

# Non Pharmacological Therapies and Evidence-Based Medicine: Challenging Current Approaches and Outcome Measures

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**Neuro-Cog**

<http://www.neuro-cog.com>

Selección y actualización de diapositivas para  
las clases impartidas en el curso

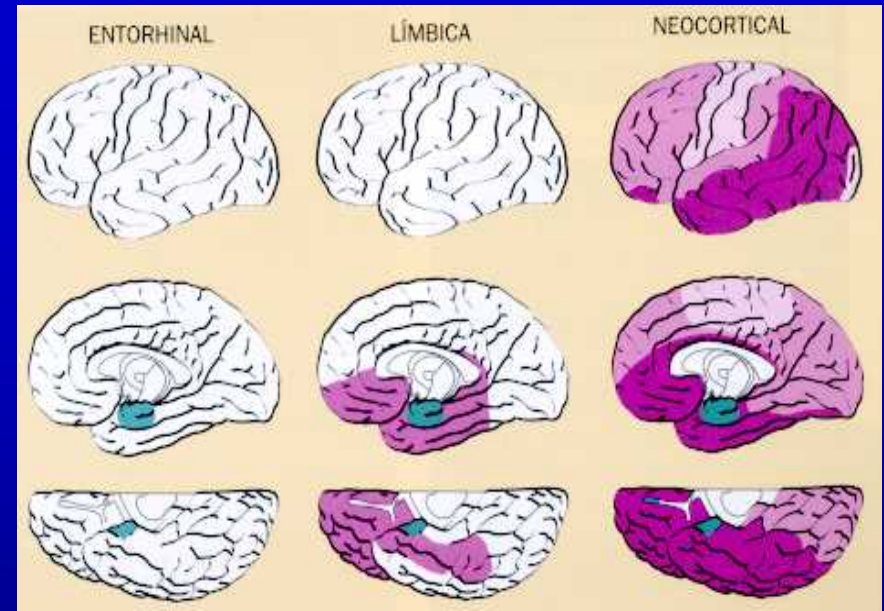
**NEUROBIOLOGIA DE LA CONDUCTA,  
FUNDAMENTOS Y AVANCES RECIENTES**

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**Pattern of brain destruction in Parkinson's and  
Alzheimer's diseases**

H. Braak<sup>1</sup>, E. Braak<sup>1</sup>, D. Yilmazer<sup>1</sup>, R. A. I. de Vos<sup>2</sup>, E. N. H. Jansen<sup>2</sup>,  
and J. Bohl<sup>2</sup>



**Early lesions:  
Transentorhinal region  
(medial temporal lobe)**

**Predictable pattern  
of evolution**

**Distribution of lesions  
in the brain**

**Symptoms**

## AD: A global (retrogenetic) approach

GDS	Diagnosis	Clinical characteristics
1	Normal	No subjective complaints or memory deficit
2	Normal ageing	Subjective complaints of memory deficit
3	Mild memory impairment	Earliest subtle deficits
4	Mild AD	Clear-cut deficit in clinical interview. Inability to perform complex tasks
5	Moderate AD	Patient can no longer survive without some assistance (e.g. choosing proper attire)
6	Moderately severe AD	Dressing, bathing properly, mechanics of toileting, urinary incontinence, fecal incontinence
7	Severe AD	All verbal abilities are lost over the course of this stage.

# NP-Therapy objectives

Etiology

(Time – Evolution) - Localization  
Extension & Intensity

Neurobiological pattern

Clinical pattern  
(symptoms)

Neurological  
*Medical*

Cognitive  
(Functional architecture)

Behavioral &  
Psychological

Activities of daily living: advanced, instrumental, basic

Health status

**QUALITY OF  
LIFE**

Environment  
(Physical & social)

**VALUES**  
- Dignity, personhood, self esteem...

caregivers

# Therapy: General objectives...

- Cognition
- Functional capacities (daily living)
- Physical, motor & sensory status
- Psychological and behavioral symptoms
- ... **Values**
- Quality of life (patient / caregiver)
- Burden (caregiver / staff)

**Outcome measure:** variable relevant to the research question that may be affected by the intervention

OUTCOMES MUST BE CLINICALLY RELEVANT

Global measures

Non Pharma Therapies for  
Alzheimer's  
METHODS. APPROACHES



Resolution therapy Pet-therapy Mental gymnastics  
Life revision Relax Occupational therapy  
Validation therapy Physical exercise Spouse support  
Brain activation Horse-Therapy Reflexology  
Cognitive training Bach Remedies Remotivation  
Behavior modification ADL training Psychotherapy  
Thalaso-therapy Reminiscence  
Music-Therapy REIKI Aroma-therapy  
ART-THERAPY Light-therapy Psycho-social therapy  
Caregiver education Psycho-stimulation  
Snoezellen  
MASSAGE-Therapy Reality orientation Counselling  
Environmental manipulation Electronic | computer memory aids  
Cognitive Therapy Psycho-Motor Therapy  
Humour-therapy Speech Therapy

