

Beyond Dystonia: Are We Detecting and Managing Non-Motor Symptoms Properly?

Dr. Davide Martino



serving all dystonia-affected persons
désservant toutes personnes atteintes de dystonie



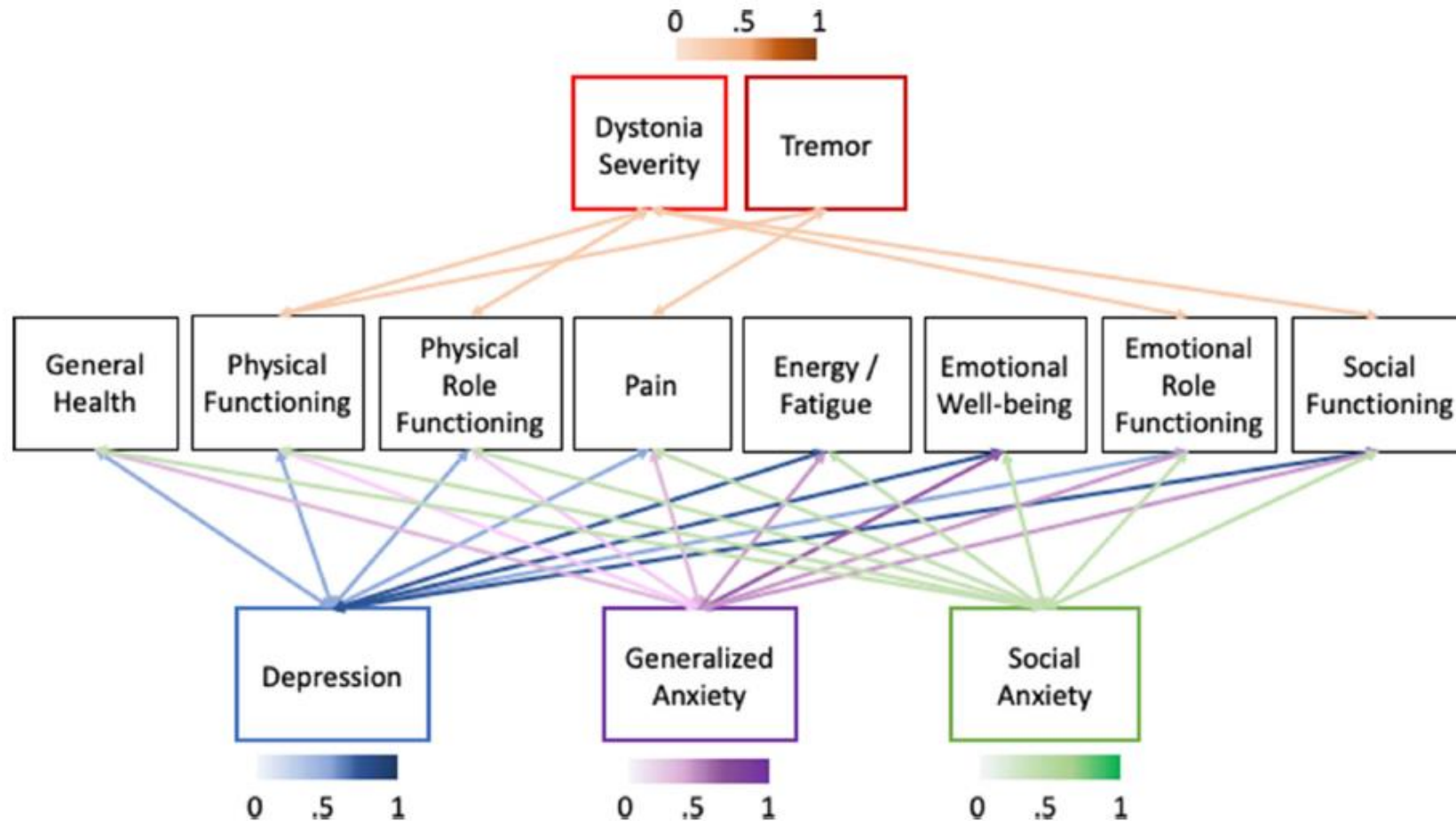
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TALK OUTLINE

- ☐ **The spectrum of non-motor symptoms in cervical dystonia and other adult-onset isolated dystonias: pain, depression, anxiety, sleep, fatigue**
- ☐ **Screening and management of non-motor symptoms in dystonia:**
 - ☐ Barriers and facilitators
 - ☐ Towards a new pathway of care
- ☐ **Special considerations on pharmacological management and mood symptoms in dystonia**

What impacts quality of life in dystonia?



Degree of depressive symptoms

Generalised and social anxiety

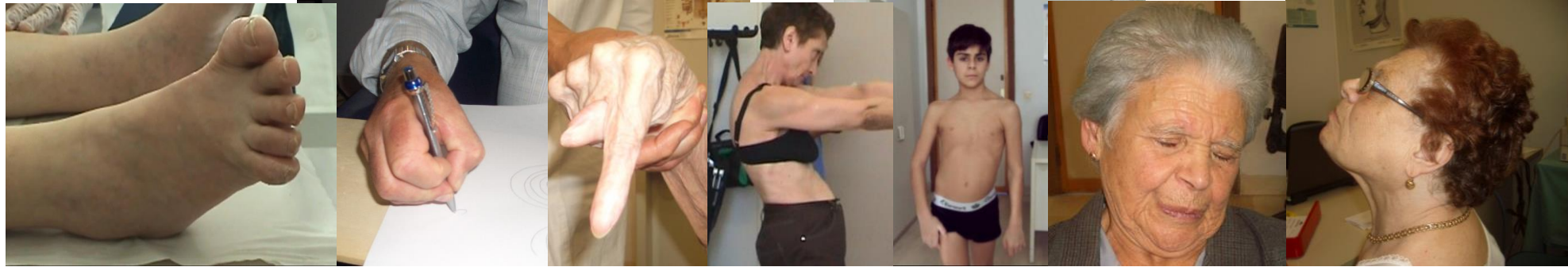
Dystonia severity

Tremor severity: only worse physical functioning and pain

Younger age: emotional well-being and vitality

No differences between sexes

What causes disability in dystonia?



- More data on cervical dystonia
- Despite motor improvements with botulinum toxin, many patients still experience difficulties with performing daily life activities
- Psychiatric features (depression, anxiety) and pain → largest contribution to disability

Much more than physical functioning and dystonia severity

[van den Dool et al., Parkinsonism Relat Disord 2016]

Non-motor symptoms

- Many people living with dystonia experience non-motor symptoms contributing to disability and reducing participation in daily activities (Smit et al. 2017a; Stamelou et al. 2012; Torres and Rosales 2017)
- Non-motor symptoms include: **pain, depression, anxiety, apathy, impaired sleep, fatigue, catastrophizing, sensorimotor disturbances, olfactory and visual problems**
- Non-motor symptoms are important when considering the overall management of dystonia as they play a significant role in quality of life (Smit et al. 2017a; Torres and Rosales 2017; Tomic et al. 2016).

Pain

- **55-89% of people** with cervical dystonia (68% in neck and shoulders → spreads to upper back, up to the head on the bent side and down to the ipsilateral upper limb)
- “exhausting”, “radiating”, “prickly”, “pulling the neck”
- 10-20% have **chronic daily headache** (occipital 79%, cervical 73%, temporal 43%, frontal 36%, vertex 25%, retroorbital 11%)
- People with blepharospasm have **painful photophobia**
- **38%** of people with focal hand dystonia have pain
- 36% of people with focal lower limb dystonia have pain
- NEVERTHELESS → No specific classification criteria

