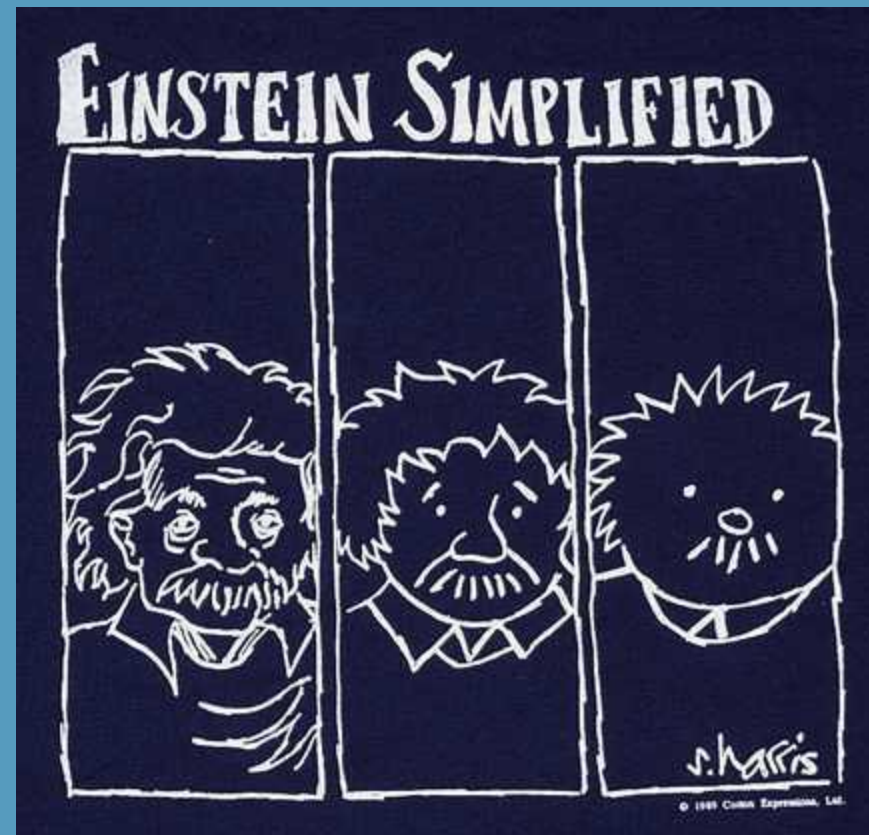


Making sense of interventions & research studies

Anna J. Esbensen, PhD

4/11/15



Overview / Purpose

- Understand how scientist conduct research to test interventions
- Help identify “red flags” that an intervention is not supported by scientific research
- Apply understanding to interventions currently being used in Down syndrome
- Considerations parents should make if interested in pursuing interventions

Disclaimer

- Not recommending for or against any therapy mentioned
- Stop me to define any concept



Scientific Model

- Determine cause of disorder or behavior
- Discover possible treatments
- Determine if treatment is effective

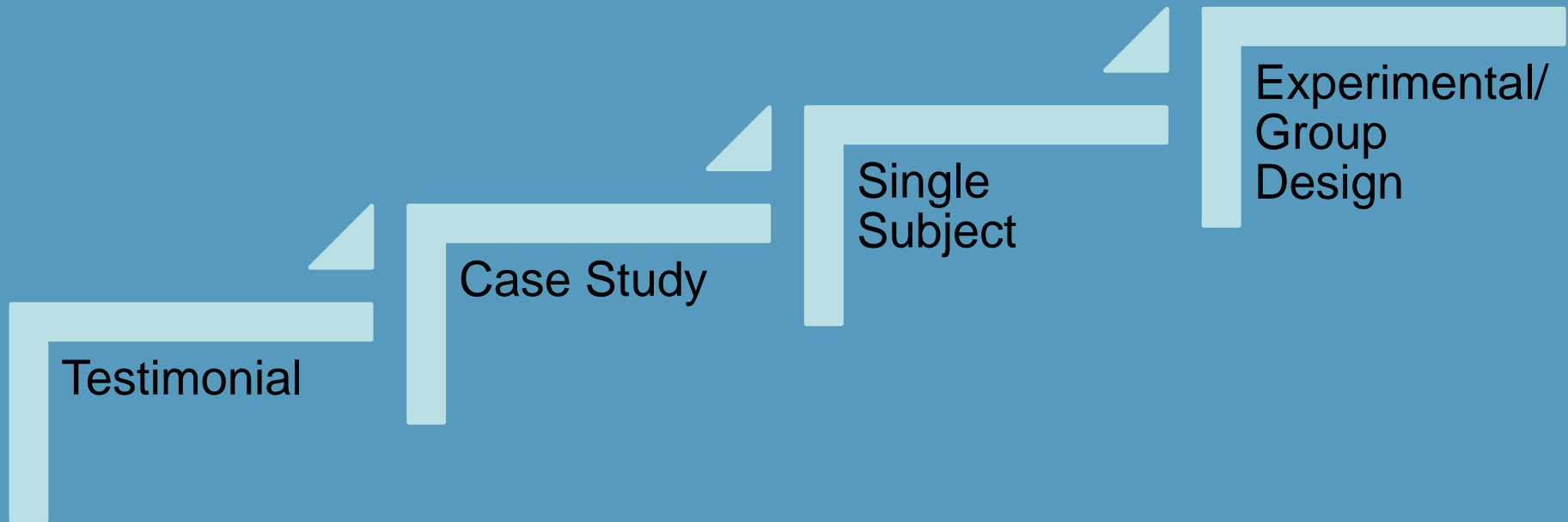
Basic Research

- Identified cause of DS
- Developed mouse models
- Test theories or interventions in laboratory

Applied Research

- Taking what we learn in basic research and applying it to real life setting
- i.e. Medication trial in adults with DS