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veritas-intel@happy.net

About

April 09, 2004. **Can Aromatherapy Help in Treating Alzheimer's Disease?**

Could the scent of cloves, lavender and frankincense help people with Alzheimer's disease eat better, sleep better and relax more?

Gerri Whidden says the answer is yes. The owner of Nature's Symphony aromatherapy shop in Boca Raton, her new mission is to encourage professional and family caregivers to tap into essential oils when caring for those with the debilitating neurological illness



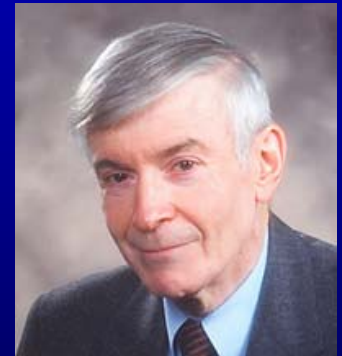
**REIKI.** August 20, 2004. Hi all! I have a good friend who is in the beginning stages of Alzheimer's & has asked me if Reiki would help it. She is taking a level 1 clas thru me next week. Thanks for any info you have.



# Quackwatch<sup>SM</sup>

Your Guide to Quackery, Health  
Fraud, and Intelligent Decisions

<http://www.quackwatch.org/>



Stephen Barrett, M.D.  
Allentown, Pennsylvania

*Nothing is more dangerous than active ignorance.*

Goethe


Quack: (Spanish = 1. *n.* charlatán, curandero / 2. *adj.* falso, fingido (remedy) de curandero:  
quack doctor: curandero. Quackery = Charlatanismo)

# Why bogus therapies seem to work...

1. The disease may have run its natural course
2. Many diseases are cyclical
3. Spontaneous remission
4. The placebo effect
5. Some allegedly cured symptoms are psychosomatic to begin with

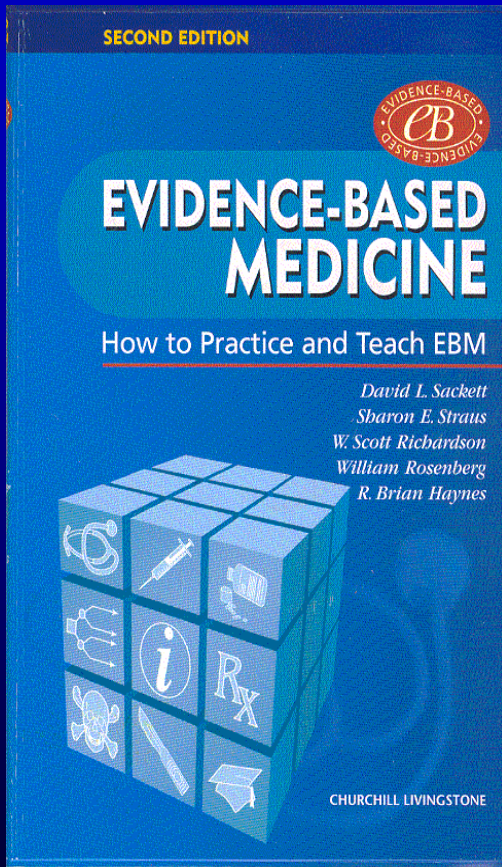
# Why bogus therapies seem to work...

6. Symptomatic relief versus cure
7. Many consumers of alternative therapies hedge their bets
8. Misdiagnosis (by self or by a physician)
9. Derivative benefits
10. Psychological distortion of reality



**OBJECTIVES**  
**METHODOLOGY**  
**OUTCOMES**  
**RECOMMENDATIONS**

# Evidence Based Medicine (EBM): Definitions...



- An approach to practicing medicine in which the clinician is aware of the evidence in support of her clinical practice, and the strength of that evidence.
- The conscientious, explicit and judicious *use of current best evidence in making decisions* about the care of individual patients

VALUES....