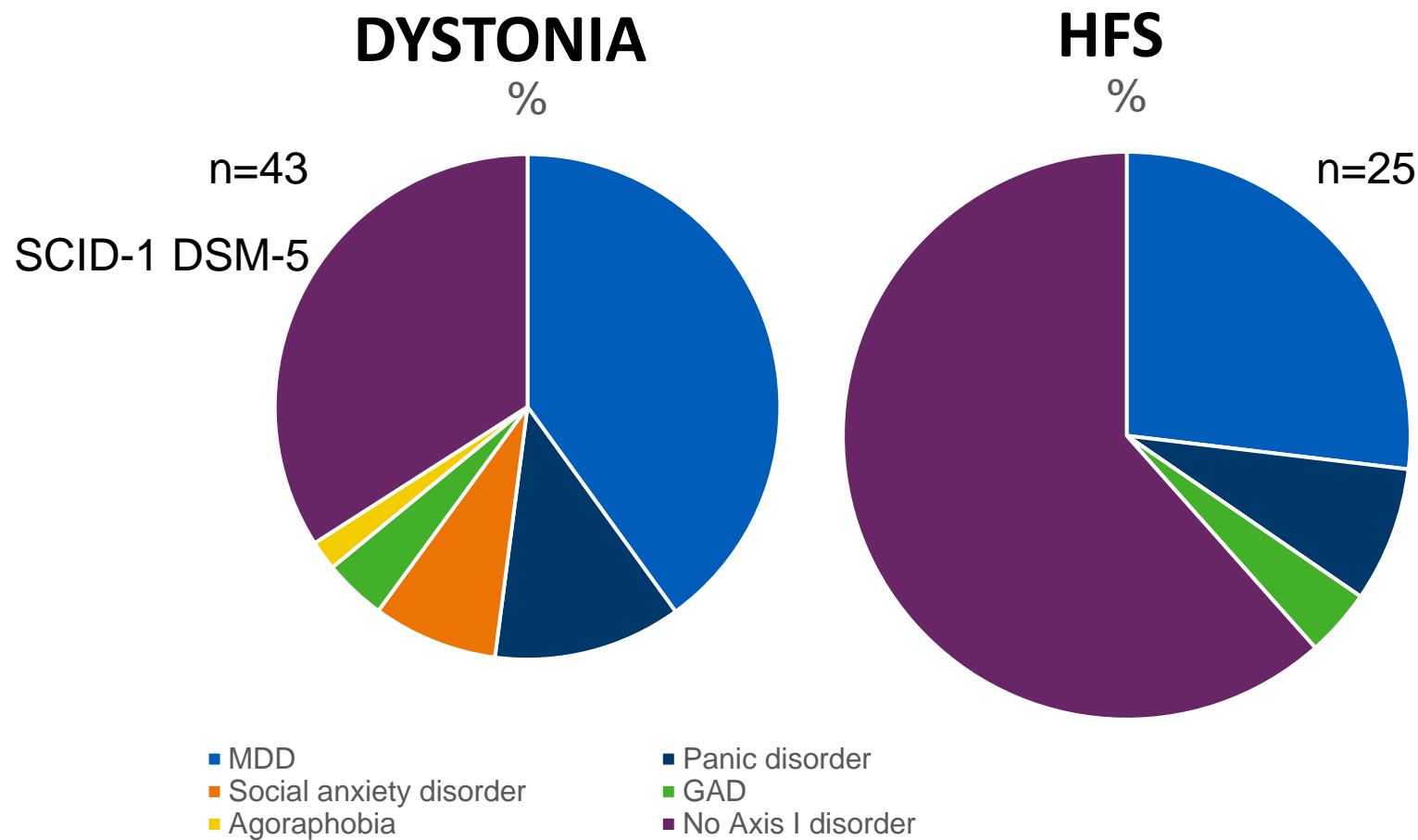
Pain: what are the risk factors/mechanisms?

- Hypothesized mechanisms include:
 - prolonged contraction of the “dystonic” muscles
 - prolonged contraction of the “compensating” muscles
 - altered brain processing of painful stimuli → reduced pressure pain tolerance in focal hand dystonia [Perez-de-Heredia-Torres et al., 2021]
- In CD, higher levels of pain acceptance co-occur with lower levels of perceived pain
- In CD, a ***catastrophic interpretation of pain*** correlates with severity of depression and anxiety [Wadon et al., 2022]

Pain: how can we treat it?

- Oral meds for dystonia are non-specific (Marciniec et al. 2019; Siongco et al. 2020)
- Botulinum toxin injections relieve pain in cervical dystonia, even before relaxing muscles (Marciniec et al. 2019; Siongco et al. 2020)
- Deep brain stimulation of the globus pallidus internus is likely to reduce pain
- Kinesiotaping and cerebellar neuromodulation: preliminary results

Depression and natural history of CD



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No obvious difference in dystonia spread between those with and those without depression

Significant difference in age at onset → presence of depression associated with earlier age at dystonia onset

[Moriarty A et al., *Mov Disord Clin Pract* 2022]

Anxiety and depression in writer's cramp

Parkinsonism and Related Disorders 100 (2022) 37–40



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Short communication

Comprehensive analysis of non-motor symptoms and their association with quality of life in Writer's cramp


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- Anxiety 51.2%
- Depression 46.2%
- Higher scores of HDRS-24 associated with lower scores of SF-36 in physical and mental determinants of QoL

Association and Familial Coaggregation of Idiopathic Dystonia With Psychiatric Outcomes

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2-fold increased risk of dx of depressive disorder
2.13 of anxiety disorder
80% greater risk of suicide attempts/death by suicide

FULL SIBLINGS

	OR (95% CI) Adjusted for Sex and Birth Year	OR (95% CI) Adjusted for Sex, Birth Year, and Idiopathic Dystonia Status in the Outcome Sibling
<i>Psychiatric Disorders of Primary Interest</i>		
Depressive disorders	1.21 (1.06–1.39)	1.20 (1.05–1.38)
Anxiety disorders	1.31 (1.15–1.49)	1.30 (1.14–1.47)
Any suicidal behavior	1.22 (1.02–1.47)	1.22 (1.01–1.46)
Suicide attempts	1.27 (1.04–1.54)	1.26 (1.04–1.53)
Deaths by suicide	0.86 (0.51–1.44)	0.86 (0.51–1.45)
<i>Psychiatric Disorders of Secondary Interest</i>		
Attention deficit hyperactivity disorder	1.06 (0.71–1.58)	1.05 (0.71–1.56)
Autism spectrum disorders	0.76 (0.36–1.59)	0.74 (0.35–1.56)
Schizophrenia and other psychotic disorders	1.45 (1.14–1.84)	1.44 (1.14–1.83)
Bipolar disorder	1.12 (0.83–1.52)	1.12 (0.82–1.51)
Obsessive-compulsive disorder	1.07 (0.61–1.88)	1.06 (0.60–1.87)
Eating disorders	1.53 (0.85–2.75)	1.50 (0.83–2.70)
Substance use disorders	1.29 (1.12–1.49)	1.29 (1.12–1.48)
Any neurodevelopmental or psychiatric disorder	1.24 (1.13–1.36)	1.24 (1.13–1.36)


Statistically significant odds ratios are highlighted in bold.
Abbreviations: OR, odds ratio; CI confidence interval.

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BRAIN 2020; 143; 2771–2787 | 2771

BRAIN
A JOURNAL OF NEUROLOGY

Dystonia genes functionally converge in specific neurons and share neurobiology with psychiatric disorders

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Movement Disorders

Official Journal of the International Parkinson and Movement Disorder Society

Hot Topics

Neurology and Psychiatry Get Closer Again: Lessons From Dystonia

Roberto Erro MD, PhD 

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The prevalence of depression in adult onset idiopathic dystonia: Systematic review and metaanalysis

