

Evidence Based Medicine

Alaska Health Care Commission
October 15, 2010
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Definition:

- Evidence-based medicine (EBM) aims to apply the best available evidence gained from the scientific method to medical decision making. It seeks to assess the quality of evidence of the risks and benefits of treatments (including lack of treatment).

en.wikipedia.org/wiki/Evidence-based_medicine

Evidence Based Medicine

- **FDA Chief Focuses on Antibiotic Resistance**
 - Wall Street Journal 10/6/10
 - FDA seeing antibiotic resistance in virtually all antibiotics
 - We no longer have effective ways to treat serious disease
 - Clearly we must encourage more judicious use of these important drugs
 - The drugs have been almost routinely used in recent years for common colds and ear infections in children

**Evidence Based Medicine
This Month's Headlines**

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- **PSA tests can cause more harm than good**
 - San Francisco Chronicle 10/1/10
 - Sadly most men are never told the facts about the test, nor are they encouraged to make their own informed decision
 - Most of the men so treated would have been just fine if they never knew about the cancer. But when they're treated (whether with surgery, radiation, or chemotherapy) the majority suffer really life-affecting effects such as impotence and/or incontinence. That is why both of the two very large trials of PSA screening published in 2009 found no (or at most a tiny) benefit but a great deal of harm

**Evidence Based Medicine
This Month's Headlines**

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- PSA Screening – additional data
 - European trial
 - 162,243 men aged 55-69
 - 1,410 men would need to be screened and 48 additional cases of prostate cancer would need to be treated to prevent one death – high risk of over-diagnosis
 - American trial
 - 76,693 men aged 55-74
 - No overall reduction in mortality in the screening arm

Evidence Based Medicine This Month's Headlines

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- The Uncritical Use of High-Tech Medical Imaging
 - New England Journal of Medicine
 - Until recently these costs were the fastest growing physician-directed expenditures in the Medicare program
 - There is broad agreement that an unknown but substantial fraction of imaging examinations are unnecessary and do not positively contribute to patient care
 - Much imaging practice is driven by habit or anecdote

Evidence Based Medicine This Month's Headlines

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- **A Surge in CT and MRI Scans Has Not Boosted Diagnosis Rates**
 - Scientific American 10/5/10
 - A new study shows that for life-threatening injuries, a threefold increase in the number of CT and MRI scans in the emergency room has not resulted in an improvement in useful diagnosis
 - One study estimated that CT scans in the US in 2007 will lead to an additional 29,000 cases of cancer

Evidence Based Medicine This Month's Headlines

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- **Too Much of a Good Thing?**
 - Washington Post 1/15/08
 - The number of (CT) scans performed each year in the US has increased sharply, rising from about 3 million in 1980 to at least 67 million in 2006.
 - The upsurge in CT use has fueled a big jump in the annual amount of radiation that each American is receiving from medical procedures of all kinds. The average level of that exposure has increased about 600-fold since 1980, according to a federal report being published this year.

Evidence Based Medicine Headlines

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- **A Simple Health-Care Fix Fizzles Out**
 - WSJ 2/11/2010
 - Courage Study – NEJM 2007
 - Applies to 1/3 who receive stents – those with chronic stable chest pain
 - 5 year study – chest pain patients –no survival, MI, or pain advantage to stents vs. drugs
 - 1st year 13% drop use of stents and drop in Boston Scientific stock price
 - Back to 1 million stents/year
 - “What is going to continue to drive practice is reimbursement” – Wm. Boden, M.D.
 - Potential saving \$5billion

Evidence Based Medicine Headlines

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- **How Medicare Could Use Comparative Effectiveness Research in Deciding on New Coverage and Reimbursement**
 - Health Affairs 10/10
 - Paying equally for comparable results is a powerful principle
 - This is not about saying “no”. It is about saying “yes and we will pay you more” or “yes and we will pay you the same” or “yes and we will give you the benefit of the doubt for (three years) to stimulate innovation

Comparative Effectiveness Research This Month’s Headlines

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- Health Care Reform: Prove it Works and CMS Will Pay
 - The Fiscal Times 10/5/10
 - The authors' proposed pricing method leaps over the roadblocks to using comparative effectiveness research that were included in the recently enacted health care reform law which specifically prohibited CMS from using comparative effectiveness research to deny patients access to any technology that has been approved by the FDA.

**Comparative Effectiveness
Research
This Month's Headlines**

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**Haven't we gotten along well
without evidence based medicine?
Some History**

**Who killed
George
Washington?**

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- extensive bloodletting, with a total of 3.75 liters of blood taken and the massive deliberate blood-loss contributing to the additional serious complication of shock
- a team of doctors for aggressive treatment. They bled him of five pints of blood, burned his neck, and gave him calomel, a mercury compound used as a purgative but which probably did little more than induce mercury poisoning.

