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

		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 and in behaviour. If symptom onset, rule out medical issues	Monitor changes in skill level and in behaviour. If symptom onset, rule out medical issues. Consider comorbid mental health problems	Monitor changes in skill level and 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 & 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 AAC. (Preverbal) speech therapy at home/school	Follow up of hearing/ conduction problems*. Continue support with AAC. (Preverbal) speech therapy at home/school	Follow up of hearing/ conduction problems*. Continue support with AAC
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
EYES & 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*
EARS & 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

		AT DIAGNOSIS	0-2 YEARS	2-12 YEARS	12-16 YEARS	>16 YEARS
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	If needed: Dietary advice, proton pump inhibitors	If needed: Dietary advice, proton pump inhibitors	If needed: Dietary advice, proton pump inhibitors	If needed: 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)	nutritional and exercise advice (dietician, physiotherapist)	nutritional and exercise advice (dietician, physiotherapist)
	Constipation	If needed: Dietary advice, laxatives	If needed: Dietary advice, laxatives	If needed: Dietary advice, laxatives	If needed: Dietary advice, laxatives	If needed: Dietary advice, laxatives. Consider testing for megacolon
HEART & 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

		AT DIAGNOSIS	0-2 YEARS	2-12 YEARS	12-16 YEARS	>16 YEARS
ENDOCRINE	Height					
	Hypothyroidism	TSH	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
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 & 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 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 anaesthetic 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. All follow-up appointments may be more often when indicated.

AAC = Augmentative and alternative communication;

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.

For background information and further details see the relevant papers in the special issue of the European Journal of Medical Genetics 2023. For prevalence of the clinical features see Schön et al EJMG 2023.
For the latest update of the Guideline for PMS see website ERN-ITHACA.