

Clinical Research in Homeopathy

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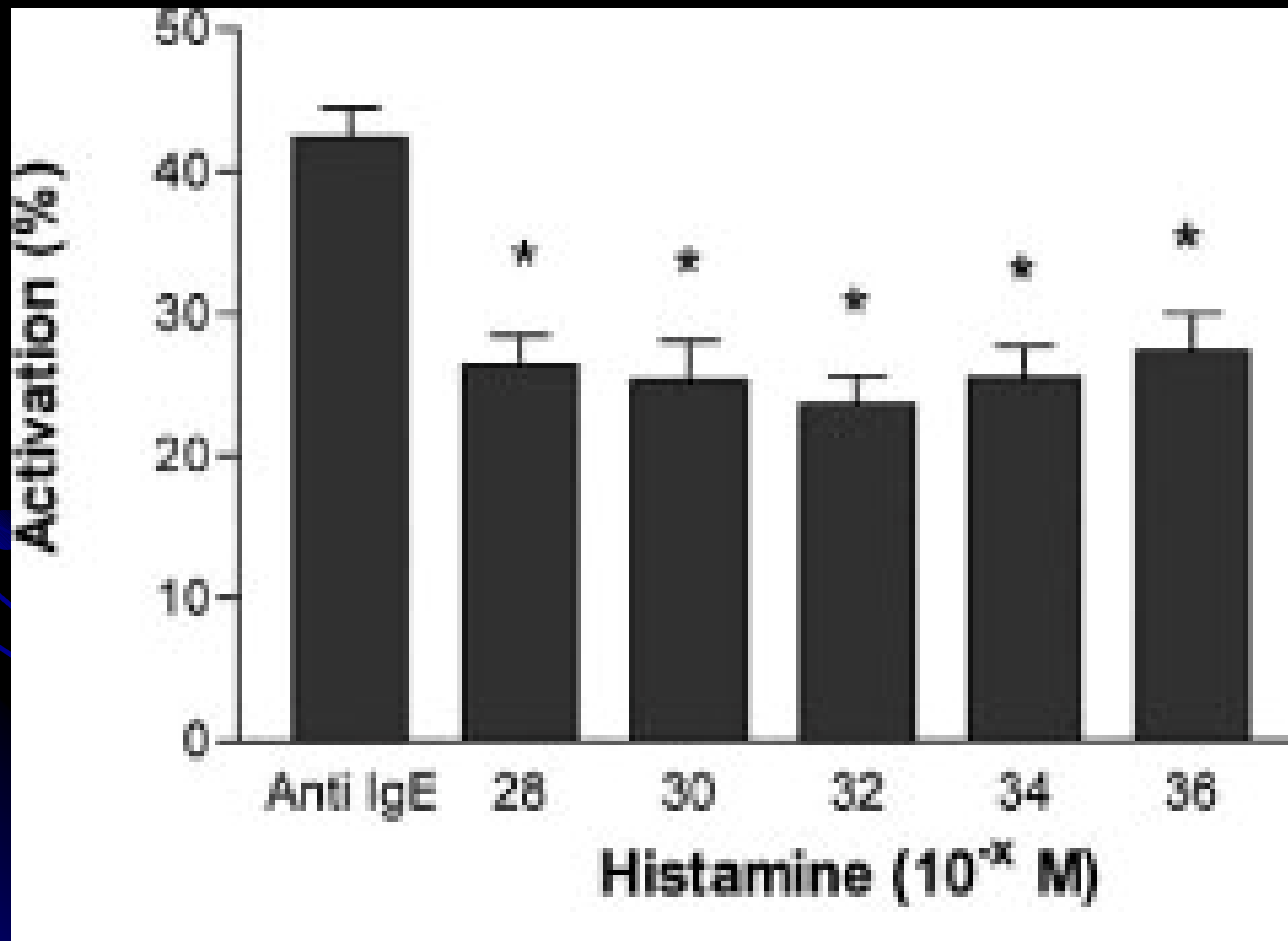
Overview of the Evidence

- | Preclinical and clinical studies demonstrate biological effects of homeopathic remedies
- | Multiple observational studies on thousands of patients are overwhelmingly positive in favor of safety and effectiveness of homeopathic treatment in real-world clinical practice
- | Randomized controlled trials (RCTs) and meta-analyses offer mixed findings and raise methodological concerns about inattention to external validity (relevance to actual homeopathic theory and practice) in deference to emphasis on internal validity criteria for judging study quality