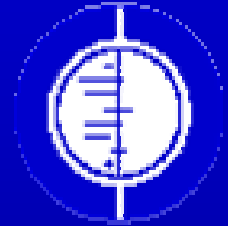
# EBM: a five steep model

1. Asking answerable clinical questions
2. Searching for the evidence
3. Critically **appraising** the evidence for its validity and relevance.
4. Making a decision, by integrating the evidence with your clinical expertise and the patient's values.
5. Evaluating your performance.

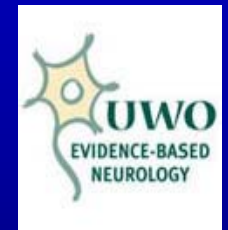
# Evidence-Based organizations/sites

(four examples)

- **The Cochrane Collaboration** ([www.cochrane.org](http://www.cochrane.org))



- **Evidence-Based Neurology Group.** University of Western Ontario. London, Ontario, Canada. ([www.uwo.ca/clinns/ebn/](http://www.uwo.ca/clinns/ebn/))



- **National Guideline Clearinghouse.** *Agency of Healthcare Research and Quality (AHRQ), with the American Medical Association (AMA) & the American Association of Health Plans.* ([www.guideline.org](http://www.guideline.org))



- **Bandolier: Neurological disorders** ([www.jr2.ox.ac.uk/bandolier/booth/booths/neurol.html](http://www.jr2.ox.ac.uk/bandolier/booth/booths/neurol.html))



# Appraising therapy articles

Is the study valid?

Are the results important?

- **Truth.** Are the conclusions substantiated by the data.
- **Validity.** Is the methodology sound and appropriate?
- **Probability.** Is the statistical analysis significant, or in the case of qualitative studies, are the findings cohesive

# Is the study valid?, I

1. Was there a clearly defined research question?
2. Was the assignment of patients to treatments randomized and was the randomization list concealed?
3. Were all patients accounted for at its conclusion? Was there an “intention-to-treat” analysis?

# Is the study valid?, II

4. Were research participants “blinded”?
5. Were the groups equally throughout?
6. Did randomization produce comparable groups at the start of the trial?

**Equipoise**



# OUTCOME MEASURES

- Is any feature that is recorded to determine the progression of the disease or problem being studied.
- Outcomes should be objectively defined and measured wherever possible.
- Often outcomes are expressed as mean values of measures rather than numbers of individuals having a particular outcome.

# Approach

## ■ Population

- Who is included/included and why?
- How were subjects recruited?

## ■ End-points

- Unequivocal, clinically significant, readily measured.

## ■ Follow-up

- Is the timescale appropriate for the purposes of the study

## ■ Analysis

- Power calculation to ensure that the study has adequate recruitment to provide significant results
- Is the statistical test appropriate?

# Are the results important?

- Three explanations for the observed effect:
  - Bias
  - Chance variation between the two groups
  - The effect of treatment

## ***p* values**

- Measure of the likelihood that the result could have occurred in the treatment was no better than the control

## ***d* values (size effect)**

- Overlapping percent

# Quantifying the risk of benefit and harm

## Event rates: calculation

	Control	Experimental
Event	<b>a</b>	<b>b</b>
No event	<b>c</b>	<b>d</b>

Control event rate

$$\text{CER} = \frac{a}{(a + c)}$$

Experimental event rate

$$\text{EER} = \frac{b}{(b + d)}$$

# Quantifying the risk of benefit and harm

- Relative risk reduction (RRR)
- Absolute risk reduction (ARR)
- Number needed to treat (NNT)
- Confidence intervals
- Relative risk (RR)

## Relative Risk Reduction (RRR)

- RRR is the percentage reduction in events in the treated group event rate (ERR) compared to the control group event rate (CER)

$$\text{RRR} = \frac{\text{CER} - \text{EER}}{\text{CER}}$$

## Absolute risk reduction (ARR)

- ARR is the absolute difference between the control and experimental group

$$\text{ARR} = \text{CER} - \text{ERR}$$

- ARR is a more clinically relevant measure to use than RRR. This is because RRR “factors out” the baseline risk, so that small differences in risk can be seem significant when compared to a small baseline risk

# Number needed to treat (NNT)

- NNT is the inverse of the ARR

$$\text{NNT} = \frac{1}{\text{ARR}}$$

- NNT is the most useful measure of benefit as it tells you the absolute number of patients who need to be treated to prevent one bad outcome.