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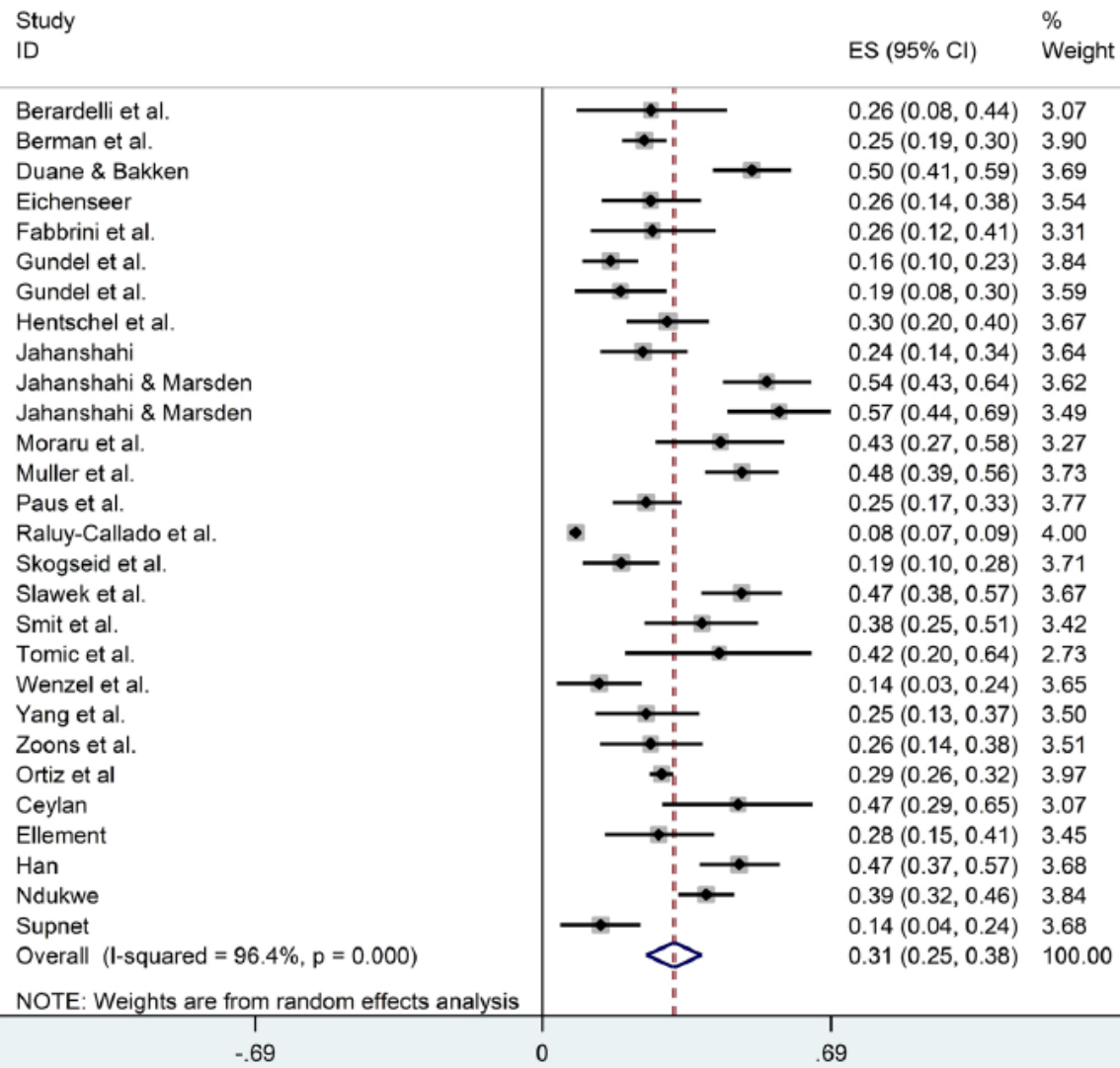
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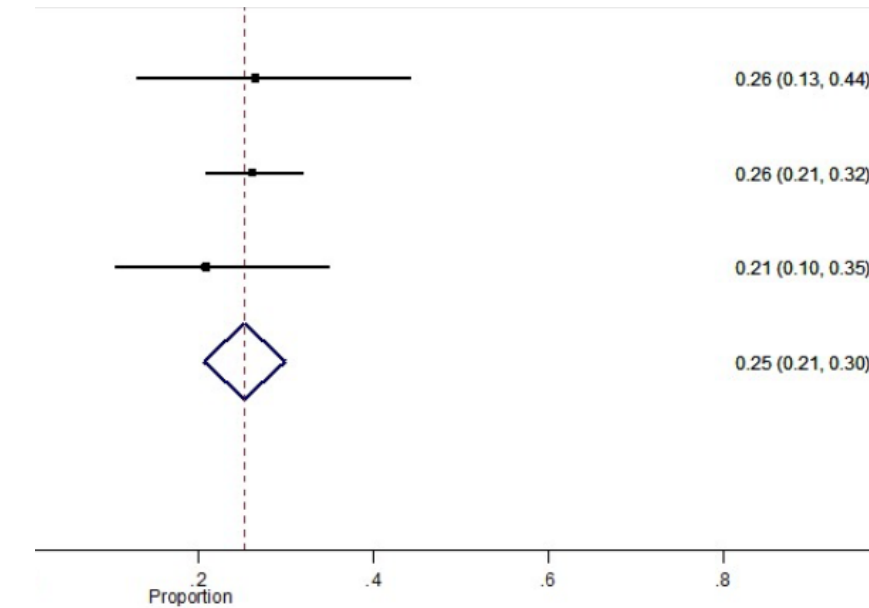
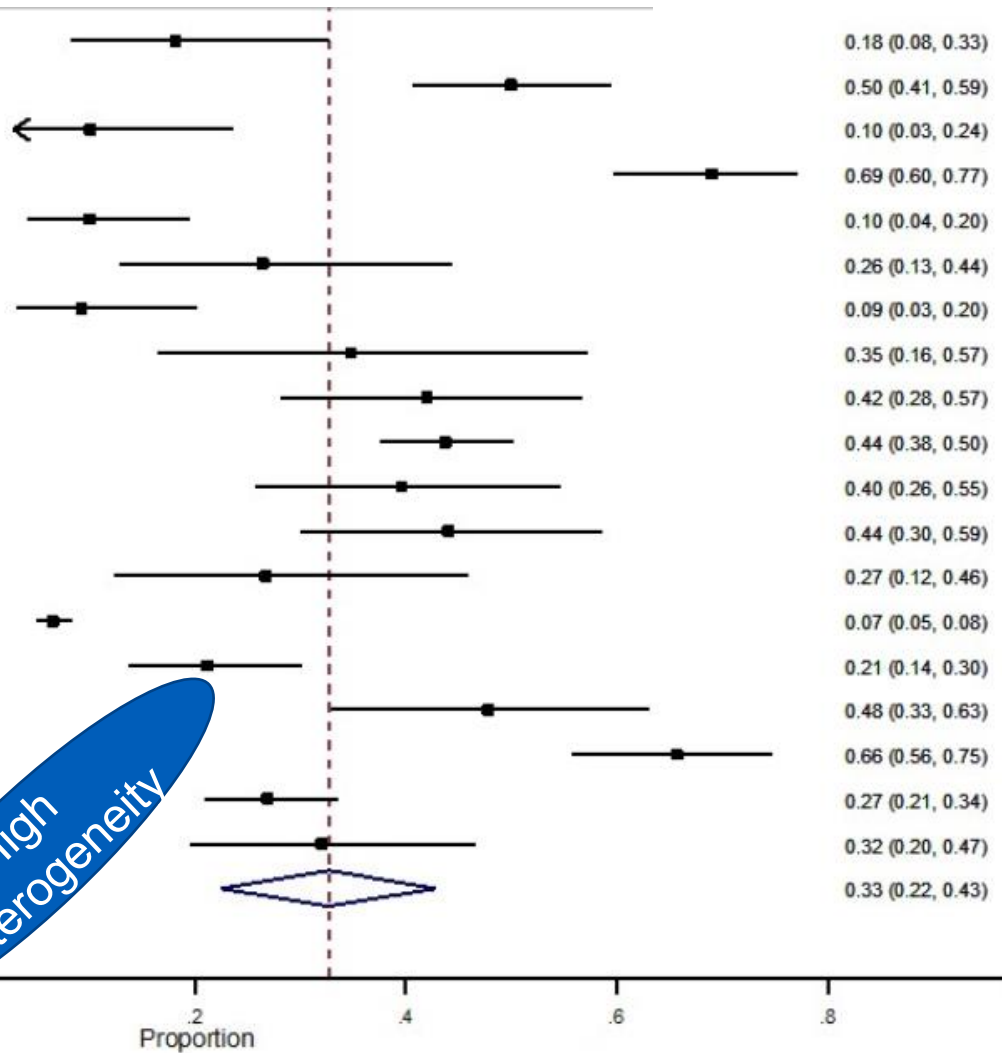
- Overall pooled prevalence of any depressive symptoms or disorders: 31.4% for cervical dystonia, 29.2% for cranial dystonia, and 30.9% for studies examining mixed forms of AOID.
- Major depressive disorder more prevalent than dysthymia across all forms of AOID.
- Prevalence of MDD higher in cervical dystonia than in other forms, whereas prevalence of dysthymia higher in cranial dystonia.



