Botulinum Toxin and Rehabilitation Therapies

Teresa Clark
Clinical Specialist & Professional Lead Physiotherapist
Brain Injury Service

Royal Hospital for Neuro-disability
A national medical charity

Our mission statement

Meeting the complex needs of people with profound disabilities arising from brain injury

Royal Hospital for Neuro-disability

A national medical charity

www.rhn.org.uk

Our current services

Brain Injury Services

Patients mostly NHSE commissioned

52 patients.

3 wards.

Continuing healthcare Service

Residents
CCG commissioned

Specialist Nursing Home – 122 residents.
6 wards.

Specialist Services
55 residents. 4 wards.

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Our current services

Total number of patients and residents: **220**

Patients and residents able to consent to their placement	Patients and residents with a feeding tube	Wheelchair-bound patients and residents	Patients and residents with a tracheostomy
48	180	217	53

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Why treat Spasticity?

- Affects approximately 1/3 of stroke patients and up to 3/4 of people with severe disability following TBI. (RCP 2009)
- Prevalence in DOC estimated as 59-89% (Martens et al 2017).
- Occurs early after stroke and associated with disability, pain and secondary impairments (Malhotra et al 2011, Cousins et al 2010, Lundstrom et al 2010)
- Assessment and treatment of spasticity recommended by 2016 RCP National Stroke Guidelines.

Why treat Spasticity in DOC?

Sample of 10 DOC patients in specialised treatment programme (Belfast)

100% presented with hypertonia in 1+ limb

45% of joints contracted on admission

Why treat Spasticity in DOC?

Sample of 210 DOC patients in specialised treatment programme (USA)

45% presented with severe hypertonia in 1+ limb

54% emerged and moved to inpatient rehab programme

Seel et al 2013

But..

‘Botulinum toxin type A plus therapy was over two and a half times the NICE cost effectiveness threshold value..’

‘…the probability of it being cost effective at the threshold value did not exceed 0.39..’

BEST Trial. Shackley et al 2012.

Effectiveness in PDOC?

brain sciences

MDPI

Review

Spasticity Management in Disorders of Consciousness

Géraldine Martens *, Steven Laureys and Aurore Thibaut

Coma Science Group, GIGA Research (Interdisciplinary Cluster for Applied Genoproteomics)–GIGA Consciousness & Neurology Department, University and University Hospital of Liege, 4000 Liege, Belgium; steven.laureys@ulg.ac.be (S.L.); athibaut@ulg.ac.be (A.T.)

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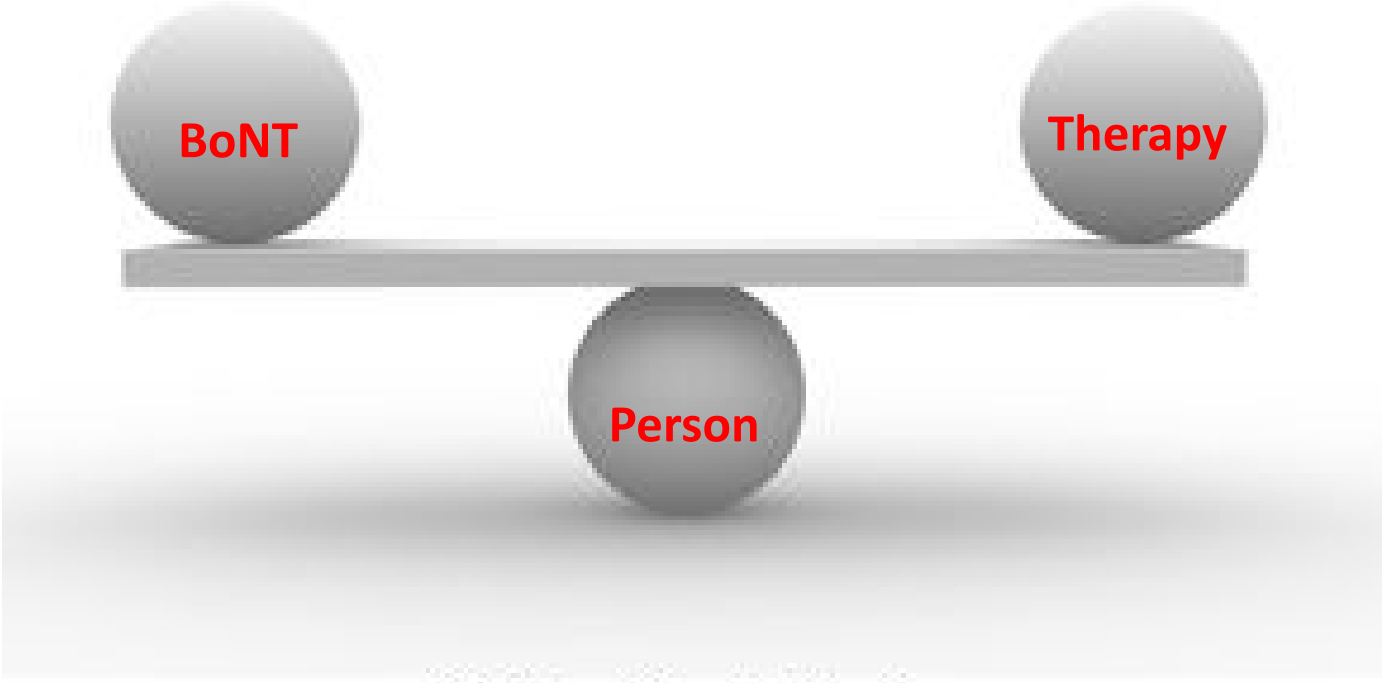
How do we get an effective outcome?



