

The European consensus guideline for Phelan-McDermid syndrome

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on behalf of the
European PMS guideline consortium

<https://ern-ithaca.eu/documentation/phelan-mcdermid-guideline>



Multidisciplinary care for:

- Diagnostics in NDD
- CHARGE syndrome
- Phelan-McDermid syndrome
- Chromosome 6 disorders

European Reference Network
ITHACA

Conflicts of interest

- This project was administratively supported by ERN-ITHACA, ERN-ITHACA is partly co-funded by the EU Health Programme
- Funding for the consensus meeting was obtained from the EU Horizon 2020 research and innovation programme under the EJP RD COFUND-EJP N° 825575
- Individual consortium member were not paid for their contributions to the guideline
- Nothing else to declare

1. How it all started

- Since 2015 UMCG is an EU-accredited Centre of Expertise for PMS
- 2018 Dutch guideline for 22q13 deletion syndrome
- 2020 ERN - ITHACA's request for European guidelines
- Email to all known professionals involved in PMS research, all ITHACA members and PMS support organisations within Europe

→ European consortium

- Administrative support by ITHACA (Klea Vyshka)
- First online meeting on PMS awareness day 22-10-2020

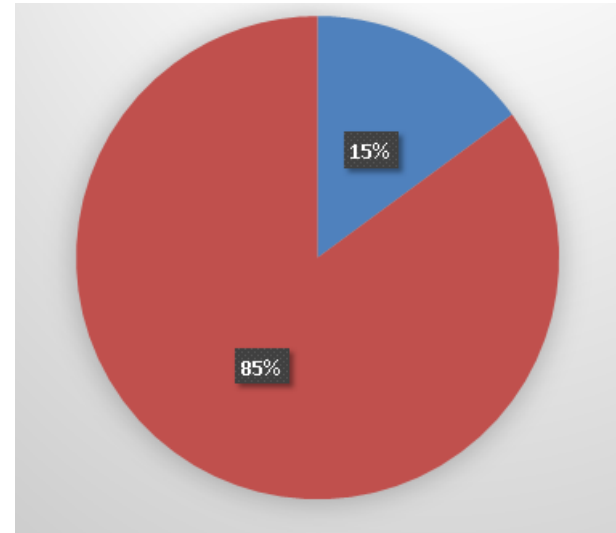


2. Patient participation

- Worldwide survey to explore the needs of families
- Patient representative in each working group
- Teams meetings of patient representatives
- Feed back on all chapters of the guideline
- Represented in organising committee of final consensus meeting (June 2022, Groningen)

3. The methods used

- AGREE II: www.agreetrust.org
- Define who are the patients and users of the guideline
- Perform a bottleneck analysis to decide
 - Based on expert opinions
 - Based on parental survey
 - E.g.: *Do professionals have enough knowledge about PMS in order to deliver appropriate care?*



4. Who are the patients? Phelan-McDermid syndrome

- *SHANK3*-related:
 - Deletion 22q13.3, including *SHANK3*
 - Pathogenic variant in *SHANK3*
- *SHANK3*-unrelated:
 - Deletion 22q13, not including *SHANK3*

4. For whom is the guideline? Professionals

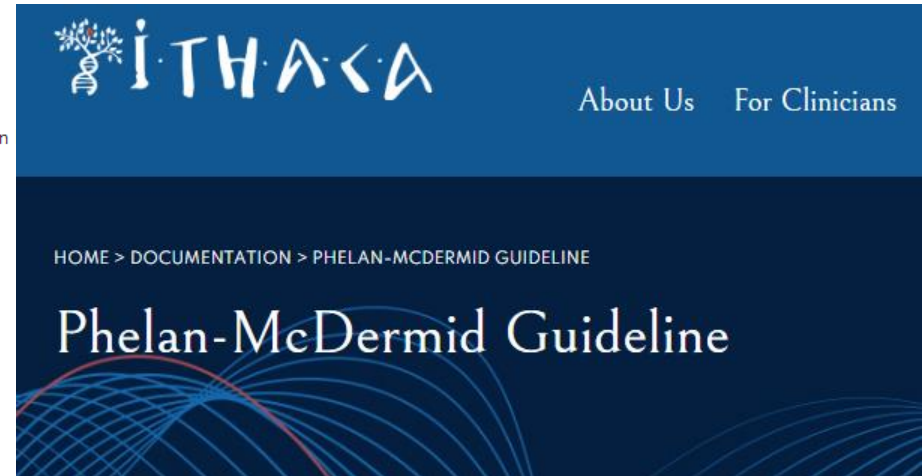


European Journal of Medical Genetics

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Phelan-McDermid syndrome; towards a European consensus guideline

Edited by Dr. Conny Van Ravenswaaij-Arts, Dr. Sarah Jesse, Dr. Maria Clara Bonaglia, Dr. Ingrid DC van



4. For whom is the guideline? Lay version for families

PHELAN-MCDERMID

☘ ☘ ☘

EPILEPSY

Many individuals with PMS life. Epilepsy is an electric the brain resulting in a r expression of the body. T be elicited by febrile pe recognize the seizures and common type of seizure. i glossary) which can be diff starts with staring into spad while the child does not r name. Symptoms can be gazing and lip smacking. T in every patient and th increases with age.