Cervical dystonia

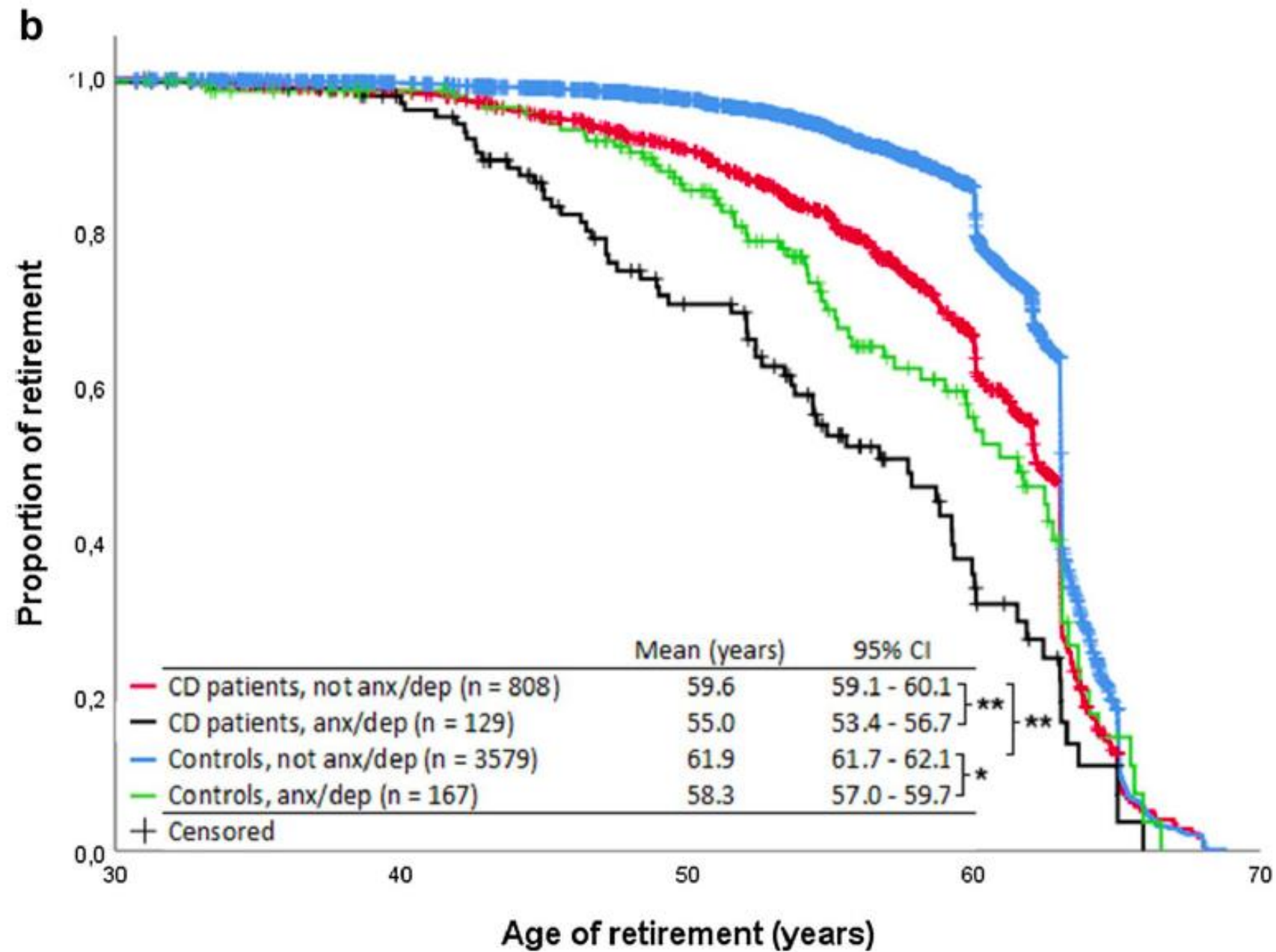
The prevalence of anxiety in adult-onset isolated dystonia: A systematic review and meta-analysis

Alex Medina Escobar¹ | Davide Martino^{1,2,3} | Zahra Goodarzi^{2,3,4,5,6}



Cranial dystonia


GENERALIZED ANXIETY DISORDER: 18%
SOCIAL PHOBIA: 25%
SOCIAL ANXIETY: part. in laryngeal dystonia



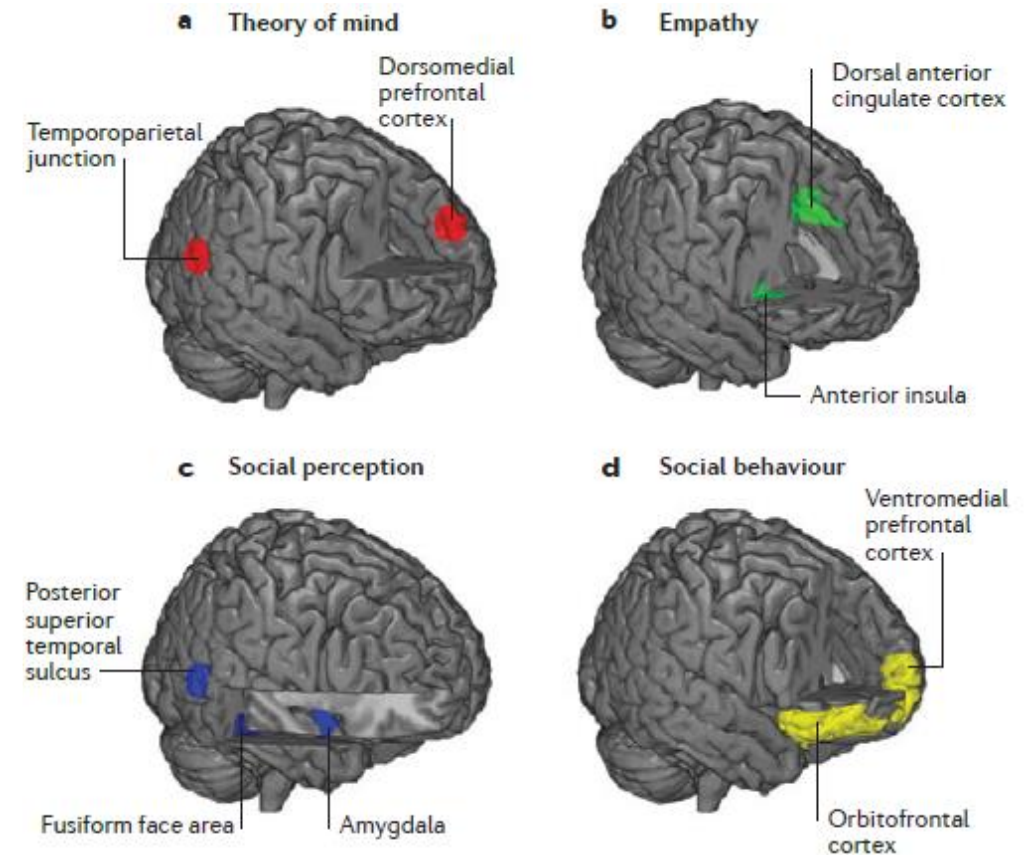
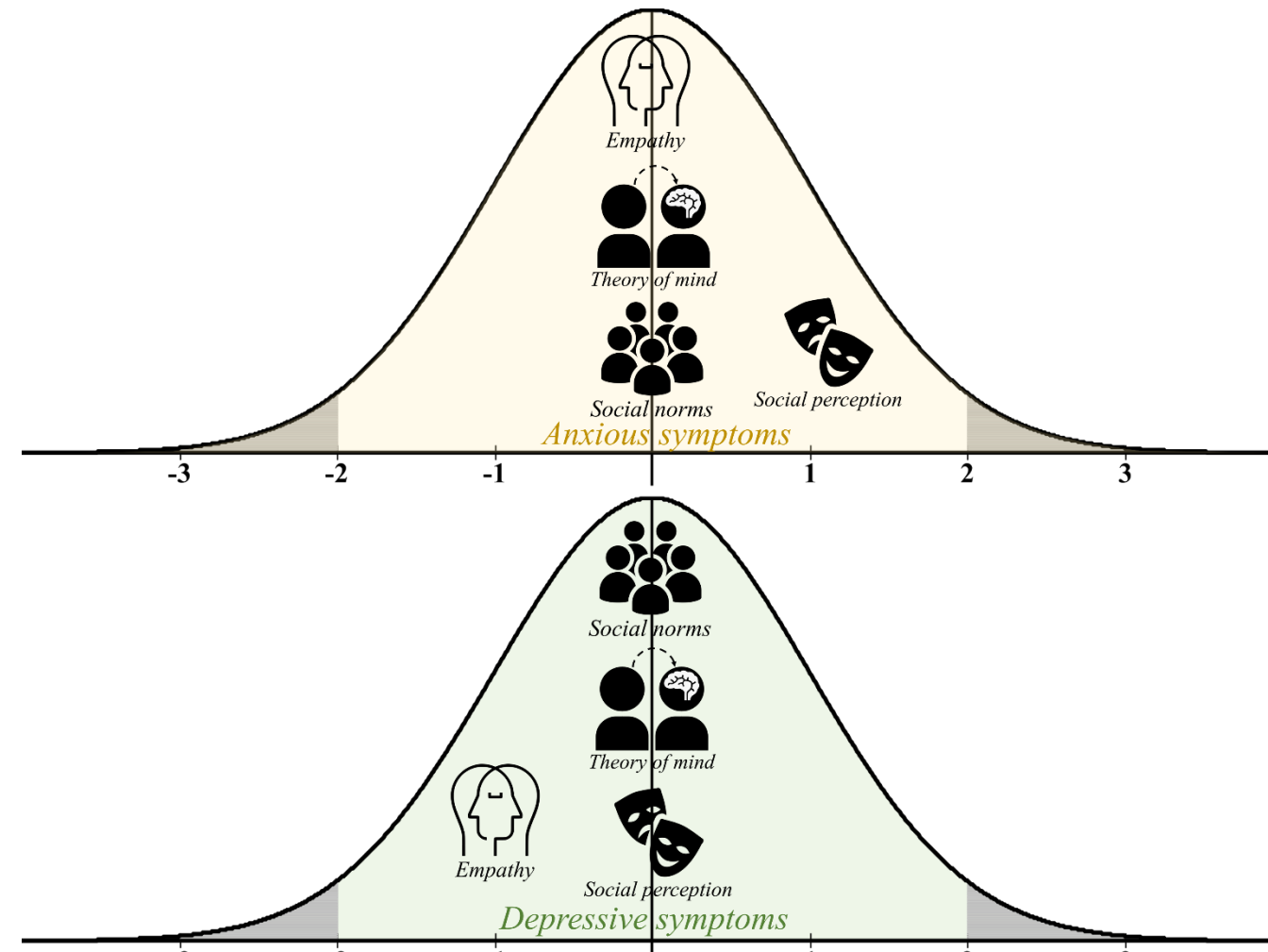
SHI-CD