Managing Adult Spasticity

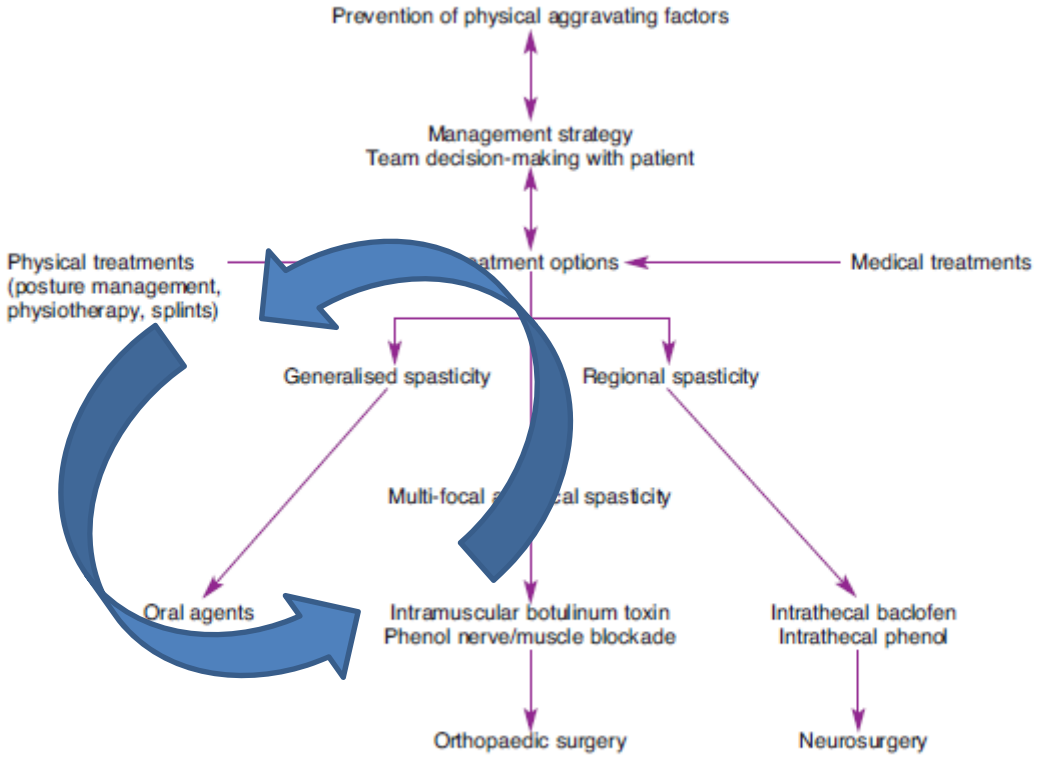
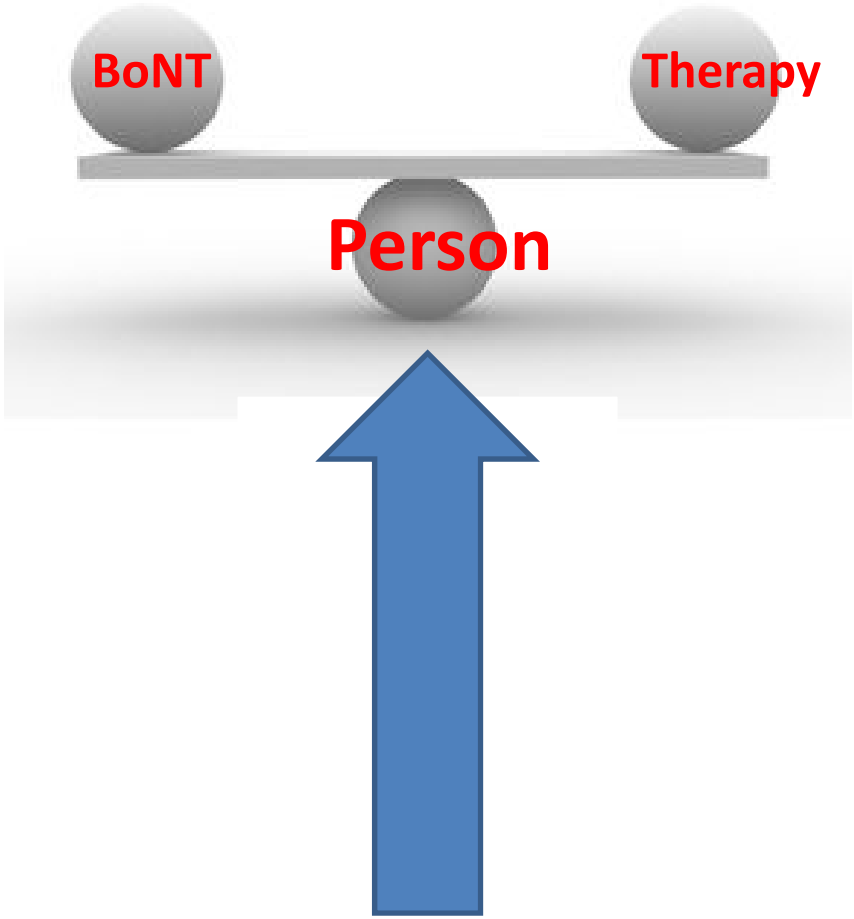


Fig 2 Management strategy for adults with spasticity. Note: It is not uncommon to have a mixed pattern of spasticity and interventions are almost always combined, eg physical management programmes and systemic medication.

Spasticity in Adults:management using botulinum toxin. National Guidelines. RCP 2009.



- Goal Identification
- Baseline Level of Function
- Secondary Impairments
- Support and Follow Up
- Acuity
  - ? Treatment of ‘evolving’ spasticity?
  - Time since brain injury

Goal Identification

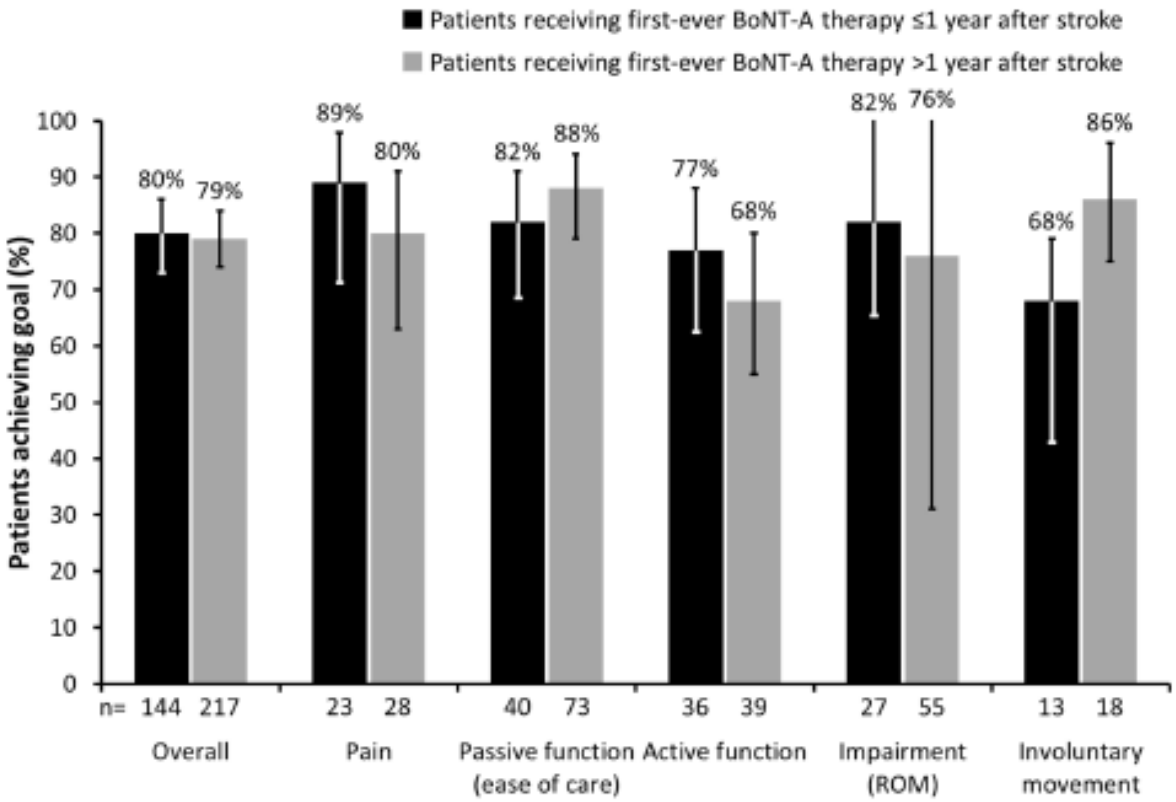


Figure 3. Proportion of patients who achieved their primary goal based on time from stroke to first-ever BoNT-A therapy. (Error bars correspond to lower and upper confidence limits of 95% CI. ROM, range of movement; CI, confidence interval).