Levels of evaluating research



Basic types of studies

1. Testimonials

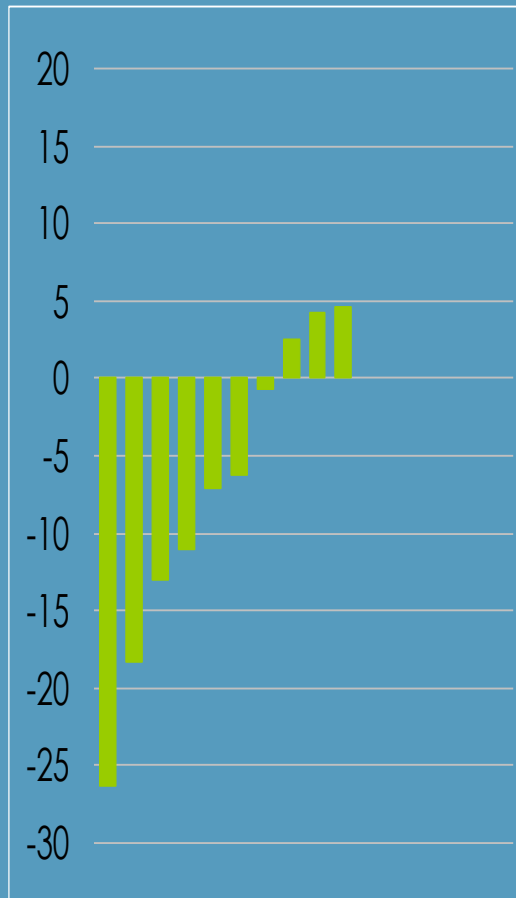
- Someone has tried a product/treatment and “testifies” about his/her experience – which is usually positive

Advantages	Disadvantages
Easy to understand	Not scientific
People just like you	Only positive responders “testify”
	Majority of people may not respond

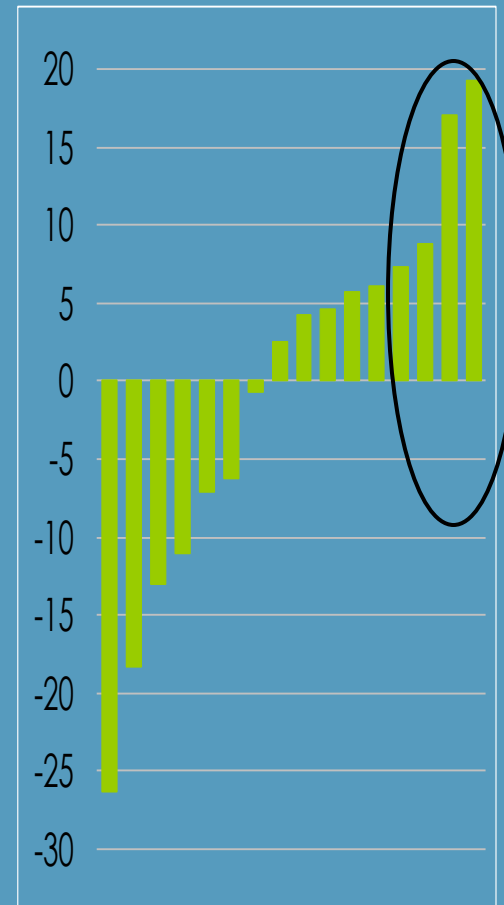
Non-testifiers are important

Change in weight, lbs

N=10



N=16





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Testimonials

Dear Luke,

I am writing to express our deep appreciation for the excellent therapy program and products TalkTools provides for families. My husband and I have five beautiful children, three of whom have Down syndrome and joined our family through adoption. Their speech and feeding needs have been many and varied. Our 15-year-old son, Benjamin, is fairly "high functioning," but struggles with hypotonia and apraxia, which makes his speech difficult to understand. Our 11-year-old son, Gabriel, has more medical challenges, but also struggles with motor planning and speech. Our 11-year-old daughter, Abigail, has many significant medical challenges and is not yet talking.

Our excellent occupational therapist, Natalie Cooper, has been using and teaching us the TalkTools program for a couple of years. We have seen solid, consistent progress with our children. In June, we had the pleasure of having all three children evaluated by Sara Rosenfeld-Johnson, who helped tailor the program for the unique needs of each of our children. She recommended that we watch the video series, *Three-Part Treatment Plan for Oral Placement Therapy*, and that we have our kids' therapists and hab techs watch them. Our speech therapist, Sheila Temple, has watched the videos and has been a wonderful ally in joining all of the parts of the program together. Even though we had been using the Oral Placement Program for a couple of years, the videos helped us fine-tune how we completed each of the activities. It was also extremely helpful to gain a better understanding of what each exercise is trying to accomplish and how these skills will help our children. We are seeing wonderful progress with all three children as they work through each of the steps of the hierarchies, at their own pace, and meeting their own needs. Benjamin and Gabriel are easier to understand and both are becoming more willing to talk to strangers. We also have some hope, for the first time in a long time, that Abigail might eventually be able to get off her feeding tube and find effective ways to communicate her wants and needs. Thank you for making these excellent resources available for the benefit of so many precious children and adults!

