Supplementary materials to: Fong N, Tan ES, Ngeow J, et al. Recommendations for the diagnosis and management of neurofibromatosis type 1 in Singapore: A Delphi consensus. Ann Acad Med Singap 2026;55:528-38. DOI: https://doi.org/10.47102/annals-acadmedsg.2026152

Table S1. Search strategy.

Search number	Query	Results 15-09-2023
1	(NF1 OR NF-1 OR "NF 1" OR "Neurofibromatosis type 1" OR "Neurofibromatosis 1" "Neurofibromatosis-1" OR "Von Recklinghausen" OR "von Recklinghausen's") OR (neurofibromatosis 1[MeSH Terms])	12,519
2	Singapore	1,44,549
3	#1 AND #2	34
4	(((((consensus[Title/Abstract] OR recommendation*[Title/Abstract] OR guideline*[Title/Abstract] OR management[Title/Abstract] OR diagnosis[Title/Abstract] OR surveillance[Title/Abstract]) OR (clinical[Title/Abstract] AND (burden[Title/Abstract] OR manifestation[Title/Abstract] OR presentation[Title/Abstract]))) OR (screening[Title/Abstract] OR epidemiology[Title/Abstract] OR prognosis[Title/Abstract] OR "disease progression"[Title/Abstract] OR "quality of life"[Title/Abstract] OR "practice pattern*"[Title/Abstract] OR surgery[Title/Abstract])) OR ((surgical[Title/Abstract] OR medical[Title/Abstract]) AND management[Title/Abstract])) OR (survival[Title/Abstract] OR mortality[Title/Abstract] OR morbidity[Title/Abstract] OR risk[Title/Abstract])) OR ("clinical characteristic*"[Title/Abstract])	91,30,391
5	**#1 AND #4**	**4310**
6	**#1 AND #4 Filter: 2018-2023 (5 year)**	**1082**

Table S2. Statements that achieved consensus in Survey 1.

Statements	Survey 1 consensus
Genetic testing	
Q. Do you agree with the following statements related to genetic testing of NF1 patients:	
Genetic testing would be of value to patients suspected to have NF1 who do not fulfil clinical diagnosis criteria.	79%
There is value in genetic testing for patients who have a clinical diagnosis of NF1.	84%
Genetic testing would be of value in patients suspected to have NF1, if cost was not a factor.	79%
Q. Do you agree that genetic testing is helpful in:	
Patients with a suspected NF1 microdeletion	81%
Complex presentations of NF1 (e.g. malignancy)	89%
Q. If an *NF1* variant is not detected, sequence analysis and deletion/duplication analysis of *SPRED1* are considered in individuals with only pigmentary features.	82%
Q. If a variant in *NF1* or *SPRED1* is not detected through DNA analysis, it is advisable to consider RNA analysis.	87%
Q. If the phenotype cannot be distinguished from those of other disorders, a multigene panel that includes *NF1*, *SPRED1*, mismatch repair, and other genes of interest should be considered.	89%
Adult management	
Q. Laser treatment for café-au-lait macules and freckles may be considered for NF1 patients.	77%
Q. For patients with CNF, clinical assessment comprising physical examination and palpation should be repeated at least annually.	79%
Q. Radiotherapy is not recommended for optic pathway gliomas due to increased risks of late-onset cerebrovascular complications and secondary malignancy.	79%
Q. Radiotherapy is not recommended for NF1-PNs due to the increased risk of secondary malignancy and moyamoya syndrome.	87%
Q. Pheochromocytoma screening is recommended in hypertensive NF1 patients under following circumstances:	