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Fheodoroff et al 2015

Baseline Level of Function

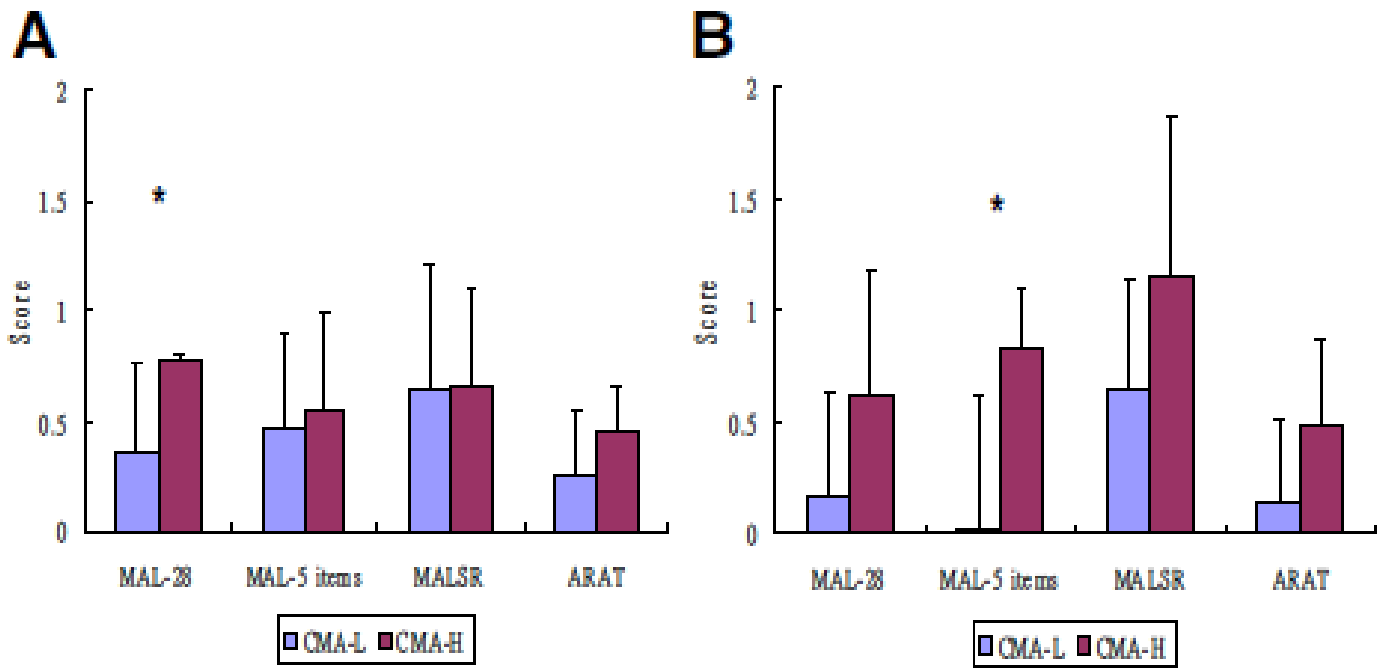

Fig 3. (A) Changes between baseline and 6 weeks after postinjection therapy (B) changes between baseline and 12 weeks postinjection. Abbreviations: CMA-L, Chedoke-McMaster Assessment Hand-Lower Function; CMA-H; Chedoke-McMaster Assessment Hand-Higher Function, MALSR, Motor Activity Log—Self Report; MAL, Motor Activity Log; MAL-28, Motor Activity Log-28.

Chang et al 2009

Secondary Impairments

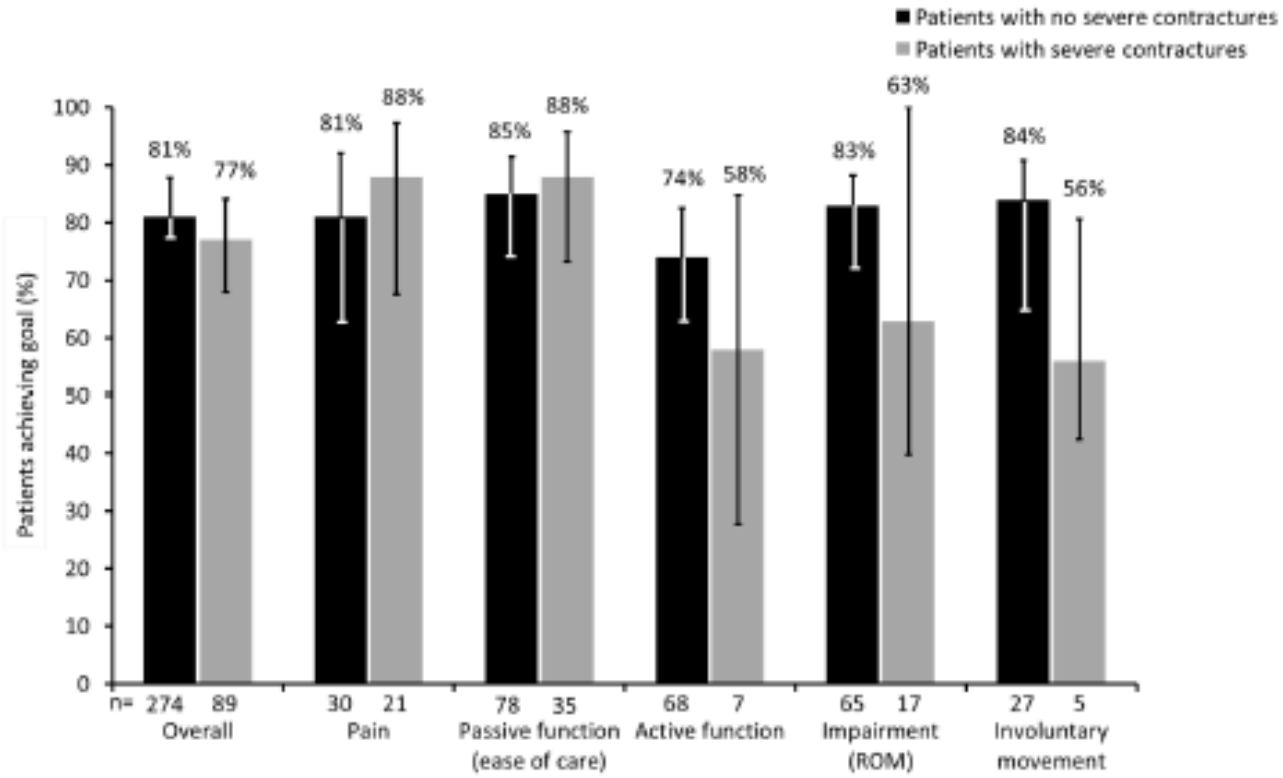

Figure 4. Proportion of patients who achieved their primary goal with BoNT-A therapy based on presence or absence of severe contractures. (Error bars correspond to lower and upper confidence limits of 95% CI. ROM, range of movement; CI, confidence interval).

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Fheodoroff et al 2015

Support and Follow Up

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY ORIGINAL ARTICLE

Determinants of responsiveness to botulinum toxin, casting, and bracing in the treatment of spastic equinus in children with cerebral palsy

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LIST OF ABBREVIATIONS

AROM	Active range of motion
DMQ	Dimensions of Mastery Questionnaire
FAQ	Functional Assessment Questionnaire
PROM	Passive range of motion
PSI-SF	Parenting Stress Index – Short Form
ROM	Range of motion
WeeFIM®	Pediatric Functional Independence Measure

AIM The objective ... child's motivation ... associated with ... 3 months after in...

METHOD Children ... evaluated before ... measures include ... function, and fun... were age, numbe...

RESULTS Thirty-... with diplegia. Tw... (GMFCS) level I a... age (p=0.015) an... change in gross ... ated with improv... gait pattern (p=0.... (p=0.004–0.027).

INTERPRETATION ... the degree of req... (personal and en...