Who Killed George Washington?

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- A footnote to history:
 - And in one final ironic twist, Martha appears to have been against bleeding. Ever a faithful student of the science of the Enlightenment, George ignored his wife's advice and followed the informed opinion of some of the best-trained physicians in the western hemisphere. If he had simply done what most husbands in history would have done and obeyed his wife, he might not have died.

Who killed George Washington?

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Haven't we gotten along well without evidence based medicine? Some Recent History

- Should we trust FDA approval?
 - Vioxx
 - September 30, 2004
 - Pharmaceutical giant Merck & Co. is pulling its arthritis drug Vioxx from the market after a study confirmed earlier concerns that it raises the risk of heart problems, including heart attacks
 - has been used by more than 84 million people around the world
 - The drug was approved by the FDA in May 1999 for the relief of osteoarthritis and menstrual pain, and later for treatment of the signs and symptoms of rheumatoid arthritis.

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Haven't we gotten along well without evidence based medicine? Some Recent History

- Should we trust FDA approval?
 - Avandia (2010)
 - **AVANDIA can cause or worsen heart failure. If you have severe heart failure (very poor pumping ability of the heart) you cannot be started on AVANDIA. AVANDIA is also not recommended if you have heart failure with symptoms (such as shortness of breath or swelling), even if these symptoms are not severe.**
 - **AVANDIA may increase your risk of other heart problems that occur when there is reduced blood flow to the heart, such as chest pain (angina) or heart attack (myocardial infarction).** This risk appeared higher in patients taking medicines called nitrates or insulin.
 - Side effects have been linked to very serious heart problems when taken with insulin. Avandia is produced by GlaxoSmithKline and was first approved by the Food and Drug Administration in 1999 to treat type II, or adult onset diabetes, Avandia quickly became one of the most popular drugs for the company GlaxoSmithKline

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"Up until about 40 years ago, medical decisions were doing very well on their own, or so people thought. The complacency was based on a fundamental assumption that through the rigors of medical education, followed by continuing education, journals, individual experiences, and exposure to colleagues, each physician always thought the right thoughts and did the right things. The idea was that when a physician faced a patient, by some fundamentally human process called the "art of medicine" or "clinical judgment", the physician would synthesize all of the important information about the patient, relevant research, and experiences with previous patients to determine the best course of action."

David M. Eddy
Health Affairs 24 no. 1 (2005)

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Medical management led by "expert opinion" or as a result of "consensus conferences"

- Prevention of purulent otitis media among Alaska Native children
- What is the proper surgery for peptic ulcer disease?
- What is the best surgery for papillary carcinoma of the thyroid gland?

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- Evidence-based medicine (EBM) aims to apply the best available evidence gained from the scientific method to medical decision making. It seeks to assess the quality of evidence of the risks and benefits of treatments (including lack of treatment).

Evidence Based Medicine

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- Is the appropriate question whose evidence?
 - No!
- The appropriate question is what is the evidence and how strong is it?
 - There are statistically and scientifically sound widely accepted norms for grading the strength of evidence
- What is meant by “grades of evidence”?

Evidence Based Medicine

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- How and where are the principles of Evidence Based Medicine applied?
- What should the health care system and health care providers be guided to do if they utilize evidence based criteria? What are the recommendations?

Evidence Based Medicine

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What is meant by "grades of evidence"?

US Preventive Services Task Force

- Level I: Evidence obtained from at least one properly designed randomized controlled trial
- Level II-1: Evidence obtained from well-designed controlled trials without randomization
- Level II-2: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one center or research group
- Level II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence
- Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

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- Evidence-based guidelines (EBG) is the practice of evidence-based medicine at the organizational or institutional level. This includes the production of guidelines, policy, and regulations. This approach has also been called evidence based healthcare.
- Evidence-based individual decision (EBID) making is evidence-based medicine as practiced by the individual health care provider.

How and where are the principles of evidence based medicine applied?

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Categories of recommendations US Preventive Services Task Force

- Level A: Good scientific evidence suggests that the benefits of the clinical services substantially outweighs the potential risks. Clinicians should discuss the service with eligible patients.
- Level B: At least fair scientific evidence suggests that the benefits of the clinical service outweighs the potential risks. Clinicians should discuss the service with eligible patients.
- Level C: At least fair scientific evidence suggests that there are benefits provided by the clinical service, but the balance between benefits and risks are too close for making general recommendations. Clinicians need not offer it unless there are individual considerations.

