# *Use of Intervention Studies in Planning Evidence-Based Treatments for the Individual Child*

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# Accumulation of Scientific Evidence in CP is a Major Advance!

- Rigorous intervention studies provide a strong basis for clinical decision making
- Will discuss why this is necessary but not sufficient!

# Getting closer to determining which interventions are best?

- Initial studies demonstrated that a given intervention produces + change
  - Lead to long list of possible treatments
- Direct comparison to alternatives: which is better? (RCTs)
  - Standard of care often variable and less intensive
  - Comparisons should ideally be true alternative and/or matched by dose
  - Many "effective" interventions not superior
- Summarize by strength, consistency & amount of evidence (Cochrane, systematic reviews)

**Proven Effective**

Preferentially use this approach

**Uncertain Effect**

Insufficient evidence

No evidence

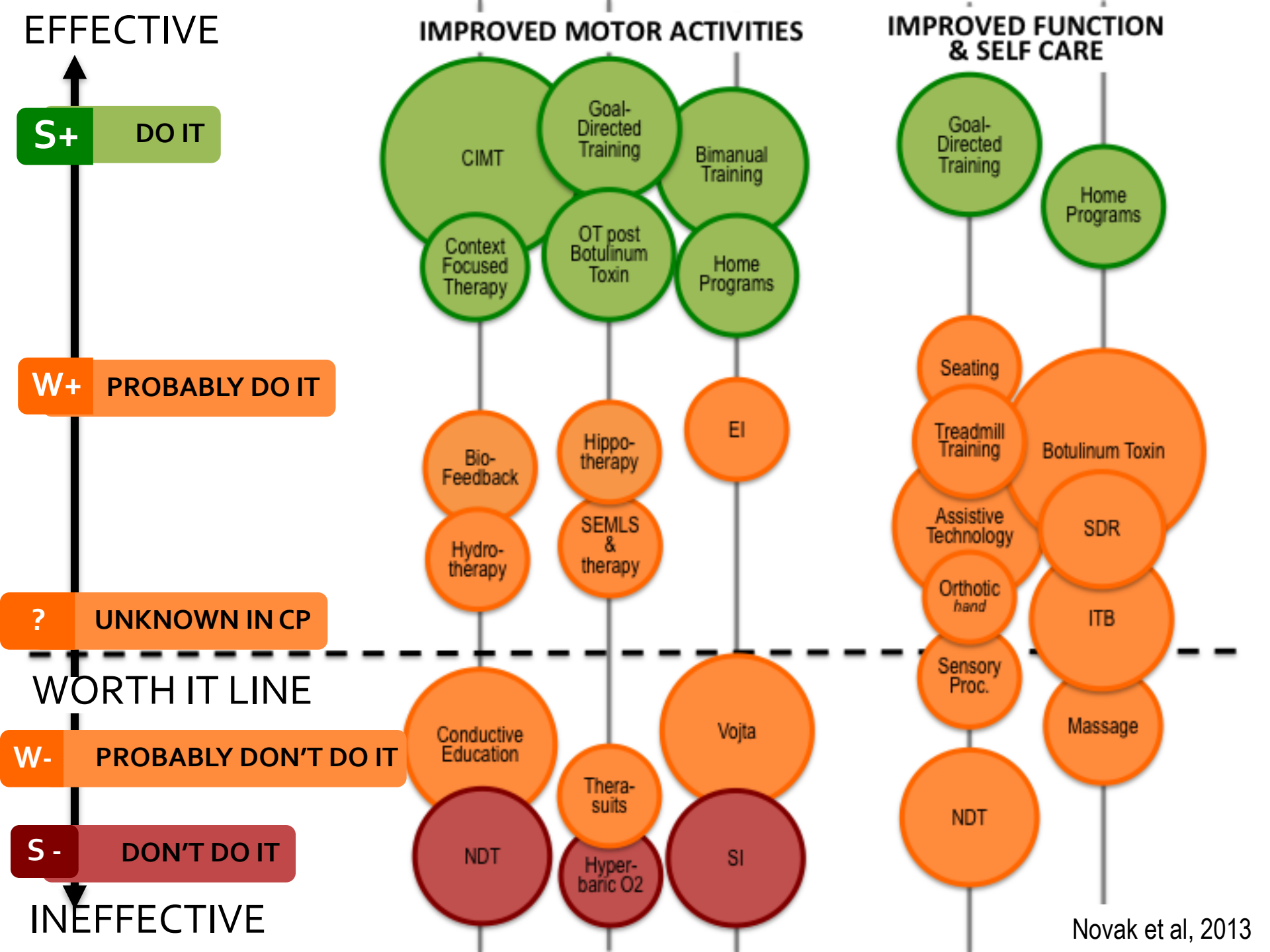
Conflicting evidence

Measure effects. Were goals met?