Statements	Survey 1 consensus
Patients over 30 years of age	75%
Pregnant patients	75%
Patients having paroxysmal hypertension	88%
Patients with hypertension-associated headache, palpitations, or sweating	94%
Q. Listed therapies may be considered in treating NF1-PN patients, based on their clinical and safety outcomes: Selumetinib (MEK inhibitor)	83%
Q. Surgical resection is the treatment of choice for NF1 patients in the selected conditions:	
MPNSTs	83%
Optic pathway glioma cases in the presence of proptosis or hypertensive hydrocephalus	77%
CNFs	78%
Gastrointestinal stromal tumours	85%
Q. Current treatment options for CNF include:	
Surgical excision	84%
Laser removal	77%
Electrodesiccation	80%
Q. For NF1 patients' health, the following points may be considered:	
Vitamin D supplementation	76%
Monitoring for curve progression for the management of scoliosis	94%
Treatment for osteoporosis for the general population	76%
Annual clinical evaluation of the back with Adam's forward bend test	93%
Q. The initial step in pain management is to use age-appropriate pain intensity assessment tools to determine the level of pain.	95%
Q. The following are the statements related to NF1-PNs:	
NF1-PN with rapid growth (>20% increase in volume per year) and impending morbidity is likely a candidate for intervention	95%
A slowly growing NF1-PN (<5% increase in volume per year), without actual or impending morbidity may be suitable for observation.	89%
Q. Risk-reducing bilateral mastectomy for woman without breast cancer should not be performed in NF1 patients.	87%

Statements	Survey 1 consensus
Q. MEK inhibitors, such as selumetinib, can be considered as treatment option for adult patients with NF1:	
Symptomatic NF1-PN	76%
Inoperable symptomatic NF1-PNs	82%
NF1-PN that remains symptomatic following partial resection	82%
Q. MRI is preferred over CT to assess NF1-PNs.	89%
Q. Among different types of neurofibromas, NF1-PNs exhibit the highest tendency to evolve into MPSNTs.	88%
Q. Treatment for adult patients with NF1 may include:	
Surgery for NF1-PN	94%
Pharmacotherapy for headaches or seizures	89%
Therapeutic counselling for managing pain	89%
Therapeutic counselling for addressing low self-esteem concerns and negative body image	94%
Psychosocial counselling	94%
Childhood management	
Q. Children diagnosed with NF1 should undergo a speech and language assessment, followed by appropriate intervention if necessary.	78%
Q. Persistent headache in a child with NF1 requires urgent attention because it can indicate an underlying life-threatening condition such as vasculopathy, hypertension, or a space-occupying brain lesion.	89%
Q. Treatment for NF1 depends on child's needs and the treatment may include:	
Surgery for NF1-PN	89%
Pharmacotherapy for headaches or seizures	94%
Educational assessment and support in school	95%
Pharmacotherapy or non-pharmacological options for managing pain	89%
Therapeutic counselling for addressing low self-esteem concerns and negative body image	95%
Early intervention for speech, physical or occupational therapy	95%
Q. Surgical resection is a preferred treatment option for children with NF1-PN when it is feasible.	76%

Statements	Survey 1 consensus
Q. MEK inhibitors, such as selumetinib, can be considered as treatment option for childhood NF1:	
Symptomatic NF1-PN	89%
Inoperable symptomatic NF1-PNs	95%
NF1-PN that remains symptomatic following partial resection	94%
Q. Assessment of hypertension in the childhood NF1 should include:	
Doppler ultrasonography of the aorta	82%
Doppler ultrasonography of the renal arteries	94%
Renal arteriography	75%
Magnetic resonance angiography	80%
Children with NF1 should be monitored for cognitive and behavioural difficulties, including:	
Development, ideally before school	95%
Progress at school	95%
Sleep patterns	94%
Ability to focus on an activity	94%
Distractibility	94%
Social interaction	95%
Motor skills	95%
Management of cognitive problems and behavioural difficulties in childhood NF1 patients may require:	
A special educational needs coordinator may be involved at an early stage	79%
Close liaison between teachers, educational psychologists, occupational therapists, and community paediatricians	89%
Cognitive behavioural therapy	84%
Methylphenidate under experienced supervision	88%
Addressing the effects of NF1 on psychosocial and neuropsychological functioning can involve:	
Psychosocial well-being and neuropsychological functioning should be addressed at each clinic visit	84%
Advisable to include a psychologist as a member of the multidisciplinary team	89%

