



# Natural History Project

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Sponsored by the NINDS and ORDR-NCATS at NIH, PAG, Industry, Professional Societies, and/or other sources.

# Natural History Project

**Goal:** Collect clinical and exam data to better understand:

- phenotypic spectrum of all dystonias
- how symptoms change over time
- if other family members are affected
- researchers to use data for research

# Natural History Recruitment Goals

(isolated dystonia): 200 cases/year

## New cases

Focal  
Multifocal  
Segmental  
Generalized  
Hemidystonia

*Must have started in:*

*Face (Craniofacial/Blepharospasm/Oromandibular)*

*Larynx (Laryngeal)*

*Limbs (Limb dystonia)*

## Follow-up cases

Focal  
Multifocal  
Segmental  
Generalized  
Hemidystonia

*Must have started in:*

*Neck (Cervical Dystonia)*

*Face (Craniofacial/Blepharospasm/Oromandibular)*

*Larynx (Laryngeal)*

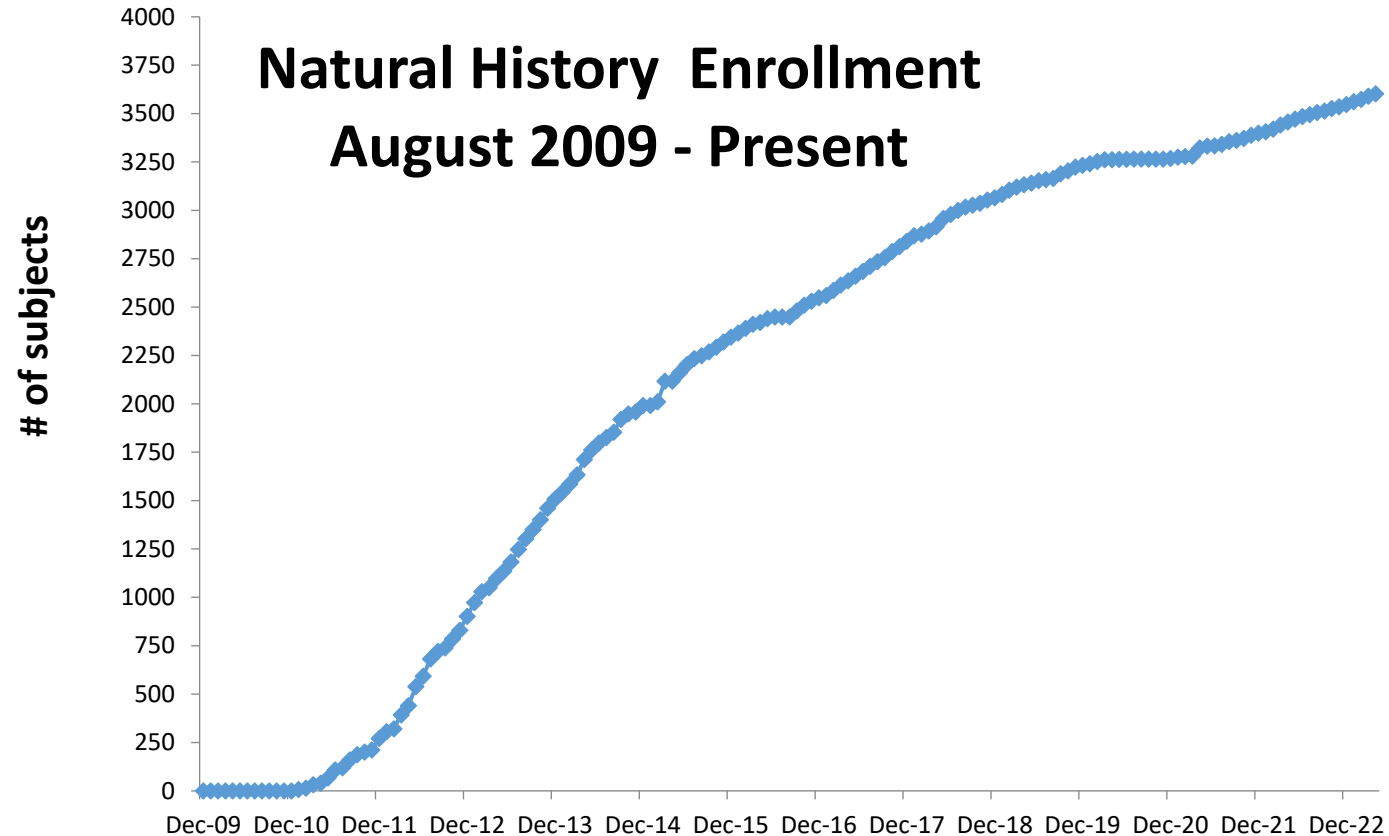
*Limbs (Limb dystonia)*

# Natural History: To Date

- The Natural History Study began recruitment in 2010
  - Natural History/Biorepository
  - Natural History Early Stage/Late Stage, 2016
  - *DCP3, 2020 to present*
- Minimal changes to data collection and video protocols
- No change for sample NINDS Coriell collection
  - Biobank at WUSM (2020)
- Follow-up visits, determined by a sliding scale

If onset of symptoms was	Subsequent follow-up visit should be
0 to < 3 years ago	1 year from last visit
3 to < 5 years ago	2 years from last visit
5 to < 7 years ago	3 years from last visit
At least 7 years ago	4 years from last visit

# Natural History Enrollment: 2010-2022



42 Sites recruited 3607 cases, 1396 follow-ups

# Distribution of Isolated Dystonia (March 2023)

Types of Isolated Dystonias enrolled	
Type	Amount
Focal Dystonia	2563
Generalized	165