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Continued

- Level D: At least fair scientific evidence suggests that the risks of the clinical service outweighs potential benefits. Clinicians should not routinely offer the service to patients.
- Level I: Scientific evidence is lacking, of poor quality, or conflicting, such that the risk versus benefit balance cannot be assessed. Clinicians should help patients understand the uncertainty surrounding the clinical service.

Categories of recommendations US Preventive Services Task Force

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- Base decisions on evidence of effectiveness and benefit
 - When there is evidence of benefit, **do it**
 - When there is evidence of no benefit or harm, **don't do it**
 - When there is insufficient evidence to determine if there is benefit, be conservative: **use individual discretion, but if there are harms or costs, don't do it**

Recommendations Paraphrased Courtesy Neil Calonge, MD, Chair US Preventive Services Task Force

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- Define the question about the provision of a therapeutic or preventive service within an analytic framework
- Define and retrieve relevant evidence
- Judge the quality of individual studies and the adequacy of evidence for key questions
- Synthesize and judge the adequacy of the body of evidence across key questions

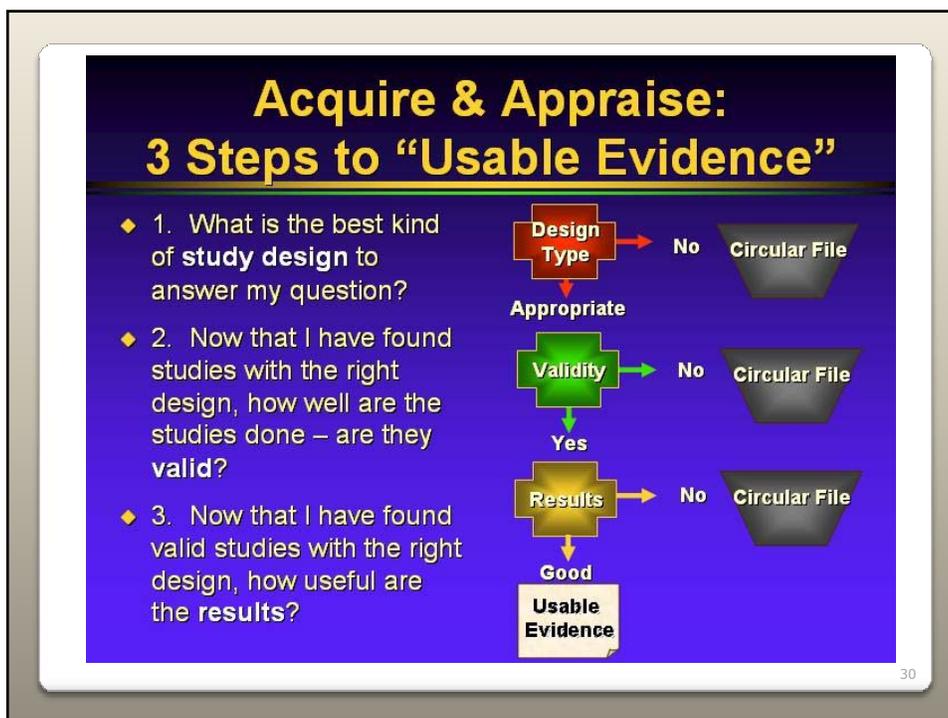
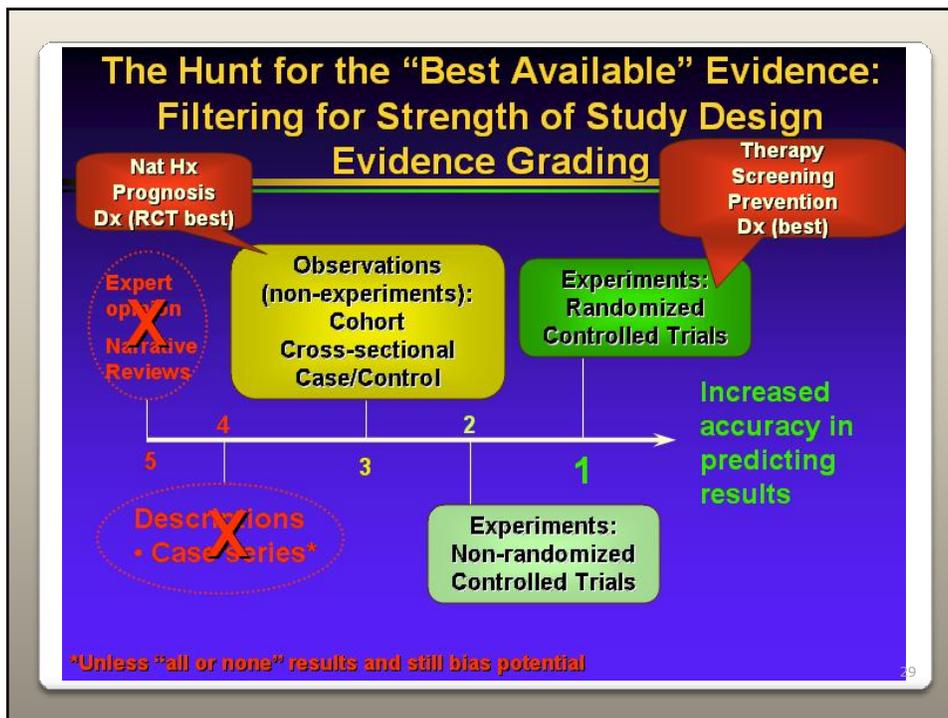
Steps in a formal evidence based analysis