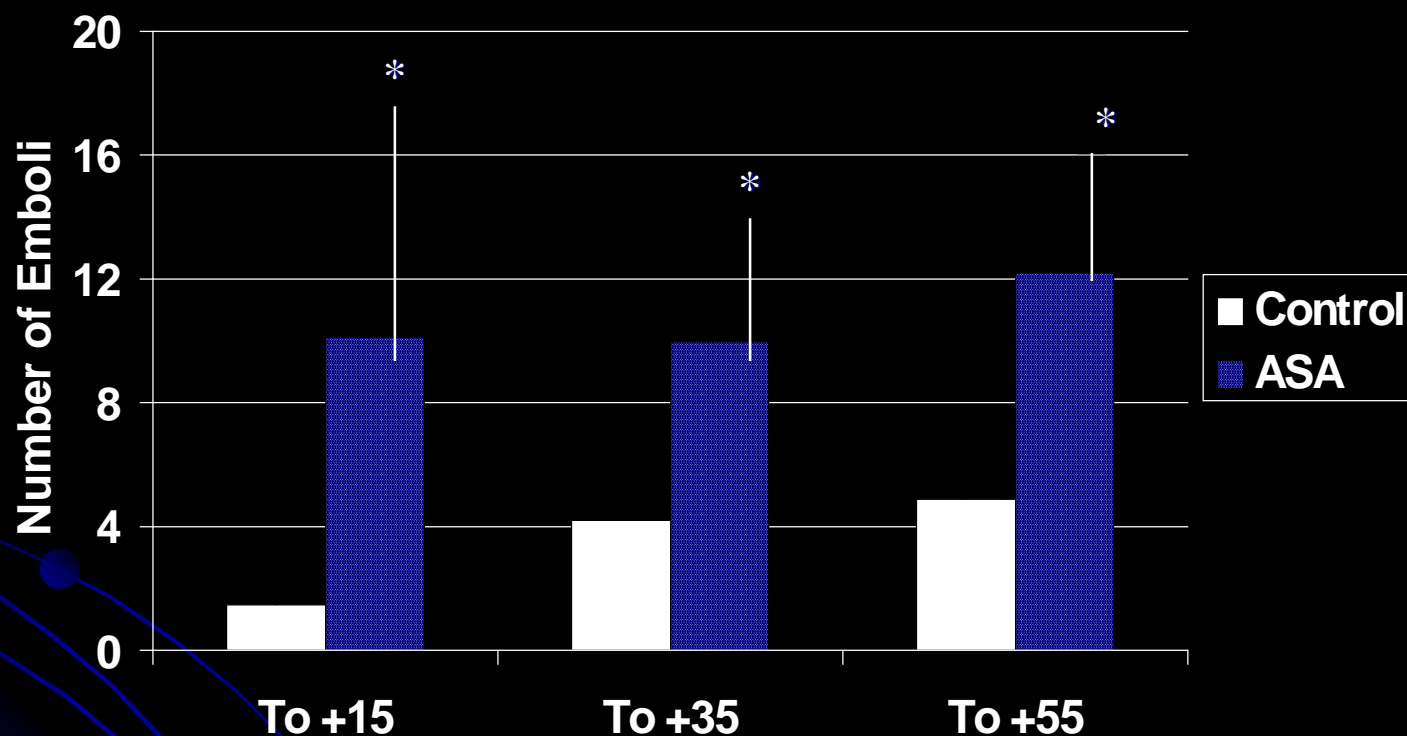
**Homeopathic Remedies
Exhibit Biological Activity
across Multiple *in vitro* and
in vivo Models**

Histamine Dilutions Modulate Basophil Activation Nonlinearly in Multi-Center Study

(Belon et al Inflammation Res 2004)



Thrombogenic Effects of Ultra-High Dilution Aspirin (ASA): A Nonlinear Dose-Response Relationship



Increased number of emboli after injection of saline buffer (control) or 10^{-10} nM ASA. Laser-lesions were induced 15, 35, 55 min. after ASA injection (T_0). Results are expressed as the mean \pm SD of 10 experiments.

* $p < 0.05$ as compared with the control group (Mann-Whitney test).

(Doutremepuich et al, *Thrombosis Research* 1994)

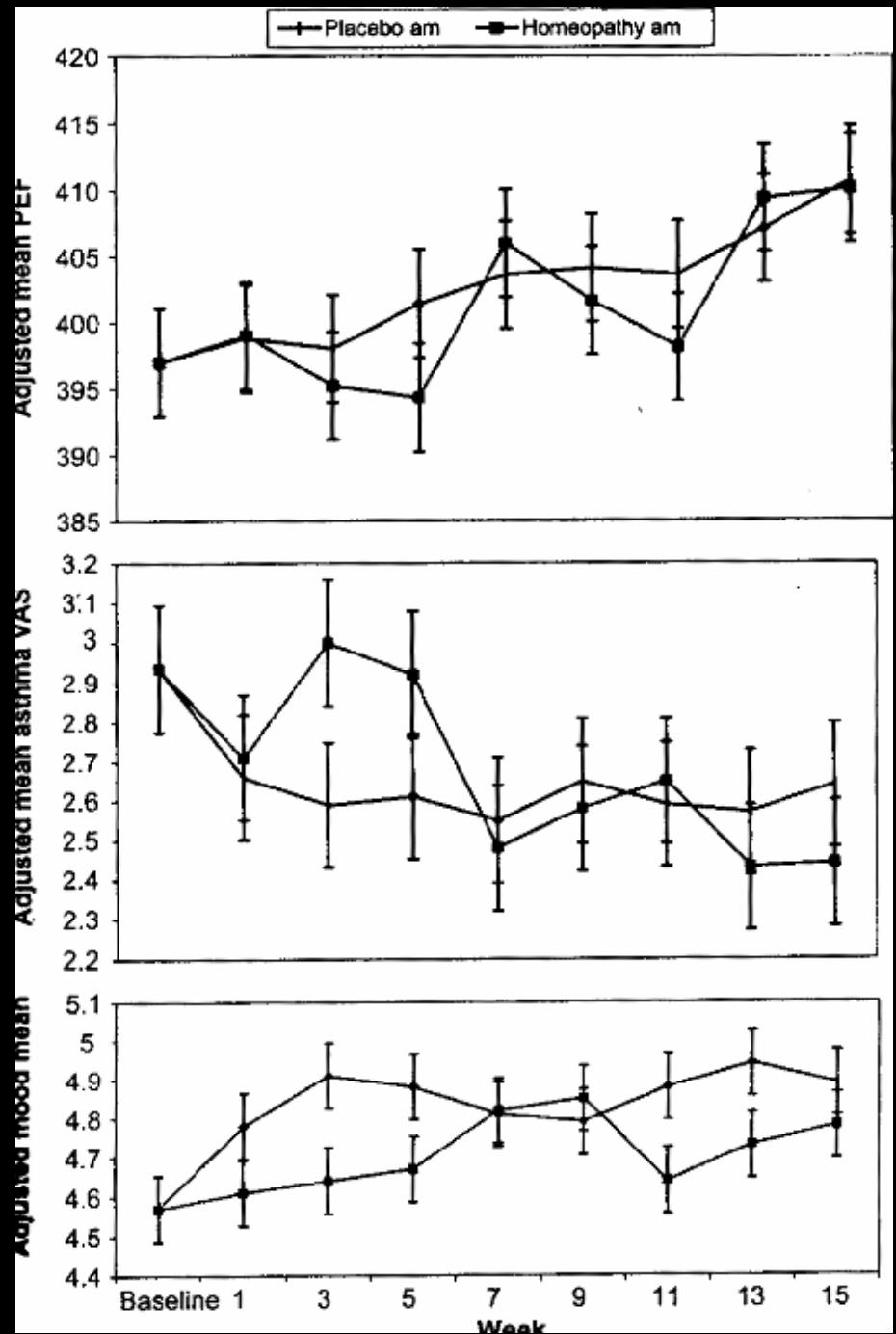
Animal Studies Demonstrate Biological Effects of Homeopathic Remedies

