Surveillance scheme summarizing recommendations for follow-up of individuals with *SHANK3*-related Phelan-McDermid syndrome (PMS).

For background information see Special issue EJMG

		AT DIAGNOSIS	0-2 YEARS	2-12 YEARS	12-16 YEARS	>16 YEARS
GENETICS	Genetic counselling of relatives to discuss: - phenotype PMS - Recurrence risk: FISH and karyotyping (also to exclude ring 22) - reproductive options - family support groups					
	Referral to (PMS) centre of expertise (CE) for follow-up, general updates on PMS, participation in research, collecting data and providing (new) information to families.		Yearly	Every 2 years	Every 2 to 3 years	Every 3 to 5 years
MENTAL HEALTH	Cognition and development	Comprehensive evaluation. Baseline measurement of functioning level.	Assessment of development. Initiate early intervention.	Assessment and follow-up of development. Continue intervention.	Assessment and follow-up of development. Continue intervention.	
	Adaptive and sensory functioning	Comprehensive evaluation. Baseline measurement of functioning level.	Assessment of development. Initiate early intervention.	Assessment and follow-up of development. Continue intervention.	Assessment and follow-up of development. Continue intervention.	
	Psychiatric and behavioural status	Baseline measurement.	Monitor changes in skill level. Monitor changes in behaviour. If symptom onset, rule out medical issues.	Monitor changes in skill level. Monitor changes in behaviour. If symptom onset, rule out medical issues. Consider comorbid mental health problems.	Monitor changes in skill level. Monitor changes in behaviour. If symptom onset, rule out medical issues. Consider comorbid mental health problems.	If symptom onset, rule out medical issues. Consider comorbid mental health problems.

COMMUNICATION, SPEECH AND LANGUAGE	Difficulties with communication, language and speech	Refer to an audiology specialist. Assess and initiate intervention by (preverbal) speech therapist.	Follow up of hearing/ conduction problems*. Assess and initiate intervention by (preverbal) speech therapist.	Follow up of hearing/ conduction problems*. Consider support with augmentative/ alternative communication. (Preverbal) speech therapy at home/school.	Follow up of hearing/ conduction problems*. Continue support with augmentative/ alternative communication. (Preverbal) speech therapy at home/school.	Follow up of hearing/ conduction problems*. Continue support with augmentative/ alternative communication.
SLEEP DISORDER	Sleep disorders/problems at all ages: - Check somatic causes - Check mental health issues - Use structured questionnaires - Check parental stress	Check for sleep problems & parental stress.	Sleep clinic or sleep specialist.	Sleep clinic or sleep specialist.	Sleep clinic or sleep specialist.	Sleep clinic or sleep specialist. Check for: - Apnoea - Parasomnias
EYE AND VISION	Strabismus, refraction errors and cortical visual impairment	Refer to eye specialist.	Refer to eye specialist if indicated. Check vision*.	Refer to eye specialist if indicated. Check vision*.	Refer to eye specialist if indicated. Check vision*.	Refer to eye specialist if indicated. Check vision*.
EAR AND HEARING	Recurrent middle ear infections, hearing problems	Refer to an ENT specialist: audiometry and tympanometry.	Refer to ENT specialist if indicated. Check hearing*.	Refer to ENT specialist if indicated. Check hearing*.	Refer to ENT specialist if indicated. Check hearing*.	Refer to ENT specialist if indicated. Check hearing*.
	Delayed response to verbal and auditory clues	Keep in mind in communication.	Keep in mind in communication.	Keep in mind in communication.	Keep in mind in communication.	Keep in mind in communication.
ALTERED SENSORY FUNCTIONING	Reduced pain response	Be extra alert for (underlying) somatic problems.	Be extra alert for (underlying) somatic problems.	Be extra alert for (underlying) somatic problems.	Be extra alert for (underlying) somatic problems.	Be extra alert for (underlying) somatic problems.
	Heat regulation problem, decreased perspiration	Be aware of overheating.	Be aware of overheating.	Be aware of overheating.	Be aware of overheating.	Be aware of overheating.
	Hypersensitivity to touch	Take into account while examining.	Take into account while examining.	Take into account while examining.	Take into account while examining.	Take into account while examining.
	Altered sensory functioning	Refer to a sensory integration specialist.				