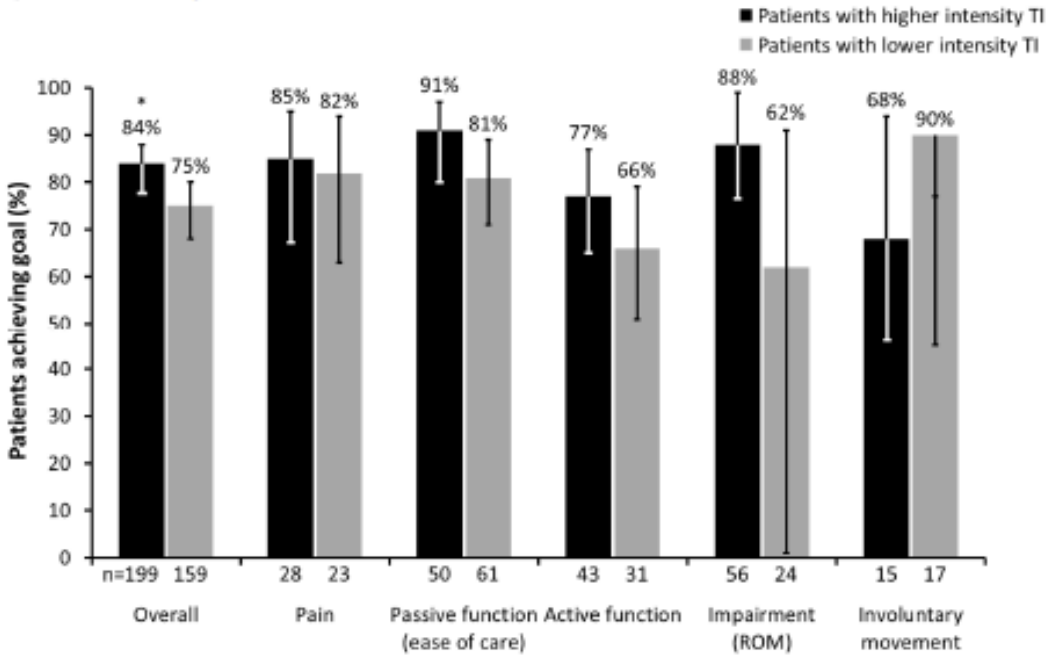

Figure 5. Proportion of patients who achieved their primary goal with BoNT-A therapy based on intensity of therapeutic input (TI). (* $p < 0.05$; Error bars correspond to lower and upper confidence limits of 95% CI. ROM, range of movement; CI, confidence interval).

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Fheodoroff et al 2015

Acuity

- **Spasticity present early - ? 11 days** (Lindsay et al 2015, Lundstrom et al 2010, Malhotra et al 2011, Cousins et al 2010)
- **Early intervention increasingly supported** (Rosales et al 2011, Cousins et al 2010)
- **Later intervention (>1 year) still effective in achieving primary goal** (Fheodoroff et al 2015)

Acuity

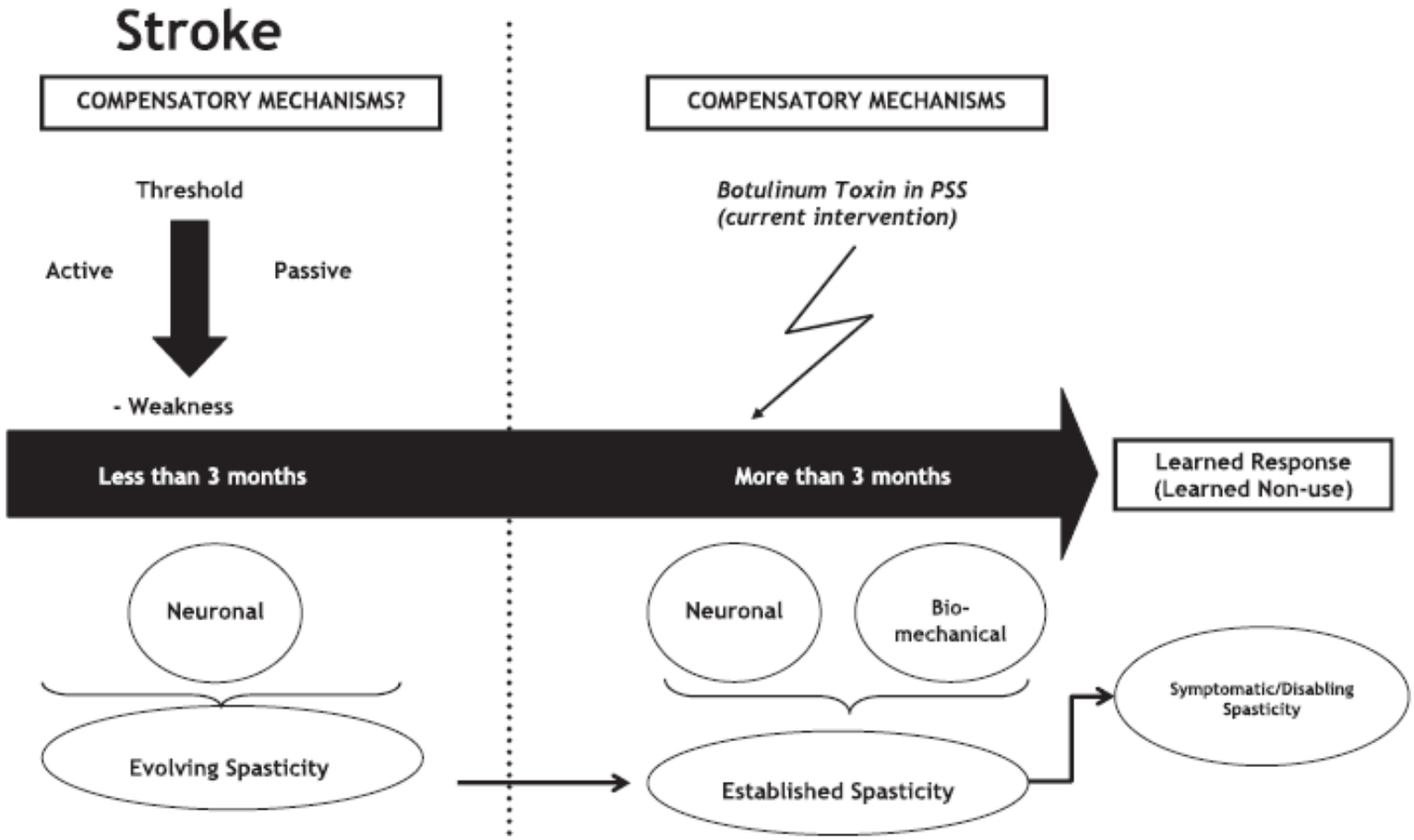
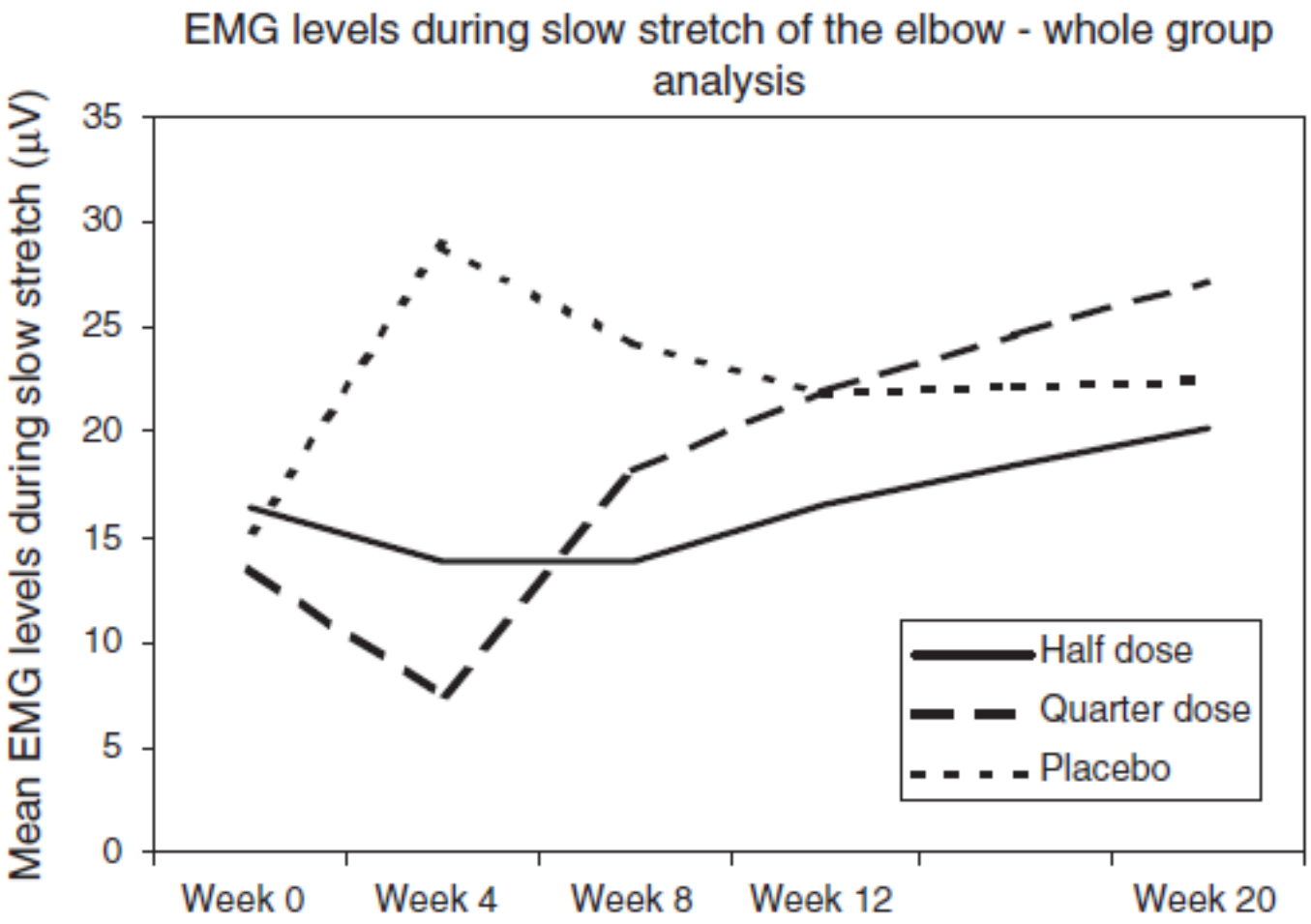