SLEEP DISORDERS

Most people with PMS suffe the good functioning of provoke fatigue, sleepiness concentration and perfo affect patient and the well- parents and caregivers.

WHAT IS THE BEST TREATMENT FOR LYMPHEDEMA?


- Physical activity to incre stimulate fluid circulation.
- A healthy diet to avoid ove
- Compression therapy garments and Velcro wraps
- Skin care to prevent skin in
- Surgical treatment is ger regular treatment is n multidisciplinary expertise

WHAT IS THE BEST TREATMENT FOR MENTAL HEALTH ISSUES?

☘ ☘ ☘



WHAT IS RECOMMENDED TO MANAGE SLEEP DISORDERS?

- Develop a constant bedtime routine with fixed bedtimes.
- Control the noise/sounds/smells, ambient light, room temperature, mattress, bed linens, etc.
- Use techniques such as gradual distancing or bedtime fading (glossary).
- Treat other physical conditions that may affect sleep.
- Investigate possible mental health difficulties, such as anxiety or depression.
- Check side effects of current medical treatments.
- Do not offer caffeine or caffeinated drinks or stimulate activities before bedtime.



WHAT IS RECOMMENDED TO MANAGE LYMPHEDEMA?

- Follow a healthy diet and do regular physical exercise to prevent obesity.
- Use a soap-free cleanser and carefully dry the skin to avoid infections or tissue maceration.
- In case of fluid retention in the legs, elevate the foot-end of the bed.
- Check the skin daily for any changes such as breaks in the skin (scratches, cuts, burns, abrasions), leakage of lymph fluid, pressure points from compression garments or changes in colour.
- Pay attention with nail care, obtain a medical pedicure, or see a podiatrist for toenail problems.
- Seek medical attention when there is a suspicion of a skin infection (redness, rash, warmth, or tenderness/pain).
- Seek medical attention if there is a leakage of lymph fluid. Seek a doctor and keep the skin clean and dry while still applying compression garments or bandages.

Intro

Participation


Methods

For whom

5. What are the main topics?

- AGREE II: www.agreetrust.org
- Define who are the patients and users of the guideline
- Perform a bottleneck analysis
 - A. Review of literature
 - B. Parental survey
 - C. Expert opinion

→ selection of **topics** for the guideline




ELSEVIER

Contents lists available at [ScienceDirect](#)

European Journal of Medical Genetics

journal homepage: www.elsevier.com/locate/ejmg



Definition and clinical variability of *SHANK3*-related Phelan-McDermid syndrome

Michael Schön^{a,*}, Pablo Lapunzina^b, Julián Nevado^b, Teresa Mattina^c, Cecilia Gunnarsson^d, Kinga Hadzsiev^e, Chiara Verpelli^f, Thomas Bourgeron^g, Sarah Jesse^h, Conny M.A. van Ravenswaaij-Artsⁱ, the European Phelan-McDermid syndrome consortium^{i,1}, Raoul C. Hennekam^j