- ▮ Various homeopathic remedies reduce experimental, carrageenan-induced paw edema (Bertani et al 1999; Lussignoli et al 1999; Conforti et al 2007)
- ▮ Reduced experimental stroke damage with ultra-dilute glutamate, but not Arnica (Jonas et al 1999; see also Jonas et al 2001)
- ▮ Increased excretion & reduced toxicity of arsenic poisoning with Arsenicum Album 30c and higher potencies (Kundu et al 2000; Mallick et al 2003)
- ▮ Carcinisin and/or Chelidonium 200c ameliorate cytogenetical endpoint findings in a mouse liver cancer model (Biswas et al 2005)
- ▮ Homeopathic Histamine or Nux Vomica alter EEG sleep stages (Ruiz-Vega et al 2005; Ruiz & Torres 1997)
- ▮ Higher potencies (200c) of several homeopathic remedies prolong cataleptic effects of haloperidol (Sukul et al 1986)

Isopathic Dust Mite, but not Placebo, in Asthmatics Perturbs System into Oscillating Dynamical Behavior Without Clinical Improvements

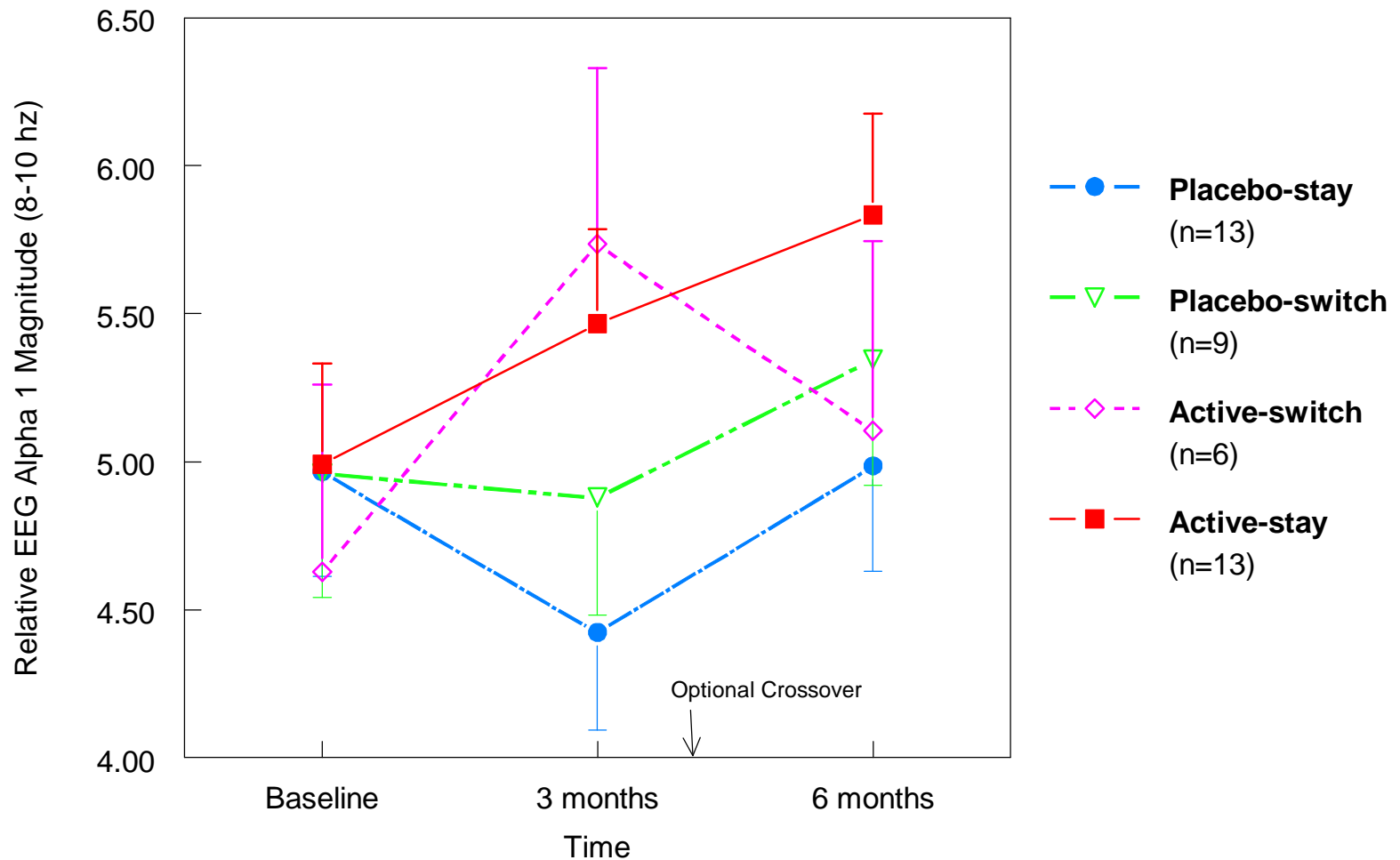
Conclusion: Disease-centered, non-individualized treatment with a homeopathically-prepared remedy is biologically active, but not clinically effective