Basic types of studies

2. Case studies or case reports

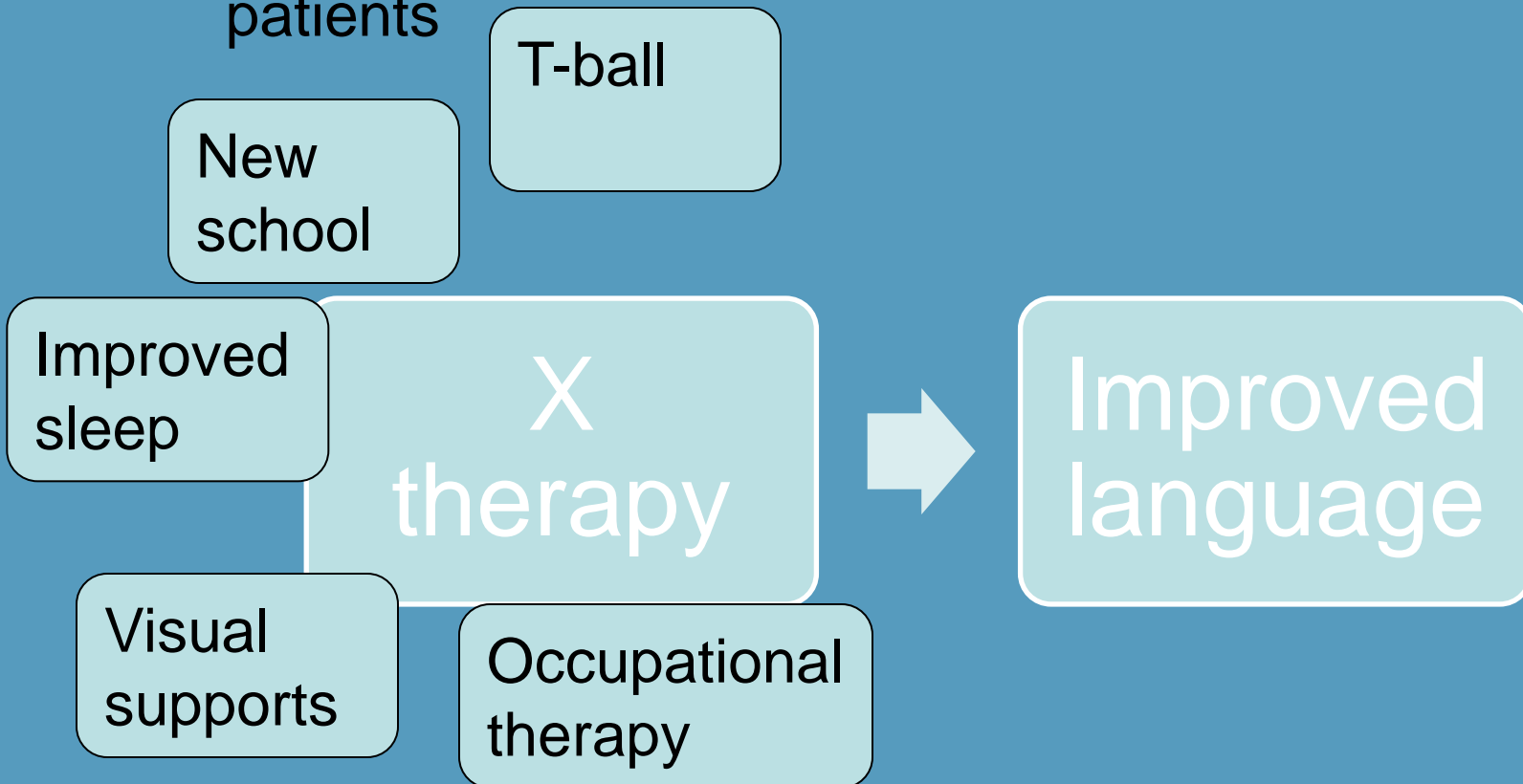
- Uncontrolled study where researcher describes results of a treatment that was conducted with a small number of patients

Advantages	Disadvantages
Easy to understand	Cannot prove that treatment led to improvements in patients
Provides ideas for future research	Uncontrolled, other factors could lead to improvement

Basic types of studies

2. Case studies or case reports

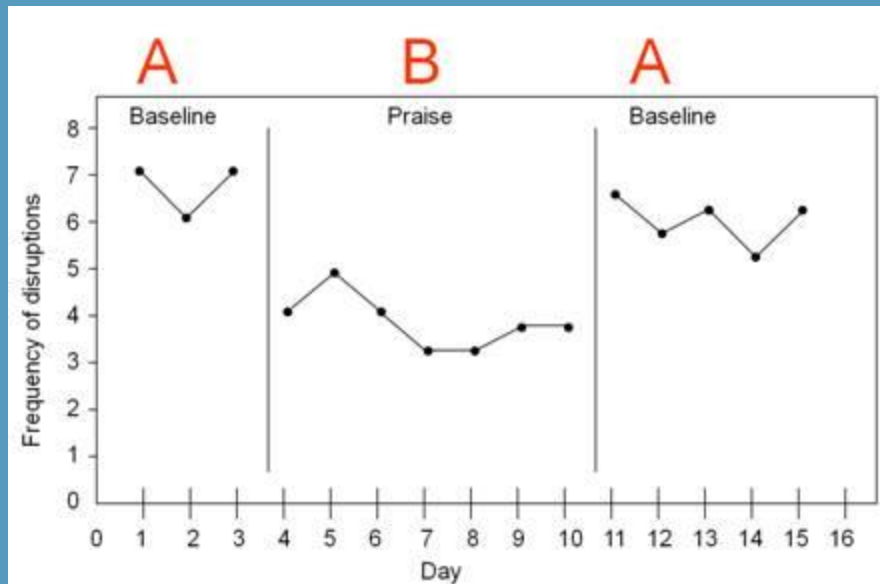
- Uncontrolled study where researcher describes results of a treatment that was conducted with a small number of patients



Basic types of studies

3. Single Subject Designs

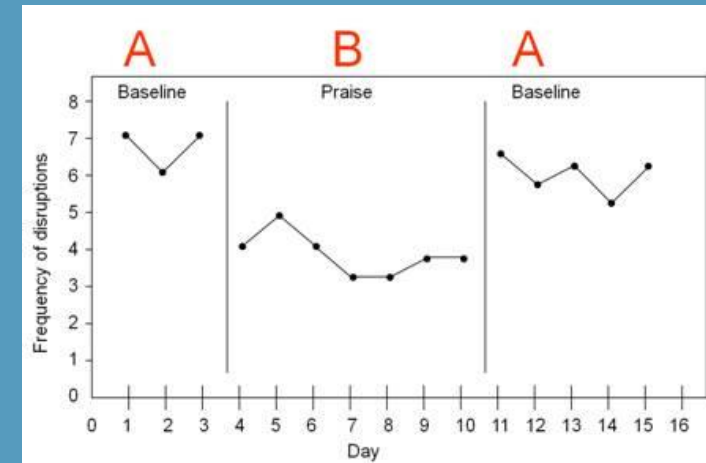
- Generally only a few subjects, controlled
- Generally in Applied Behavior Analysis (ABA)
- Treatment given, withdrawn, re-given in order to demonstrate treatment related effect on subject's behavior (ABAB)



Basic types of studies

3. Single Subject Designs

- Generally only a few subjects
- Generally in Applied Behavior Analysis (ABA)
- Treatment given, withdrawn, re-given in order to demonstrate treatment related effect on subject's behavior (ABAB)



Advantages	Disadvantages
Clear relationship between treatment and change in behavior	Generalizability to other subjects or settings
Controlled study	Often requires replication of study to show effectiveness