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- Judge the certainty of net benefit (balance of benefits and harms)
- Link magnitude and certainty of net benefit to a recommendation statement/letter grade (A, B, C, D, I)

Steps in a formal evidence based analysis (continued)

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Anatomy of an Article

Title – Useful to determine relevance

Abstract – Only useful for deciding you want to review the study – data is often not verifiable in body of article!

Body – Critically appraise key elements of the study e.g., population, methodology, possible biases, etc.

Tables – Highly useful (be sure to look for baseline comparisons, for example)

Results – Vital importance (*if study is valid!!!*)

Conclusions – NOT evidence! This is opinion

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- Hypothetical case:
 - 100 people have condition X. All are treated with treatment Y. At the end of five years 10% of those treated die from the disease and 15 percent of those not treated die from the disease.

**How big is the difference –
Different ways to say the same
thing**

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- **Relative Risk Reduction (RRR)**
 - If 15 die without treatment and 10 die with treatment the RRR is 33%
- **Absolute Risk Reduction (ARR)**
 - The ARR is 5%
- Measures of outcomes
 - In five years 90% are living with treatment and 85% are living without treatment (assuming no other cause of death)

**How big is the difference –
Different ways to say the same
thing**

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- Examples of RRR of 33%:
 - (A) At five years 85% are alive without treatment and 90% with treatment
 - (B) At five years 40% are alive without treatment and 60% with treatment
 - (C) At five years 10% are alive without treatment and 40% with treatment
 - Dead 15% vs. 10%; 60% vs. 40%; 90% vs. 60%
 - All examples are of a 33% risk reduction

**How big is the difference –
Different ways to say the same
thing**

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- **Number Needed to Treat (NNT)**

- The number of individuals you need to treat to have one individual have the desired outcome
- Methodology is 100% divided by the Absolute Risk Reduction
- Example (A) = $100\%/5\% = 20$ NNT
- Example (B) = $100\%/20\% = 5$ NNT
- Example (C) = $100\%/30\% = 3.3$ NNT
- All three examples have a relative risk reduction of 33%

**How big is the difference –
Different ways to say the same
thing**

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- We look at the peer reviewed scientific literature

- How strong is the evidence in terms of the grades of evidence we are looking for?
 - A double blinded randomized control study with a sufficient number of participants to achieve statistical significance is the strongest evidence
 - Means therapist, evaluator, and subject do not know if agent or placebo is administered and subjects are assigned totally randomly but are otherwise comparable to each other.
 - This is relatively easy to achieve for some kinds of therapies such as pharmaceuticals or for certain screening testing procedures.
 - This is difficult to achieve for some kinds of therapies such as surgical procedures (we don't like to subject people to sham procedures).

How is this applied?

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- We subject the results to statistical analysis to see how likely it is the results are just due to chance. Commonly we want to see a likelihood of 5% or less that the results are due to chance. (p value of .05 or less)
- We look at RRR (Relative Risk Reduction), ARR (Absolute Risk Reduction), NNT (Number Needed to Treat)
- With Comparative Effectiveness Research we also look at comparisons of both relative effectiveness and cost for alternative therapies or tests.

How is this applied?

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- Evidence based medicine experts initially stayed away from relative or absolute cost issues.
- With the reality that resources are not unlimited and that we probably have the technical ability to justifiably spend our total GDP on health care, cost issues and comparisons cannot be avoided.
- This reality led many to the term Comparative Effectiveness Research

How is this applied?

