellent result
Posterior wall	87	6	3	4	17	117	74%
Posterior column	9	-	1	1	-	11	81.82%
Anterior wall	6	-	1	1	1	9	66.67%
Anterior column	12	1	1	-	2	16	75.00%
Transverse	17	1	-	-	1	19	89.47%
T-shaped	20	3	-	-	3	26	76.92%
Transverse and posterior wall	49	16	10	9	17	101	48.51%
Posterior column and posterior wall	5	1	2	1	8	17	29.41%
Anterior column and posterior hemitransverse	26	5	4	3	3	41	63.41%
Both-column	76	21	14	11	13	135	56.30%
Total	307 62.40%	54 10.98%	36 7.32%	30 6.10%	65 13,21%	492 100%	62.40%



## **Mangled Extremity**



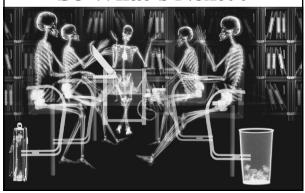
#### **Case Series**

- Prognostic information
- Important for patients
- Guide decision making
  - Population
  - Reproducible
  - Outcomes important



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#### So What's Next??



#### So What's Next??

- Collectively
  - Consider the big questions
  - Put egos aside
  - Organize well designed trials
  - Get real answers
  - Benefit our patients

#### So What's Next??

- Individually
  - Question everything
  - Listen to our patients carefully
  - Consider better ways
- Tell everyone!!



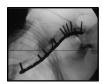
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#### **Our Responsibility**

- Read and interpret
- Stay current!



- Act on REAL evidence
  - Self appraisal
  - Benchmarking
  - Re-evaluation



#### **Above All Else**

- Surgery
  - Art

  - Science
- Make the best decision
- Each individual patient
- Don't know the right choice

#### **Individual Needs**

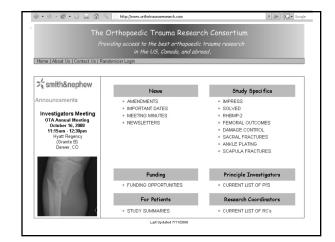


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#### **Orthopaedic Surgery**

- Art
- Patients are all individuals
- Goals
  - Return to function
- Healthy skepticism
- Look for better ways
- Prove that they are better!!







#### **Hippocrates**

"One must attend in medical practice not primarily to plausible theories, but to experience combined with reason"

Thank You
Boston Medical Center