(Lewith et al. *BMJ* 2002;
Hyland & Lewith *Homeopathy* 2002)



Individualized Homeopathic Treatment in Fibromyalgia Patients Produces Differential Changes in qEEG over Time vs Placebo

Changes in Eyes Closed EEG Alpha 1 during Bottle Sniffs Controlled for Baseline Mood, Emotional Neglect, & Medications



(Bell et al. *Int J Neuroscience* 2004)

Systematic Review of *in vitro* Homeopathic Studies (Witt et al. 2007)

- | CONCLUSIONS: “Even experiments with a high methodological standard could demonstrate an effect of high potencies [beyond Avogadro’s number].
- | No positive result was stable enough to be reproduced by all investigators.
- | A general adoption of succussed controls, randomization and blinding would strengthen the evidence of future experiments.”

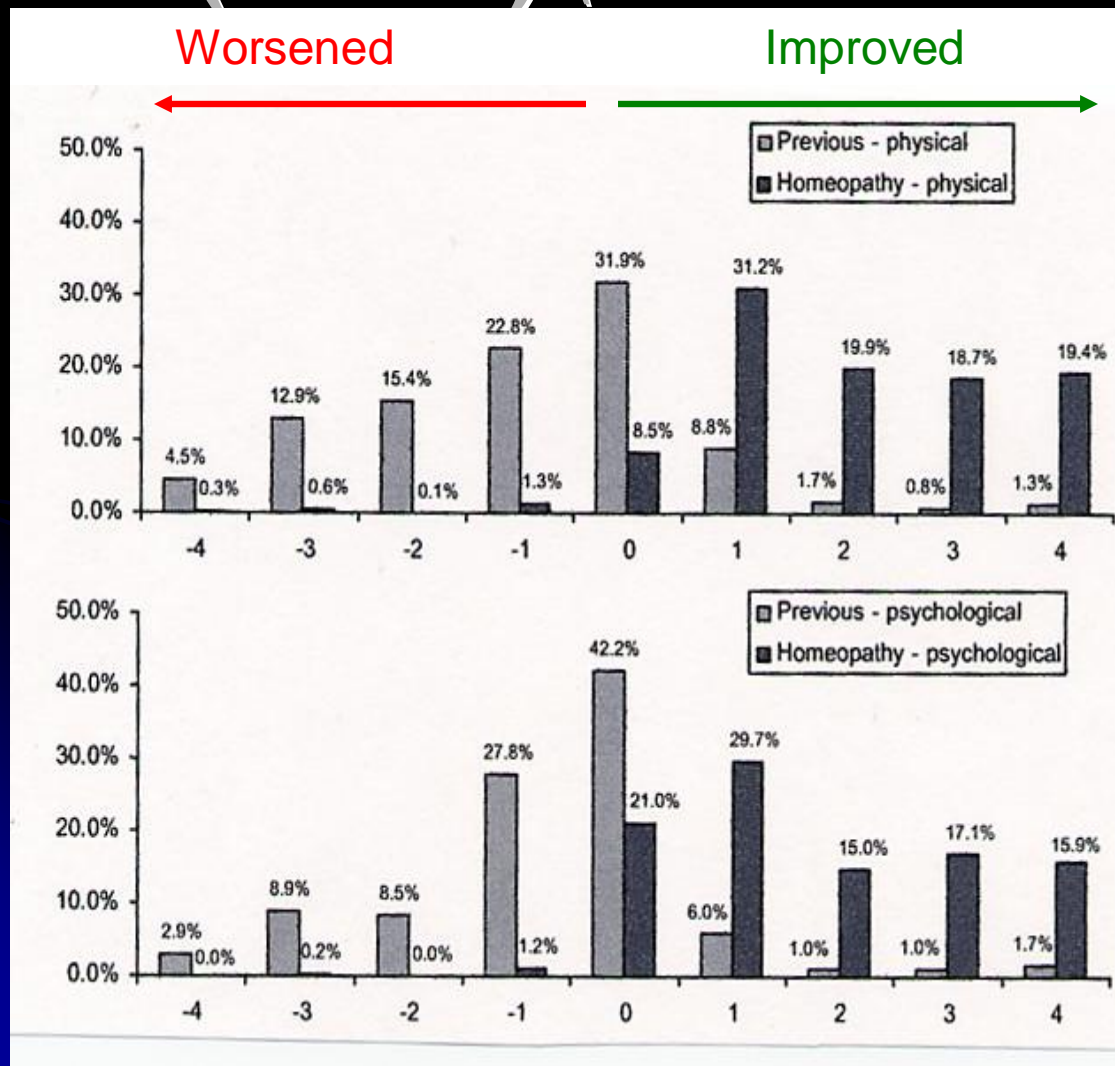
**Observational Studies Show
Real-World Effectiveness of
Individualized Homeopathic
Treatment across Multiple
Conditions with Longer-Term
Follow-Up**