5A. Clinical signs

Sign / Symptom	22q13.3 deletions (%)	SHANK3 variants (%)	Sign / Symptom	22q13.3 deletions (%)	SHANK3 variants (%)
Development			External phenotype		
Developmental delay	493/504 (98%)	48/50 (96%)	Dolichocephaly	84/319 (26%)	2/28 (7%)
Speech impairment	507/572 (88%)	31/44 (70%)	Long eyelashes	149/312 (48%)	19/39 (49%)
Neurology			Down-slanting fissures		
Seizures (one or more)	148/542 (27%)	14/53 (26%)	Periorbital fullness	69/239 (29%)	7/39 (18%)
Hypotonia	333/451 (74%)	42/51 (82%)	Ptosis	62/286 (22%)	2/28 (7%)
Structural brain anomalies	118/223 (53%)	12/42 (29%)	Epicanthal folds	122/378 (32%)	8/39 (21%)
Senses			Ear anomalies		
Vision disturbances	70/316 (22%)	9/34 (26%)	Wide nasal bridge	156/349 (45%)	15/42 (36%)
Strabismus	59/243 (24%)	4/28 (14%)	Broad nose	169/349 (48%)	15/40 (38%)
Hearing loss	32/372 (8%)	3/29 (10%)	Short philtrum	22/138 (16%)	0/21 (0%)
Increased pain tolerance	204/314 (65%)	38/48 (79%)	Thin upper vermillion	15/56 (27%)	3/11 (27%)
Behaviour			Thick lower vermillion		
ASD	162/282 (57%)	26/33 (79%)	Malocclusion	109/297 (37%)	10/29 (34%)
Hyperactivity	33/112 (29%)	21/29 (72%)	Retrognathia	29/115 (25%)	0/31 (0%)
Aggression	50/267 (19%)	18/49 (37%)	Pointed chin	154/309 (50%)	18/29 (62%)
Self-injury	10/80 (13%)	8/27 (30%)	Large fleshy hands	180/392 (46%)	11/28 (39%)
Sleep disorder	62/237 (26%)	24/46 (52%)	Clinodactyly 5 th finger	79/405 (20%)	10/28 (35%)
Internal organs			2-3 Syndactyly of toes		
Gastro-oesophageal reflux	31/122 (25%)	5/29 (17%)	Sandal gap	30/56 (54%)	6/9 (7%)
Cardiac anomalies	49/387 (13%)	3/46 (7%)	Small / malformed nails	138/438 (32%)	13/29 (45%)
Freq. airway infections	75/280 (27%)	15/47 (32%)	Lymphedema	29/270 (11%)	0/34 (0%)
Urogenital problems	9/62 (15%)	0/24 (0%)	Eczema	48/225 (21%)	14/46 (30%)
Renal abnormalities	20/137 (15%)	0/17 (0%)	Hypohidrosis	31/84 (37%)	2/24 (8%)
Growth			Hyper-extensible joints		
Short stature (≤ P3)	37/392 (9%)	4/41 (10%)			
Tall stature (≥ P98)	84/392 (21%)	3/41 (7%)			
Macrocephaly (≥ P98)	55/329 (17%)	6/39 (15%)			
Microcephaly (≤ P3)	53/329 (16%)	5/52 (10%)			

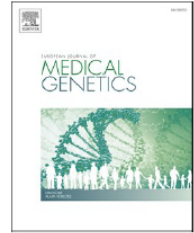


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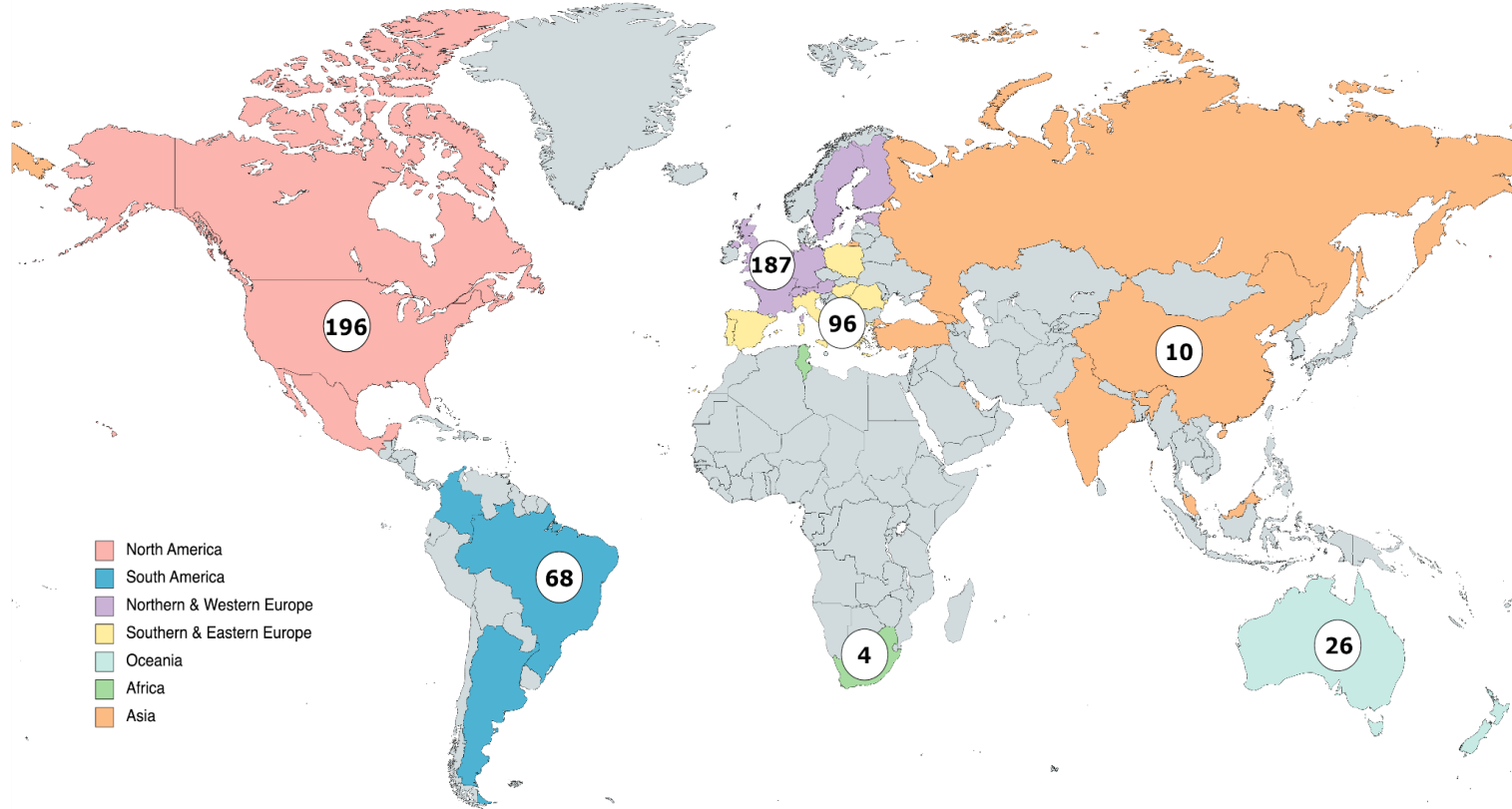
journal homepage: www.elsevier.com/locate/ejmg



