

# Medicinsk behandling av dyskinesi och spasticitet

Lena Westbom och Kate Himmelmann

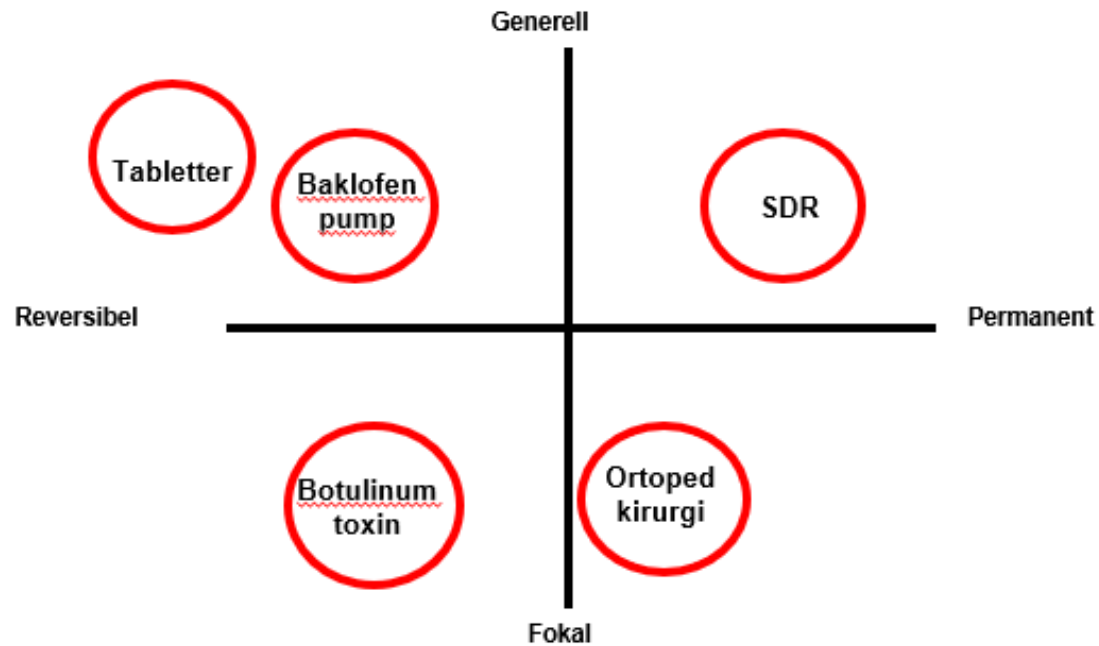
Malmö 18-10-22

Session C

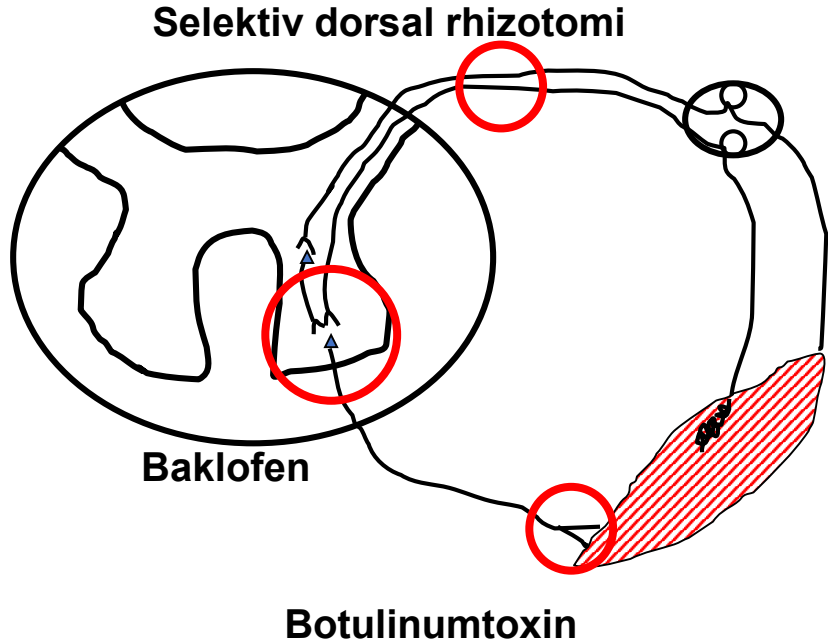


UPPFÖLJNINGSPROGRAM FÖR CEREBRAL PARES

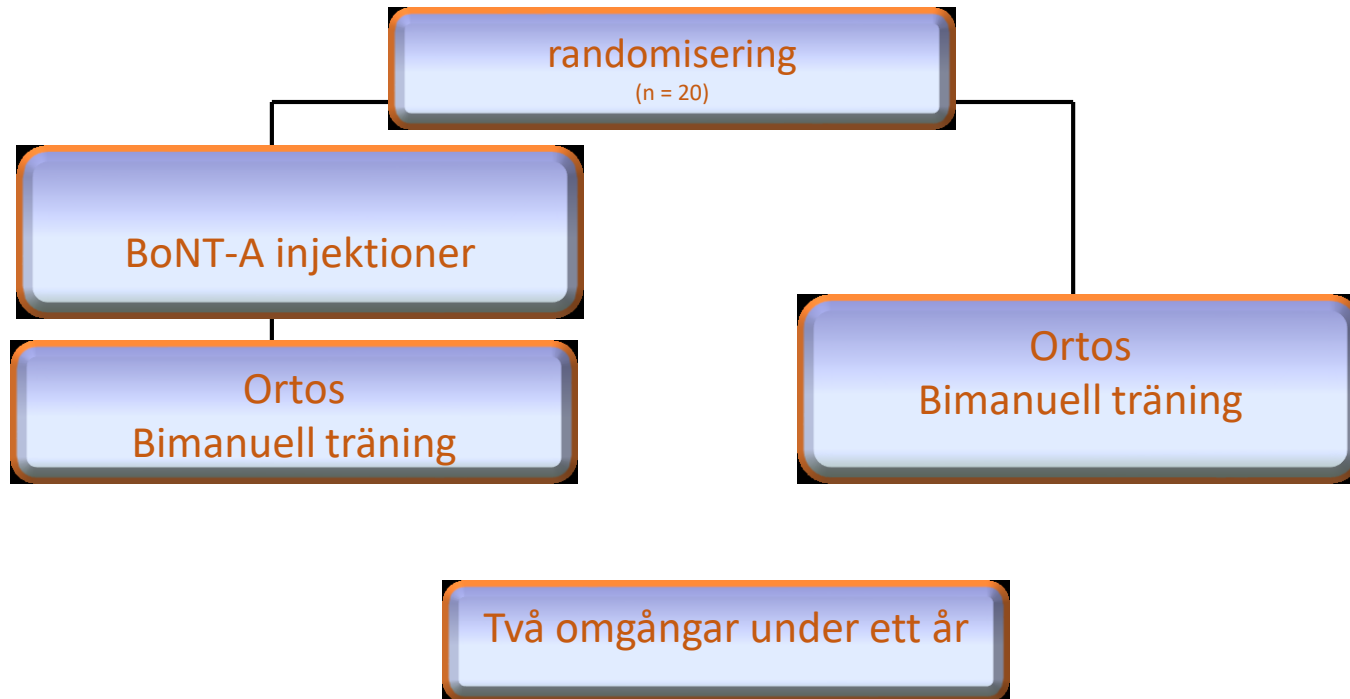
# Behandling av muskelspänningar



# BEHANDLING AV MUSKELSPÄNNINGAR



# RCT-studie



## Learning for life

How children with unilateral spastic cerebral palsy learn to master bimanual activities

Git Lidman

Institute of Neuroscience and Physiology at the Sahlgrenska Academy, University of Gothenburg

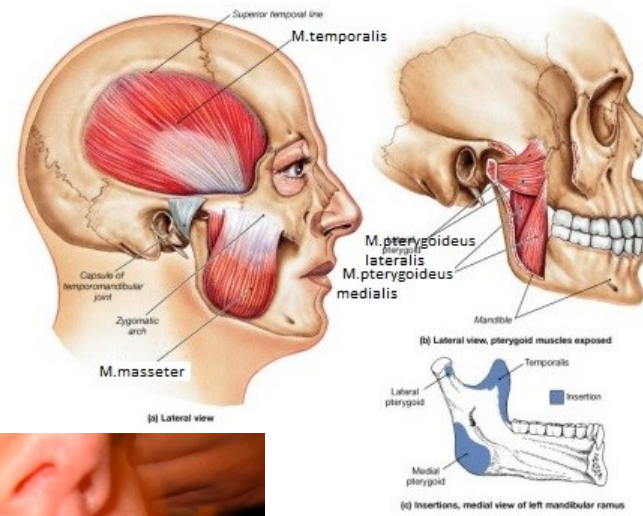


UNIVERSITY OF GOTHENBURG



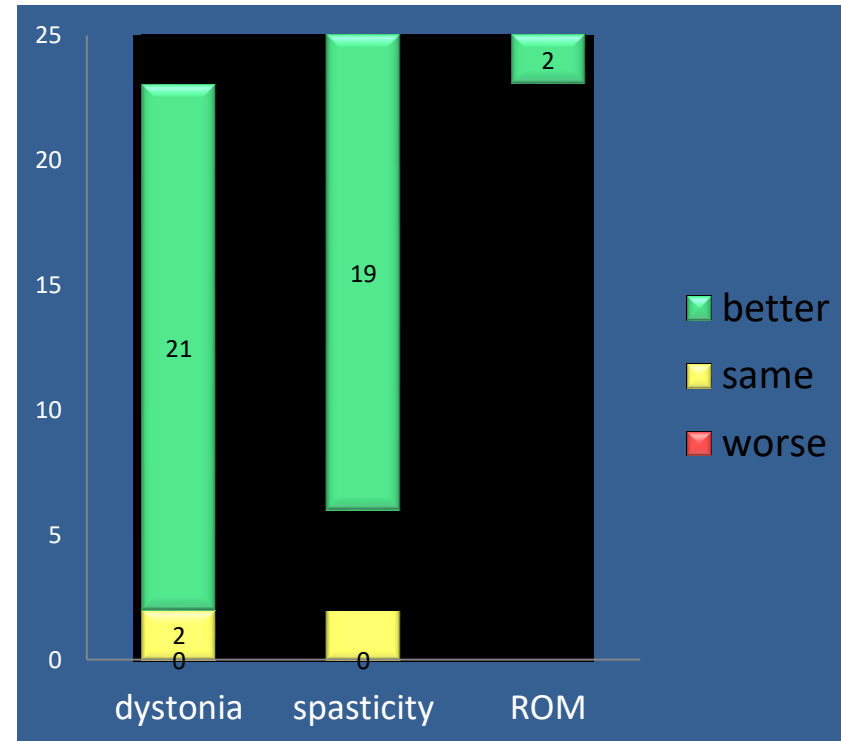
### • Efter interventionsåret:

- Upprepad BoNT-A i kombination med intensiv arbetsterapi gav bättre effekt på bimanuell handfunktion jämfört med enbart arbetsterapi
- ROM aktiv supination och målinriktade aktiviteter förbättrades i båda grupper

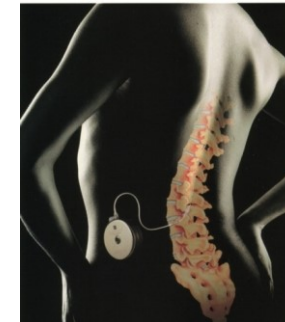


Borttagna bilder från  
SCPE-videoer  
om dyskinetisk CP/dystoni

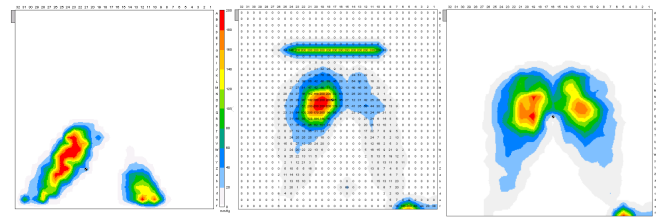
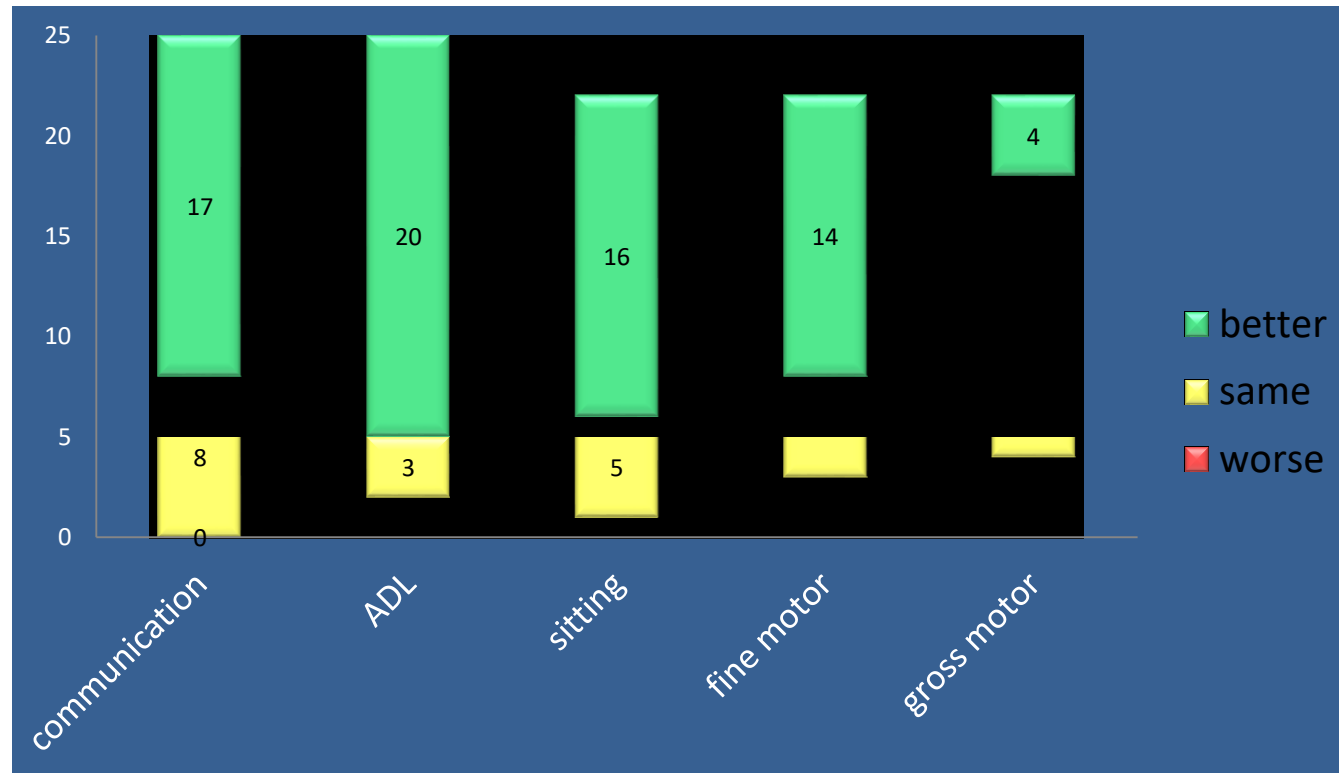
## Våra resultat efter baklofenpump – muskelspänningar och rörelseomfång



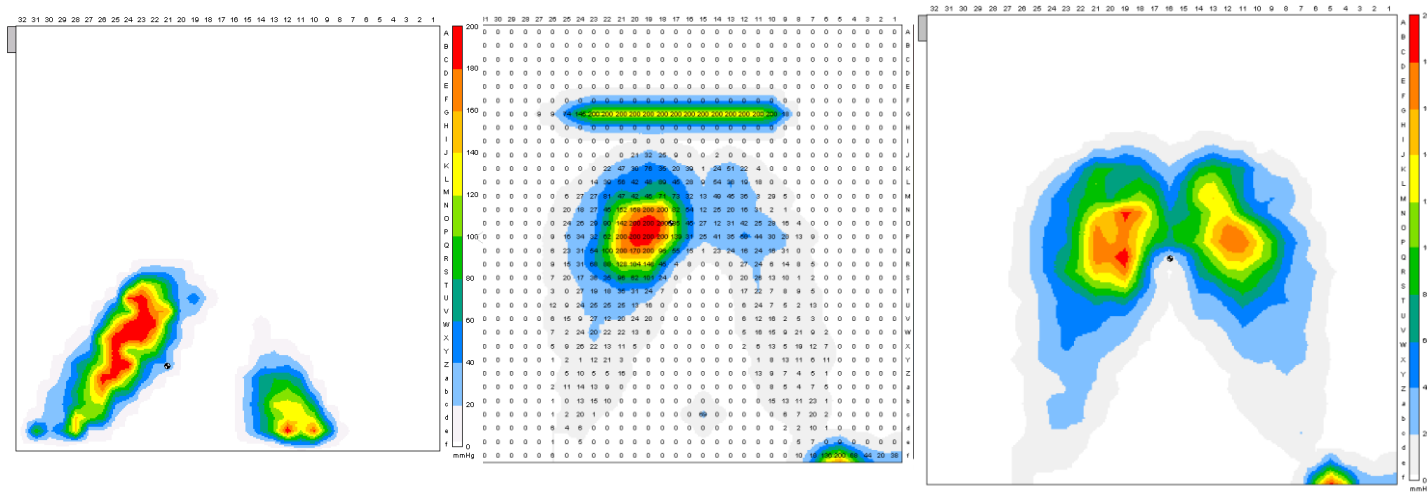
25 barn och ungdomar med dyskinetisk CP



## Våra resultat – funktion och aktivitet

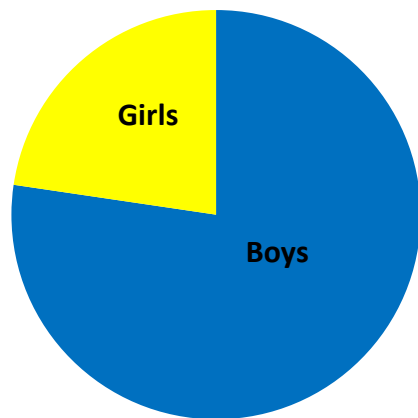


# Sittande före och efter pump tryckregistrering, Ida, snart 7 år



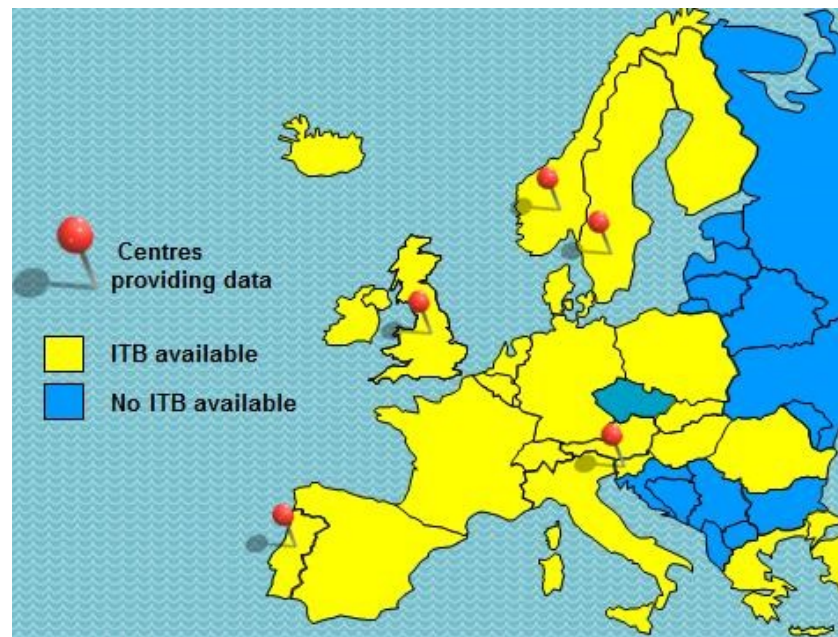
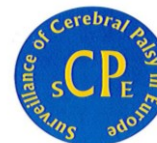
Kate Himmelmann





0,4-4%

## Tillgång till ITB i Europa

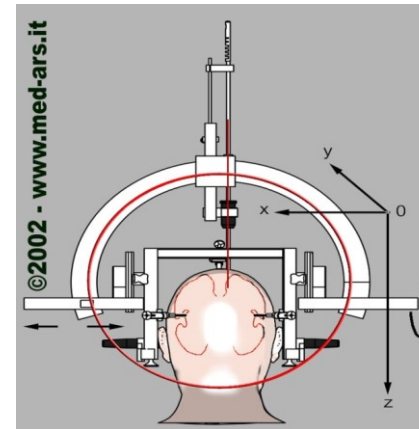


Kate Himmelmann

# Deep brain stimulation

2 elektroder i globus pallidus internus

5 d senare: Implantation av 'internal pulse generator': som producerar en högfrekvent elektrisk strömpuls