**Proven Ineffective**

Do NOT use this approach. Choose alternative

Novak & McIntyre, 2010




Novak et al, 2013

# Take away messages

- Intensive, goal-directed & activity based interventions are more effective than more passive interventions
- Interventions that reduce impairments (e.g. spasticity, PROM) may not directly improve daily functioning
- Several traditional therapies are now known to NOT be effective, but still  prevalent in some parts of the world (through lack of knowledge or active resistance)

# Evidence-Based Practice (EBP)

"Conscientious, explicit & judicious use of current best evidence in making decisions **about the care of individual patients**".

(Sackett, 1996)

# Using Evidence in Clinical Practice

1. Child & family identify a functional **goal**
2. Physiotherapist uses the most reliable & valid **assessments** to determine the child's capabilities and training needs to achieve goal
3. Together develop a **treatment plan** that includes evidence-based strategies
4. Monitor **progress** towards goal & whether child/family are satisfied with this
5. Adjust plan accordingly – may need to change dose or alter intervention strategy

# How do we decide WHO is most likely to benefit from a therapy?

- No clear guidance from scientific literature; few strong predictors of individual outcomes reported
- Need to better define treatment effect or "benefit"
  - Absolute amount of change in an objective measure, with all children considered equal?
  - Based on personal goal attainment or "meaningfulness" of change to an individual?
  - Outcomes in trials may not be at all important to families – we need to know what they want!

# Narrowing Our Focus in CP: From a population to a person

- **Population:** Children with early brain injury and motor disability
- CP is a "group" of disorders
- Weeding out what is/ is NOT CP (Diagnostic precision)
- Including more homogeneous groups in studies (e.g. uni/bilateral, PVL or stroke, age or functional groups)
- Subgroup or phenotypic prescriptions for individuals still inadequate for predicting response to intervention

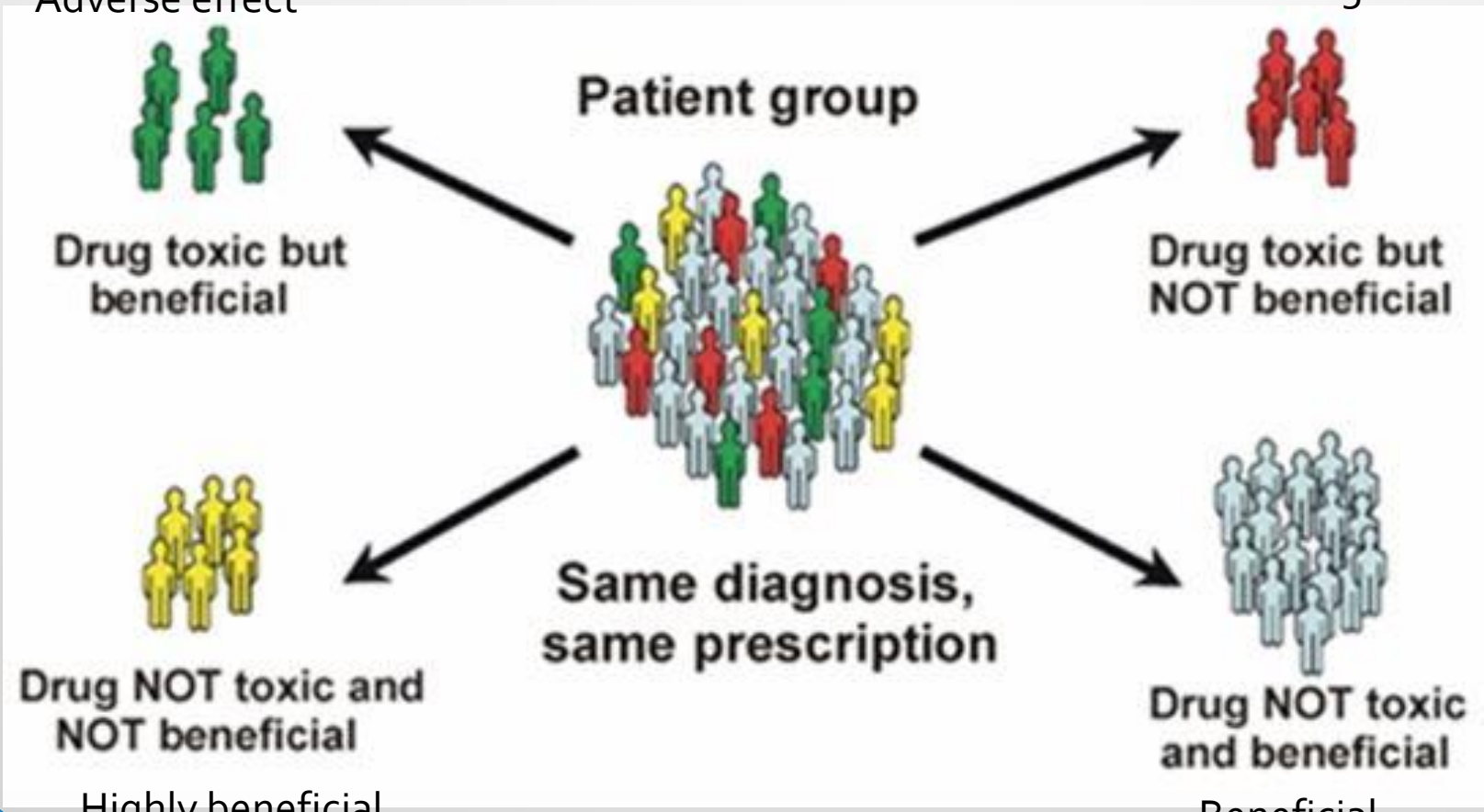
# Developing & Using Evidence to Improve Rehabilitation Practice