Parental perspectives on Phelan-McDermid syndrome: Results of a worldwide survey

Annemiek M. Landlust^{a,b,1,*}, Sylvia A. Koza^{b,1}, Maya Carbin^c, Margreet Walinga^b, Sandra Robert^d, Jennifer Cooke^e, Klea Vyshka^f, the European Phelan-McDermid syndrome consortium

5B. worldwide survey



- 10 languages; 35 countries
- Completed by 587 caregivers, mainly being parents (98%)

- Median age at completion survey 12 years (0-60)
- Median age at diagnosis 3 years (0-59)
- 56% female 44% male

- Near normal IQ/mild delay 10%
- Moderate delay 19%
- Severe delay 71%

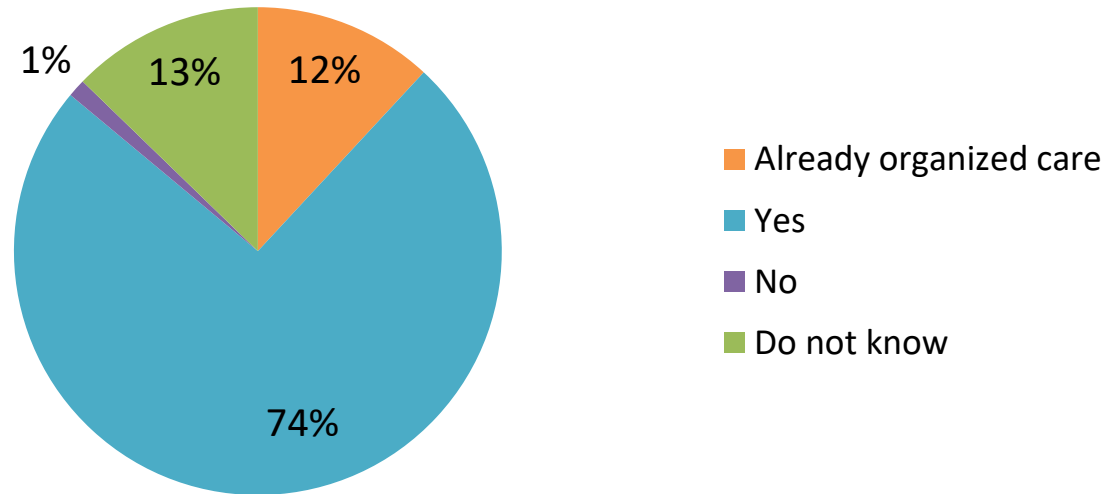
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57% in survey

5B. Opinion on the usefulness of the guideline

Would a PMS guideline help to better organize and personalize care? (n=587)







5. The main topics → working groups

- Introduction: Definition and clinical overview of PMS
- Genetic counselling, including ring chromosome 22
- Communication, language and speech problems
- Chewing, swallowing and gastrointestinal problems