Consistently Positive Outcomes for Homeopathy in Observational Research

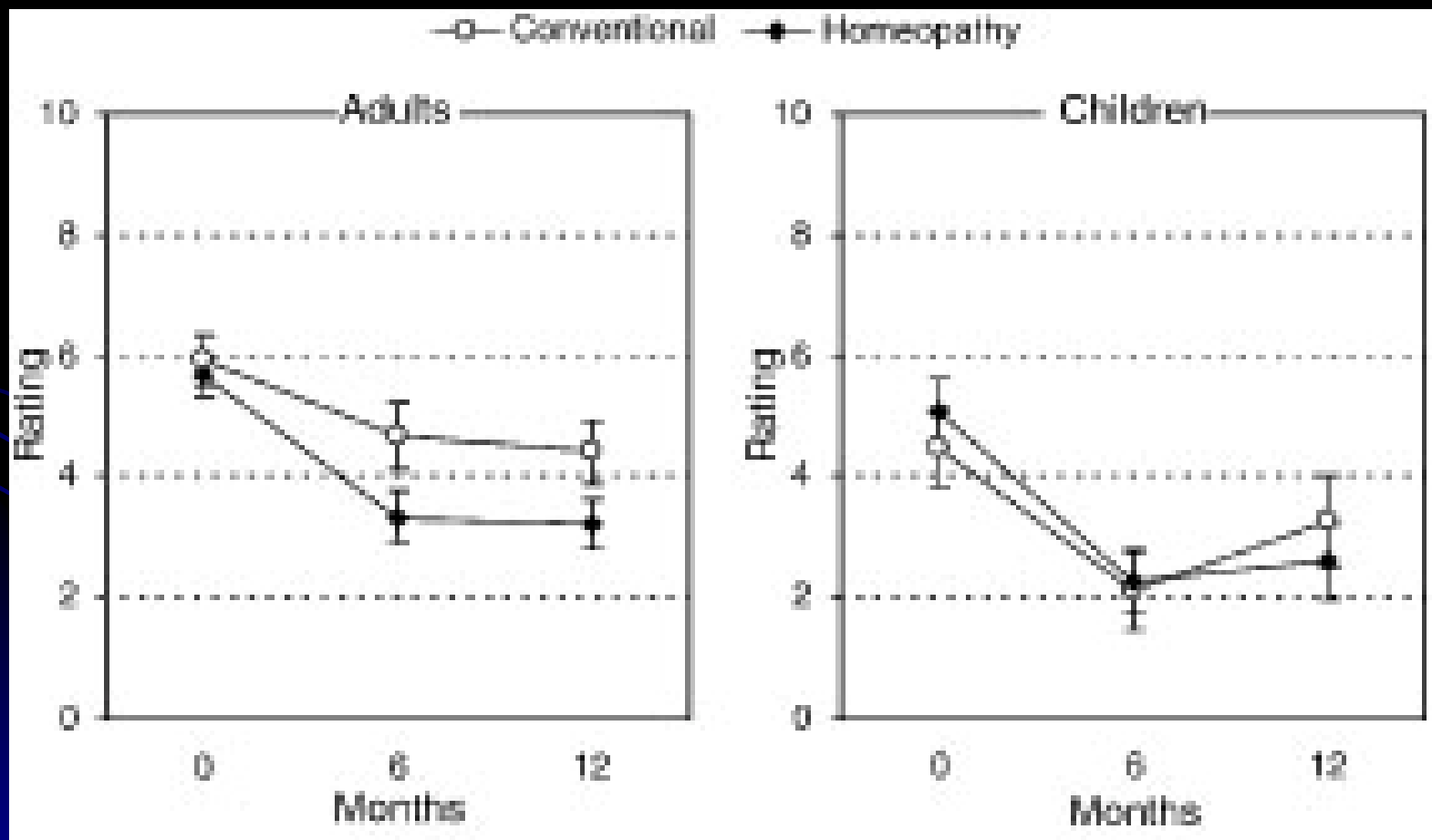
- | Multiple observational studies show moderate to marked improvement in the majority of patients, a good safety record, high satisfaction, and, in many but not all cases, lower overall costs of care
- | Goldstein & Glik (1998) and van Wassenhoven & Ives (2004) report sustained good outcomes in homeopathically-treated patients who had failed other CAM and conventional treatment
- | **Well-designed cohort or case-control observational studies do not overestimate treatment effects compared with “gold standard” randomized, controlled trials on same topic (Concato et al, NEJM 342:1887-92, 2000)**

Perceived Effectiveness in Belgian Primary Care Observational Study (N=782) (van Wassenhoven & Ives 2004)

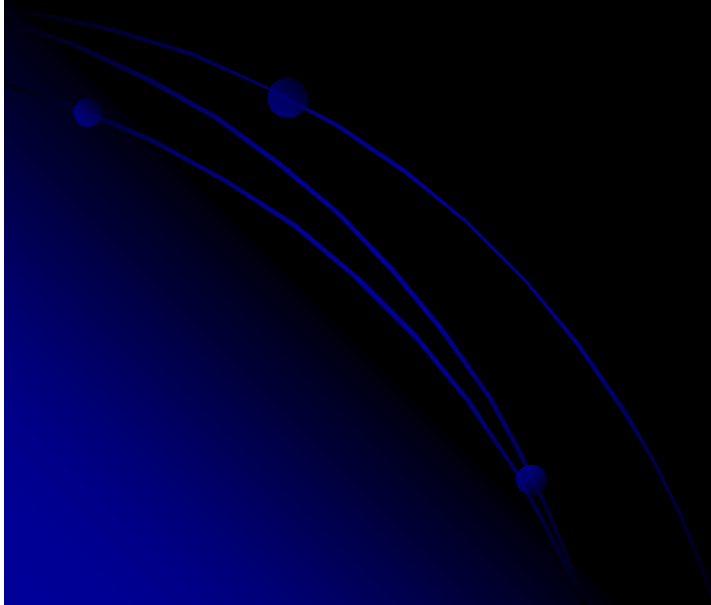


- % patients rated perceived effectiveness of homeopathy higher (with fewer adverse effects) than previous conventional primary care for same conditions
- *Homeopathy lowered drug costs, with high patient satisfaction*