# Confidence intervals (CIs)

- A 95% CI specifies that there is a 95% chance that the population's "true value" lies between the two limits.
- The 95% on a  $NNT = 1 / \text{the 95\% CI on its ARR}$ :

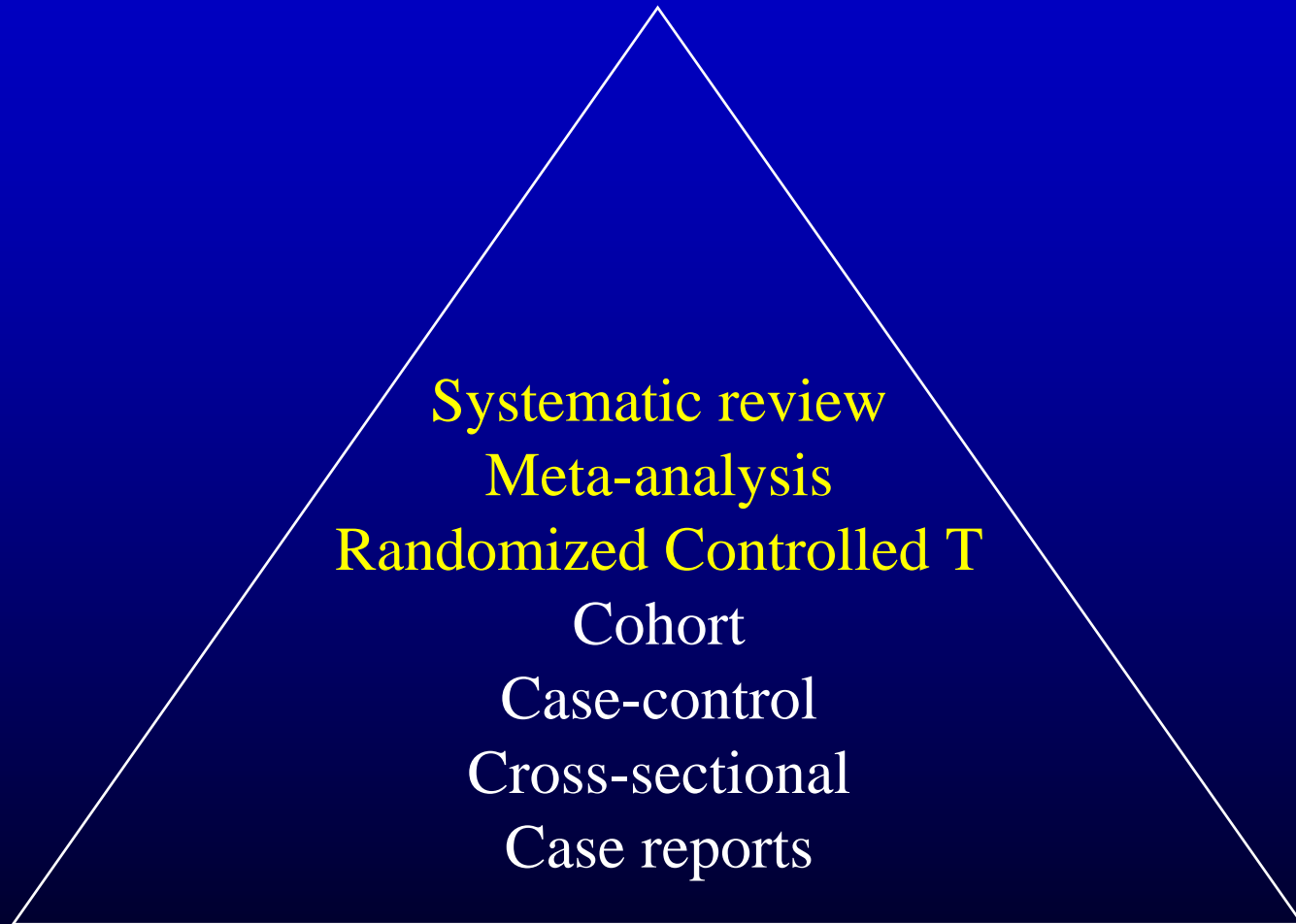
$$95\% \text{ CI on the ARR} = \pm 1.96 \cdot \sqrt{\frac{\text{CER} \cdot (1 - \text{CER})}{\# \text{ of control patients}} + \frac{\text{EER} \cdot (1 - \text{EER})}{\# \text{ of exper. patients}}}$$