Hemidystonia	15
Multifocal	296
Segmental	858

# Distribution of Focal Dystonia Subtypes

All subjects categorized by site affected		
Body Site	Affected at onset of illness	Affected at time of study
Foot	123	207
Hand	527	836
Jaw	189	304
Larynx	406	645
Lower Face	316	729
Neck	2081	2460
Pelvis	15	47
Shoulder	199	740
Tongue	59	144
Trunk	62	227
Upper Arm	164	354
Upper Face	729	958
Upper Leg	56	97

# Natural History Available Data

## **Completed by Neurologist**

- Global Dystonia Rating Scale (GDRS)
- Burke-Fahn Marsden Dystonia Scale (BFM)

## **Completed by participant**

- Short Form Health Survey 36 (SF-36)
- Beck Depression Inventory II (BDI-II)
- Hospital Anxiety and Depression Scale (HADS)
- Liebowitz Social Anxiety Scale (LSAS)
- Patient Health Questionnaire 9 (PHQ-9)



# Natural History Available Data

## **Completed by Coordinator**

### ➤ DCP Data Collection Form

*demographic, medical history, medications, exam, family history*

### ➤ Neurological Exam Video

*over 3,000 videos available*

# Data Accessibility - Who

- Enrolling Sites
  - Access to site data and videos
- New Research Projects
  - IRB approval
  - Data Access Agreement form
  - Executive Committee approval
    - Data
    - Videos (restricted access)
    - Biospecimens
- REDCap Data Interface / Chiron Interface
  - Publically available non-PHI data*
  - Full research data, de-identified*

# Data Accessibility - Where

- Washington University in St. Louis
  - REDCap
  - Video Repository
  - REDCap
    - Full data set for research
- NINDS Coriell Institute for Medical Research, *New Jersey*
  - DNA samples
  - De-identified data
- Data Management and Coordinating Center (DMCC), *Cincinnati Children's Hospital Medical Center*
  - De-identified data for public (Chiron)
  - De-identified data for research (Chiron)