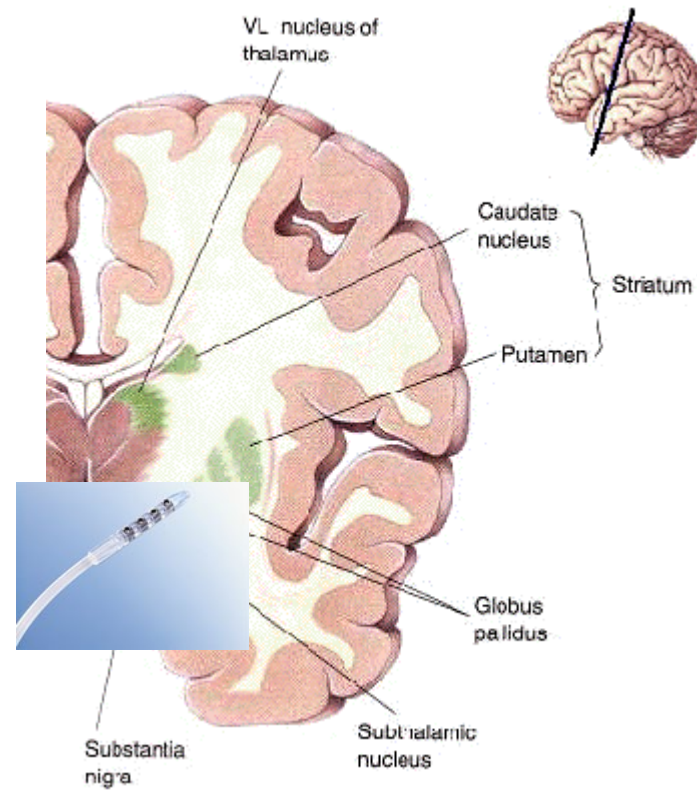
# DBS



Elektrod  
m 4 poler

Neurostimulator  
pulsgenerator

# DBS globus pallidus int bilat



# Systematisk review

## DBS (n=14+1meta-analysis)

- Vidailhet 2009 (n=13) pilot study, adults
- Air 2011 (n=6/31)
- Gimeno 2012 (n=5/6) smärta/komfort, sittande etc.
- Olaya 2013 (n=6)
- Marks 2013 (n=9/17) jfr DYT 1 och CP
- Lumsden 2013 (n=28?/70) tidig debut sämre resultat
- Martinez 2013 (10/33)
- Koy 2013 (n=8) young adults
- Gimeno 2014 (n=14/30) COPM 1 year follow-up
- Keen 2014 (n=5)
- Romito 2014 (n=15) 5 year follow-up
- Kim 2014 (n=5/12)

**Meta-analys (Koy et al.) av 68 patienter/20 artiklar (Burke-Fahn-Marsden) visar att DBS gav effekt på dystonin men mycket varierande grupper i studierna**

	Mechanism of action	Dystonia	Chorea	Side-effects
Dopamine agonists (levodopa) <sup>55</sup>	Enhances the activity of dopamine	Used	..	Nausea, orthostatic hypotension, and constipation
Anticholinergic (trihexiphenidyl, benztropine) <sup>53,55</sup>	Blocks acetylcholine muscarinic receptor	Used	..	Drowsiness, confusion, memory difficulty, blurred vision, hallucinations, urinary retention, and worsening chorea
Benzodiazepine receptor agonists (diazepam, clonazepam) <sup>55,56</sup>	Enhances GABA-A inhibition	Used	Used	Sedation, confusion, depression, ataxia, and dependence
GABA-B receptor agonist (baclofen) <sup>53,55-57</sup>	Enhances the activity of GABA-B receptor	Used	..	Worsening chorea, incontinence, sedation, dizziness, dry mouth, and increased blood glucose
Dopamine and serotonin antagonist (clozapine) <sup>56</sup>	Binds to serotonin and dopamine receptors and prevents release	Used	..	Decreased white blood cell count, sedation, hypotension, myocarditis, cardiomyopathy, drooling, arrhythmia, seizures, and diabetes mellitus
Pre-synaptic $\alpha$ 2 receptor agonist (clonidine) <sup>58</sup>	Enhances the activity of pre-synaptic $\alpha$ 2 receptor	Used	..	Orthostatic hypotension, bradycardia, sedation, fatigue, and headache
Dopamine antagonists (pimozide, haloperidol) <sup>55</sup>	Antagonist of the D2, D3, and D4 dopamine receptors, and the 5-HT <sub>2</sub> receptor	..	Used	Hypotension, sedation, QT interval prolongation, and ventricular arrhythmias (including torsades de pointes); overdose causes severe extrapyramidal symptoms
Monoamine blockers (tetrabenazine) <sup>51,55,56</sup>	Inhibits vesicular monoamine transporter 2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine storage	Used	Used	Drowsiness, parkinsonism, depression, insomnia, anxiety, and akathisia
Monoamine depleters (reserpine) <sup>51</sup>	Blocks the vesicular monoamine transporter	..	Used	Nasal congestion, nausea, vomiting, weight gain, gastric intolerance, gastric ulceration, stomach cramps and diarrhoea, hypotension, bradycardia, and worsening of asthma
Voltage-gated sodium and calcium channel blocker (carbamazepine) <sup>55</sup>	Blocks voltage-sensitive sodium channels	Used	..	Decreased white blood cell count and platelets; increased risk of suicide
Calcium channel blocker (levetiracetam) <sup>53,54</sup>	Binds to a synaptic vesicle glycoprotein and inhibits presynaptic calcium channels, reducing neurotransmitter release and acting as a neuromodulator	..	Used	Somnolence, decreased energy, headache, dizziness, and (mild) ataxia
Muscle tone reducer (dantrolene) <sup>59</sup>	Reduces skeletal muscle tone at the muscle fibre level	Used	..	Speech and visual disturbances; depression and confusion; hallucinations; headache; insomnia and exacerbation or precipitation of seizures, and increased nervousness
Voltage-gated calcium channel blocker (gabapentin) <sup>60</sup>	Antagonises binding of thrombospondin to voltage-gated calcium channel $\alpha$ 2d-1 receptors and inhibits synthesis of glutaminergic excitatory synapses	Used	..	Dizziness, drowsiness, sedation, fever, fatigue, viral infection, ataxia, and nystagmus




**Table: Medications used to manage dystonia and choreoathetosis in patients with dyskinesic cerebral palsy**

Föregående tabell finns i:

Monbaliu E, Himmelman K et al. Clinical presentation and management of dyskinetic cerebral palsy. Lancet Neurology 2017; 16: 741-49.



# Pharmacological and neurosurgical interventions for managing dystonia in cerebral palsy: a systematic review

DARCY FEHLINGS<sup>1</sup>  | LEAH BROWN<sup>1</sup> | ADRIENNE HARVEY<sup>2</sup> | KATE HIMMELMANN<sup>3</sup> | JEAN-PIERRE LIN<sup>4</sup> | ALEXANDER MACINTOSH<sup>1</sup> | JONATHAN W MINK<sup>5</sup> | ELEGAST MONBALIU<sup>6</sup> | JAMES RICE<sup>7</sup>  | JESSICA SILVER<sup>1</sup> | LAUREN SWITZER<sup>1</sup> | ILANA WALTERS<sup>1</sup> 



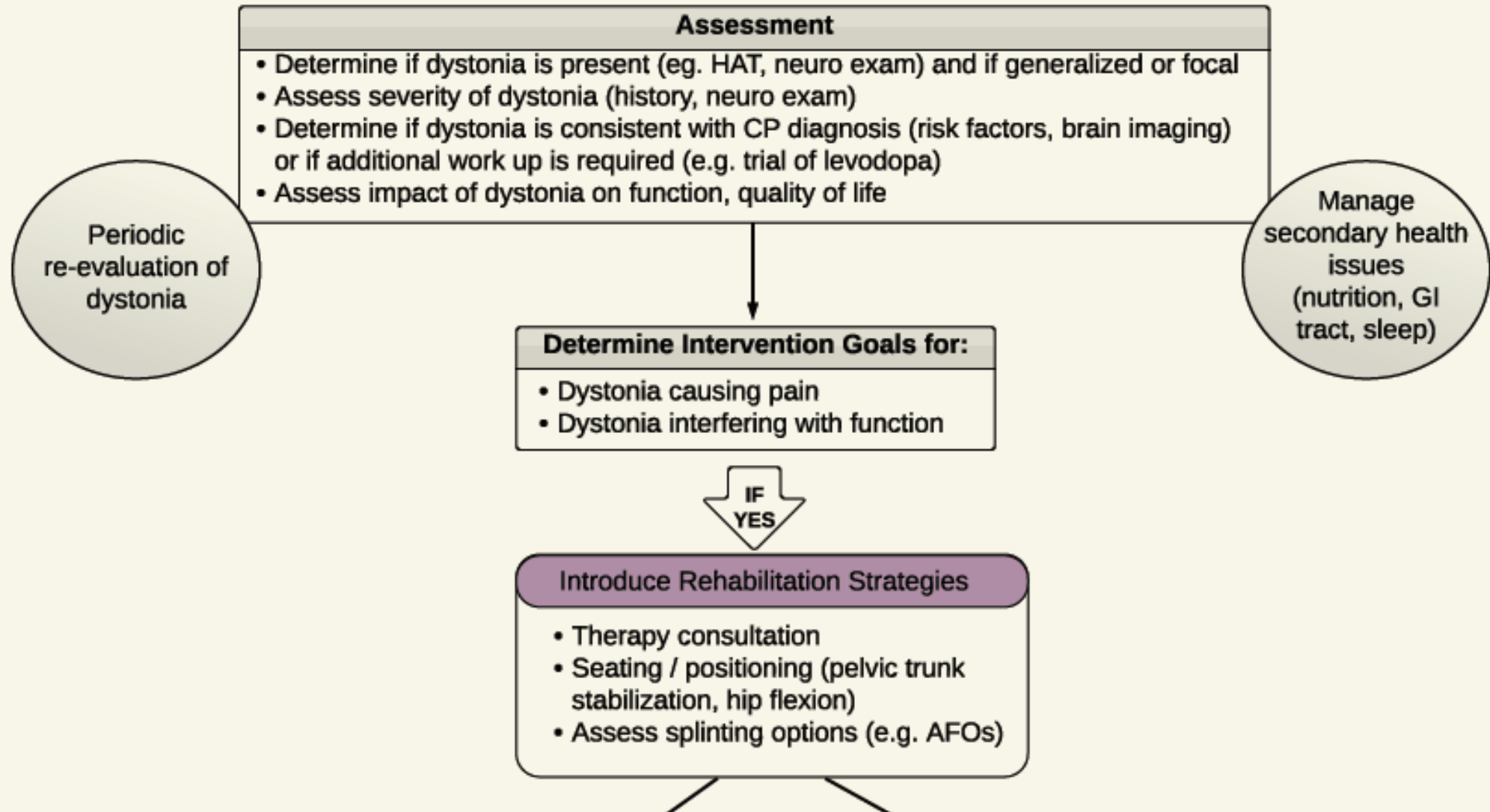
<http://www.aacpdm.org/resources/care-pathways/dystonia#>