Basic types of studies

4. Experimental Group Designs
 - Randomly assigning subjects to treatment or control/comparison group



Enrollment

Assessed for Eligibility

Excluded

Randomized



Allocated to Intervention

Allocated to Intervention

Allocation

Did Not Receive Intervention

Did Not Receive Intervention

Received Intervention

Received Intervention

Follow-Up

Discontinued Intervention

Discontinued Intervention

Lost to Follow-Up

Lost to Follow-Up

Followed Up

Followed Up

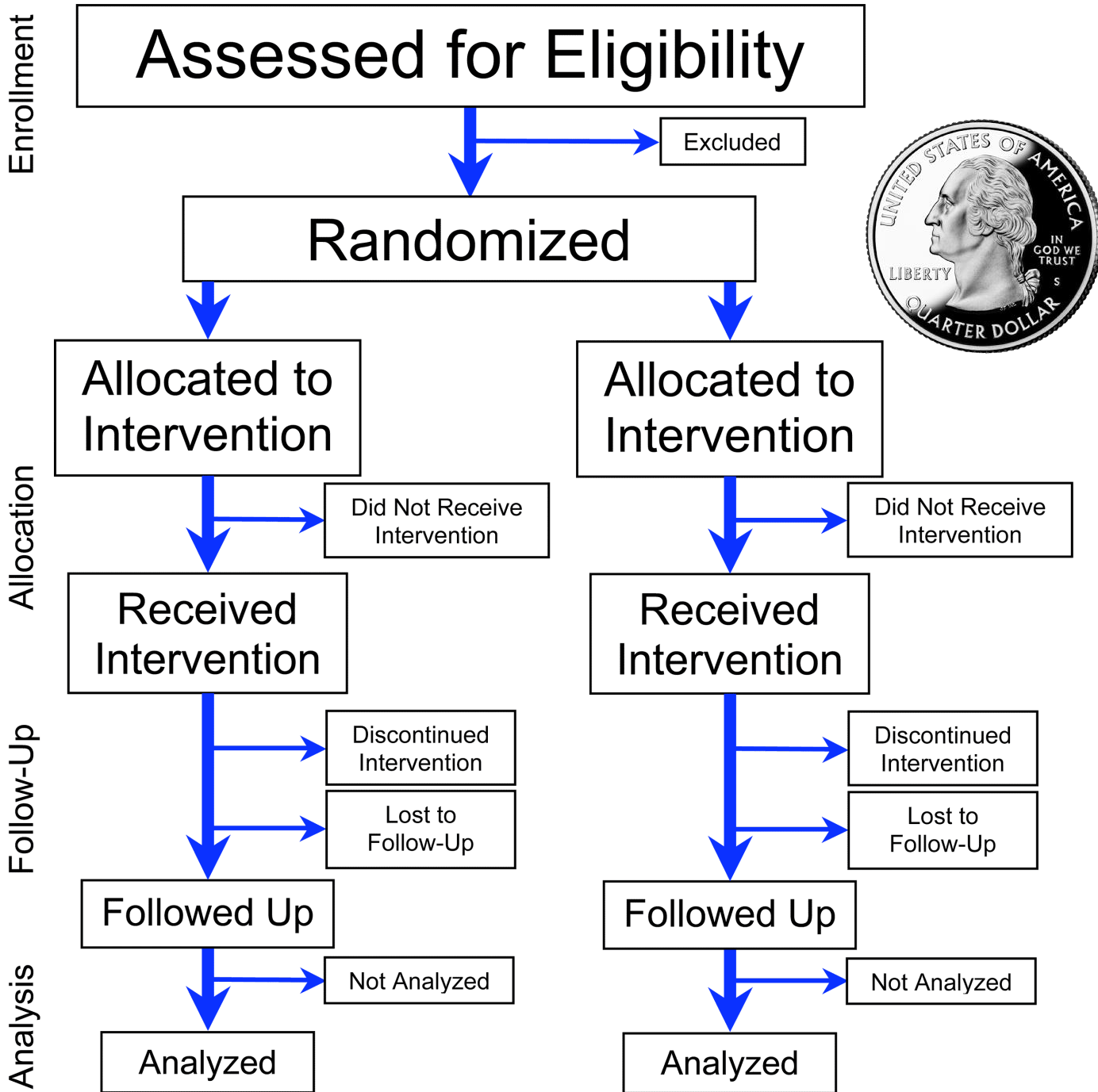
Analysis

Not Analyzed

Not Analyzed

Analyzed

Analyzed



Basic types of studies

4. Experimental Group Designs

- Randomly assigning subjects to treatment or control/comparison group
- Blinded
 - What if you knew what treatment you were getting?
 - What if the researcher knew what treatment you were getting?

Advantages	Disadvantages
Demonstrates cause and effect between treatment and change in outcome	Generalizability to other subjects
	Generalizability to other settings

Scientific Model

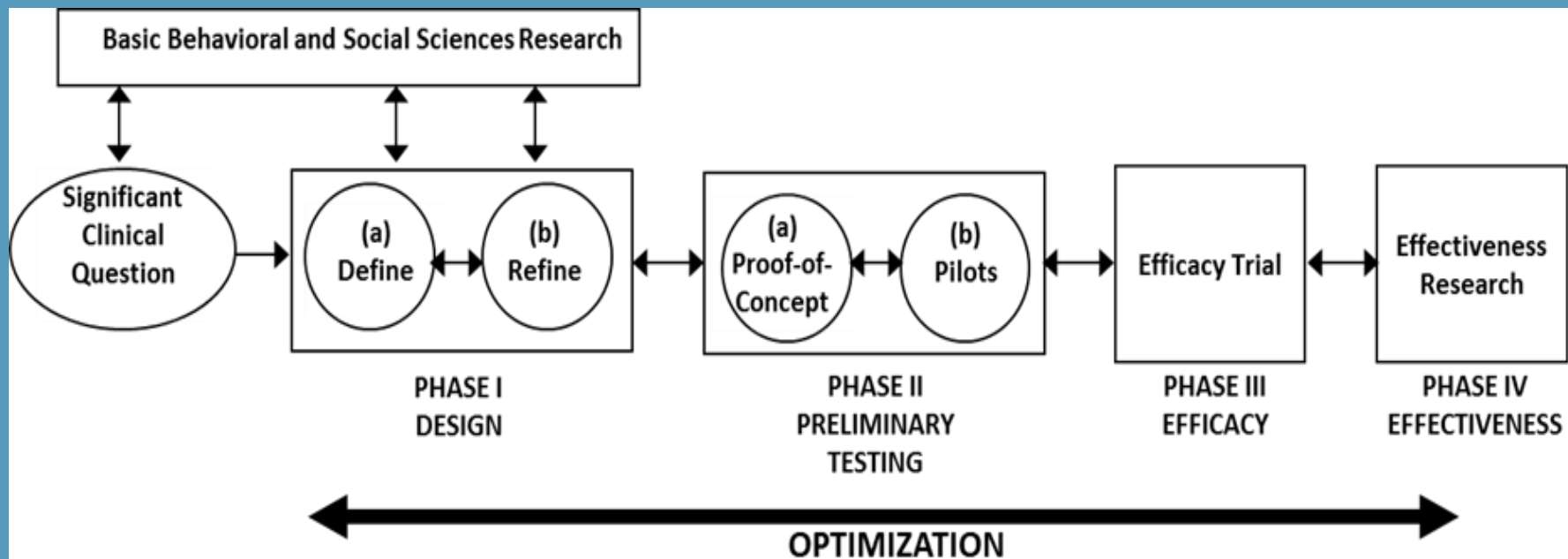
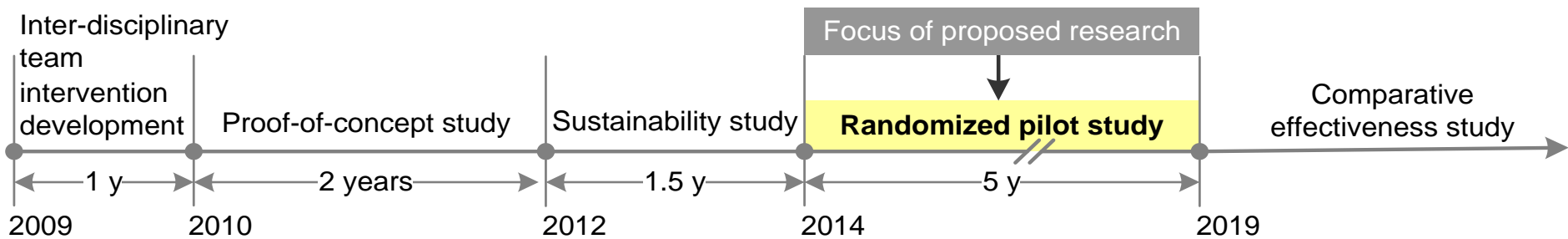