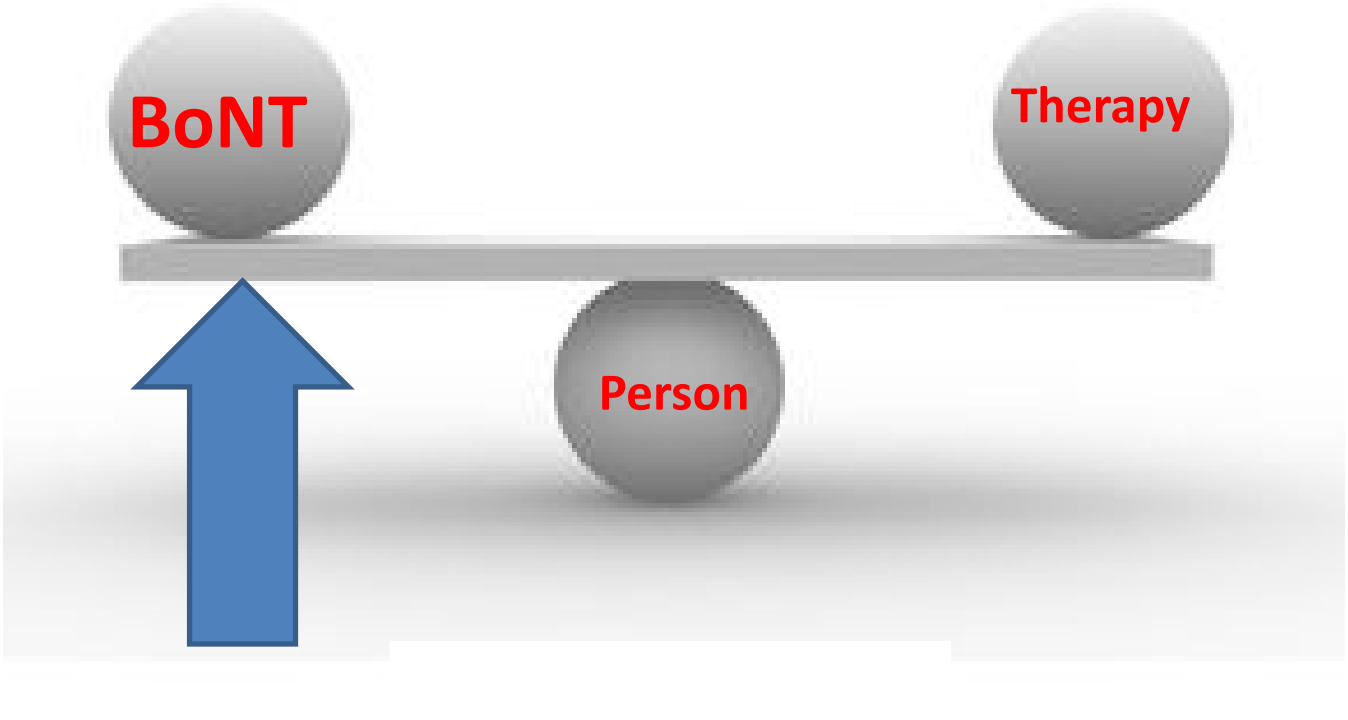
Fig. 1. Evolution of Spasticity after stroke and where botulinum toxin therapy is currently administered; PSS-post-stroke spasticity.

Cousins et al 2010

Acuity



Cousins et al 2010


BoNT
Therapy
Person

UL Function

UL Passive Function		Strong evidence of decreased disability and carer burden Ie: - Hand hygiene & nail cutting - Washing/Dressing - Limb positioning & splint application Effects lasting at least 12 weeks, often longer.	Sheean et al 2010, Foley et al 2013, Brashear et al 2002, Hesse et al 2001, Bhakta et al 2000, Simpson et al 2008, Shaw et al 2011.
UL Active Function		No RCT showing clear benefit. Systematic review with pooled meta analysis of 4 studies showing small improvement in motor function. General consensus – BoNT does not improve active UL function.	Sheean et al 2010. Foley et al 2013, Shaw et al 2011, Shackley et al 2012

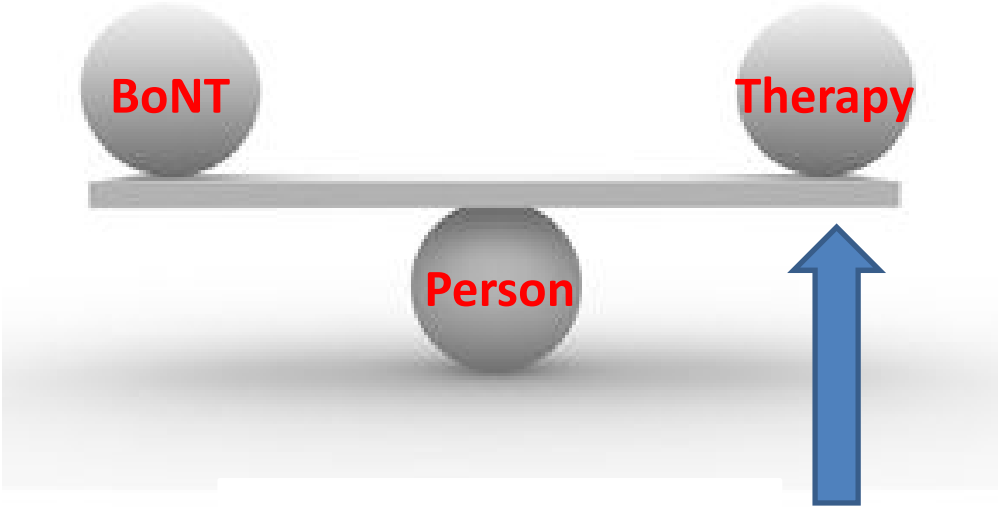
LL Function

LL Passive Function		Evidence that BoNT helps passive goal achievement including: - Decreasing carer burden - Improving positioning and comfort - Seating - Splint application	Simpson et al 2008, Hesse et al 2001
LL Active Function	?	Difficult to separate effects of BoNT from therapy. Small trends indicating improvements in gait speed, walking ability, knee swing, efficiency and balance. Differences tend to be modest and variable. Some evidence suggesting no change.	Foley et al 2010, Hesse et al 2001, Caty et al 2008, Rousseaux et al 2005, Kaji et al 2010