Statements	Survey 1 consensus
Counselling as an intervention	95%
Childhood bullying	94%
Surveillance – All ages	
Q. Systematic clinical assessment by NF1 experts, which includes skin and neurological examinations, blood pressure, height, weight and pubertal development, is carried out as a minimum:	
Annually in children up to 10 years	82%
Once every 2 years in children >10 years	76%
Yearly for children up to 18 years old, when transitioning	89%
Once every 3 years in adults	83%
Q. In NF1, biochemical or imaging screening for pheochromocytoma in asymptomatic, non-hypertensive individuals is not recommended.	79%
Q. In NF1, measurement of plasma free metanephrines as a single test is more sensitive and specific in an individual clinically suspected to have pheochromocytoma.	82%
Q. For NF1 patients with hypertension and vasculopathy, following should be performed:	
MRI is the preferred imaging modality for the evaluation of renovascular hypertension	91%
Spiral CT and CT angiography may be used, for individuals with impaired renal function (GFR <30 mL/min)	80%
Selective imaging (e.g. ultrasound) should be performed for individuals who are clinically suspected to have a vascular lesion	79%
Q. Pain assessment for NF1 symptoms should be conducted during clinic visits.	95%
Surveillance – Adults (aged >18 years)	
Q. For adults (>18 years) with NF1, symptom check should be performed as a minimum:	
Annually by primary care physician	83%
Once every 3 years by NF1 expert	83%
Q. Breast cancer surveillance should consider:	
Screening with annual breast MRI should be the primary approach	83%
Mammography is the second best alternative when MRI is not available.	82%
Annual screening in NF1 should begin at the age of 30 years.	81%

Statements	Survey 1 consensus
Screening to be performed for NF1 once every 2 years after the age of 50 years.	75%
Risk-reducing bilateral mastectomy should not be performed in NF1 patients.	75%
Q. Clinical assessment for optic pathway glioma should include age-appropriate assessment of:	
Visual acuity	94%
Visual fields	94%
Pupillary testing	94%
Eye movements	88%
Optic disc appearance	88%
Surveillance – Children (aged 0–16 years)	
Q. Children with NF1 are recommended to follow a surveillance protocol that includes:	
Physical examinations at least twice a year until the age of 5 years, and at least annually thereafter.	78%
Child's growth and overall development.	95%
Children to undergo yearly neurologic examinations, which may help to detect the presence of tumours forming on the nerves.	89%
Child's head circumference should be checked regularly.	95%
Annual neurological examination for headaches and seizures.	89%
Annual visits with an ophthalmologist throughout childhood to screen for optic gliomas.	84%
Doctors should suggest screening for learning disorders and attention deficit hyperactivity disorder when children start school.	94%
Annual review should include a pain score assessment for children.	89%
Annual cardiac assessment by evaluating blood pressure and/or echocardiography.	82%
Q. Clinical evaluation of childhood NF1 patients suspected of having orbital and periorbital PN, comprises:	
Physical examination looking for blepharoptosis, proptosis, eyelid oedema, orbital dysplasia and/or dystopia, distortion of the (peri)orbital skeleton, pulsation of the eye, and strabismus	95%

Statements	Survey 1 consensus
Clinical testing of vision and refractive error, visual field, ocular motility and alignment, and evaluation of the optic disc to exclude glaucoma or optic neuropathy	89%
MRI of the brain and orbits should be performed in all suspected children.	79%
Q. Surveillance for pheochromocytoma in patients with NF1 should include an annual blood pressure check starting at the age of 10 years.	89%
Surveillance – Transition age (16–18 years)	
Q. Considering the heightened risk of MPNST associated with a high internal tumour burden:	
Q. It is advisable to contemplate whole-body MRI for evaluating NF1 patients aged 16–20 years	83%
Q. Surveillance for NF1 patients with scoliosis consists of:	
X-ray imaging	95%
Orthopaedic opinion	94%
Statistical analysis of the spinal curvature	87%

CT: computed tomography; CNF: cutaneous neurofibroma; DNA: deoxyribose nucleic acid; GFR: glomerular filtration rate; MEK: mitogen-activated protein kinase; MPNST: malignant peripheral nerve sheath tumours; MRI: magnetic resonance imaging; NF1: neurofibromatosis type 1; NF1-PNs: NF1-plexiform neurofibromas; PN: plexiform neurofibroma; RNA: ribonucleic acid; SPRED1: Sprouty-related EVH1 domain-containing protein 1

Table S3. Statements that did not achieve consensus in Survey 1 and achieved/did not achieve consensus in Survey 2.