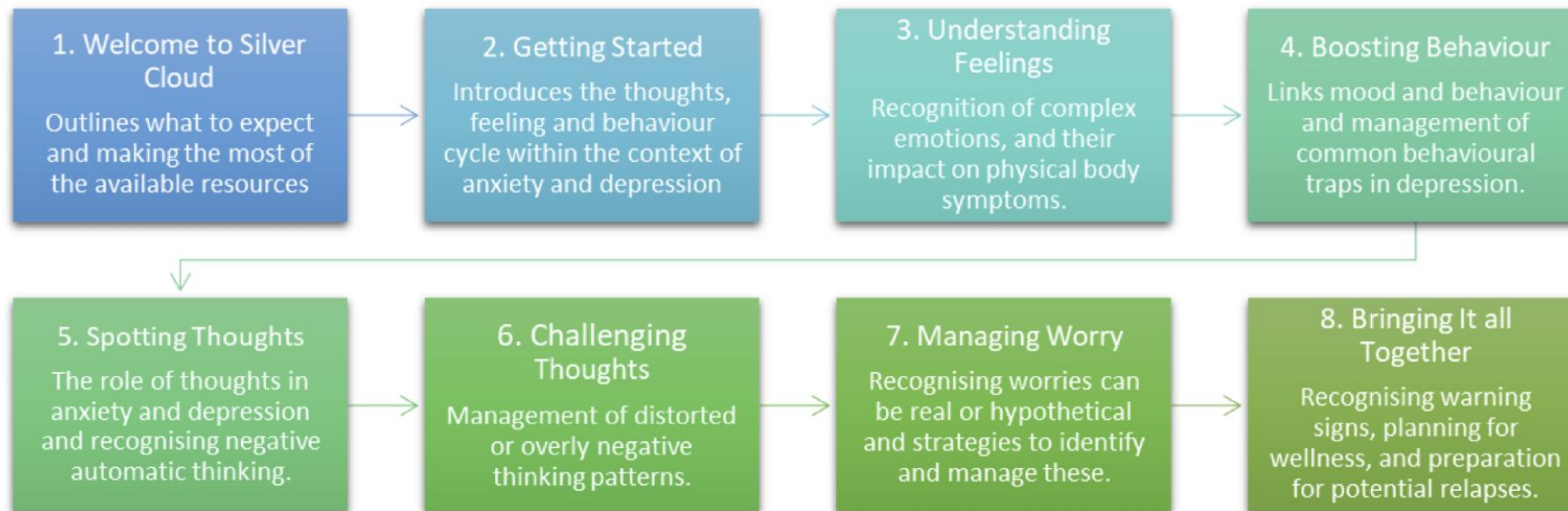
(Social cognition and Habituation to social stimuli In Cervical Dystonia)

Social cognition in cervical dystonia: phenotype and relationship to anxiety and depression

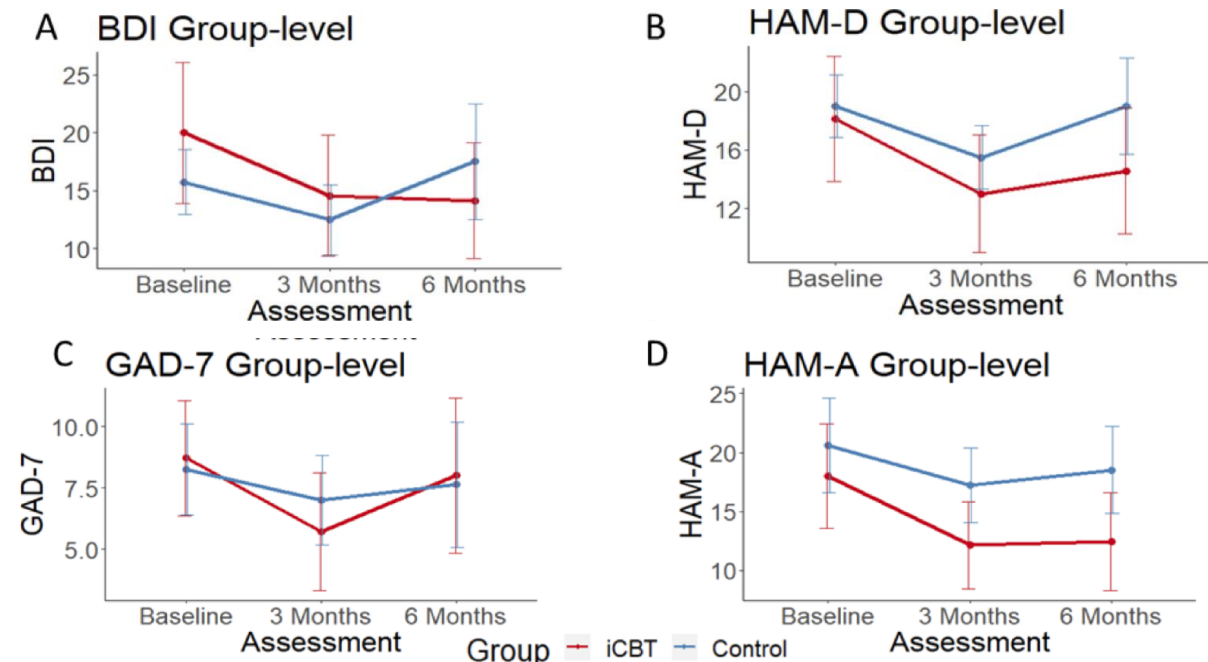
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iCBT for depression/anxiety in CD



Wadon et al.,
Clin Parkinsonism Relat Disord 2021

Are people with dystonia who also have depression and anxiety more prone to use meds?

- Dystonia Coalition cross-sectional study → 37 centres in US, Canada, Europe and Australia → 2,026 participants (76% focal [61% cervical, 12% laryngeal, 10% limb, 9% cranial, 8% blepharospasm])
- If anxiety/depression was present, patients were ***twice as likely to be taking oral medications*** (also useful) for dystonia
- Particularly:
 - BENZODIAZEPINES
 - OTHER SLEEP-INDUCING MEDS (e.g. zopiclone)
 - MUSCLE RELAXANTS
 - ANTICHOLINERGICS (e.g. trihexyphenidyl)

May/should people with dystonia who also have depression and anxiety be treated with antidepressants?