Prospective Comparative Cohort Study in Patients with Chronic Disorders (N=493) (Witt et al 2005)



RCTs and Meta-Analyses Reveal Methodological Issues and Mixed Findings



Shang et al Lancet Meta-Analysis: *Criticisms (per Fisher 2006)*

- | Does not meet QUOROM standards
 - | Quality of reports of meta-analyses of randomized controlled trials, published in Lancet 1999!
- | Meta-analyses should:
 - | present “descriptive data for each trial”
 - | “data to calculate effect sizes and confidence intervals”
- | Shang et al do not report these
 - | or excluded trials
 - | or quality assessments and odds ratios of included trials

Moher D et al. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. Lancet 1999;354:1896–1900.

Additional Flaws in Homeopathic Meta-Analyses

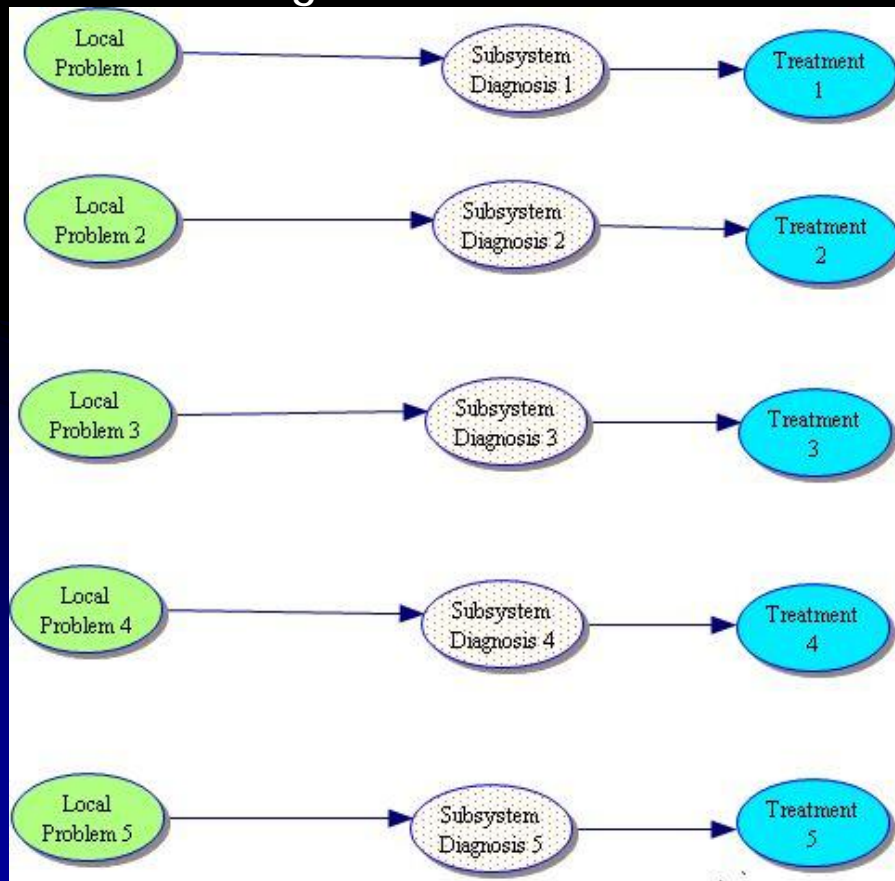
- | Insufficient numbers of published homeopathic studies with high internal validity and good trial reporting (should improve with Dean et al 2007 supplement to CONSORT for homeopathic studies)
- | Inappropriate pooling of studies across multiple different clinical conditions and patient types
 - | Langman 1997 criticism of positive meta-analysis by Linde et al applies to Shang et al negative meta-analysis as well
- | No ratings for external validity in study selection
 - | Does the study reflect actual clinical practice?

Implications for Measuring “Specific” versus “Non-Specific” Effects (Bootzin & Bailey, *J Clin Psychol* 2005)