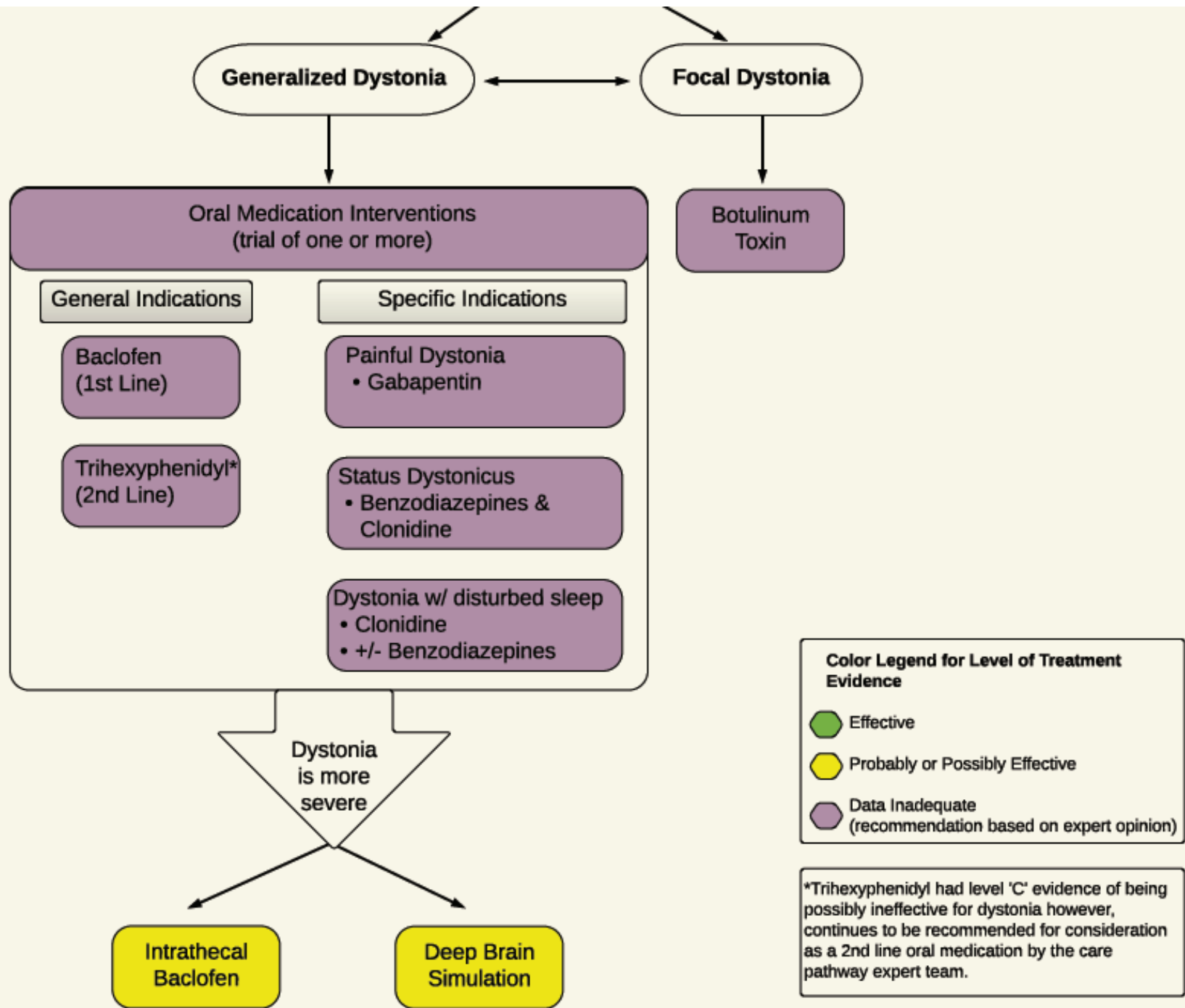


Oral meds	Dystonia	Chorea
Dopa agonists (L-Dopa)	☹️	☹️
<b>Anticholinergics</b> (Trihexiphenidyl, benz(a)tropine)	😊	☹️
Benzodiazepines (diazepam, clonazepam)	😊	😊
<b>Baclofen</b>	😊	
Clozapine	😊	
Dopa antagonists (Pimozide, Haloperidol)		😊
<b>Monoamine blockers</b> (Tetrabenazine)	☹️	😊
<b>alpha 2 receptor agonist</b> (Clonidine)	😊	
Monoamine depleters (Reserpine)		😊
AED (Carbamazepine)	😊	
AED (Levetiracetam)		😊
Dantrolene	😊	
<b>Gabapentin</b>	😊	

References: 1984, Marsden - 2001, Hoon - 2002, Chuang - 2003, Edgar - 2007, Sanger - 2009, Rice - 2010, Cloud - 2011, Ben Pazi - 2011, Carranza-del Rio - 2011, Kölker - 2012, Roubertie - 2013, Jankovic - 2014, van Karnebeek - 2016, Liow - 2016, Lumsden - 2016, Koy

# Flow Diagram for an Evidence-Informed Care Pathway for Dystonia in Cerebral Palsy





Create Open Add Files Convert To Save Print Hand Edit Text Box Add Image Comment Bates Numbering Redaction Password Security

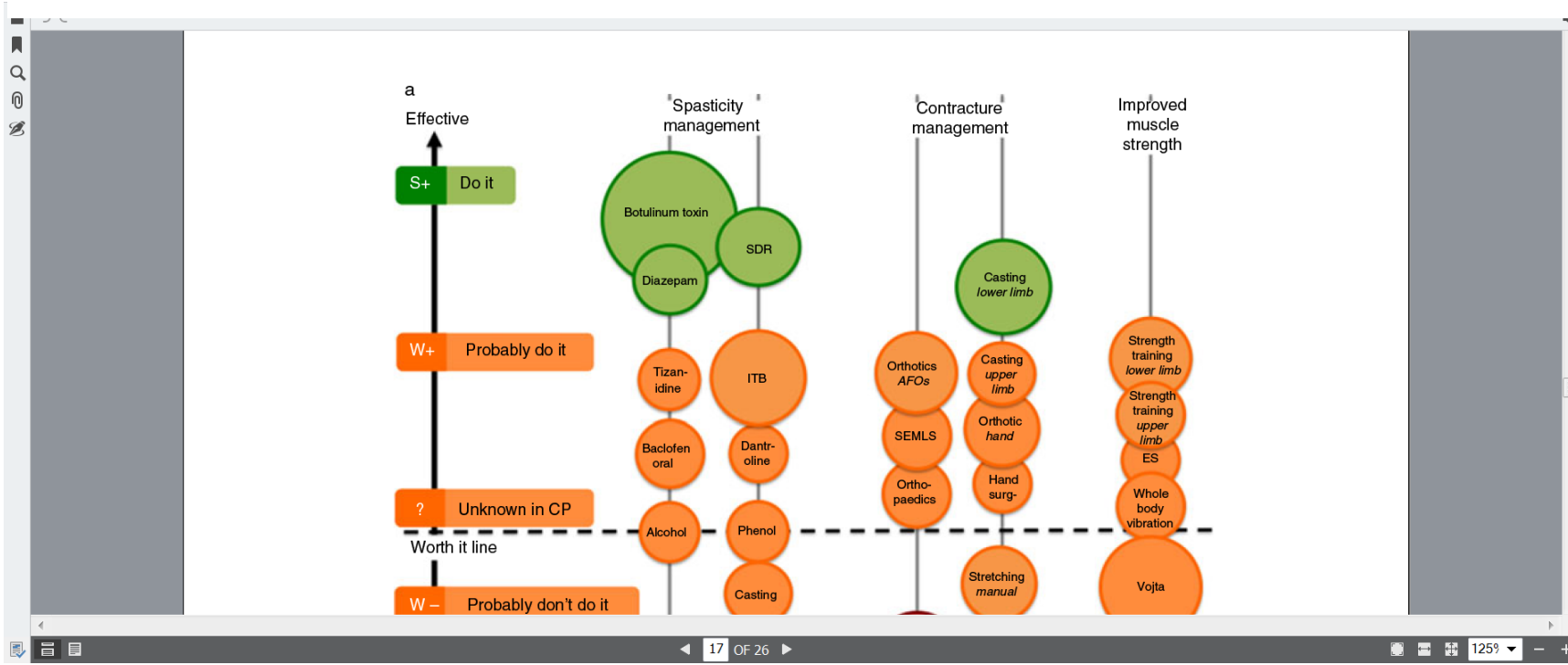
DOCUMENT SAVE/SEND MODIFY REVIEW PROTECT

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY REVIEW

## A systematic review of interventions for children with cerebral palsy: state of the evidence

IONA NOVAK<sup>1,2</sup> | SARAH MCINTYRE<sup>1,2</sup> | CATHERINE MORGAN<sup>1,2</sup> | LANIE CAMPBELL<sup>2</sup> | LEIGHA DARK<sup>1</sup> | NATALIE MORTON<sup>1</sup> | ELISE STUMBLES<sup>1</sup> | SALLI-ANN WILSON<sup>1</sup> | SHONA GOLDSMITH<sup>1,2</sup>

SDR: Spasticity reduction, gait kinematics – green light – GO!  
 SDR: Improved function and self-care – yellow light – probably do it – measure!  
 DMCN 2013



# Indications for SDR

- Bilateral spastic CP (legs more involved than arms = CP spastic diplegia)
- Spasticity interfering with functional development
- Age 3 – 6 years ideal (older persons sometimes)
- Any gross motor function level GMFCS I-V
- Enough muscle control and strength under the spasticity to reach the individually formulated goals
- Available rehabilitation service