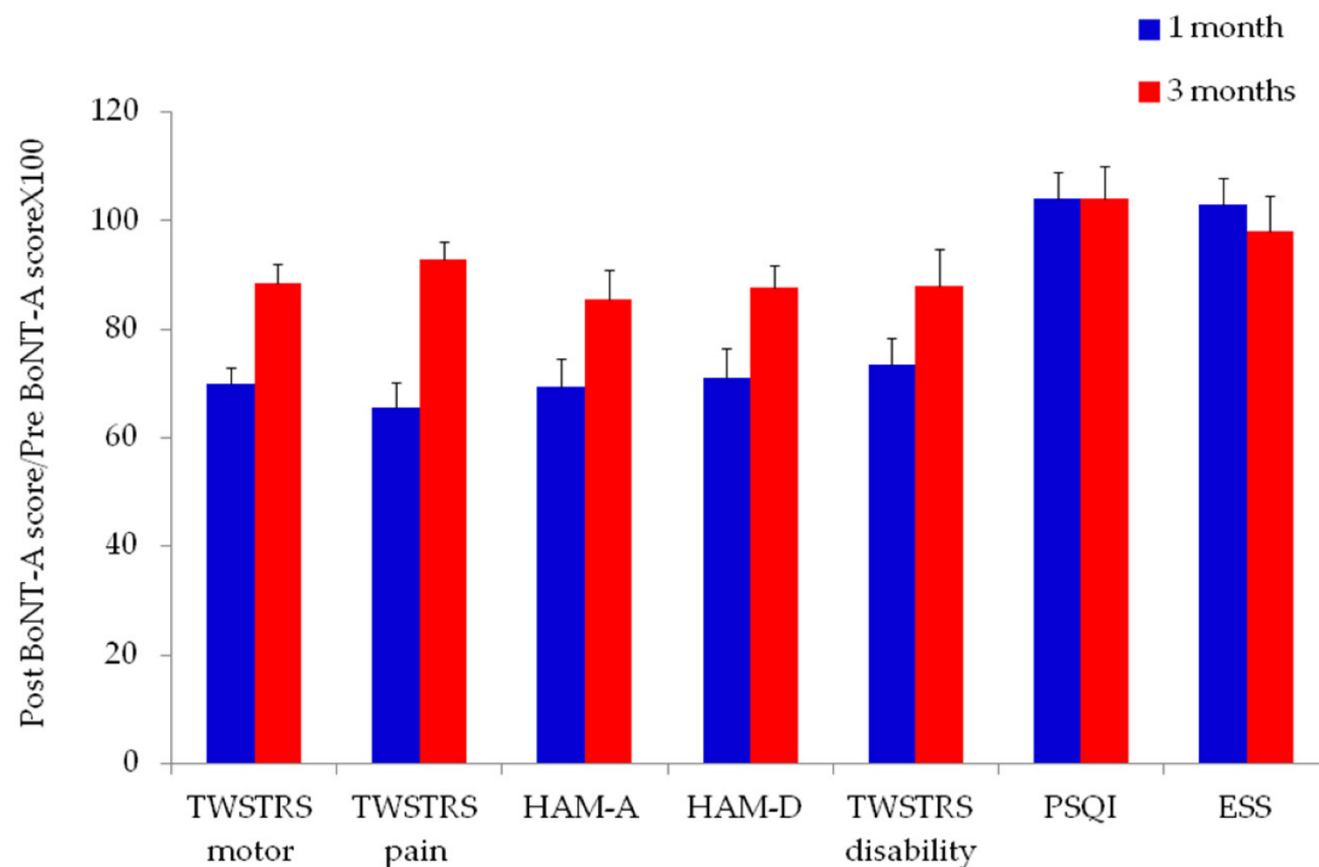
- There is no valid reason to be extra cautious to treat depression and anxiety with antidepressants (SSRIs) in patients with cervical dystonia
- Still no clear evidence confirming that antidepressants improve depression in patients with dystonia, compared to placebo, but evidence is limited
- More evidence of safety of SSRIs in patients with dystonia

[Zoons et al. J Neurol Neurosurg Psychiatry 2018; Duarte et al., Parkinsonism Relat Disord 2018]

Can BoNT-A improve depression and anxiety in AOID?

Costanzo et al., *Toxins* 2021

BoNT-A-induced motor and non-motor changes



- Promising evidence in favour of efficacy, but no change on TWSTRSpsych
- Overall, still not uniform
- No correlation between motor change and non-motor change (incl. pain and depression/anxiety) or between different NMS

Does deep brain stimulation surgery improve depression and anxiety in people with dystonia?

- Overall, anxiety, mood and cognition seem to remain stable postoperatively
- There may be some improvement if patients with moderate-severe depression are included (?due to different causes)
- Caution for neuropsychiatric problems in the screening for DBS remains very important

[Eggink et al., Parkinsonism Relat Disord 2018]

Do people with dystonia have sleep problems?

- Poor night sleep quality in at least half of the patients with cervical (and cranial) dystonia (increased sleep latency, decreased sleep efficiency, with more awakenings and less REM sleep)
- Independent from the severity of dystonia
- Poor sleep quality influenced by concurrent depression / may worsen quality of life in dystonia
- Excessive daytime sleepiness less common complaint

[Hertenstein et al., Sleep Med Rev 2016; Antelmi et al., Sleep 2017]

Do people with dystonia have sleep problems?

- Inverse relationship between quality of sleep and efficacy of sensory trick (→ poorer sleep leads to less effective tricks? → vicious cycle of fatigue and diminished ability to exploit the trick?)

[Benadof et al., Trem Other Hyperkin Mov 2019]

- BoNT-A, even if successful in reducing motor symptoms, may not eliminate sleep problems
- Effect of GPi-DBS upon sleep: limited evidence (on Meige sdr)
- How much can the use of other medications, e.g. benzodiazepines, explain these sleep disturbances?

[Hertenstein et al., Sleep Med Rev 2016]

Do people with dystonia suffer from excessive fatigue?

- Moderate-severe fatigue: >40% of adults with dystonia
- More fatigue correlates with poorer quality of life, regardless of depression and sleep problems
- We don't know whether this improves with treatment
- Fatigue as significant barrier to engagement in exercise and physical activity
- Writer's cramp → greater fatigue, lower scores on mental component summary of SF-36

[Wagle Shukla et al., Int J Neurosci 2016; McCambridge et al., Front Neurol 2019, Zhang et al., Park Relat Disord 2022]

Depression and anxiety: barriers and facilitators to screening and management

- Health professionals recruited from 4 Canadian MD clinics in Calgary, Edmonton, Vancouver and Montréal
- All experience of >1 AOID patient with co-morbid depression and/or anxiety
- Patients with AOID + current/past anxiety or mood disorder from DMRF Canada local support groups and MD clinics

[Martino et al., submitted 2022]

Depression and anxiety: barriers and facilitators to screening and management

- Focus groups and interviews: 45 participants (31 F): 10 MD neurologists, 4 psychiatrists, 5 MD nurses, 8 allied health/primary care practitioners, 18 patients
- Framework analysis approach → summarizing and classifying data within a thematic framework approach
- Indexed based on the Theoretical Domains Framework and the Capability, Opportunity, Motivation and Behaviours (COM-B) system
- Behaviour change techniques identified to overcome the identified barriers and promote the implementation of facilitators

[Martino et al., submitted 2022]

Theme 1: Gaps in Knowledge

Theme 2: Beliefs on the origin of emotional symptoms in AOID

- *“The worst part is not knowing whether it is normal or abnormal to feel depressed with my dystonia. Probably anyone would feel depressed walking around with their head on their shoulder. So, I always thought that it was inevitable feeling like this when you have dystonia and that I had to pull myself together with my own resources”. → PRECONCEPTION OF MOOD ISSUES AS SECONDARY TO OTHER ‘PHYSICAL’ SYMPTOMS*
- *“An excellent seminar was put on just a few years ago in my city. They did a really good job at describing many of the aspects of dystonia, including depression, and how you could mitigate them by activities, exercise, diet. etc. If the opportunity to follow similar events were available again, I would certainly take it.” → DEARTH OF COMPREHENSIVE EDUCATIONAL INTERVENTIONS*
- *“The neurologist is very busy, and the time is very short, but it is almost like after you see the neurologist it would be nice to go to another person who can give you more information or something to read or direct you towards information online”. [Martino et al., submitted 2022]*

Theme 3: Self-isolation and stigma

- *“I will have the odd person that will come up to me and ask me if I have Parkinson’s, if I am under a lot of stress, or even if I have just come out of rehab [...] I have learned over time that people are inquisitive or simply commiserate you, and as a result have become quiet and withdrawn”.*
- *“Well, there is always difficulty in getting help for mood symptoms because usually most people, as you know, especially as they grow older, are reluctant to discuss that.”* → ACCESSING SOCIAL SUPPORT WITHIN PATIENTS’ ORGANIZATIONS [Morgan et al., *Disabil Rehabil* 2021]
- *“What is it that you are anxious about?”* Participant [Patient 6]: *“The pain, the people staring, questions, but mostly the pain”.* [Martino et al., *submitted* 2022]

Theme 4: Physicians' communication skills

- *“And he kept giving me pills. And he did not have the time to talk. That level could be looked at. I think it is not the doctors' fault. The way we pressure doctors to see a patient every 10 minutes. They haven't got the time. And nurses maybe have more time [...] to talk to the patient for half an hour and then have the doctor come in for 10 minutes.”*