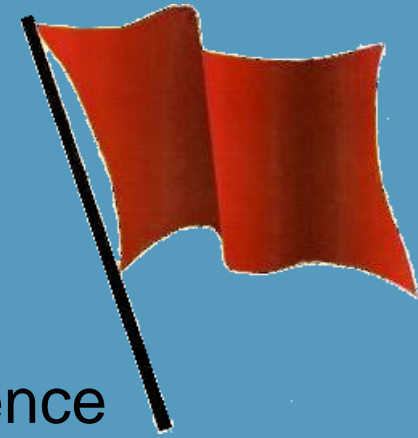
Figure 1. The ORBIT Model for Behavioral Treatment Development

Scientific Model



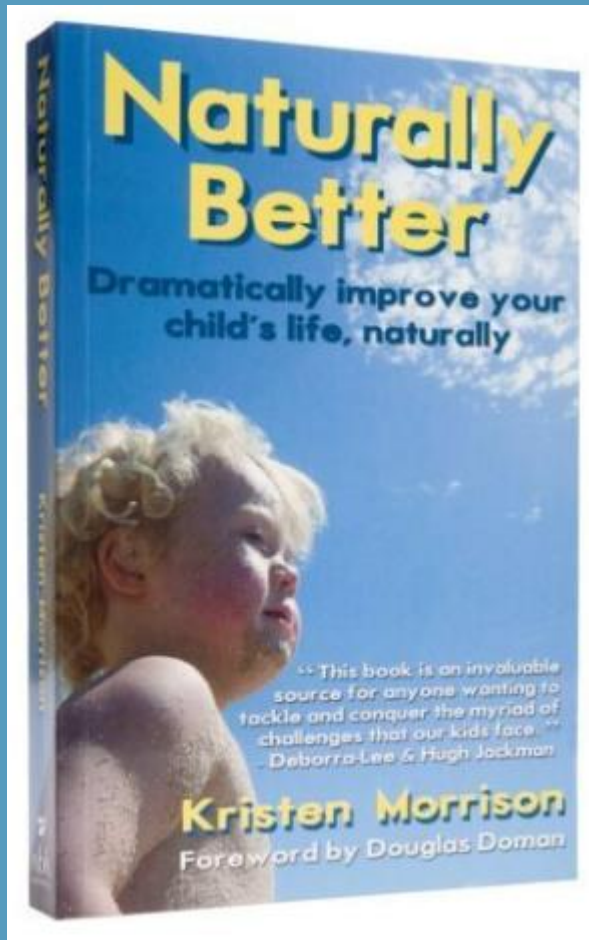
**THERE IS NO
SUBSTITUTE
FOR HARD WORK**

Thomas Edison



Red flags

- Personal experience given as evidence
- Treatment claims go beyond available evidence
- Studies on the treatment appear on internet/media, instead of scientific journals
 - Peer review process
- Treatment based on grandiose claims or poorly described outcomes
 - Research must be replicatable
- Treatment is described in vague, mystical way
- Check the degree. All Drs are not the same.
- List generated.
- Then sought examples in Down syndrome field.



Personal experience
given as evidence



“how [parents] can help their
developmentally delayed child
catch up to their peers”

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Treatment claims go beyond evidence



Prozac

1:

[Related Articles](#), [Links](#)

[Clark S](#), [Schwalbe J](#), [Stasko MR](#), [Yarowsky PJ](#), [Costa AC](#).

Fluoxetine rescues deficient neurogenesis in hippocampus of the Ts65Dn mouse model for Down syndrome. *Exp Neurol*. 2006 Jul;200(1):256-61. Epub 2006 Apr 19. PMID: 16624293 [PubMed - indexed for MEDLINE]

2:

[Related Articles](#), [Links](#)

[Kodama M](#), [Fujioka T](#), [Duman RS](#).

Chronic olanzapine or fluoxetine administration increases cell proliferation in hippocampus and prefrontal cortex of adult rat. *Biol Psychiatry*. 2004 Oct 15;56(8):570-80. Erratum in: *Biol Psychiatry*. 2005 Jan 15;57(2):199. PMID: 15476686 [PubMed - indexed for MEDLINE]

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[Santarelli L](#), [Saxe M](#), [Gross C](#), [Surget A](#), [Battaglia F](#), [Dulawa S](#), [Weisstaub N](#), [Lee J](#), [Duman R](#), [Arancio O](#), [Belzung C](#), [Hen R](#).

Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. *Science*. 2003 Aug 8;301(5634):805-9. PMID: 12907793 [PubMed - indexed for MEDLINE]

4:

→ [Ginkgo Biloba](#)

→ [Phosphatidylcholine](#)

→ [Prozac](#)

→ [Focalin XR](#)

→ [B12/Folinic Acid](#)

Targeted Nutritional Intervention (TNI) in the Treatment of Children and Adults with Down Syndrome

Principles behind its use, treatment protocols, and an expanded bibliography.

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Genetics and Disabilities Diagnostic Care Center
520 Jose St #11
Santa Fe, NM 87501
505-467-8637

[E-Mail: larry@leichtman.org](mailto:larry@leichtman.org)

Introduction and Background

You may have been approached by one of your patients to discuss the issue of Targeted Nutritional Intervention and the use of Piracetam in Down syndrome. You may have, in most cases, drawn a blank or have self-referred back to the era of mega-vitamin therapy and drawn an immediate negative reaction. What is all of this and does it have any grounding in medical science or is it nothing but snake oil?

First of all, it isn't snake oil. The TNI formulation, NuTriVene-D, was designed originally by Dixie Lawrence Tafoya. All subsequent modifications were based on journal articles or research and reviewed and approved by the SAC (Scientific Advisory Committee) of Trisomy 21 Research Foundation, Inc. (TRI). Dixie Tafoya first developed this formula based on the work of Henry Turkel, M.D. carried out from the 1940s to the 1970s in which he used a formulation based on some educated guesses. These guesses were made without benefit of formal knowledge of the biochemistry or genetics of Trisomy 21. In fact, when Dr. Turkel first developed his formula, the correct number of human chromosomes was not known nor was it known that Down syndrome was produced by an extra chromosome 21. Today, the ongoing Genome Project in association with improved metabolic assaying techniques has afforded us a better view of the genetics and biochemistry of chromosome 21 in order to make more accurate estimations of what supplementation may help in the treatment of Trisomy 21.

Gene Overexpression in Trisomy 21

Most recent gene mapping has sequence all of the genes on chromosome 21 This doesn't mean that they are all known, that process will take more time. But within a few years we should know all of the genes and their protein products. Already several gene families of developmental genes have been found. Some of these because they are turned on only prenatally cannot be influenced



Internet article,
Not scientific journal



Q: How will we recognize any results and when should we expect to see a change?

Poorly described
outcomes

A: You will see some changes right away, probably. Most people report that they do. If not, at least by 3 months you will. We hear people say "it's as if the lights just went on" with the ginkgo. Your child should seem more alert, connected with his environment, his eyes will be brighter. He will begin to learn new words and new skills little by little. Be patient. For some, the results come more slowly. If your child is older when he/she starts the protocol, they will have a lot of catching up to do. The babies show the fastest results.



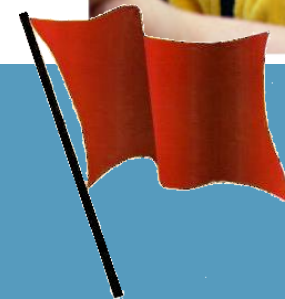
WHAT IS NACD?

Vague, mystical

The NACD Neurodevelopmental Approach to Human Development

The National Association for Child Development, under the direction of founder Robert J. Doman Jr., has, over its twenty-nine years of existence and work with over 30,000 clients, developed a unique and effective view of and approach to enhancing the development and function of children and adults. Because the fields of education and health care have become more and more compartmentalized in recent years, and treatment approaches are driven more by symptom and label rather than by cause, their methods often fail to serve the uniqueness and totality of the individual.

NACD has created an approach to human development, the achievement of human potential, and the remediation of developmental, educational, and neurological problems that is based upon the gestalt of the individual. Our Neurodevelopmental Approach utilizes a neurologically-based, individually targeted, eclectic treatment methodology. The efficacy of NACD's Neurodevelopmental Perspective has been demonstrated with over 30,000 clients—from infant to geriatric—whose function has ranged from comatose to gifted. The NACD Neurodevelopmental Approach is based on the following model:



No red flags...

- Do I go with an intervention for my child?
- What else do I need to look at?

- Considerations parents should make if interested in pursuing interventions

Questions to ask

- Any controlled research supporting intervention?



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Family/Caregiver
Support

Education

What is the NDT approach?

The NDT Approach is used for management and treatment of individuals with central nervous system (CNS) pathophysiology. The individual's strengths and impairments are identified and addressed in relation to functional abilities and limitations. The NDT Approach continues to evolve with the emergence of new theories, models, research, and information in the movement sciences. NDT is a hands-on, problem solving approach. Intervention involves direct handling and guidance to optimize function. The approach is guided by the client's reactions throughout every treatment session.

An NDT Trained or NDT CertifiedTM therapist's education in neurology, physiology, and current research is translated into daily practice. They work collaboratively with patients, families, caregivers, and other healthcare professionals to develop individualized comprehensive treatment programs based on NDT theory and philosophy.

The Mission of NDTA

The purpose of the Association is to promote the unique qualities of the Neuro-Developmental Treatment (NDT) approach by:

- Providing specialized clinical training to health care professionals
- Supporting Clinical Research
- Supporting client's and families with education, resources and information

// NDT
Certification
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Research Article Summaries

1999 - 2009

NDTATM is pleased to make the following research article summaries available as a NDTATM Members-Only benefit. This bibliography was compiled and each article summarized in response to the many requests NDTATM has received. It is the first report of research articles published by NDTATM in over twenty years.

This bibliography includes summaries of articles from 1999-2009 identified through searches of on-line journal databases (such as PubMed) or NDTATM member recommendations. Articles included in this bibliography are either experimental or quasi-experimental studies or

Research Article
Summary Titles

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It is important to note that all studies that met the criteria were included regardless of the quality of the research and that we have not provided any study critiques. We encourage the reader to carefully evaluate the contribution of each study to the research evidence on NDT based on analysis of such factors as the appropriateness of (a) the research design, (b) the control group, (c) those providing the NDT interventions, (d) the data analyses, and (e) the conclusions drawn by the researchers. All of the studies are relatively small and thus run the risk of not identifying a difference even when one exists. However, these small studies are a critical part of research development as they help determine the important questions and lay the groundwork for larger scale studies.

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Those who wish to have more information about a specific study may access many of the original abstracts through PubMed free of charge. We have provided the PMID, the PubMed citation identifier number when available, to assist with this process.

Unfortunately, NDTATM is not able to provide copies of the original articles because of copyright restrictions imposed by the journals. However, full length copies of articles may often be ordered for a fee through the library of local medical facilities and/or universities or colleges.

