Research, Learning Health Care Systems and PBRNs in the Age of Electronic Data

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- Off Label Medication Use: Off label medication findings from PBRN members will be discussed
US Health Care: Less for More?

- USA spends ~100% more than any other country on health care
- USA ranks poorly in all major health outcomes compared to all other industrialized countries
- Has any country ever received so little for so much as what we get from our health care dollar?
National context

- Health care value assessment critical
- Improved methods for comparative effectiveness, quality and dissemination
- New models of data acquisition
- Systems that combine basic scientists, clinical researchers, clinicians, patients and communities
- Approaches that can drive quality and effectiveness while expanding knowledge
Can’t Be Business as Usual

- Payment system and clinical care delivery system must fundamentally change
- Hospitals become cost centers **NOT** profit centers
- New collaborative models to ask and answer questions must be formed
- **Research and practice advances must be united and transformed**
How Did We Get Here?
I wonder what is was like...

In The Beginning...
The first research project
The effect of deception in a group of educationally naïve humans
The apple
Wanting to do this right, God sought the approval of the interplanetary group of responsible top brass.
Benefit: Knowledge

Risk: Death

...not sure it would have met today's safety standards
Dear God:

Fascinating and innovative! But the title is not working for us. Too long and "researchy". And we definitely don’t get the apple. Why not something exotic, like....
The Pomegranate
God prepared a resubmission
The effect of deception in a group of educationally naïve humans
The **Effect of Deception in a group of Educationally Naïve humans**

.....or........
The EDEN Project
The apple
The Pomegranate
Dear God:

We are writing to you about the EDEN project. We LOVE it!!!!! But what’s the deal with the pomegranate… Why not something more simple and delicious – like…
The apple
God responded

“But the Angels are the ones who wanted the pomegranate”
That was the Angels from California. We sent the resubmission to a different review group.
The apple is BACK!
Human beings’ insatiable drive to acquire new knowledge was confirmed
God thought

“We need a neater way to investigate questions about human behavior”
A Neater way to Investigate questions about Human behavior

....or.........
And you might wonder if there really is an interplanetary group of responsible top brass
An Interplanetary group of Responsible top Brass
IRB

... so here we are!

Thanks to Richard Wender, MD for this story
Main Focus of NIH Research for 30 Years

- **Cells**
  - What’s possible?
  - Biochemistry
  - Cells/Tissues
  - Exp. Animals

- **Diseases**
  - Can it work?
  - Phase I Trials
  - Phase II Trials
  - Phase III Trials

**Basic Research** ↔ **Human Research**

T1
Come down to the contest ye Humorists: Let us take out of the Hospitals or the camps or elsewhere, 200, or 500 poor People, that have Fevers etc. Let us divide them in Halfes, let us cast lots, that one half of them may fall to my share and the other to yours; I will cure them without bloodletting...; but do you do as ye know. We shall see how many Funerals both of us shall have: But let the reward of the contention or wager, be 300 Floreens, deposited on both sides: Here your business is decided.

Van Helmont JA. Oriatrike London: Lodowick-Loyd, 1662, p.526
It had been so arranged, that this number was admitted, alternately, in such a manner that each of us had one third of the whole. The sick were indiscriminately received, and were attended as nearly as possible with the same care and accommodated with the same comforts. Neither Mr. Anderson nor I ever once employed the lancet. He lost two, I four cases; whilst out of the other third [treated with bloodletting by the third surgeon] thirty five patients died.”

Milne I and Chalmers I. J Epidemiol Community Health 2002;56:1a
Over 100 Years Later
During the last decades we have certainly bled too little
William Osler, MD
“It's hard not to scream when you see how many physicians, pharmaceutical companies, [and] medical-device makers...seem to hate science... These days the science that inspires fear and loathing is comparative-effectiveness research.”
Acute MI and the Occluded Artery
What to Do with a Blocked Artery?

Researchers tried to organize a randomized study of the benefits of angioplasty for patients who had suffered a heart attack three days or more before... 

Many doctors were so convinced of the value of this procedure...that they thought it would be unethical to assign any patients to the control group, which would get all the best medicines for this condition but not the artery-reopening procedure.
The Results! (n=2,166)

Hazard ratio, 1.16; 95% CI, 0.92–1.45; P=0.20

PCI group

Medical therapy group

Antman EM et al. JACC 2008;51:210-47
Basic Research

Human Research

Practice-Based Research

Practice

Cells

Diseases

People

Practices

What’s possible?

Can it work?

Will it work?

Who does it work for?