Impairments

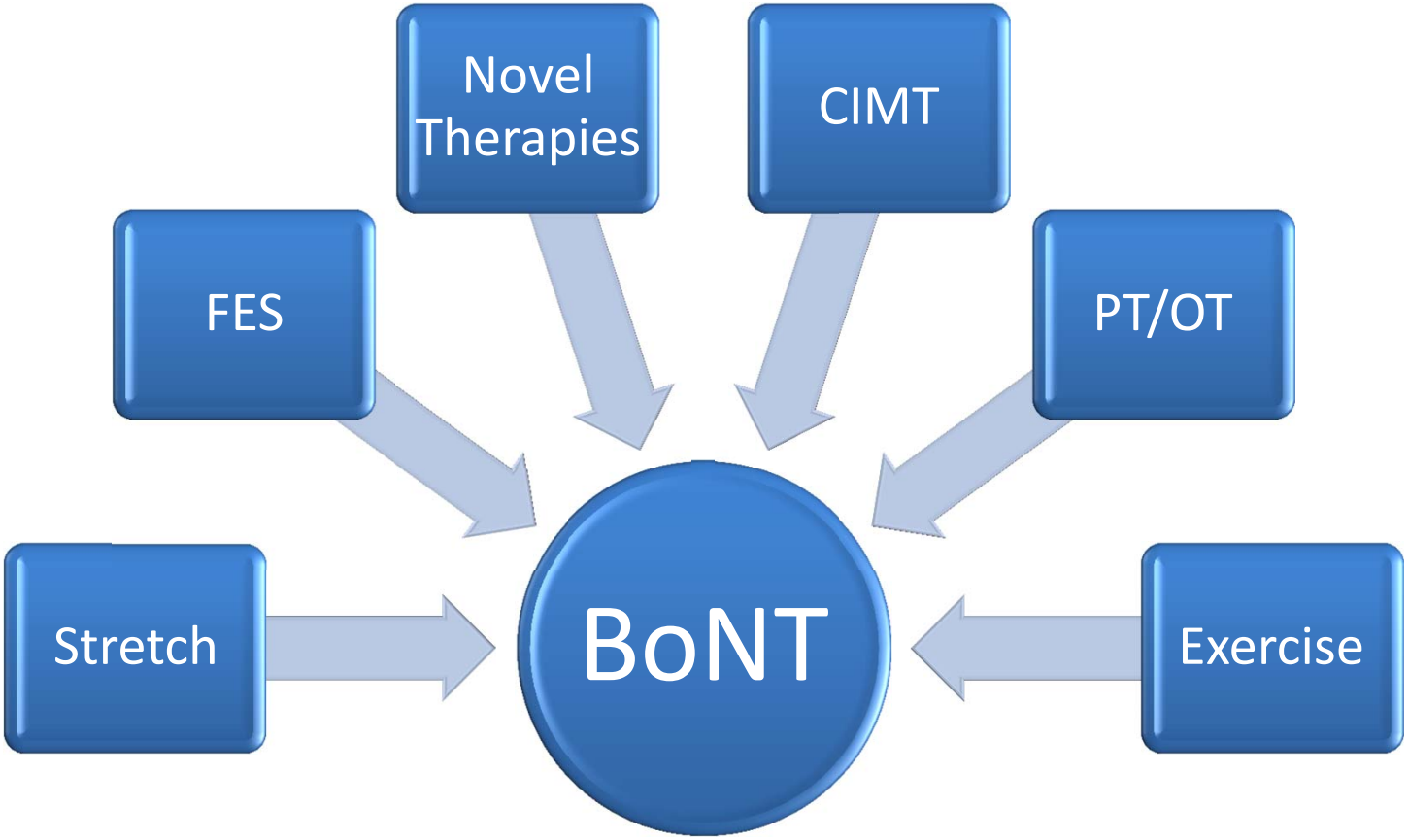
Spasticity		Large body of level 1 evidence - Spasticity will reduce by ~ 1 on MAS, and on EMG - Effects within 2 weeks - Lasting at least 12 weeks, possibly longer	Bhakta et al 2000, Esquenazi et al 2013, Childers et al 2004, Brashear et al 2002, Shackley et al 2012, Hesse et al 2001, Shaw et al 2011, Simpson et al 2008, Bakheit et al 2000, Caty et al 2008, Rousseaux et al 2005, Kaji et al 2010, Pandyan et al 2002
PROM	?	Evidence of improvements in PROM in wrist and LL, lasting 12 weeks. Evidence that BoNT helps preserve PROM in the LL (compared to splinting alone).	Bhakta et al 2000, Esquenazi et al 2013, Verplancke et al 2005
Pain	?	Growing body of evidence that BoNT decreases spasticity pain. Indications that there may be a slower onset of symptom relief with longer duration of effect. ? Separate anti-nociceptive effect?	Shaw et al 2011, Wissel et al 2000, Rosales et al 2011, Wissel et al 2016

Can Therapy Help?



- Improve BoNT outcomes?
- Prolong BoNT effect?
- Reduce the need for repeat treatments?
- Reduce dose requirements?

Can Therapy Help?



Systematic Reviews
Randomized Controlled Trials
Cohort Studies
Case-Control Studies
Case Series, Case Reports
Editorials, Expert Opinion

Cochrane Library

Cochrane Database of Systematic Reviews

Systematic review of adjunct therapies to improve outcomes following botulinum toxin injection for treatment of limb spasticity

Patricia Branco Mills[1–4], Heather Finlayson[1,3], Malgorzata Sudol[1,3] and Russell O'Connor[1,3]

Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity (Review)

Demetrios M, Khan F, Turner-Stokes L, Brand C, McSweeney S

Rehabilitation Therapies After Botulinum Toxin-A Injection to Manage Limb Spasticity: A Systematic Review

Bianca Z. Kinnear, Natasha A. Lannin, Anne Cusick, Lisa A. Harvey, Barry Rawicki

EBP: BoNT and Rehab Therapies

- Evidence scarce and of low quality
- Low level evidence for multidisciplinary rehabilitation for active function and impairment
- Low level evidence for intensive forced UL use.
- Preliminary evidence to suggest BoNT + stretch more effective than BoNT alone.
- Optimal types and intensity of therapy unclear

Demetrios et al. Cochrane Library 2013., Mills et al 2015, Kinnear et al 2014

Tre BoNT + Casting spastic equinus with BoNT + casting (compared to BoNT alone):

- improves spasticity, PROM and ability
- prolongs positive effects

Singer et al 2003, Carda et al 2011, Bottos et al 2003, Park et al 2010, Glanzman et al 2004

BoNT + Casting

Treatment of spastic equinus with BoNT + casting:

- Casting prevents equinovarus
- Effects of BoNT needs further Ix

Verplancke et al 2005

Stretch

Four weeks of daily stretch has little or no effect on wrist contracture after stroke: a RCT. Horsley et al. (2007)
Stretch had no effect on pain, activity or ROM
The effect of casting combined with stretching on passive dorsiflexion in adults with traumatic head injuries. Mosely et al (1997).
Passive ankle DF increased by 13.5 degrees*
7 day cast
Twelve weeks of nightly stretch does not reduce thumb web space contractures in people with a neurological condition: a RCT. Harvey et al. (2006)
Worn for 8 hours per night, 12 weeks.
1 degree change in 12 weeks. No sig change.
Effectiveness of a bed positioning program for treating older adults with knee contractures who are institutionalized. Fox et al (2000)
40 mins 4 x a week
No change in knee range. BPP is not supported for Mx of knee contractures.