		AT DIAGNOSIS	0-2 YEARS	2-12 YEARS	12-16 YEARS	>16 YEARS
HEART AND LUNGS	Cardiac ultrasound					
	Congenital abnormalities (including TI- tricuspid insufficiency, ASD- atrial septal defect, PDB- Persistent ductus Botalli)	Consult cardiology; ECG, US (<2 years) if indicated.				
	Recurrent upper airway infections					

- Mental health issues
- Organization of care

5. Task of working groups:

- Write a chapter with:
 - Introduction: what is the chapter about?
 - Fundamental questions 
 - Search and selection of literature sources 
 - Conclusions from literature 
 - Recommendations 
 - References & other sources

6. How consensus was reached

- Each chapter was reviewed at least twice
 - by the members of the European consortium
 - including patient representatives
 - and discussed at Teams meetings every 6 weeks
- Final consensus meeting
 - in Groningen (June 2022)
 - 30 participants, including 5 patient representatives, representing 12 European countries
 - Fine-tuning of the text of the recommendations and voting until consensus was reached (hybrid)

6. How consensus was reached



7. Recommendations

<https://ern-ithaca.eu/documentation/phelan-mcdermid-guideline>



Link to all PMS guidelines materials

8. Clinical synopsis



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12 extensive papers:

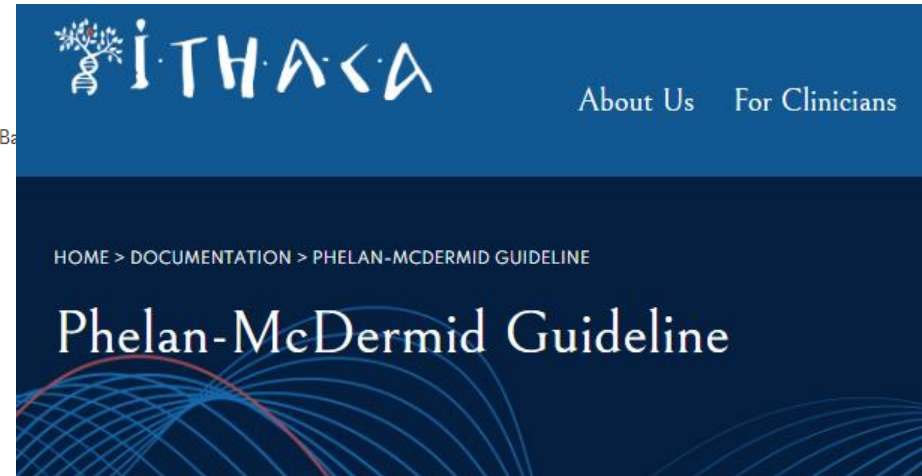
- Good background information
- Not practical

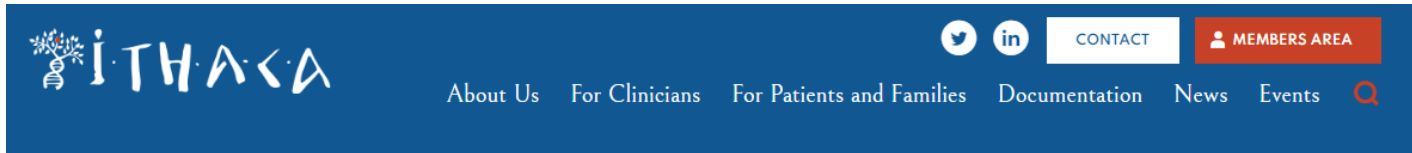
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Website with:

- **Clinical synopsis**
- Surveillance scheme
- Emergency card





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Introduction to the European Consensus Guideline for Phelan-McDermid syndrome

Members of the European Phelan-McDermid syndrome guideline consortium

Clinical synopsis of the European consensus guideline for Phelan-McDermid syndrome

Surveillance scheme summarizing recommendations for follow-up of individuals

Clinical synopsis of the European consensus guideline for Phelan-McDermid syndrome

Introduction

This is a shortened version of the European consensus guideline for Phelan-McDermid syndrome (PMS). More information including extended background information, methods and literature references can be found in the [Special Issue](#) of the European Journal of Medical Genetics published in 2023.

This guideline covers recommendations for individuals with **SHANK3-related PMS**, but may also partly be applicable for non-*SHANK3*-related PMS. It is written for professionals. A [clinical surveillance scheme](#), [emergency card](#) and lay versions in multiple languages are available.

A pdf of this clinical synopsis can be down loaded here



<https://ern-ithaca.eu/documentation/phelan-mcdermid-guideline>

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Raoul Hennekam

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