Cells

Diseases

People

Practices

Cells/Tissues

Biochemistry

Exp. Animals

Phase I Trials

Phase II Trials

Phase III Trials

Meta-analyses

Guidelines

Cost-effectiveness

Best Practices

Implementation

Comparative Effectiveness

Facilitation

Re-engineering

Phase IV Trials

Meta-analyses

Guidelines

Cost-effectiveness

Best Practices

Implementation

Comparative Effectiveness

Facilitation

Re-engineering

Practice

Not ready for humans

Not ready for patients

Not ready for practice
Two Way Arrows?

- DPP-IV inhibitors effect on psoriasis
- Effect noted by PBRN physicians shortly have release (Oct. 2006)

- Sitagliptin, a Dipeptidyl Peptidase-IV Inhibitor, Improves Psoriasis
  Noshioka T et al Dermatology 2012; 224:20-21
What happened here?
Anti-inflammatories for DM?

- Patient A
- Patient B
- Patient C
Arrests for illegal opioids up markedly
75-80% of the drugs are prescription medications being diverted
Could the medical community do something?
Worked with Local QI/Network Team

- Taught use of state registry
- Taught use of rule of 7
- Taught use of urine testing
- Other activities

- One year later prescription arrests down 300%

Research Focus of PBRNs Differs

- PBRNs study the “sharp end” of practice, using data gathered in the course of providing care to unselected patients.
- Health services research tends to focus on the blunt end of practice, using secondary analysis of administrative data sets.
- Randomized Controlled Trials typically enroll non-representative patients.
Why do we Care?: Selection Bias in Clinical Trials

- SHEP Trial: large RCT of treatment of HTN in elderly, only 24% participation rate
- Diabetes Prevention Trial: approximately 10,000 patients screened for <1000 enrollees
- 10 studies in regional PBRN participation rates were 84% to 96%
- AAFP NRN trials typically >80% participation rates with almost no exclusion criteria
The Ecology of Medical Care

1000 people, one month
800 with symptoms
327 consider care
113 receive primary care
13 go to ER
8 are hospitalized
< 1 at Academic Center
What we Need: PRACTICAL CLINICAL TRIALS

- Bold in the issues studied
- Creative in your intervention approach/synthesis
- Practical in intervention delivery
- Thorough in selecting a design
- Broad in what they measure
- Transparent (TREND*) in reporting

What to Look For: PRACTICAL CLINICAL TRIALS

- Do They Include **Multiple** Relevant Health Outcomes?
  - More than knowledge and blood assay
  - Outcomes relevant to patients, purchasers, clinicians, policy makers and the public
  - Include quality of life
  - Include economic outcomes
Taking Research to Scale

- Kidney Disease Outcomes Quality Initiative (KDOQI) are a mixture of evidence based information and expert opinion
- Reproducibility of efficacy studies has been variable
- No trials that look at impact of implementing the entire set of guidelines
Cluster randomized trial to implement KDOQI guidelines in 36 primary practices through clinical decision support versus full TRANSLATE model

- Tracking all outcomes through EHR and claims data
- Currently 24,000 patients with CKD in the study
Information Systems Support

- Clinical decision support at point of care
  - Adjust recommendations to new information or nuanced situations – high K⁺ and ACE/ARB
- Registries are highly desired
- Feedback reports at practice and clinician level
  - Missed opportunities reports may work better than traditional quality metrics
Broad Array of Outcomes

- Intermediate outcomes
  - Increased screening
  - Improved diagnosis (less under and over)
  - Change in eGFR
  - Change in ACR

- Patient outcomes that matter
  - Stage 5 / ESRD
  - Death – linkage to NDI
Adverse Outcomes

- Adverse effects
  - Number of individuals who develop hyperkalemia
  - Rate of Hip, forearm or clavicle fractures on and off ACE/ARB
  - Instances of acute renal failure
Look to a New Model of Research

- Study / improve care in real settings
- Look for a long-term relationship with the research team
- Look for designs that are inclusive
- Expect interventions that can be maintained
- Find measures important to patients
- Have fun
How can I get involved?

- "Hard work spotlights the character of people: some turn up their sleeves, some turn up their noses, and some don't turn up at all." - Sam Ewing
  - *Show up!*

- “Men occasionally stumble over the truth, but most of them pick themselves up and hurry off as if nothing had happened.”
  -- Winston Churchill
  - *Pay attention and don’t hurry off!!!*
Why should I get involved?

- **F.P. Jones:** “Experience is that marvelous thing that enables you to recognize a mistake when you make it again.”
  - Get involved to share your experience

- **P.L. Berger:** "In science as in love, too much concentration on technique can often lead to impotence.”
  - Get involved to do research without knowing how

- **Confucius:** “Tell me and I'll forget; show me and I may remember; involve me and I'll understand.”
  - Get involved to learn how
Help Generate New Knowledge

- Question the status quo
- Collect data that matters
- Share your observations
- Participate in research

JOIN A PBRN!
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