GASTROINTESTINAL	Feeding problems (reduced sucking reflex, chewing)		Speech therapy.	Speech therapy.		
	Gastroesophageal reflux	If needed: Dietary advice Proton pump inhibitors	Dietary advice Proton pump inhibitors	Dietary advice Proton pump inhibitors	Dietary advice Proton pump inhibitors	Dietary advice Proton pump inhibitors
	Cyclic vomiting		Refer to paediatrician to exclude somatic cause	Refer to paediatrician to exclude somatic cause		
	Overweight: nutritional and exercise advice (dietician, physiotherapist)					
	Constipation	If needed: Dietary advice laxatives	Dietary advice laxatives	Dietary advice laxatives	Dietary advice laxatives	Dietary advice laxatives Consider testing for megacolon.
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					
NEUROLOGY	Brain structural abnormalities	Low-threshold MRI of the brain at indication (paediatric)neurologist.				
	Hypotonia: poor head control, feeding problems, fatigue, insufficient movement.		Paediatric physiotherapist, occupational therapy, speech therapy.	Paediatric physiotherapist, occupational therapy, speech therapy.	Advise sports, possibly under the supervision of a physiotherapist.	Advise sports, possibly under the supervision of a physiotherapist.
	Delayed motor development, motor dyspraxia, hyperlax joints		Paediatric rehabilitation doctor, child physiotherapist, occupational therapy.	Paediatric rehabilitation doctor, child physiotherapist, occupational therapy.		
	Epilepsy, frequent febrile seizures		Paediatric neurologist and EEG at indication.	Paediatric neurologist and EEG at indication.	Paediatric neurologist and EEG at indication.	Paediatric neurologist and EEG at indication.

ENDOCRINE	Height		Investigate only if behavioural changes consistent with thyroid dysregulation.	Investigate only if behavioural changes consistent with thyroid dysregulation.	Investigate only if behavioural changes consistent with thyroid dysregulation.	Investigate only if behavioural changes consistent with thyroid dysregulation.
	Hypothyroidism	TSH				
RENAL UROGENITAL	Congenital abnormalities: vesicoureteral reflux, cystic or dysplastic kidneys, or hydronephrosis	Perform US of kidneys/urinary tract at least once				
	Recurrent urinary tract infections					Exclude underlying problems and consider prophylaxis.
	Birth control and family planning					
SKIN AND LYMPH	Dysplastic, thin toenails that frequently become ingrown					
	Primary lymphedema, prevalence increasing with age				Consider referral to a CE for lymphedema.	Consider referral to a CE for lymphedema.
	Be alert to overheating and/or decreased perspiration					
TUMOURS (In ring chromosome 22)	Monitoring for potential NF2-tumours, including eye and neurological examinations				Every 1 to 2 years.	Every 1 to 2 years.
	Baseline cerebral/spinal imaging (MRI)					
	MRI in case of symptoms of lethargy, unilateral weakness and/or ataxia and hearing loss					
ANAESTHESIA /MRI	Assistance with preparing the individual for procedures like an MRI or anaesthesia should be discussed with parents.					
	Close monitoring of aesthetic depth[#]					

General note: The coloured boxes in the scheme indicate when a specific check is recommended. The columns contain items that are advised at least once when making the diagnosis. For background information and further details see the relevant papers in this special issue, listed in the references. For prevalence of the clinical features see Schön et al (2023 this issue). All follow-up appointments may be more often when indicated.

ECG: electrocardiogram; EEG: electroencephalogram; US: ultrasound

* According to national guidelines

[#] Close monitoring of anaesthetic depth seems useful because there may exist an increased sensitivity to anaesthetics, based on hypersensitivity for isoflurane in *Shank3*-haploinsufficient mice (Li et al. 2017). However, to date there is no clear hint of anaesthesia complications in humans with PMS.