## Absolute contraindications for SDR:

- Ataxia or dyskinesia

## Contraindications:

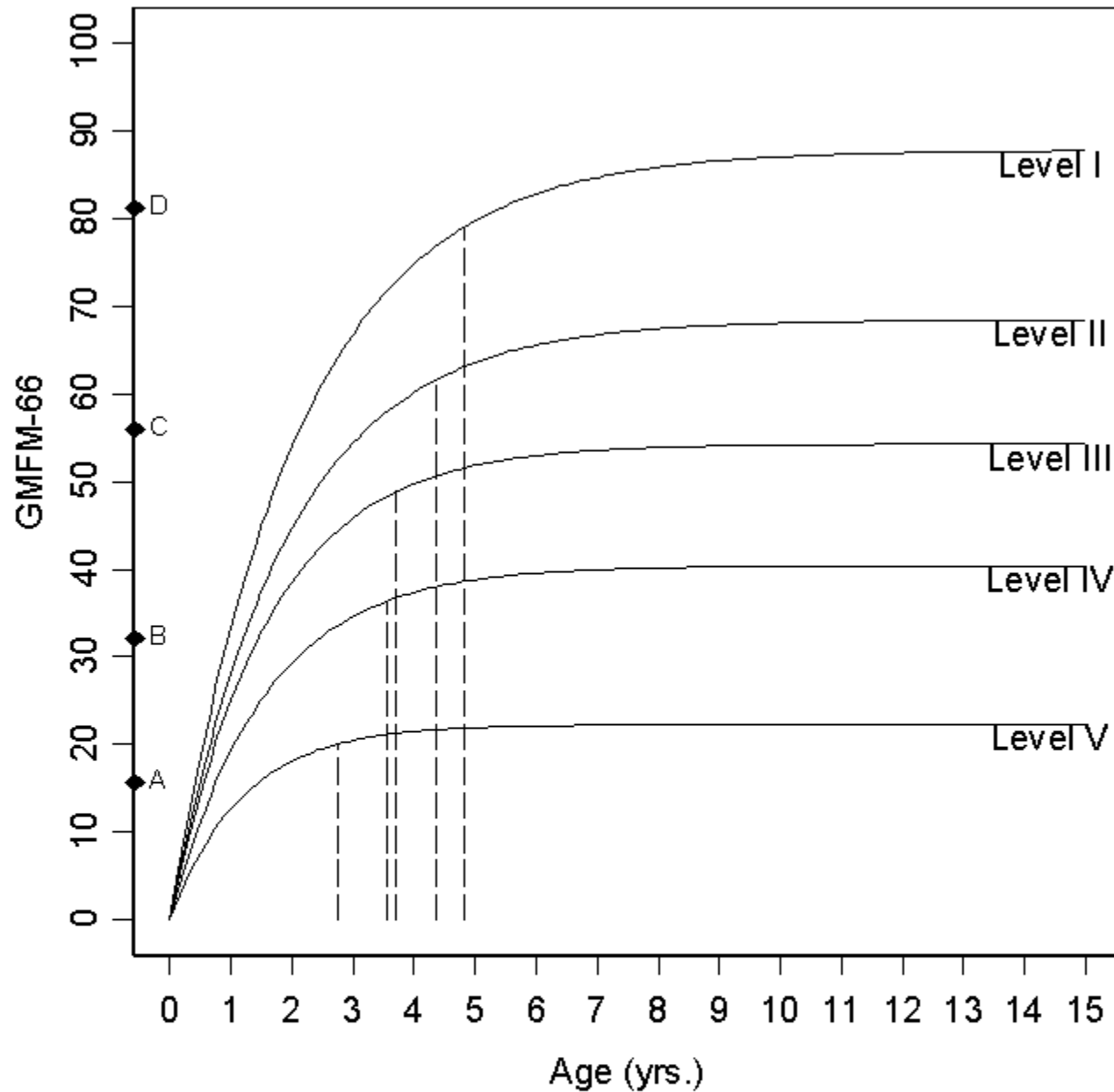
- Trunk weakness/hypotonia
- Dependent on spasticity for antigravity control
- Severe contractures and joint deformities
- Prior orthopaedic surgery (muscles, tendons)
- Lack of prerequisites to carry out post-op therapy
- Unrealistic expectations

Establishing the goals of the intervention, together with the family and local therapists

Based on

- child's actual function (a.o. GMFCS level)
- family priorities
- increasing knowledge of outcome in previously SDR-operated children
- knowledge regarding the natural course without SDR or with other treatment options
- three slides on "natural course development":

# GMFCS Level I to V



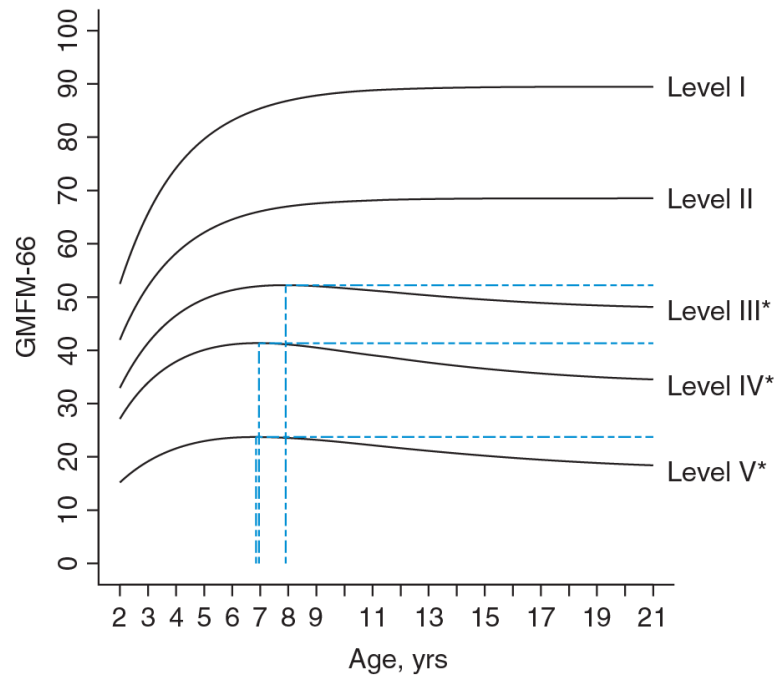
Motor developmental curves

Rosenbaum et al JAMA 2002

This graph shows the observed and predicted GMFM-66 scores for children in GMFCS Levels I through V. The curved solid lines indicate average performance. The horizontal dotted lines on the right of the figures indicate the band expected to encompass 50% of children's limits of development. The solid vertical lines indicate the average age 99.4th percen



Functional deterioration with age due to increased body size, contractures and joint deformities



Hanna et al, DMCN 2009



Contractures, starvation, pain correlates to the deterioration (Bartlett et al DMCN 2009)

# Contracture development with age

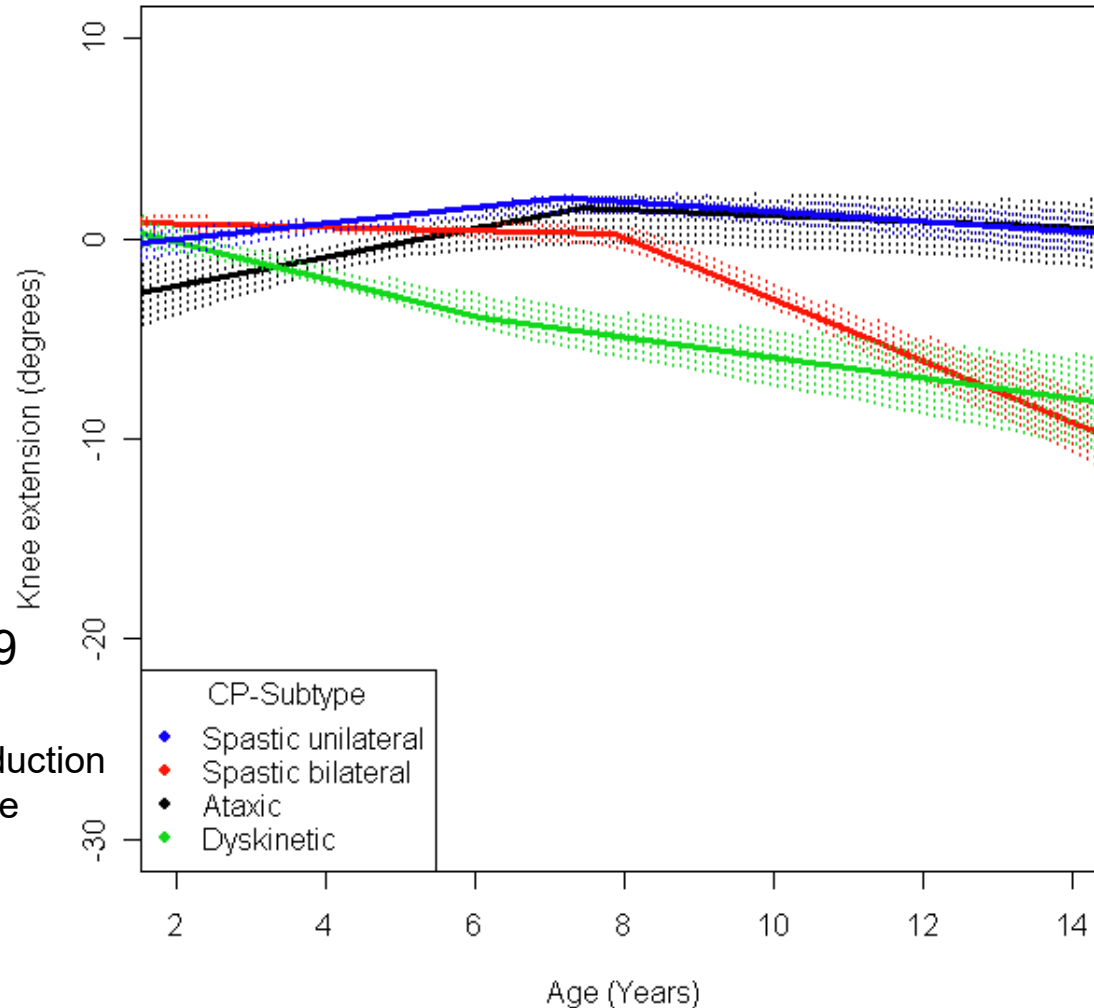
- total population with CP, 359 children, 5075 assessments

Mean PROM in  
knee extension  
 $\pm 2$  SD

**BSCP red**

Nordmark et al 2009

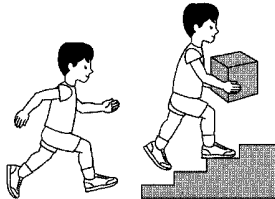
One aim with spasticity reduction  
/SDR s to make contracture  
prevention easier



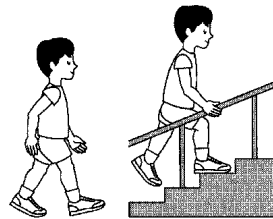
## SDR – functional goals, general

- GMFCS I-II: Improve balance, endurance and flexibility in standing, walking, running, jumping
- GMFCS III: Stability and variability in sitting, attain and maintain standing, walking and enabling self-propelled wheeled transfers
- GMFCS IV-V: Independent sitting, supported standing and enabling wheel-chair transfers. Reduce pain emerging from spasticity. Ease care burden.