# Relative risk (RR)

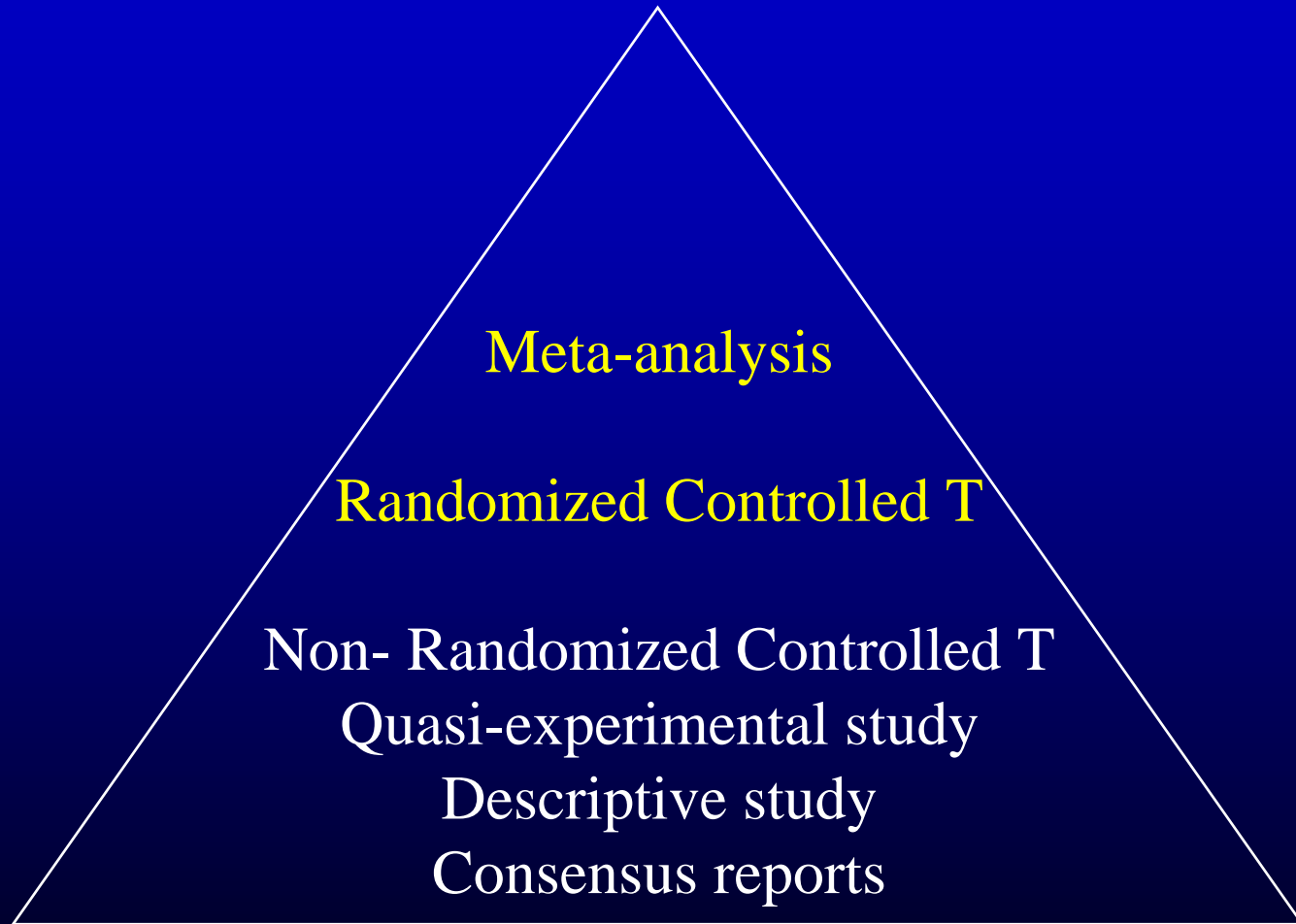
- RR is a ratio of the risk in the experimental group to the risk in the control group

$$RR = \frac{EER}{CER}$$

# Hierarchy of evidence in quantitative studies



# Categories of evidence



# Quality of evidence ratings for therapeutic modalities (AAN)

- **Class I:** Evidence provided by one or more well-designed randomized, controlled clinical trials, including reviews (meta-analyses) of such trials
- **Class II:** Evidence provided by one or more well-designed observational studies with concurrent controls (e.g., case control or cohort studies).
- **Class III:** Evidence provided by expert opinion, case reports, and studies with historical controls.

# Levels of recommendations (AAN)

- **Standard.** Principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical questions, or overwhelming Class II evid. when circumstances preclude randomized clinical trials).
- **Guideline.** Recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evid.)
- **Practice Option.** Strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).

A last point:

## Therapy as a life-empowering process

- Pragmatism
- Sensitive to everyday life needs
- Realistic objectives

*Nothing is more dangerous than active  
ignorance.* Goethe