Our plan is to update the article summaries on an annual basis to keep this resource as useful as possible for our members. We hope that this resource is helpful to all NDTATM members in seeking information on NDT-related research whether it is for self-study, graduate research, and/or clients and employers.

Marcia Stamer, NDTA Publications Committee Chair

// Testimonials

See How NDT Has
Changed Lives...



Effects of neurodevelopmental treatment (NDT) for cerebral palsy: an AACPDm evidence report

Table II: Levels of evidence. Maximum level of evidence is determined by research design; conduct of study may result in reduction of level of evidence by one level

<i>Level</i>	<i>Non-empirical</i>	<i>Group research</i>	<i>Outcomes research</i>	<i>Single subject research</i>
I		Randomized controlled trial All or none case series		N-of-1 randomized controlled trial
II		Non-randomized controlled trial Prospective cohort study with concurrent control group	Analytic survey	ABABA design Alternating treatments Multiple baseline across participants
III		Case-control study Cohort study with historical control group		ABA design
IV		Before and after case series without control group		AB design
V	Descriptive case series/case reports Anecdotes Expert opinion Theories based on physiology, bench, or animal research Common sense/first principles			

<i>Study</i>	<i>Research design</i>	<i>Level of evidence</i>	<i>Treatment duration</i>	<i>NDT Rx n</i>	<i>Control Rx n</i>
1973 Wright ¹²	RCT (3 groups)	II	–	–	–
	External comparison 1		6 mo	16	31
	External comparison 2		12 mo	7	10
	Internal comparison		6 mo	9	9
1975 Carlsen ¹³	RCT (Paired then assigned to 2 groups)	II	6 wk	6	6
1976 Scherzer ¹⁴	RCT (2 groups)	II	7–21 mo	14	6
1981 Sommerfeld ¹⁵				10	–
					9
					10
1983 DeGangi ¹⁶				4	^a
1985 Laskas ¹⁷				1	^a
1987 Herndon ¹⁸				12	None
1988 Palmer ¹⁹					
	Part I	I	6 mo	25	23
				25	23
1989 Hanzlik ²⁰				10 ^c	10 ^c
1990 Palmer ²¹				25 ^c	22 ^c
1990 Lilly ²²				2	^a
1990 Embrey ²³				1	^a
1990 Kluzik ²⁴	AB design	IV	4 wk	5	^a
1991 Law ²⁵	RCT (2 of 4 groups reported: intensive vs regular amount NDT)	I	9 mo	18	18
1994 DeGangi ²⁶	Case study	V	8 wk	1	0
1994 Bower ²⁷	Concurrent cohort study (4 groups)	III	1–6 mo	8	22
1996 Fetters ²⁸	Multiple crossover trial	II	4 wk	8	^a
1997 Jonsdottir ²⁹	Multiple crossover trial	II	4 wk	8	^a
1997 Law ³⁰	RCT (2 groups) crossover with washout	I	4 mo ^b	50	^a
1999 Trahan ³¹	Before and after case series	IV	8 mo	50	0
2000 Adams ³²	Before and after case series	IV	6 wk	40	0

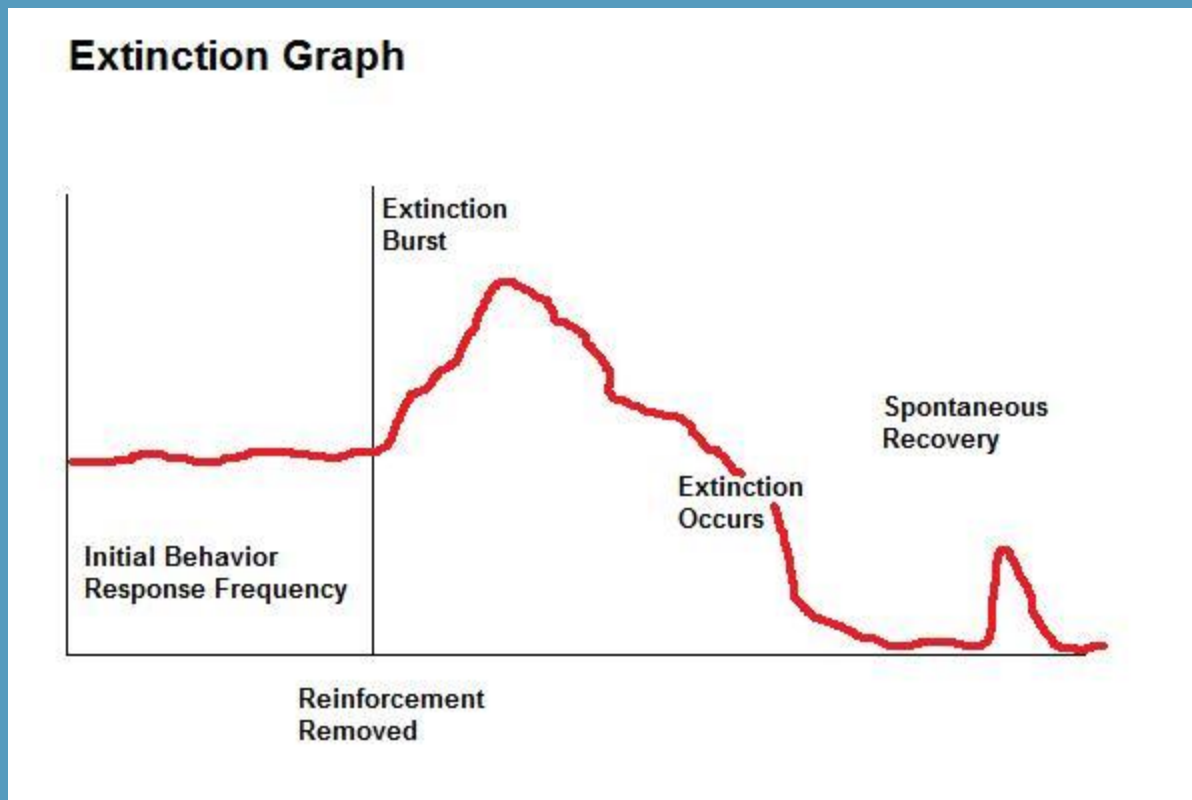
Case comparisons designs found NDT sometimes being helpful compared to control

Strongest study designs found NDT not helpful, and sometimes hurtful

Rx, treatment; RCT, randomized controlled trial. ^aParticipants were their own controls; ^bEach group received 4 months of treatment then crossed over to opposite treatment after a 2-month washout period; ^c Mother–infant dyads.