Statements	Survey 1 consensus	Survey 2 consensus
Adult management		
Q. Patients with NF1 usually do not exhibit KIT or PDGFRA overexpression in gastrointestinal stromal tumours, limiting the use of imatinib in this population.	50%	100%
Q. When feasible, surgical resection may be the preferred treatment option for NF1 patients under specific conditions, such as:		
NF1-PN	47%	76%
Bone dystrophic changes (e.g. kyphosis)	33%	62%
Q. *Surgical resection can be a treatment option, if feasible, for symptomatic NF1-PN.	17%	82%
Q. *Listed therapies may be considered in treating patients with NF1-malignant peripheral nerve sheath tumours, based on their clinical and safety outcomes:		
*Surgery	44%	88%
Chemotherapy	33%	81%
Radiotherapy	27%	64%
#Empirical targeted therapy (e.g. MEK inhibitors and/or mTOR inhibitors)	NR	69%
#Targeted therapy based on tumour molecular profiling	NR	67%
Q. *For which of the following NF1-associated conditions is medical treatment generally approached the same way as in patients without NF1, assuming standard clinical guidelines and no NF1-specific complications?		
Migraine, seizures, or sleep disorders	29%	65%
Osteoporosis	50%	82%
Glioblastoma	42%	43%
Breast cancer	47%	50%
Leukaemia and lymphoma	46%	69%
Surveillance		
Q. *Risk assessment of juvenile myelomonocytic leukaemia should be performed in children with xanthogranulomas for surveillance of JMML.	57%	71%

Statements	Survey 1 consensus	Survey 2 consensus
#Specific clinical features should guide the need for further investigations, such as full blood count.	NR	83%
#Clinical advice alone is sufficient.	NR	33%
Q. Patients with presence of NF1-PNs may receive below by the age of up to 21 years or before transition to adult services		
Whole-body MRI	71%	94%
Regional MRI	67%	100%
FDG PET scan	33%	31%
Q. Surveillance for NF1 patients with scoliosis consists of: MRI?	63%	63%

FDG PET: fluorodeoxyglucose positron emission tomography; JMML: juvenile myelomonocytic leukaemia; KIT: KIT proto-oncogene receptor tyrosine kinase; mTOR: mechanistic Target of Rapamycin; MEK: mitogen-activated protein kinase; MRI: magnetic resonance imaging; NF1: neurofibromatosis type 1; NF1-PNs: NF1-plexiform neurofibromas; NR: no response; PDGFRA: platelet-derived growth factor receptor alpha

** Question is modified in Survey 2*

 # New question added in Survey 2

Fig. S1. Open-ended question 1.