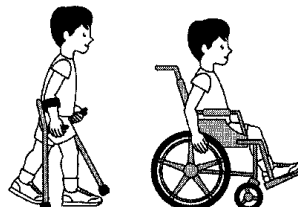
**GMFCS I**



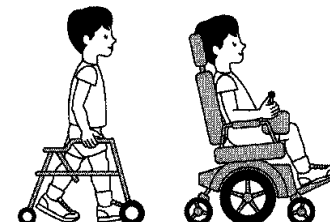
**GMFCS II**



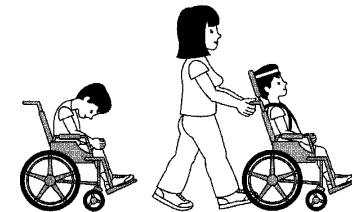
**GMFCS III**



**GMFCS IV**



**GMFCS V**



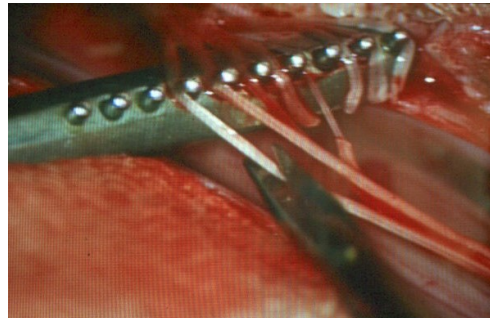
# Instruments

- Tonus - modifierad Ashworth + Tardieu
- Passive Range of Motion (PROM) - goniometer
- Gross Motor Function Measure (GMFM)
- Pediatric Evaluation Disability Inventory (PEDI)
- Gait analysis



# Procedures - neurosurgery

- Unilateral laminoplasty L2-L5 laminae flap fastened in the end of op
- Posterior roots in cauda equina identified, anatomical level confirmed
- EMG-recording of muscles incl anal sfincter
- Roots divided into 4-10 rootlets → "comb" to stimulate all rootlets before cutting those with most pathological response



Nordmark et al BMC Pediatrics 2008, 8:54

# Procedures - post-op

- 3-4 days continuous infusion intrathecal bupivacain and morphine by a pump
- Physiotherapy day 5 + 3 weeks
- Physiotherapy at home included in functional and play activities
- Individualized 1 h sessions with the PT twice a week for 6 mths, then once a week  
for at least one year

# Postoperative treatment

- Strength training
- Using newly learned functions in daily activities
- Long-time controlled standing in a standing shell - muscle stretching-  
contracture prevention
- Ortooses for optimal positioning of the feet in free standing



# Ref från SDR-op i Lund

Nordmark E, Josenby A L, Lagergren J, Andersson G, Strömblad LG, Westbom L. Long-term outcomes five years after selective dorsal rhizotomy. BMC Pediatrics 2008;8:54 (beskriver urval, op-teknik, FT-uppföljning, och 5års resultat GMFM)

open access: <https://bmcpediatr.biomedcentral.com/articles/10.1186/1471-2431-8-54>

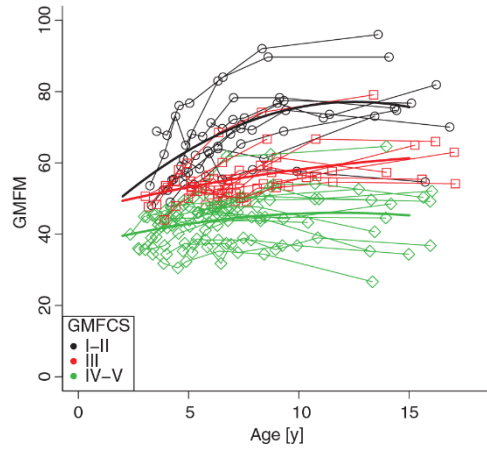
Josenby AL, Wagner P, Jarnlo GB, Westbom L, Nordmark E. Motor function after selective dorsal rhizotomy: a 10-year practice-based follow-up study. Dev Med Child Neurol. 2012; 54:429-35.

Josenby AL, Wagner P, Jarnlo GB, Westbom L, Nordmark E. Functional performance in self-care and mobility after selective dorsal rhizotomy: a 10-year practice-based follow-up study. Dev Med Child Neurol. 2015; 57:286-93.



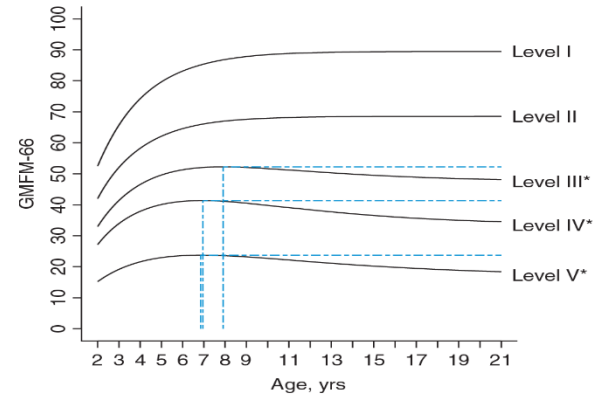
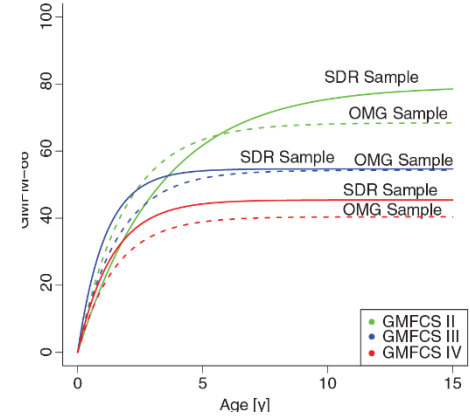
# Motor growth curves