[Martino et al., submitted 2022]

Theme 5: Organization of activities at the level of the MDC

- *“And I think one of the challenges is that our patients are mixed in in our movement disorders clinic, or the patients that come every three months for toxin treatment. For sure having a screening tool with a few questions that they can fill out would make everything easier. So, I would love to have a good conversation with them, but time is limited”. [Neurologist]*

[Martino et al., submitted 2022]

Theme 6: Local networks of providers

- *“Around the time of my diagnosis of dystonia, I started feeling anxious around people and often tearful and depressed. My GP told me it was because I had dystonia and to talk to my neurologist. My neurologist disagreed and threw the ball’s back into the GP’s court. I lived like this for more than 3 years, feeling increasingly hopeless”.*

[Martino et al., submitted 2022]

Theme 6: Local networks of providers

- *“I think that behavioural treatments (like mindfulness-based or cognitive-behavioural) are under-used in these patients, and family physicians may not always have great training in non-medical modalities of treatment.”* [Psychiatrist]

[Martino et al., submitted 2022]

Code	Domain in the Theoretical Domain Framework	Behaviour change technique
Under-diagnosis of depression/anxiety	Skills	Periodical screening with self-rated tools
Lack of nurses' involvement	Professional role	Nurses act as case managers
Lack of coordination of local resources	Environmental and Context Resources	Neurologists act as coordinators of local network of providers
Limited communication with family physicians	Environmental and Context Resources	Timely documentation on screening and treatment
Limited patients' and family physicians' knowledge on mood/anxiety issues in AOID	Knowledge	Multimodal educational package

[Martino et al., submitted 2022]

Moving towards improvement in screening



- In Calgary, symptoms charted only for 20% of patients screened positive for depression/anxiety (in a research study – clinical screening is random)
- Only 31% received a management plan (>80% by family physicians)
- Under-detected without rigorous screening and, as a result, under-treated
- BDI-II and PHQ-9 highest sensitivity for depression
- BAI and STAI highest sensitivity for anxiety

[Martino et al., *submitted* 2022]



	YES	NO
1. Do you feel NOT refreshed after an overnight sleep?		
2. Do you have difficulties falling or staying asleep?		
3. Do you experience light - headedness or dizziness?		
4. Does fatigue (tiredness) or lack of energy limit your daytime activities?		
5. Do you feel nervous, worried or frightened for no apparent reason?		
6. Do you feel sad or depressed?		
7. Do you suffer from loss of self-confidence due to stigma of visible (cervical) dystonia?		
8. Do you have flat moods without the normal "highs" and "lows"?		
9. Do you have difficulty while eating such as chewing or swallowing?		
10. Do you experience unpleasant sensation such as numbness, tingling or pins and needles in the body area or nearby the body area of your dystonia?		
11. Do you have any speech problems?		
12. Does your dystonia affect your vision for instance when your head is turning to one side?		
13. Do you suffer from pain (painful tension) of the body area or near to the body area of your dystonia (without any other condition in this body area that could cause the pain)?		
14. Do you suffer from any walking difficulty or balance problem?		

RESEARCH ARTICLE

Validation of a self-completed Dystonia Non-Motor Symptoms Questionnaire

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Reliability of DNMSQuest as a Screening Tool for Mood Disorders in Cervical Dystonia

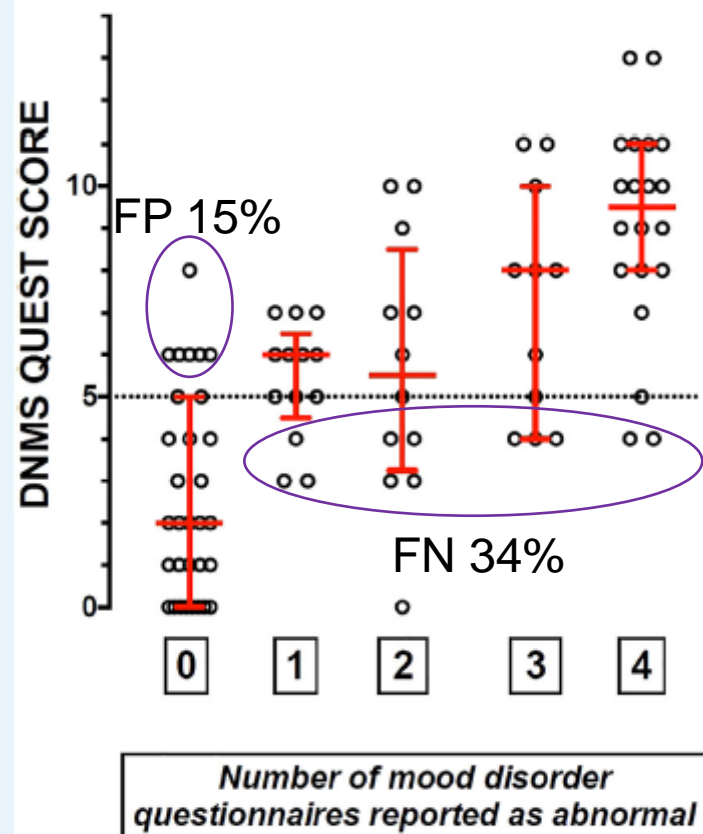
Shameer Rafee, MRCPI,  Ihedinachi Ndukwe, MBBS, Sean O'Riordan, MD, FRCPI, and Michael Hutchinson, FRCPI 

Assessment tool (total = 88)	Men (27)	Women (61)
BAI \geq 10	10 (37%)	30 (49%)
BDI \geq 14	11 (41%)	24 (39%)
HADS-A \geq 8	9 (33%)	30 (49%)
HADS-D \geq 8	9 (33%)	29 (48%)
HADS-Total \geq 16	10 (37%)	29 (48%)

- 88 CD patients, tested within 1 week of previous BoNT-A treatment
- 70% women and 52% men met criteria for mood disorder on \geq 1 assessment tool

Reliability of DNMSQuest as a Screening Tool for Mood Disorders in Cervical Dystonia

Shameer Rafee, MRCPi,  Ihedinachi Ndukwe, MBBS, Sean O'Riordan, MD, FRCPI, and Michael Hutchinson, FRCPI 



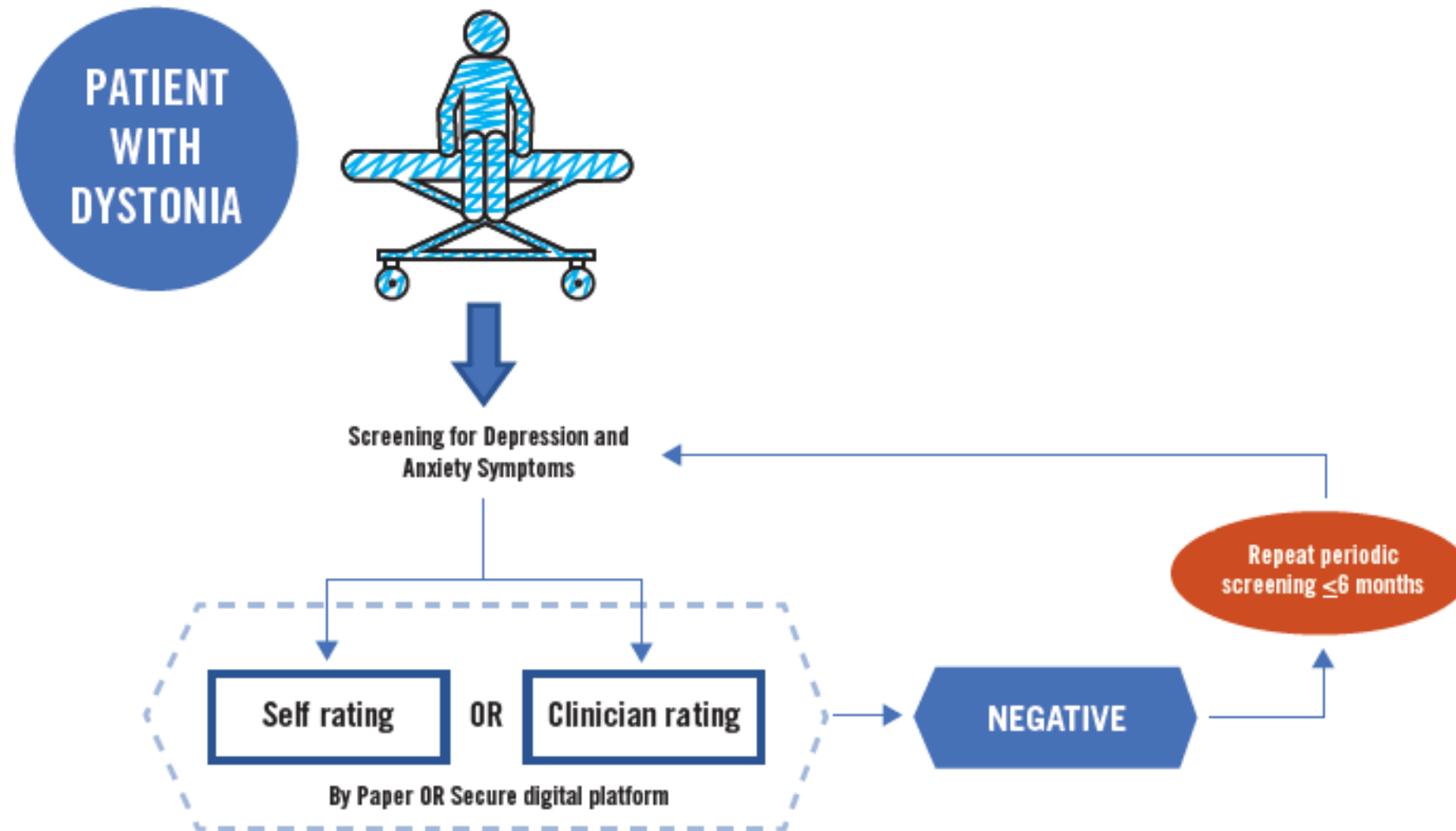
Tool	Sensitivity	Specificity
BAI ≥ 10	85%	60%
BDI-II ≥ 14	85.7%	56.6%
HADS-Anx ≥ 8	76.9%	53.1%
HADS-Dep ≥ 8	78.9%	54%