# Data Accessibility – Video Repository

Restricted access

 Washington University in St. Louis • School of Medicine



Search by site

Search by diagnosis

Search by project

Search by Comments

Site

# Data Sharing/Access

**Public Access: Chiron (DMCC)**

## **Full Data or Video Access**

- Application
- Data access agreement
- IRB approval
- Executive Committee approval
- Only project specific data release
- Video: only streaming, not downloading

# Investigator Responsibilities

- Use data for proposed studies only
- No secondary release
- No attempt to identify participants
- Adequate staff training
- Share findings with Dystonia Coalition and publish data
- Acknowledge source

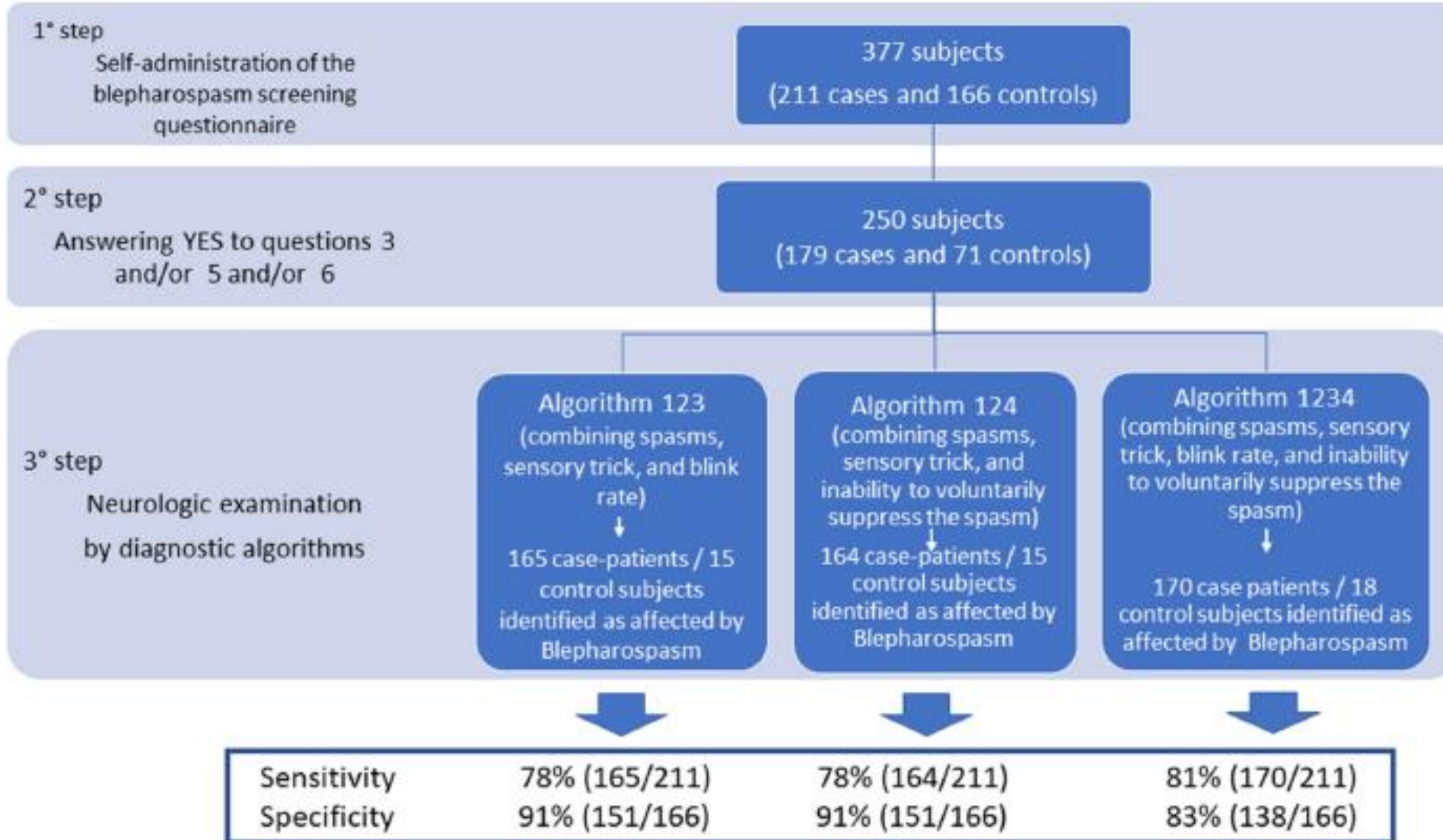