– 10 yrs post SDR Lund and OMG 2002 and 2009

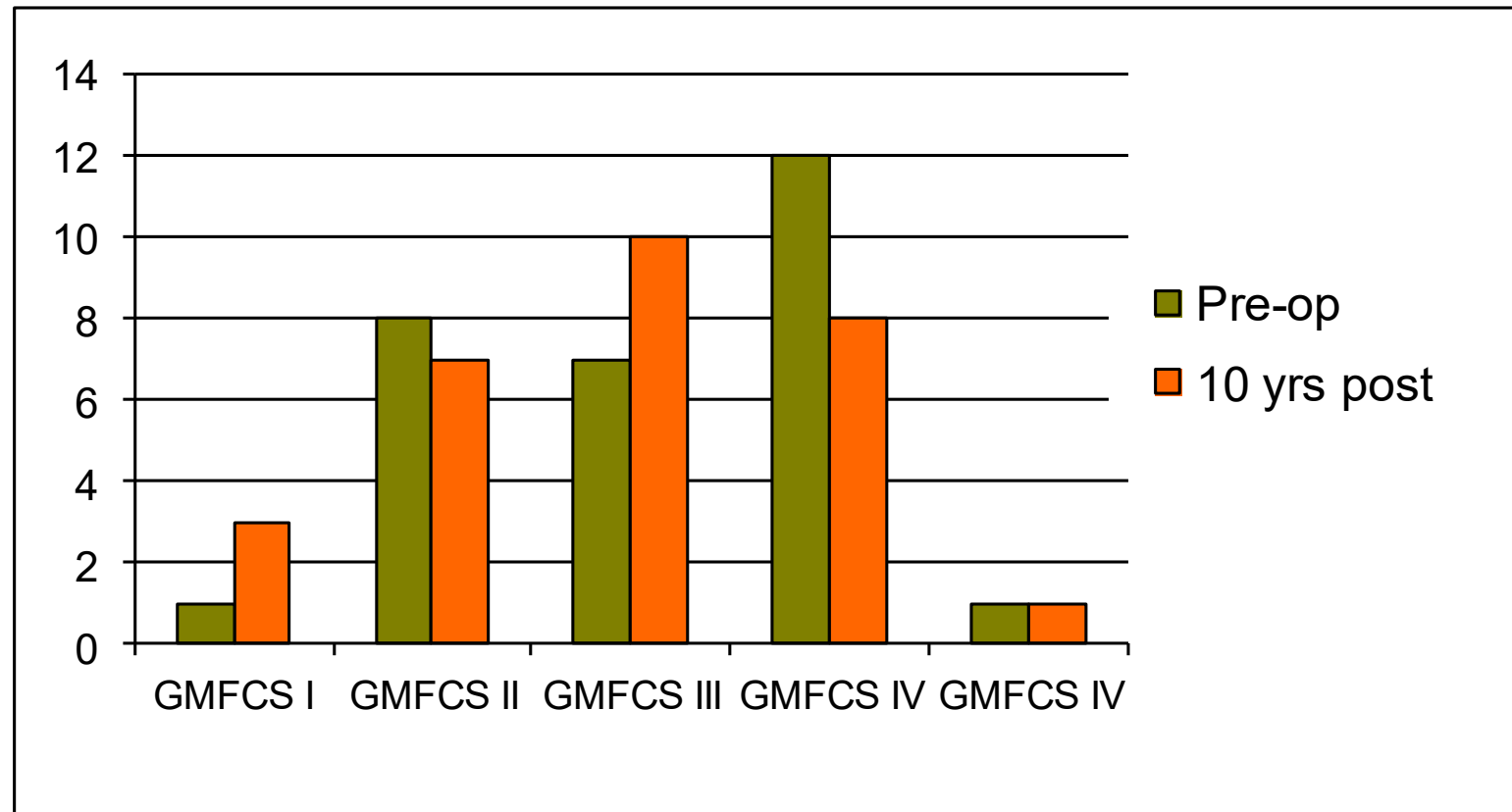


The GMFM scores increased more than expected from OMG 2002

and especially from OMG 2009



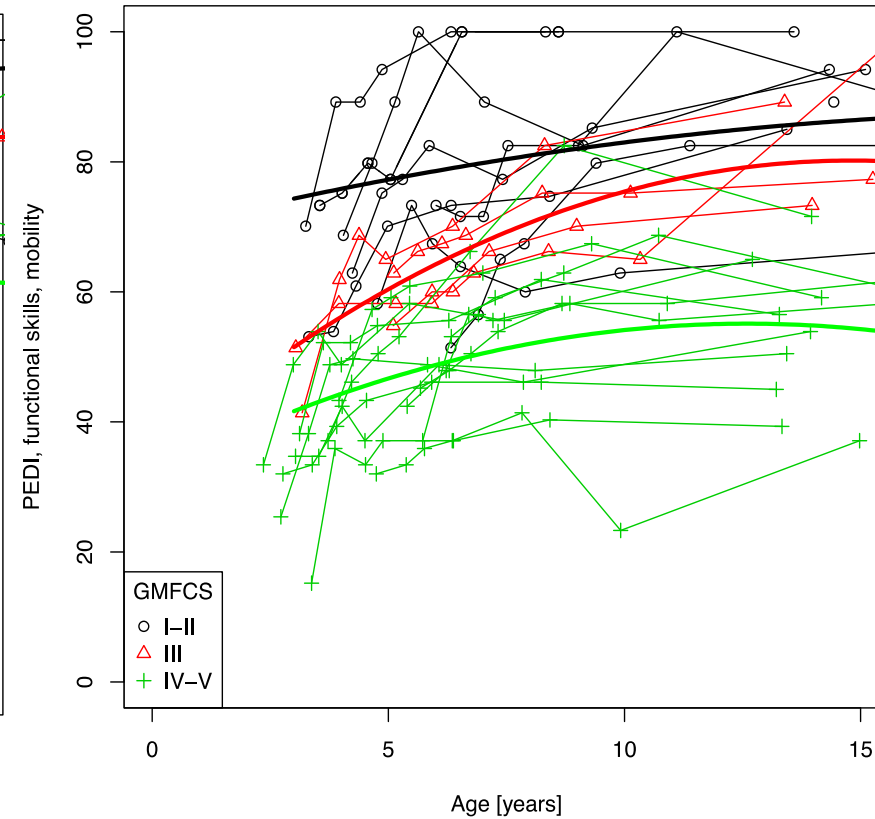
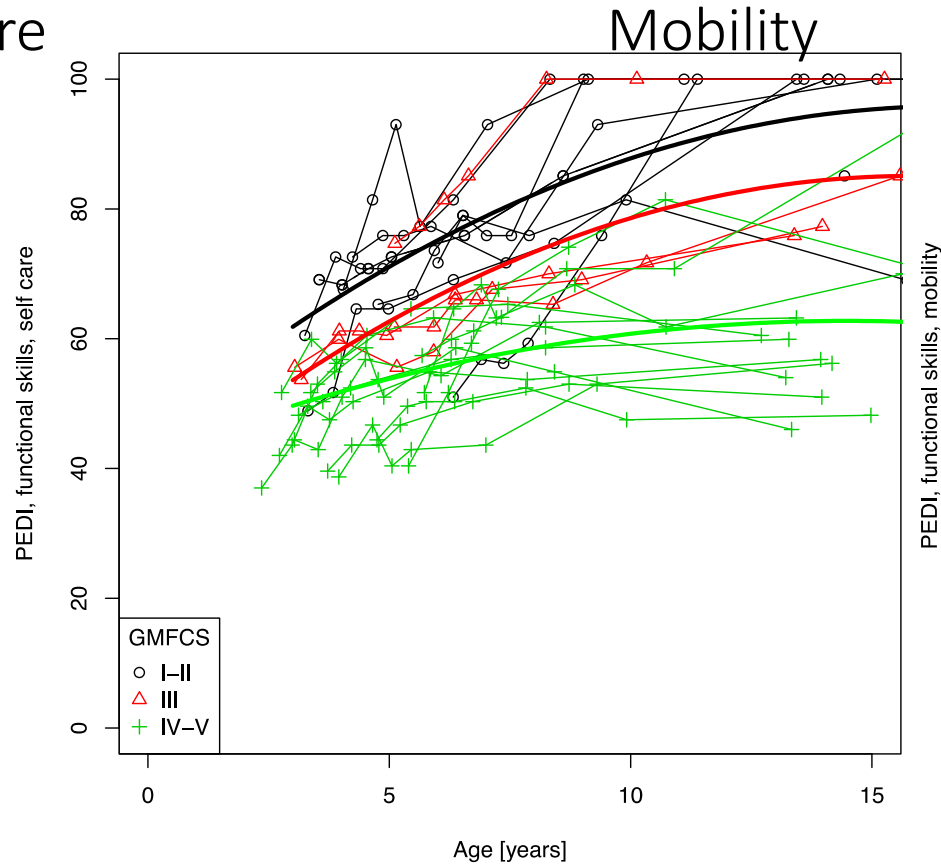
# GMFCS-levels at 10 years post SDR – number of children in each GMFCS level



Improved in 7/29 children, in two children by two levels. One deteriorated level II→III

# PEDI - performance in functional skills, 10 years post SDR

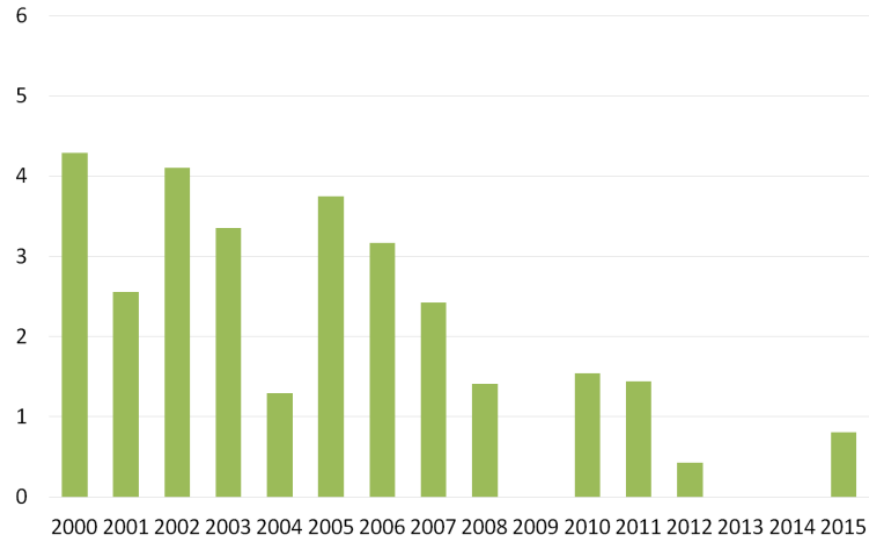
## Self care



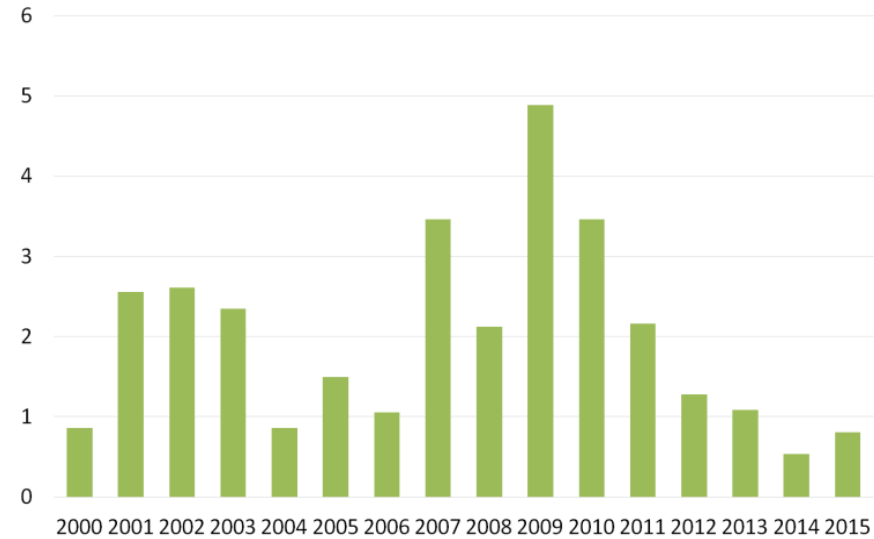
Ten years after SDR, irrespective of GMFCS level, children undergoing SDR and PT continued to improve in functional skills and were more independent in complex functional activities of daily life.

# UR CPUP rapport 2018

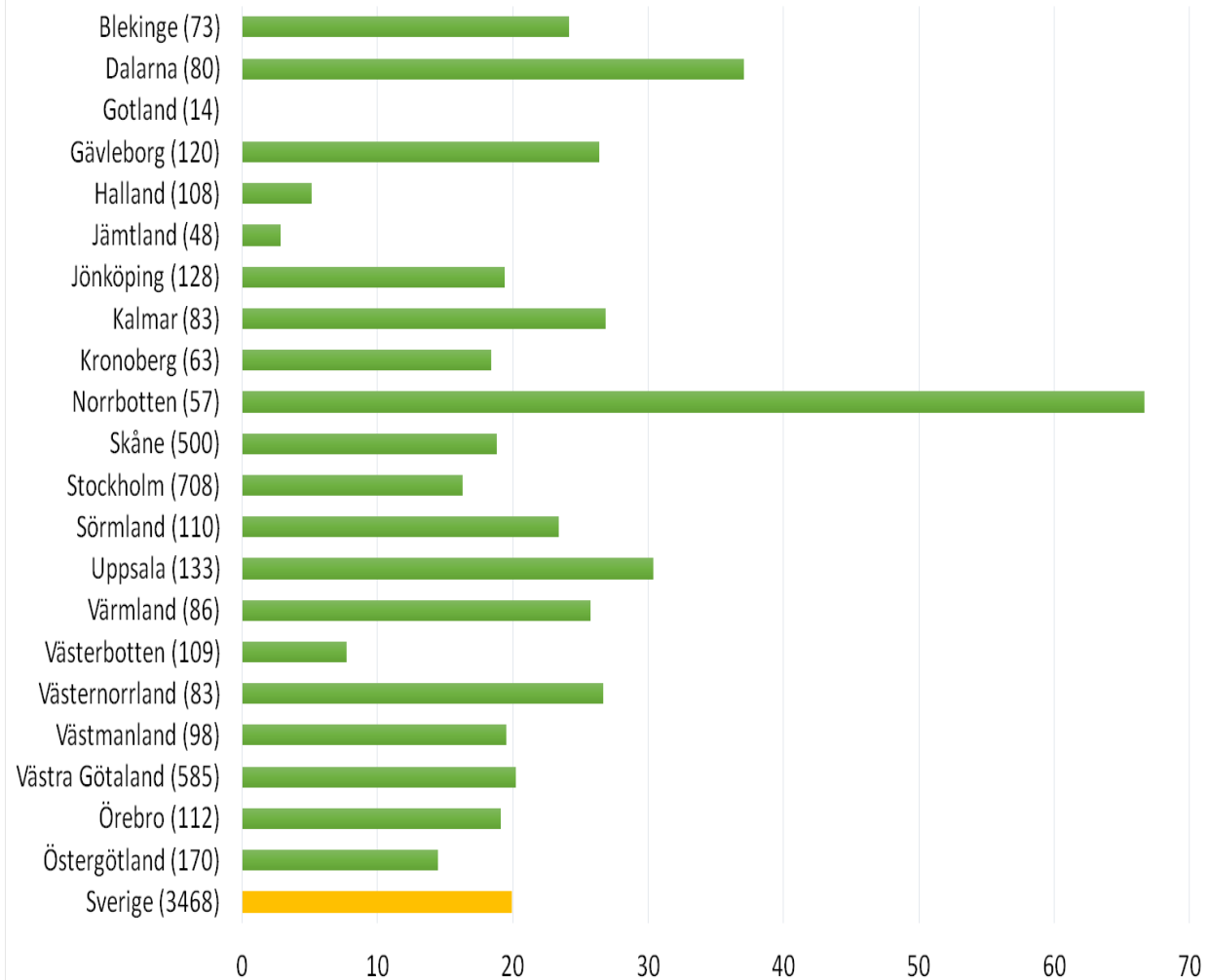
Andelen barn opererade med baklofenpump relaterat  
födelseår (%)



Andelen barn opererade med rhizotomi relaterat  
födelseår (%)