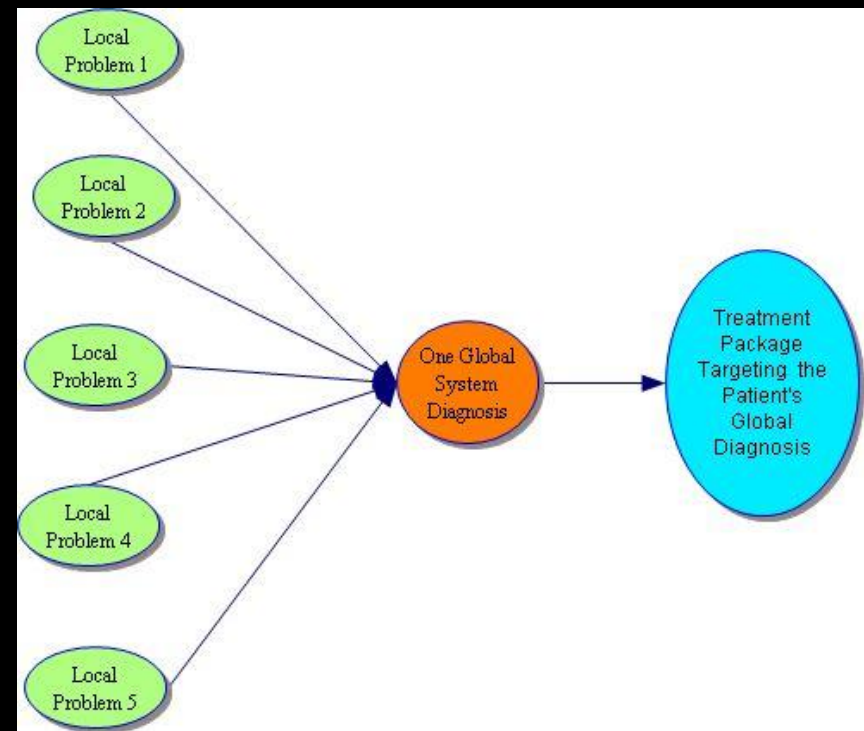
- **Specific effects**: Effects of treatment that are predicted *by the theory* about how the treatment produces change
- **Nonspecific effects**: Effects that are not related to the causal pathways specified in the theory about how the treatment produces change. Nonspecific effects can refer to broad psychological effects of a treatment as well as contextual factors present in the delivery of treatment.
 - **Common Factors**: The factors in the delivery of treatment that are common to different therapeutic endeavors such as the patient-therapist relationship and expectations of receiving help. Common factors are a subset of nonspecific effects.

Western Medical versus CAM Systems: Local versus Global Diagnosis and Treatment

Western Medical Approach to Drugs or CAM Modalities



CAM System Approach to Multimodal Treatment



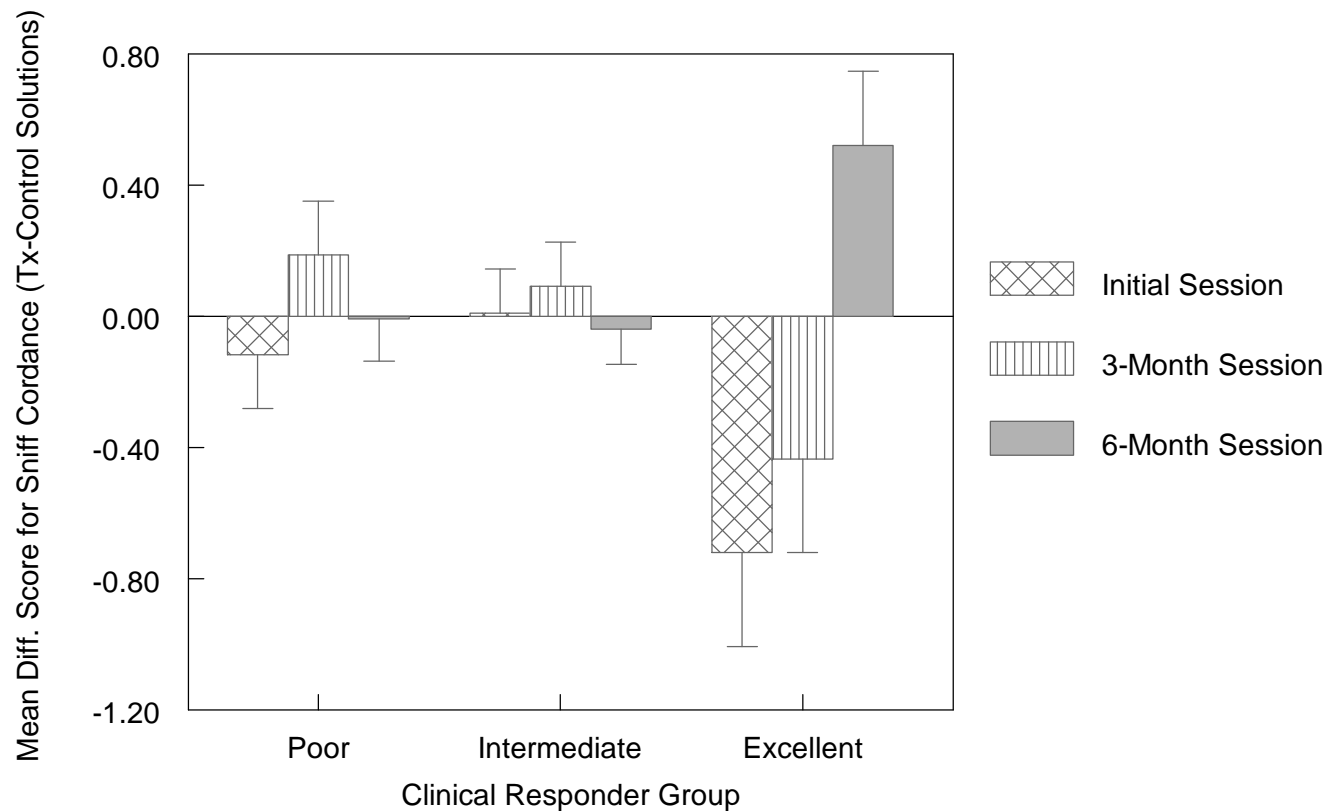
Clinician Treatment Expectations for Dynamical Whole System CAM Patient-Centered Care in Chronic Illness