# Data Utilization

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# Blepharospasm Diagnostic Criteria: (bleph: n =211; control: 166)



**Prof Giovanni Defazio**

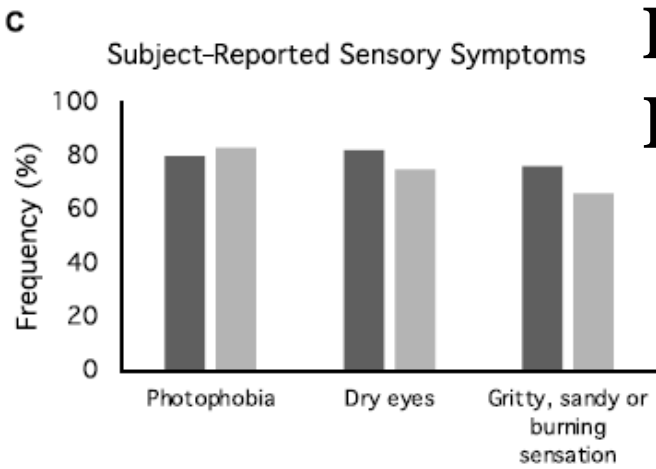
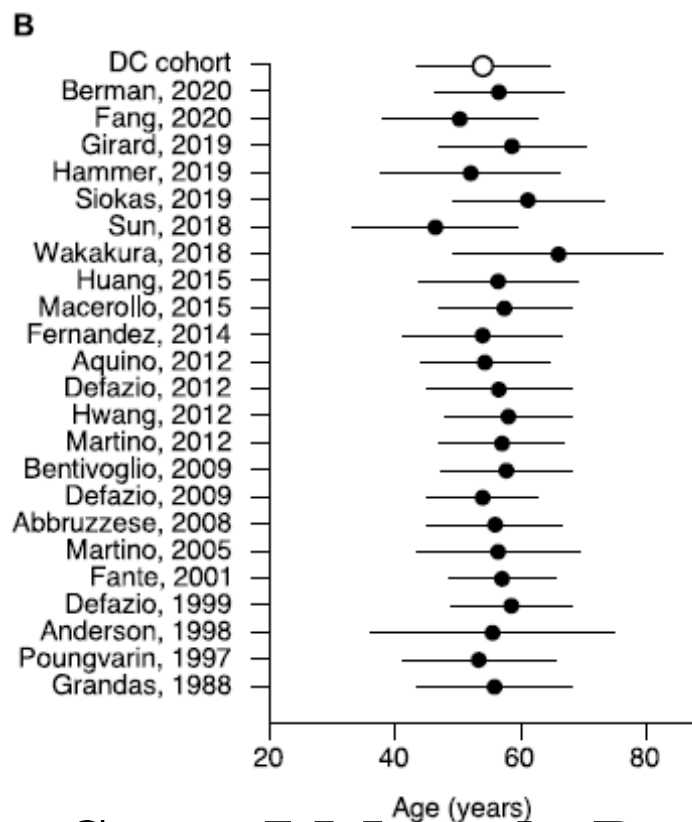
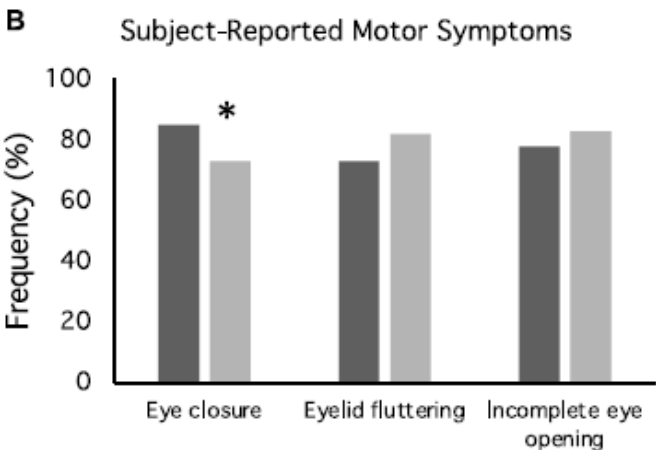
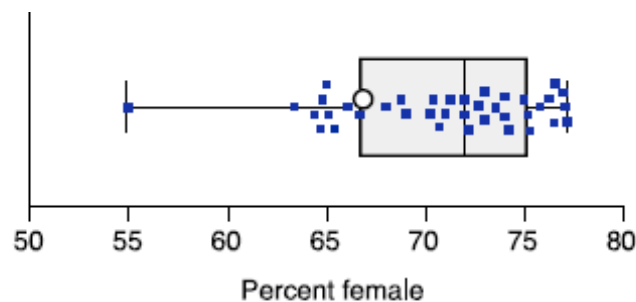
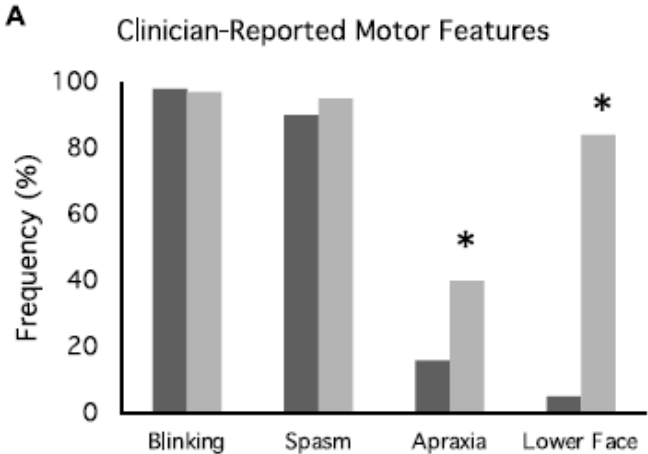