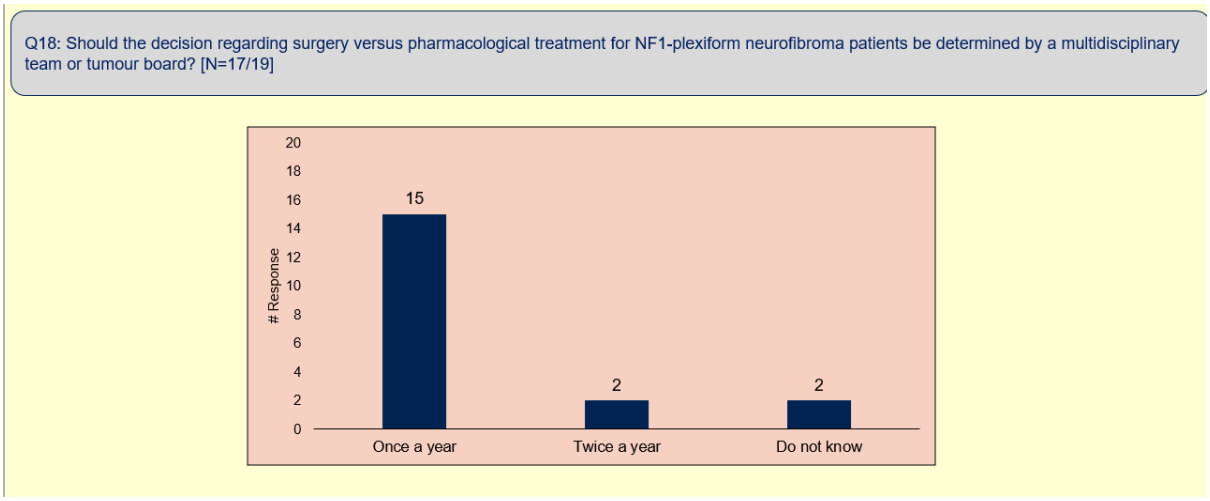


Fig. S2. Open-ended question 2.

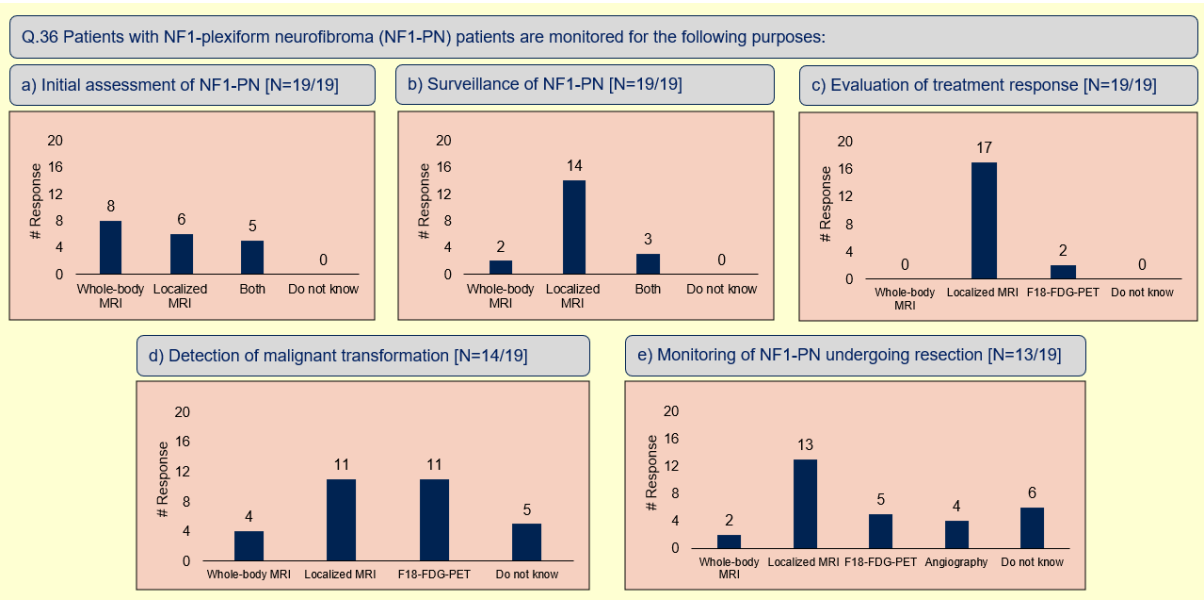


Fig. S3. Open-ended question 3.