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- The next several slides deal with cost issues that are usually ignored but that in reality all come with a trade off related to some other potential or real perceived good – on an individual or societal basis. Because it is easy to understand, I have selected pharmaceutical examples
 - E.g.
 - Education
 - Roads
 - Retirement
 - Anything

How is this applied?

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- Bob Svensson is an 80 year old with incurable prostate cancer
 - Provenge was approved by the FDA for advanced prostate cancer 4/10.
 - Provenge will cost \$93,000 for the one dose that will help Bob
 - The studies show that Provenge will extend Bob's life by four months
 - Bob says he has elected the therapy since his insurance covers it but "I would not spend the money because the benefit doesn't seem worth it".

Real Life

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- Revlimid has been approved by the FDA for relapsing multiple myeloma
 - Revlimid costs \$10,000 a month and is given monthly
 - Revlimid plus methotrexate results in average survival for these patients of more than 29 months
 - Methotrexate alone results in average survival for these patients of more than 20 months
 - Nine months added survival for average cost of an additional \$290,000 plus administration fees

Real Life

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- Tarceva is FDA approved for pancreatic cancer
 - Tarceva costs \$4,000 a month plus administration fees.
 - Tarceva plus standard therapy results in average survival of about 192 days
 - Standard therapy alone for comparable patients results in average survival of 180 days

Real Life

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- Erbutix has been approved by the FDA and is effective for prolonging life for lung cancer patients
 - Erbutix costs between \$300,000 and \$800,000 a year for the drug and administration costs

Real Life

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- Rheumatoid arthritis –a common diagnosis
 - Treatments include NSAIDS, patient education, pain management, low dose glucocorticoids, DMARDS, and the newer biologic drugs – in increasing order of cost
 - Concept of QALY (Quality Adjusted Life Year)
 - Addition of DMARD (methotrexate) costs \$4,849 per QALY
 - Addition of biologic agent (e.g. HUMIRA – adalimumab or Embrel – etanercept) costs \$157,350 per QALY (Annals of Internal Medicine)

Real Life

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- Resistant hemophilia
- Healthy adolescent male Medicaid enrollee
- Goes to school, engages in sports (his right?, develops hemarthroses)
- Superbly medically managed by Puget Sound Blood Center
- Over a four year period medication costs alone ran two to five million dollars a year

Real Life

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- “Primum non nocere”
 - Virtually everything a physician does for or to a patient carries some risk
 - Blood letting
 - Prefrontal lobotomy
 - Thalidomide (Phocomelia)
 - Vioxx
 - Avandia
 - Sibutramine (Meridia)(hot off the griddle - October 8, 2010 — Abbott Laboratories has withdrawn the obesity drug sibutramine (*Meridia*) from the market in light of clinical trial data pointing to an increased risk for stroke and myocardial infarction, the US Food and Drug Administration (FDA) announced today.

Why do we need EBM?

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- Society trusts the health care sector with a huge portion of our national treasure.
- The costs of health care are placing a heavy financial burden on federal and state governments and on employers.
- We need to assure that policy and clinical decision making consider both effectiveness and cost effectiveness of health care interventions. EBM and CER allows us to do that objectively.

Why do we need EBM?

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- **Archie Cochrane** - Scottish Epidemiologist - Published *Effectiveness and Efficiency: Random Reflections on Health Services* (1972)
- **David Sackett & Gordon Guyatt** - Canadians - McMaster University
- **David Eddy** - USA - Duke University, Kaiser Permanente - first used term "Evidence Based" in 1990
- **Anna Gordon** - Australian - Founded BMJ's *Clinical Evidence*, the *Journal of Evidence Based Healthcare*, and *Evidence Based Policy*
- **John Wennberg** - USA - Dartmouth - Leading researcher in unwarranted variation in the healthcare industry. Founded Center for Evaluative Clinical Services in 1988

EBM Pioneers

Examples

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- Organizational Technology Evaluation Committees
- Cochrane Collaboration and Library
- Hayes, Inc. – Directories, reviews, briefs, research
- Technology Evaluation Center – Blue Cross Blue Shield Association and Kaiser
- Delfini – Assistance with how organizations can become an evidence based system capable of finding and closing quality and cost gaps.

Resources

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What is the role for the HCC related to Evidence Based Medicine in Alaska?

- Understand the potential for enhancing the quality of health care clinical and policy decision making
- Understand the potential of EBM/CER for assuring that health care resources are used most effectively and efficiently and that the resources available achieve the greatest health good for Alaskans

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What is the role for the HCC related to Evidence Based Medicine in Alaska?

- Recommend in our annual report the increased use of EBM/CER by Alaskan physicians and other providers, health care facilities, and governmental and private payers

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Questions?

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