**Defazio G et al,  
Parkin Relat Dis,  
2021**



# Blepharospasm: Clinical features

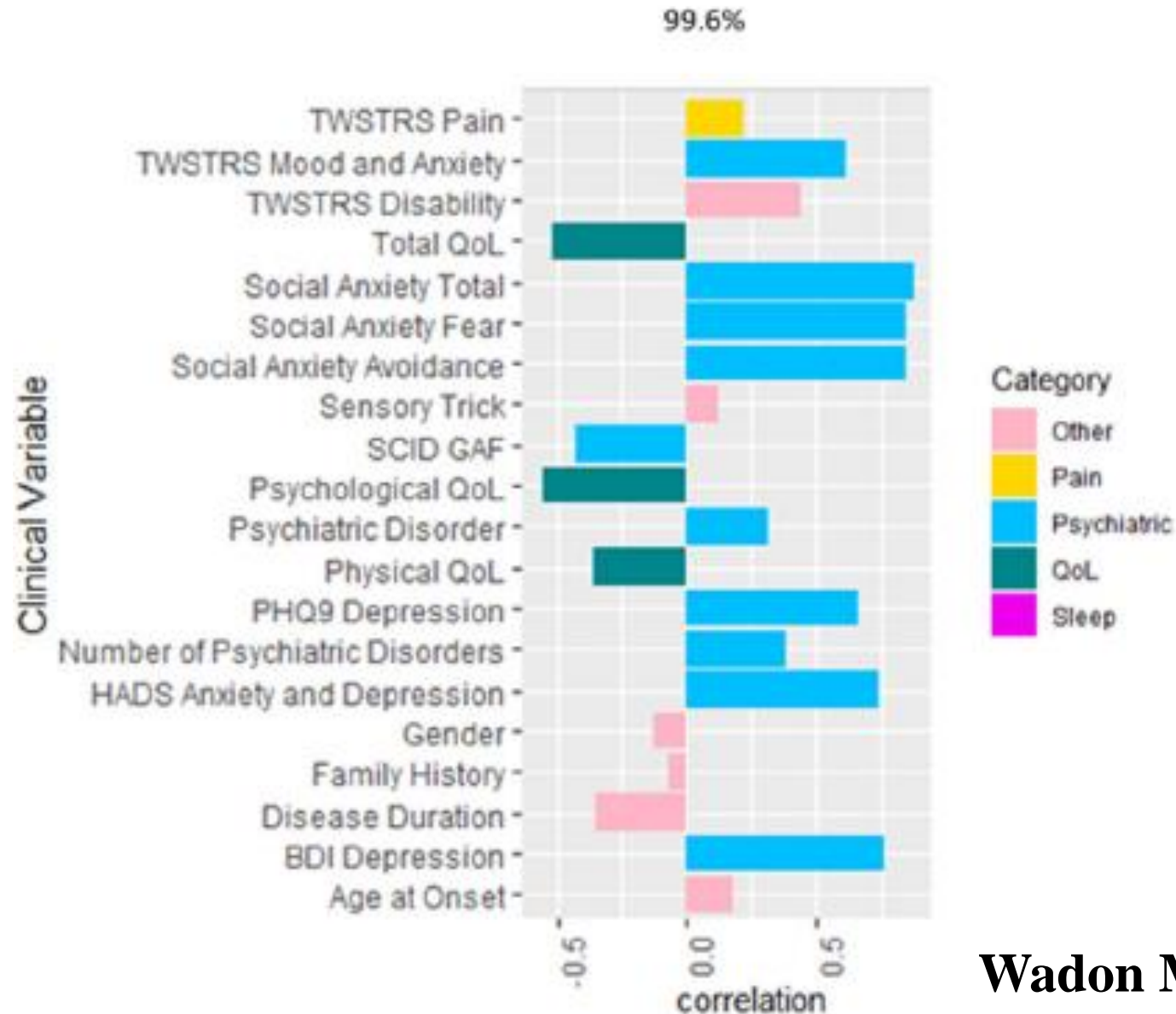
**N = 884**



**Dark: focal bleph**  
**Light: spread**

# CD: Non-motor phenotypic subgroups

(N =183 (DC), 114 dystonia wales)



# CD: classification & Diagnosis:

Cases with CD

N =1258

Body region affected on exam	Cases with dystonia	Cases with tremor
Neck	1245	720
Shoulder	226	8
Hand	69	157
Larynx	36	21
Upper face	51	10
Lower face	37	5
Upper arm	28	38
Trunk	23	10
Jaw	16	7
Foot	5	5
Upper leg	4	6
Tongue	4	5
Pelvis	0	0