Stretch

Effectiveness of Stretch for Treatment and Prevention of Contractures in People with Neurological Conditions: Systematic Review. Owen et al. (2011)
Regular stretch does not produce clinically important changes when applied for less than <7/12
Effects of longer programs unknown
The effect of stretching in spasticity: A systematic review. Bovend'Eerdt et al. (2008)
Evidence is inconclusive
Regular stretch does not increase muscle extensibility: an RCT. Ben & Harvey (2010).
No change in muscle extensibility. Improved stretch tolerance.

Constraint Induced Movement Therapy

RCT: CIMT + BoNT .v. BoNT alone

- Significantly greater improvements in UL spasticity and arm function in CIMT group at 6 months post injection.

Sun et al 2010

Case Study: CIMT + BoNTA (Chronic Stroke)

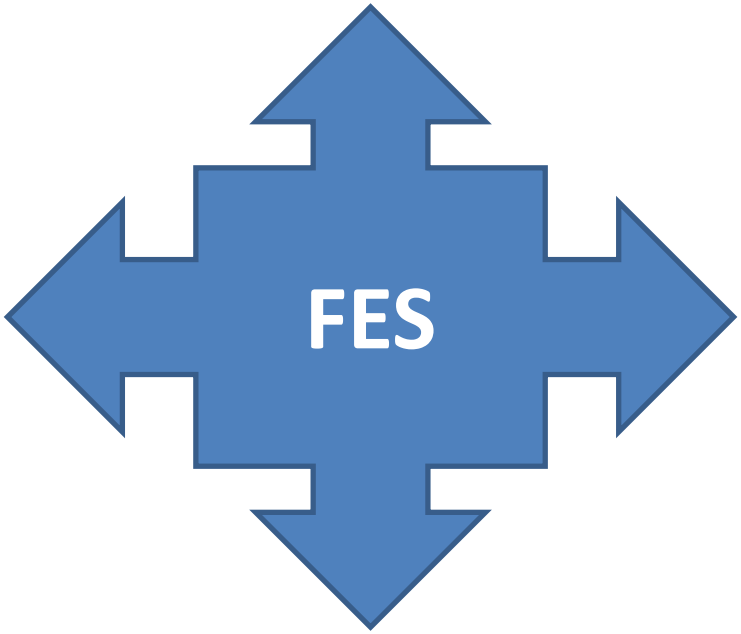
- Improvements in MAS, Fugyl Meyer, ARAT and AOU- MAL over 1 year period
- No repeat injections necessary

Amano et al 2015

FES – Possible mechanisms for improving anti spasticity effect of BoNT

Immediately stimulate injected muscle:
Increase toxin uptake at NM junction

Stimulate agonist:
Treatment of negative symptom of UMNL ie weakness



Immediate cyclic stimulation agonist/antagonist: mechanical spread of toxin

Stimulate antagonist: Reduce tone in agonist through reciprocal inhibition

Wilkenfield 2013

BonT, FES & Walking Speed

Speed is meaningful!

'Powerful indicator of function and prognosis after stroke' Schmid et al 2007

- **<0.4 m/s** **Household Ambulation**
- **0.4-0.8 m/s** **Limited Community Ambulation**

- **>0.8 m/s** **Community Ambulation**

Gait velocity gains that lead to a change in ambulation category result in better function & QoL. Schmid et al 2007

BonT alone assoc with small but sig increase in gait speed ~ 0.044m/s. Foley et al 2010

PNS, BoNT and Walking Function

- **Lack of clear data to indicate that PNS is better than an AFO.**

Wilkenfield 2013

- **Indication that PNS + BoNT increases walking speed**

Johnson et al 2002 and 2004

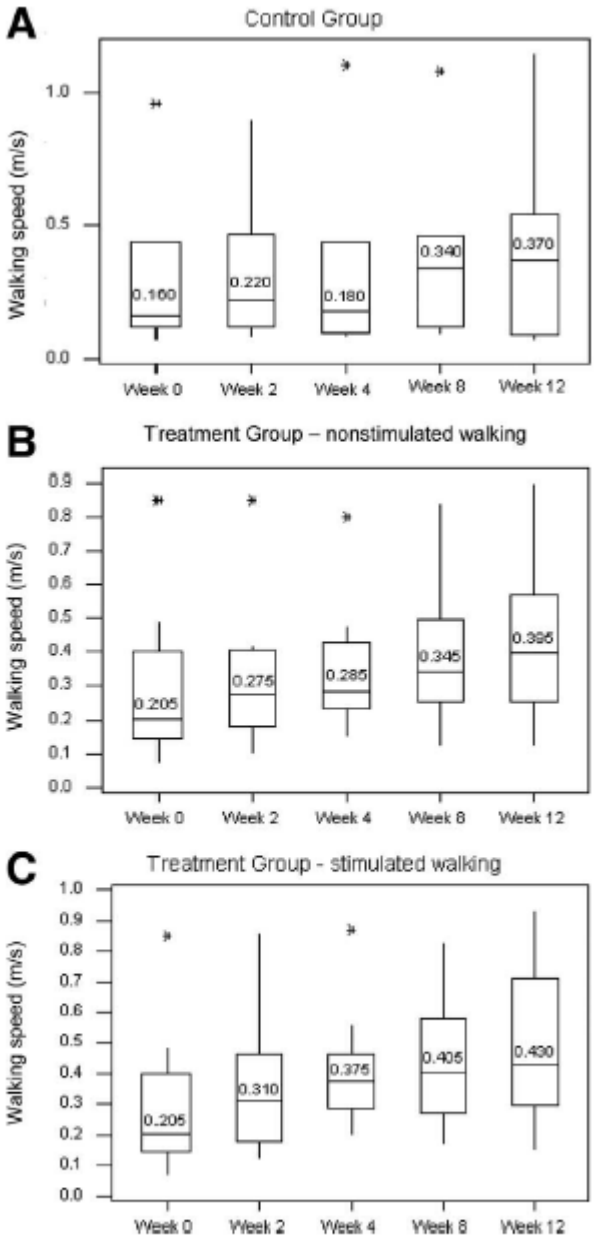


Fig 2. (A) Walking speed for the control group. (B) Nonstimulated walking speed for the treatment group. (C) Stimulated walking speed for the treatment group. Asterisks denote single outliers.

Johnson et al 2004

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ES, BoNT and Spastic Drop Foot

BoNT + post injection ES further improves spasticity and walking (speed, symmetry and stride length) compared to BoNT alone.