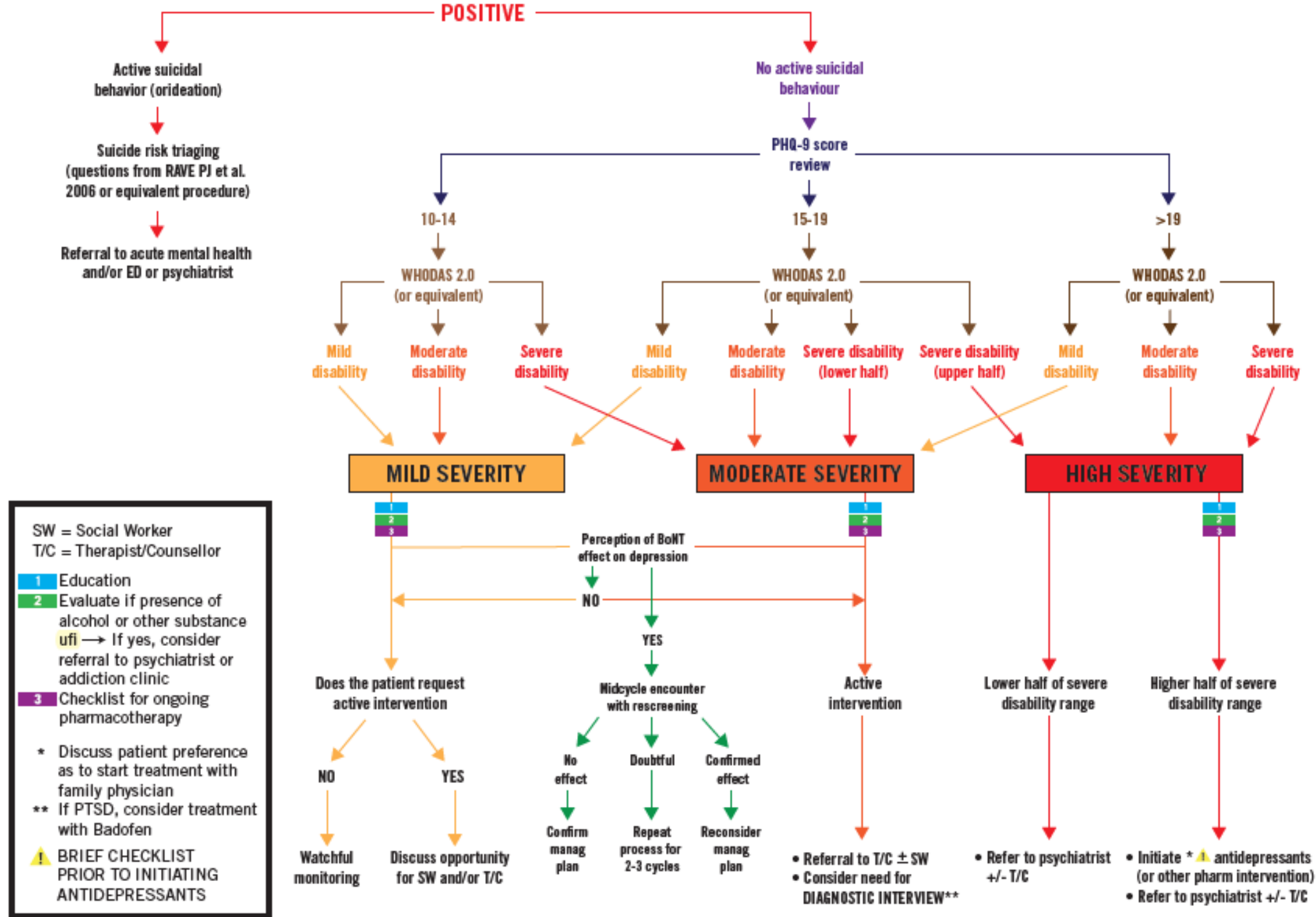
CAVEATS:

- ❖ DNMSQuest cumulative score reflects the whole NMS spectrum
- ❖ BAI, BDI and HADS may not be equivalent in detecting anxiety/depression in CD (rigorous validation studies missing)

Depression and anxiety: recommendations for screening and management

- Survey development meeting
- Delphi survey: 41 expert professionals invited → 23 participated
- 14 F, 9 M
- Neurologists, psychiatrists, clinical psychologists, family physicians and nurses
- Consensus meeting





MEDICATIONS AND MOOD SYMPTOMS IN DYSTONIA

BENZODIAZEPINES

- Is the patient using benzodiazepines regularly? If yes,
- provide education on the risk of chronic benzodiazepine intake and assess the opportunity to initiate a slow taper. If necessary, refer to existing guidelines for safe benzodiazepine taper
- if the patient clearly reports having received benefit on motor symptoms from benzodiazepines, discuss -as needed- the opportunity of future use of benzodiazepines in short-term courses

ANTICHOLINERGICS

- Is the patient on anticholinergics, reporting benefit on motor symptoms? If yes,
- has there been a temporal relationship between anticholinergic initiation or dose increase and worsening of depressive or anxiety symptoms? If yes,
 - consider dosage adjustment or drug replacement

MEDICATIONS AND MOOD SYMPTOMS IN DYSTONIA

BACLOFEN

- Is the patient on baclofen, reporting benefit on motor symptoms? If yes,
- has there been a temporal relationship between baclofen initiation or dose increase and worsening of depressive or anxiety symptoms? If yes,
 - consider dosage adjustment or drug replacement
- does the patient have a history of alcohol (or other substance) use, or of post-traumatic stress disorder (PTSD)? If yes,
 - refer to psychiatrist to assess whether these comorbidities are contributory to current depressive or anxiety symptoms, and whether baclofen therapy can be optimized (e.g. increase dosage -if appropriate- to improve mood symptoms in the context of substance abuse or PTSD; adjust dosage to minimize risk of hypomania)

MEDICATIONS AND MOOD SYMPTOMS IN DYSTONIA

ANTIDEPRESSANTS

- Is the patient on antidepressants with partial or insufficient control of depressive or anxiety symptoms? If yes,
- consider change in dosage or change of agent within the same category or switching categories (e.g. from SSRI to NSRI)
- consider referral to psychiatrist to adjust medications
- If the patient is not on antidepressants but there is indication to start treatment, has the patient been treated in the past with antidepressants? If yes,
- did he experience worsening of dystonia or tremor while on antidepressants? If yes,
 - consider switching agent or category
- is there a precedent or a risk for hypomania? If yes,
 - refer to psychiatrist before initiating treatment

DYSTONIA RESEARCH PROGRAM IN CALGARY

Local PI collaborators

- Dr. Tamara Pringsheim
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- Dr. Justyna Sarna
- Dr. Brandy Callahan
- Dr. Giuseppe Iaria
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