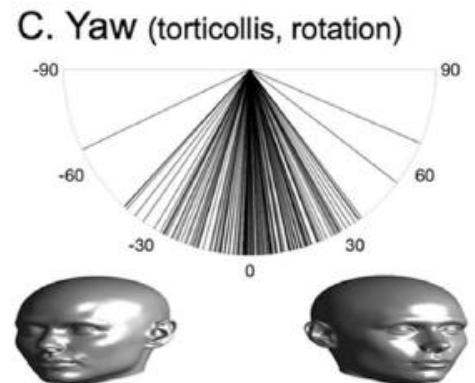
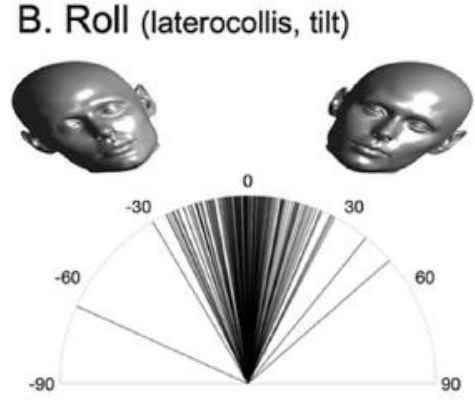
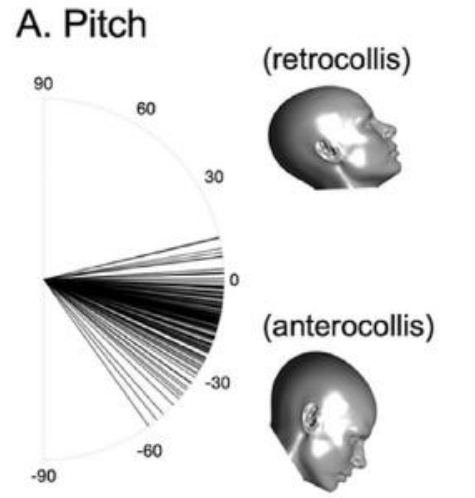
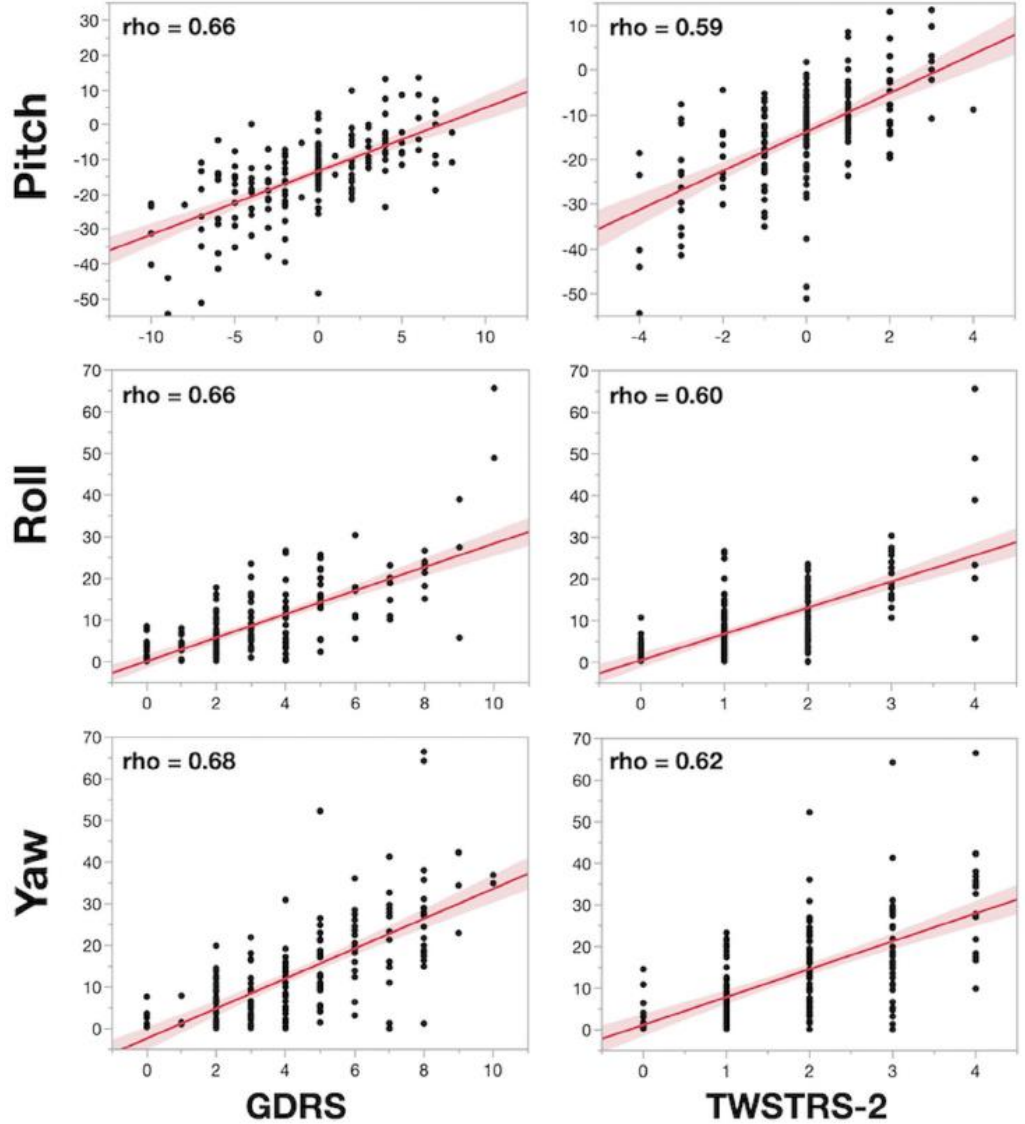
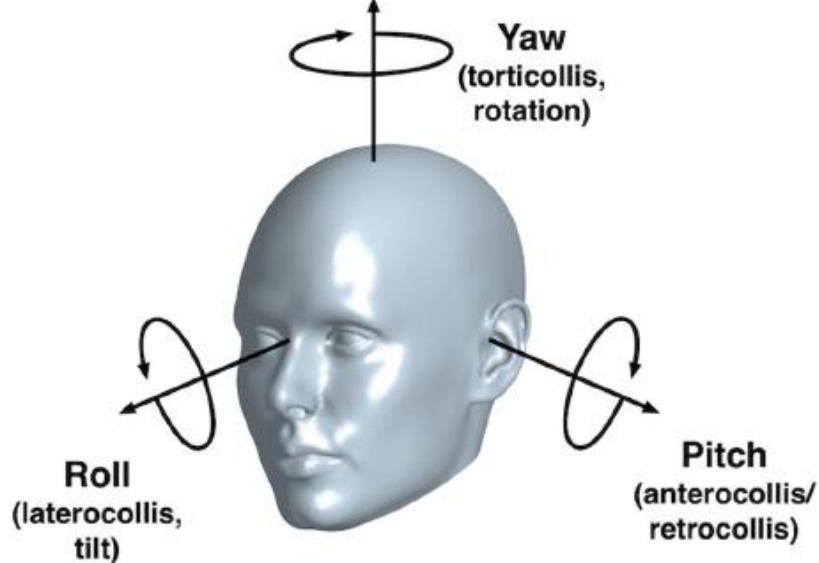
**TABLE 4** Recommendations for diagnosis of cervical dystonia according to body regions affected

Diagnosis	Body regions involved
Focal cervical dystonia	Neck only
	Neck plus shoulder
	Neck plus platysma
Segmental dystonia with neck involvement	Neck plus shoulder and upper arm
	Neck plus shoulder and whole arm/hand
	Neck plus jaw/tongue
	Neck plus lower face
	Neck plus larynx
Neck plus trunk	



Kilic-Berkmen G t al, Mov Clin Pract 2022

# Cervical Dystonia: Objective Video quantification (CMOR): n=185



Zhang Z et al,  
Ann Clin Transl Neurol, 2022

# **Bleph subtypes (motor/psych): cluster analysis (n=188)**

- **3 subtypes: mild, moderate & severe motor**
- depression/anxiety: bleph > controls**
- severity of depression/anxiety:  
moderate > severe > mild**



**Prof Giovanni Defazio**

# Q & A

## **Natural History (NH) Project**

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