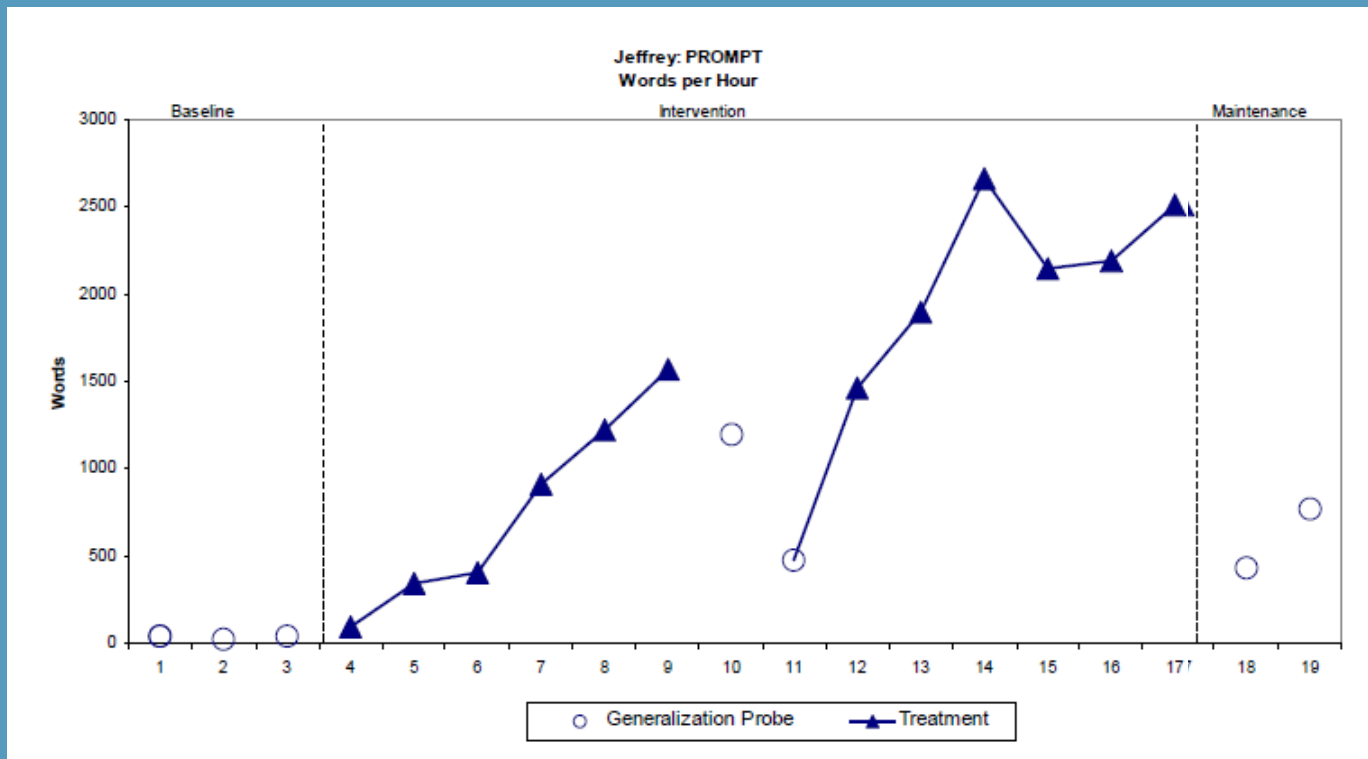
Questions to ask

- Any controlled research supporting intervention?
- How long before treatment benefits can be seen?



Questions to ask

- Any controlled research supporting intervention?
- How long before treatment benefits can be seen?
- How will improvements be measured or assessed?



Questions to ask

- Any controlled research supporting intervention?
- How long before treatment benefits can be seen?
- How will improvements be measured or assessed?
- Are there any risks to my child?
 - Check with your health care provider prior to using a supplement
 - Particularly true for certain population groups
 - Supplements can produce adverse effects when used in combination with other medication
 - Ginko biloba & aspirin thin blood and can increase risk of internal bleeding

Questions to ask

- Any controlled research supporting intervention?
- How long before treatment benefits can be seen?
- How will improvements be measured or assessed?
- Are there any risks to my child?
- Is the service covered by insurance or school district?

Questions to ask

- Any controlled research supporting intervention?
- How long before treatment benefits can be seen?
- How will improvements be measured or assessed?
- Are there any risks to my child?
- Is the service covered by insurance or school district?
- Does my pediatrician recommend it?



AAP recommends screening for symptoms

Saturday, October 15, 2011

All children not the same

Why supplement and monitor zinc?

Jett just tested low on zinc so I thought I'd do some research. OMG... Needless to say, we are buying him zinc TOMORROW morning!!! It is absolutely ridiculous that this paper, **The Role of Zinc in Down's Syndrome** by Eastland Roxanne, was written 10 years ago and that zinc isn't a mandatory supplement for everyone with DS.

I just reviewed the (recently revised) Clinical Report on the Health Supervision for Children With Down Syndrome written by the American Academy of Pediatrics to see what they say about zinc. Guess how many times zinc is mentioned? ZERO. I'm going to rewrite the Guidelines for Treatment of DS myself. (Okay, so it's on my to-do list...) You are welcome to listen to the AAP, but I feel that us parents have our children's best interest at heart and seriously wonder about whomever is on the board that created our present guidelines. Of course, I will share my Guidelines with you! (I'm sorry, I am soooooo angry right now!!) My notes are in italics.

Zinc supplements when no zinc deficiency can be harmful or cause copper deficiency

Check with pediatrician about YOUR child

Excerpts from: **The Role of Zinc in Down's Syndrome**

in-downs-syndrome&Itemid=117

arnosine to protect his
/31-for-21-l-

hp?
ublications&id=55:zinc-

VIOLENT METAPHORS

THOUGHTS FROM THE INTERSECTION OF SCIENCE, PSEUDOSCIENCE, AND
CONFLICT.

How to read and understand a scientific paper: a guide for non-scientists

<http://violentmetaphors.com/2013/08/25/how-to-read-and-understand-a-scientific-paper-2/>

(Props to Missy)

So how do we improve science?

Researchers & Families



Ask good questions

Design good studies

Participate in research

Researchers

Families