Hesse et al 1995

But…

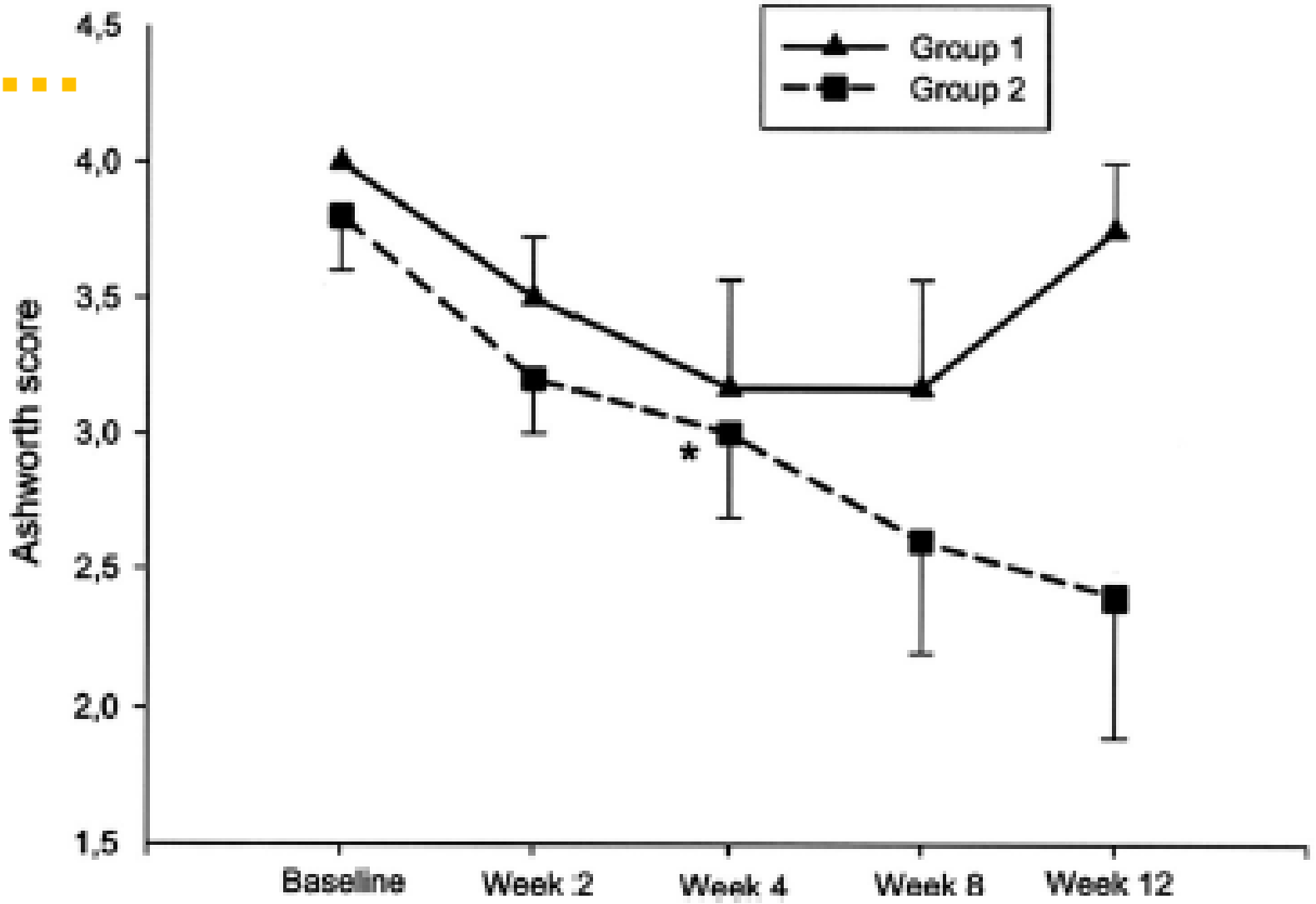

FIGURE 1 *Course of mean Ashworth Score (*P < 0.05). Error bar = 1 SEM.*

Cyclic ES, BoNT and Hand Function

Cyclic ES does not increase hand function gains made with the combination of BoNT and task practice

Weber et al 2010

BoNT and Therapy/Exercise

BoNT and Novel Therapies










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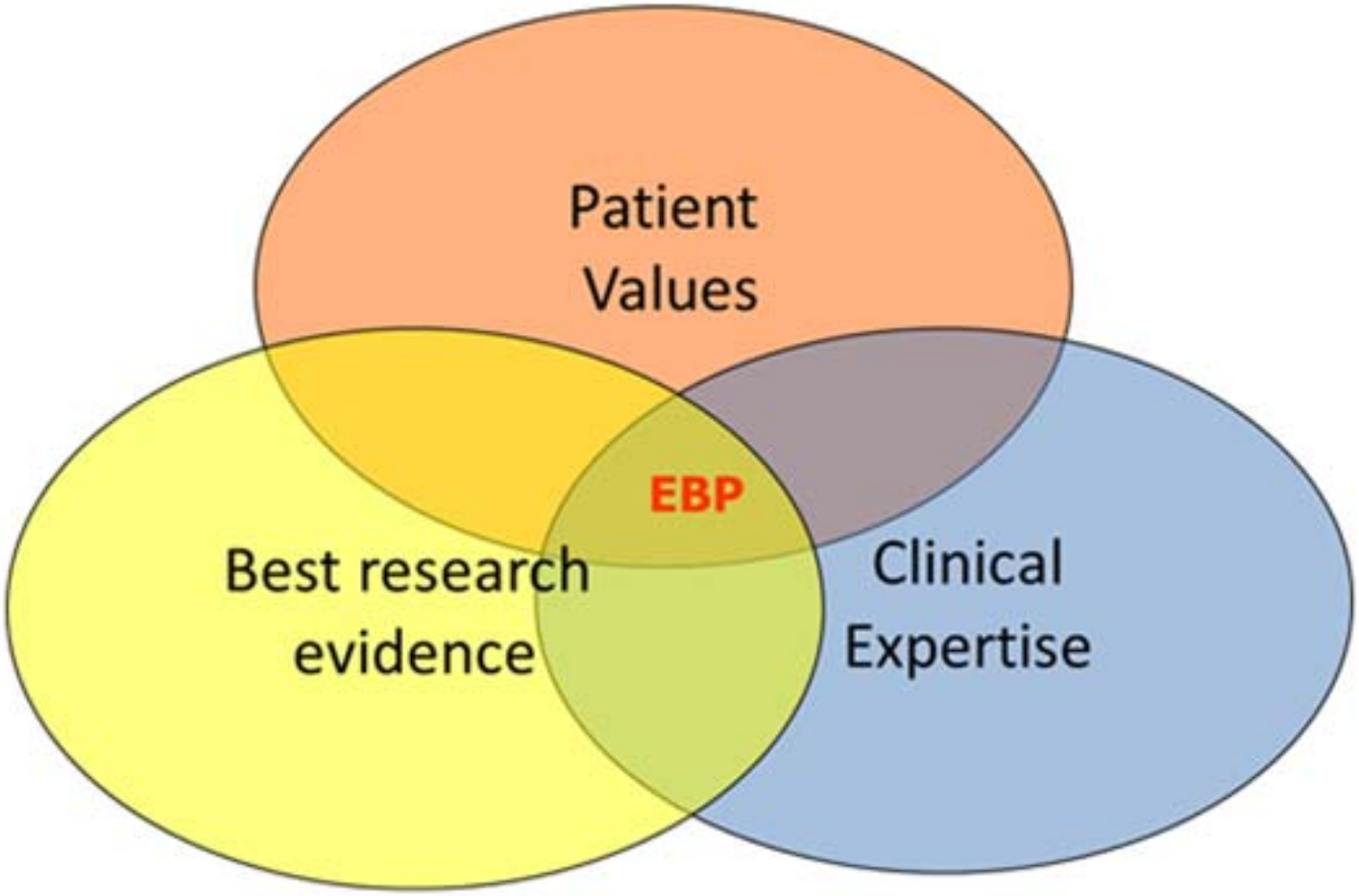

Sackett D et al (2000): Evidence-Based Medicine. Churchill Livingstone

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