- | Persistent long-term improvement in the trajectory of the person's individual global illness process over time (specific local changes emerge in a predicted pattern from above downward and from inside out)
 - | Global sense of well-being
 - | Greater overall energy
 - | Fewer relapses
 - | Less severity of each relapse or flare
 - | Gradual resolution of susceptibility to relapses
 - | Delay or prevention of additional diagnoses, complications, and drug side-effects from original illness

Individualized Homeopathic Treatment Improves Global Behavior Patterns in ADHD (*Frei et al, 2007*)

- Confirm with open label pre-screening trial that “active” homeopathic remedy is really active in a given individual under study conditions
- Then enroll responders in the double-blind RCT study, using global behavior as outcome
 - Clinically needed 5 months and open trials of 3 different sequential single remedies (on average) to find a truly active individualized treatment for most ADHD children, prior to enrolling in double-blind placebo-controlled trial
 - Frei’s modified RCT was positive, vs Jacobs’s unmodified RCT was negative

Excellent Clinical Responders to Individualized Homeopathy Exhibit Baseline Prefrontal qEEG Cordance Effects - Different from Poor Remedy Responders and Placebo Patients during Olfactory Administration of Remedies



(Bell et al JACM 2004)

Conclusions – Clinical Research

- | **Homeopathic remedies exhibit biological activity across multiple *in vitro* and *in vivo* models**
- | **Observational studies show real-world effectiveness of individualized homeopathic treatment across multiple conditions, even with long-term follow-up**
- | **RCTs and Meta-Analyses reveal major methodological Issues and mixed findings**
 - | Variability in reproducibility derives partly from the nonlinear dynamical (changing, evolving) nature of people & remedies as complex adaptive systems - and sensitivity to initial conditions

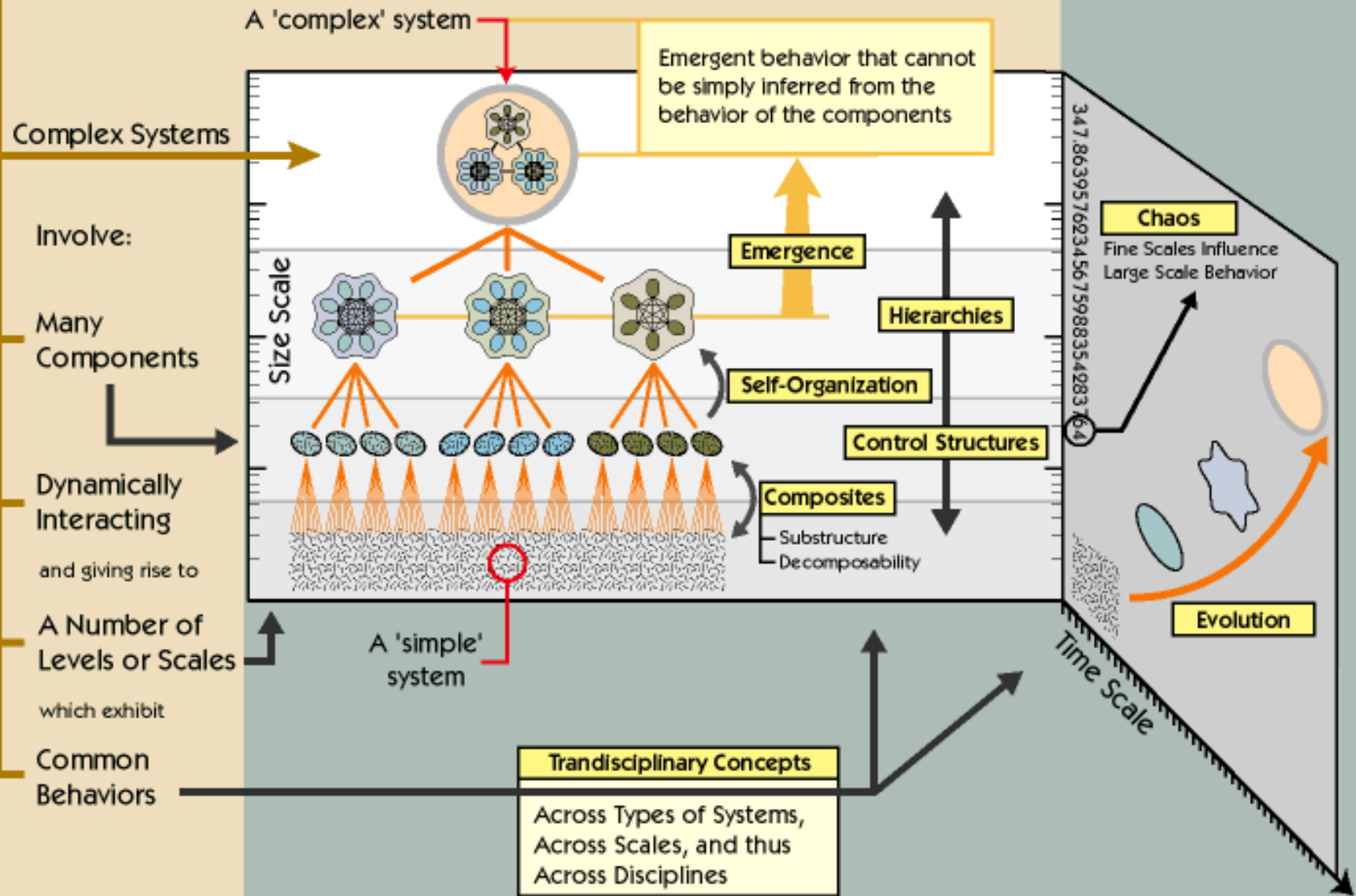
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Characteristics of Complex Systems



(Source: www.necsi.org)