- Seel et. Al, APMR, 2012; supplement
- Goal: "decrease reliance on authority, disciplinary lore & personal experience"
- Need for efficacy (RCT), single-subject (small n), & comparative effectiveness (CE) research
- Need better validated predictive models of prognosis and treatment response
- Dilemma of accumulating better evidence with grossly inadequate funding

# Randomized Clinical Trials

- Deliberately minimize effect of variability on outcomes (groups should = on as many factors as possible)
- Eliminate all possible confounders
- Goal is to demonstrate **intervention** is efficacious (better than control or comparison)
- Comparison group has a major effect on statistical significance and therefore efficacy so researcher may chose a less active control.
- Other tricks: examining change within groups when groups are not different.

# Is Response to Effective Rehabilitation Interventions Similar to Drug Response?



# What if an Intervention based on established principles is not shown to be EFFICACIOUS?

- Clear reporting bias towards + findings but this is changing
- Negative trials are important, may be due to many factors besides an ineffective treatment
  1. **dose not large enough** (unrealistic expectations)
  2. underpowered study
  3. large variability in response; outliers
- **Recommendations:**
  - Include individual data for primary outcomes (appendix)
  - Perform subgroup analyses (if powered to do so)
  - Examine associations of patient factors with outcomes

# Fidelity of Treatment

- RCT: COPCa (Coping & Caring) vs. NDT in 46 HR infants (Hielkema et al., DMCN 2011)
- No mean difference in motor outcomes
- Videos showed much blending of behaviors
- Associated therapist behaviors with outcomes
  - Coaching (+) vs. teaching techniques (-)
  - Encouraging self-initiated movement (+); passive positioning/sensory stimulation (-)
- Associations differed for CP vs. non-CP

# Considering other studies designs

- *From the micro to the macro*

# N=1 studies

- Underutilized & underappreciated in rehabilitation
- Can have high internal validity if you measure outcomes with and without intervention
- Can be replicated across subjects for external validity
- Can be easily replicated in clinical practice; can manipulate dose within person, extend duration, or try alternatives if not effective
- Can provide proof of concept for larger trials

# N=1000+ studies

- Modern innovations in designs are driven by the increasing recognition in clinical research that diseases are heterogeneous and patients who apparently have the same disease require different therapies" (Berry, Biostatistics, MD Anderson, 2016)
- Including many therapies in one trial is far more cost-effective and efficient; can differentiate responders and non-responders and allows the finding that a combination of therapies may be optimal for some.

# Lessons from Cancer Research

- New information on genes and cancer types is creating smaller and smaller patient subgroups , each of which may require different treatment approaches
- It is impossible to study each subtype & treatment in RCTs
- Bayesian approaches have revolutionized cancer research (e.g. NCI-MATCH precision-medicine trial). Therapies chosen for each patient are based on existing, continually updated outcomes data on others with similar genomics ("basket trials"); their outcomes further refine future recommendations.
- Some existing treatments may be effective in very different cancers for reasons not yet understood

# How would this look in CP?

LEARN FROM EVERY PATIENT

Cerebral Palsy Research Network (CPRN): research and quality assurance registry across 20+ major CP centers.

Most data contained in EMR with elements of interest chosen by treating clinicians; PROs assessed at clinic visits

After a large dataset is collected on interventions and outcomes, more and less successful treatment plans for different patient groupings should start to emerge. These can be adopted prospectively and further refined over time.

Collecting genetic data for future use as knowledge grows

# Point-of-Care Documentation

- Should be designed by therapists and be able to be completed in 1 minute or less after session

| Type of therapy | Time spent (minutes) |
|---|---|
| Passive Stretching<br>Strength training UE<br>Strength training LE<br>Strength training trunk<br>Constraint therapy<br>Bilateral UE training<br>Basic mobility (rolling, come to sit)<br>Transitions (sit-to-stand) | 15 |
| Locomotor training (treadmill) | 20 |
| Locomotor training (overground) | 15 |
| Balance training (static) | |
| Balance training (dynamic) | 10 |

# GOAL: Personalized Rehabilitation

- Need to determine an individual's unique characteristics and use those to determine best treatment for more successful outcomes
- Our current inability to explain variability in outcomes suggests that more predictive factors are yet to be uncovered
- Genetic factors are known to be responsible for differences in outcomes from physical training and motor learning; therefore these must play a role in CP as well as other disorders
- There are medications (e.g. levodopa)  and techniques (neuromodulation) that can stimulate plasticity and learning and may be effective when combined with intensive training (stroke early recovery trial using levodopa + therapy vs. therapy alone)