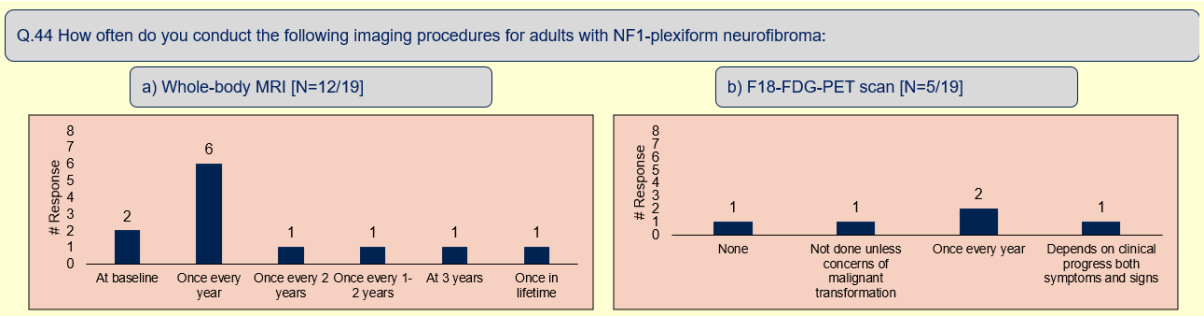


Fig. S4. Open-ended question 4.

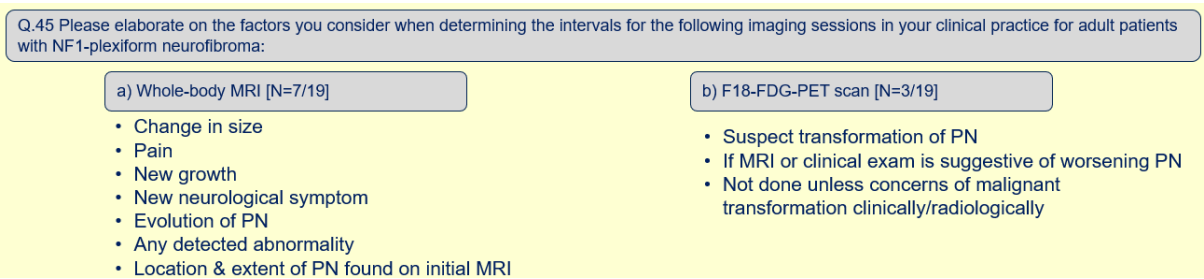


Fig. S5. Open-ended question 5.

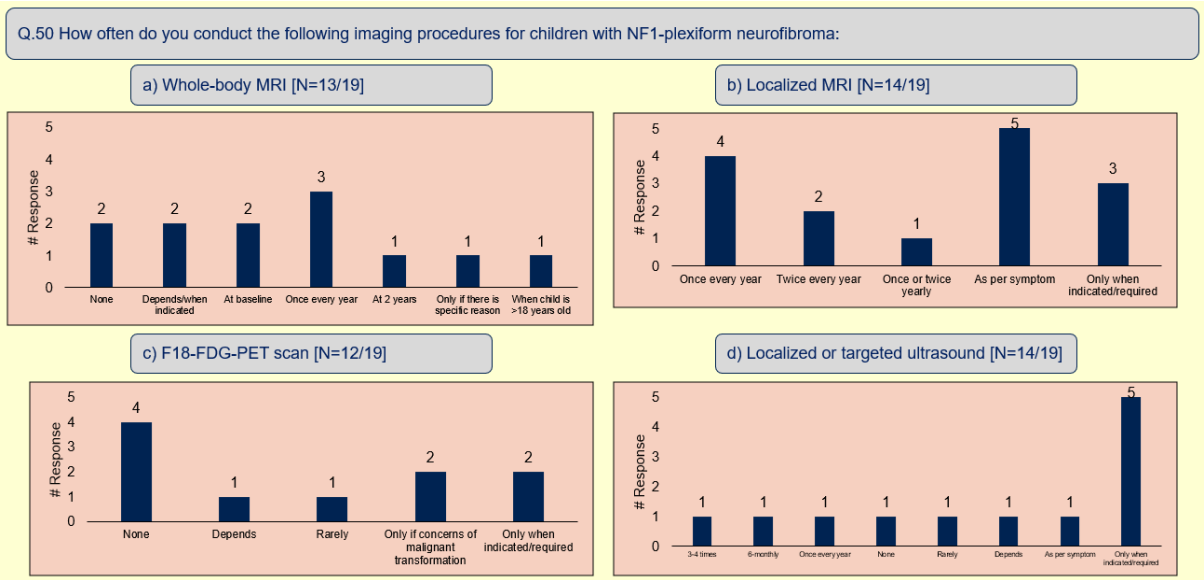


Fig. S6. Open-ended question 6.