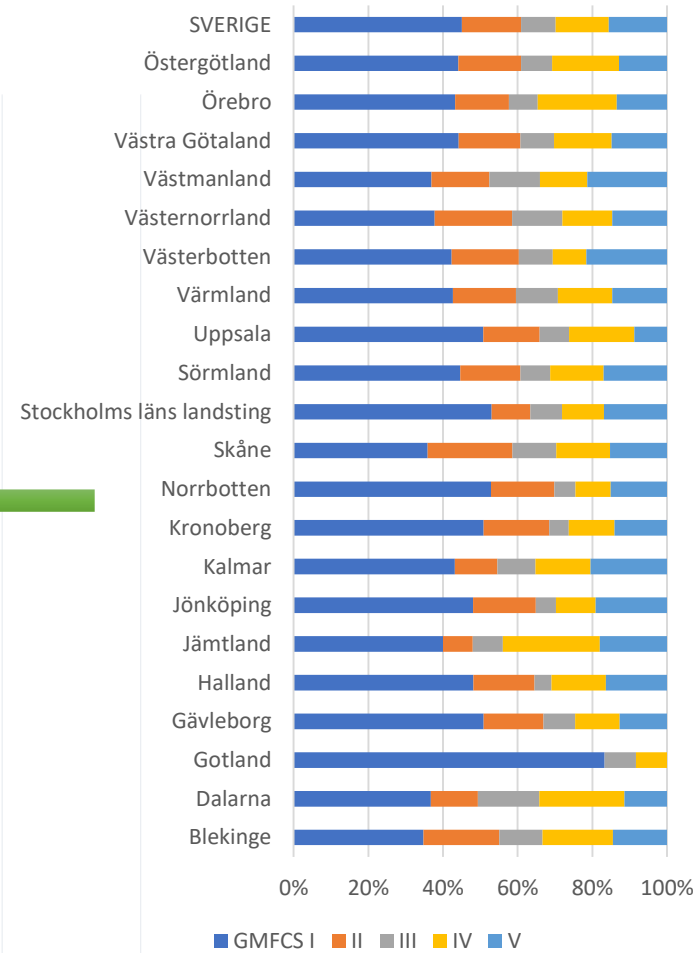
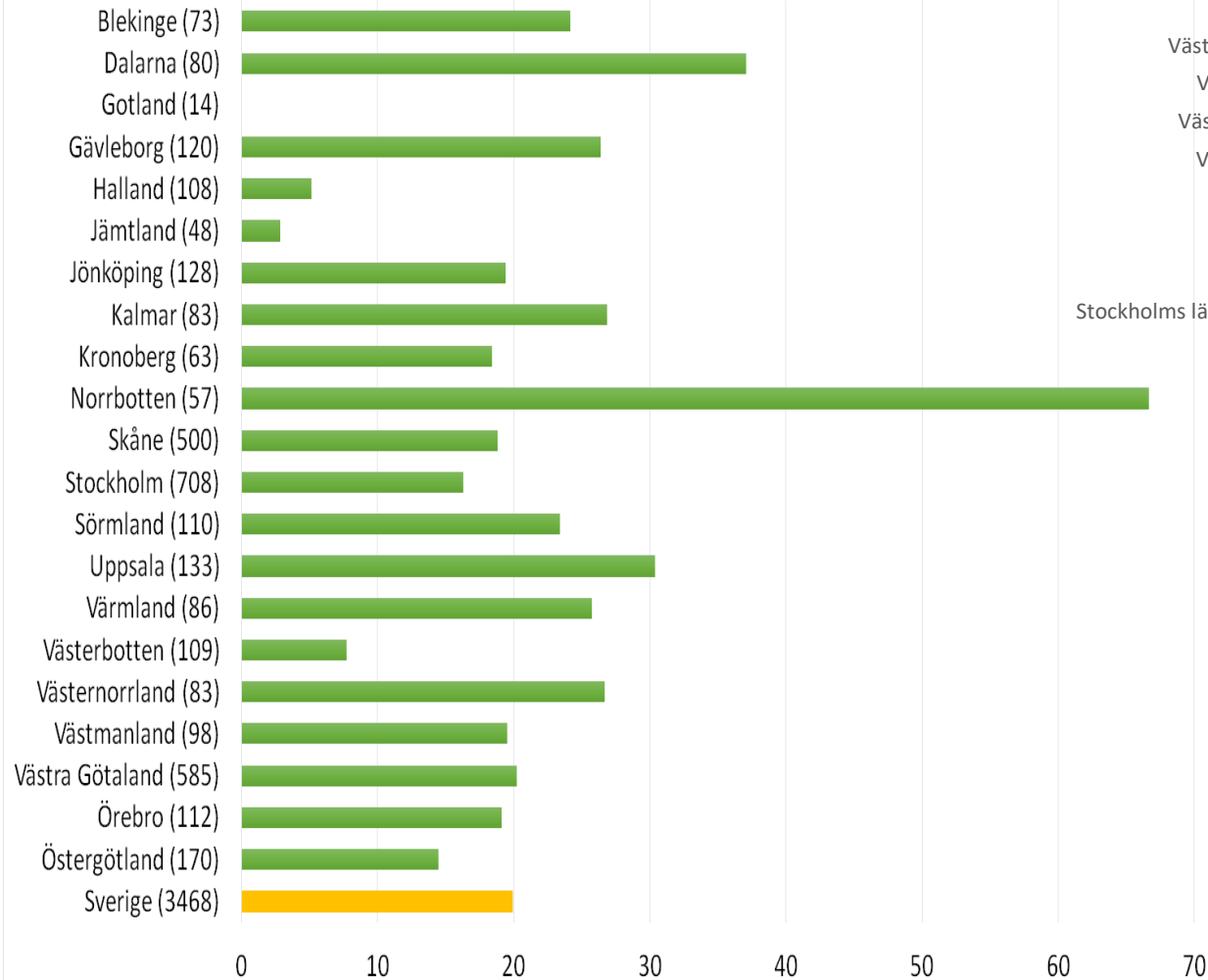


### Andelen barn födda 2001-2015 som rapporterats behandlade med botulinumtoxin i benen 2017 (%)

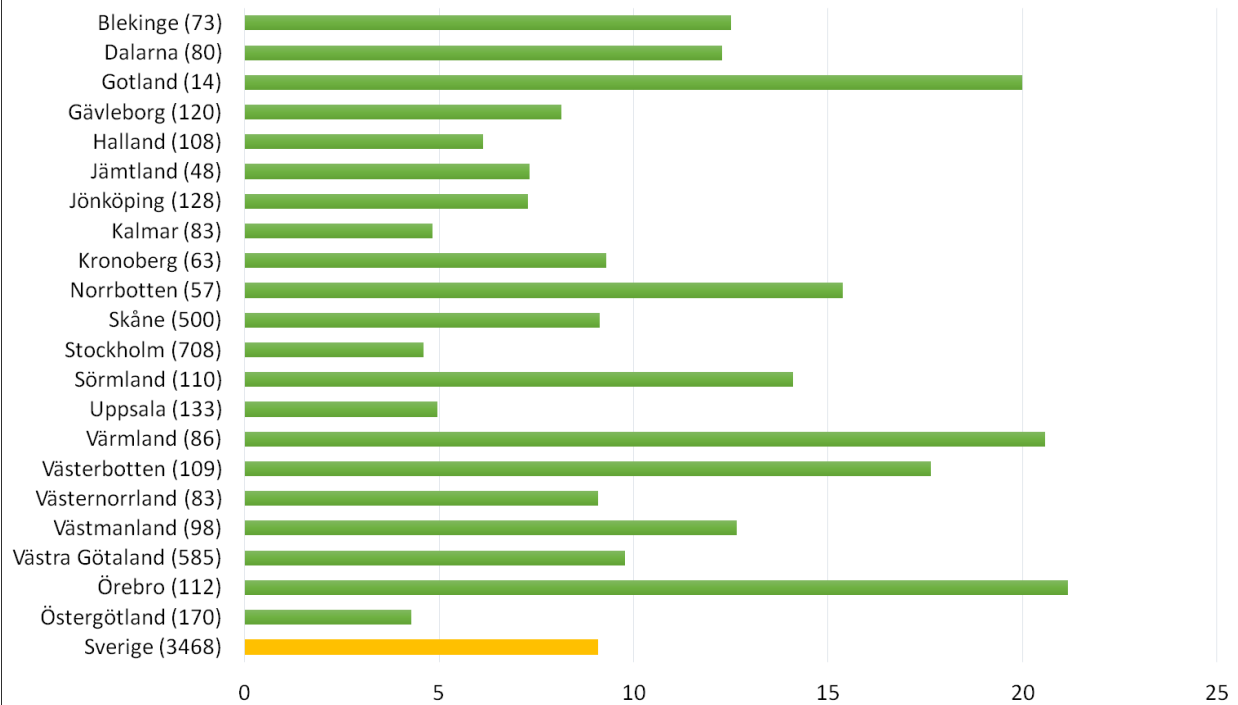


Senaste GMFCS 2017, andel (%) 1-16 år per län

Andelen barn födda 2001-2015 som rapporterats behandlade med botulinumtoxin i benen 2017 (%)



**Andelen barn födda 2001-2015 som rapporterats behandlade med botulinumtoxin i armar och händer 2017 (%)**







# *Spasticitet behövs ibland*

- Borttagen bild – flicka sp diplegi, GMFCS III, svag ”går på sin spasticitet”

# Ökande spasticitet/dystoni vid

- Otrygghet, oro
- Aspiration mat, saliv, slem - rosslighet
- Ensidig sitt- el viloställning
- Tryck av kläder, ortoser
- Kissnödighet
- Trängning till avföring
- Hunger, törst

# Allmän behandling

- Handling
- Positionering
- Sjukgymnastik
- Instruktion
- Minimera spast.utlösande faktorer

## Vanliga orsaker till svår spasticitet/dystoni

- Förstoppning
- GER med esofagit
- Tandvärk
- Urinretention
- Höftluxation
- Osteoporos med frakturer
- Skolios m smärta
- Kontrakturer
- Spända muskler

Vanligt vid svår spasticitet/dystoni

UNDERNÄRING



## Före och efter sondmatning 9 veckor

- Borttagna bilder – ca årgammalt ytterst avmagrat barn ligger med korsade ben o spetsfotställning – 9 veckor senare fått hull efter sondmatning, ingen annan spasticitetsreducerande behandling; avslappad, ej längre korsade ben eller spetsfotställningar, ser mindre ansträngd ut,
- Dvs undernäringen i sig/hunger o illabefinnande ger ökad muskelspänning

# Balances



# Devices to measure height/length





## OND cirkel

Spasticitet/dystoni slår/på och ökar  
vid oro och smärta → ännu högre  
tonus → ännu mer smärta → osv