Guideline for Growth, Heath and Developmental Follow-up for Children Born Very Preterm

Ex	Expert Review			
	Reviewer One (United Kingdom)	NHMRC Comment	Developer response	
1	(Reviewer was asked: Has the appropriate evidence been identified and reviewed in line with the scope and clinical questions posed by this guideline?) There is a huge literature on outcomes following preterm birth and of risk factors for impaired outcomes. The specific investigation considered the effects of a structured follow up service for which there is little evidence but is in my opinion self-evident. The need for health and family surveillance is clear and the breadth of outcomes is set out nicely. The specifics of a follow up programme are not really discussed and the need for national monitoring of these or key outcomes is not really discussed in detail. This may be devolved to the ANZNN data collection. Several scales (which have significant cost implications) are recommended (Table 4 emboldened items) but not justified – but as it is unclear what the clinical team are to do with the data. I suspect this is outside the terms of this review. Given that L believe the GDT have identified the data to answer their posed questions.	For noting.	Comment noted.	
2	(Reviewer was asked: Have the risks and potential harms of recommendations been fully considered in the context of clinical practice, including any medico-legal implications that you may be aware of?) This is an odd question for the subject matter in point. The rationale is to identify issues raised by clinical assessment and parental discussions given the high rate of potential impairment in this target group, thereby avoiding medico-legal issues. I cannot foresee harm from these assessments. I suspect a well set out programme will provide support and deflate anxiety for families enrolled in these schemes.	For noting.	Comment noted.	
3	(Reviewer was asked Are there relevant international or well referenced guidelines (recommendations) on the same topic that conflict with this guideline? If so, is this acknowledged and justified in the guideline?) The closest guideline is that produced by NICE in the UK, but that seeks to provide more than simple follow up evaluations and to provide a route for parents to seek advice outside the formal system and to provide data on cognitive outcomes to assist in adaptation to school based on the UK system. Several countries mainly in Europe have developed similar frameworks. These seek to capture data at key points and provide varying degrees of parental support and communication with statutory bodies which are covered in the EFCNI guidance. As each health care system is different/unique I suspect the acknowledgement [of other guidelines] is appropriate.	For noting.	Comment noted.	
4	Other comments Overall the guideline is well presented and comprehensive but limited in that much is left to the local team to organise and funding issues (which will have to be developed as appropriate) are presumably responsibility of each state. The difficulty will be in the operationalisation of the guidance.	Please consider this comment in the context of the dissemination and implementation plans for the guideline.	Commented noted for the development of the dissemination and implementation plan.	

	Reviewer Two (Australia)	NHMRC Comment	Developer response
5	(Reviewer was asked: Has the appropriate evidence been identified and reviewed in line with the	Please consider and respond to	Thank you for your comment. Recommendations for
	scope and clinical questions posed by this guideline?)	these comments and	long-term follow-up from a national or international
	The authors have conducted an extensive search of the literature related to the two clinical questions	recommendations from the	perspective were considered in addition to systematic
	posed.	reviewer.	review 1 in the development of the structured follow-
			up schedule provided. More information is provided
	The authors have provided an excellent review based on the literature available, however, I		for this as part of the Technical Report (Table 4, page
	have some comments related to the review and findings.		11-14). No amendment has been made in relation to
			this comment.
	COMMENTS Re QUESTION 1: Should children born very preterm and their Caregivers be offered		
	structured, preterm-specific post-discharge follow-up care?		In addition, a reference to a relevant Cochrane review
			that illustrates the benefit of early childhood
	This was interpreted for the purpose of the literature review as: "Is there evidence that systematic and		intervention has been added to the Current Landscape
	targeted follow-up after very preterm birth improves child or family outcomes?"		of Follow-up Care in Australia section on page 38.
	9,653 studies were screened and 116 full text studies assessed for eligibility. However, only ONE study		Reference: Spittle A, Orton J, Anderson PJ, Boyd R,
	was included in review with all others excluded as irrelevant or not providing appropriate information.		Doyle LW. Early developmental intervention programs
	The one included study provided evidence of earlier diagnosis, but no evidence of improved outcome.		post hospital discharge to prevent motor and
			cognitive impairment in preterm infants. Cochrane
	The subsequent recommendations for follow-up were then provided as Consensus Recommendations		Database Syst Review 2015; 2015(11): CD005495
	(based on expert opinion), due to lack of evidence from the literature review. The authors did not		
	provide any additional evidence from literature to demonstrate that early diagnosis and intervention		
	provides benefit to children.		
	Recommend: Due to a paucity of literature related to benefits of a structured follow-up after preterm		
	birth, it would be helpful if the researchers could provide some evidence of benefit of early diagnosis		
	and early intervention on outcomes for children born at any gestation (including term births) with		
	disabilities that are common in preterm children, e.g. hearing loss, cerebral palsy, developmental delay		
	or other disabilities.		
6	COMMENTS re QUESTION 2: What biological and environmental factors influence health and	Please consider and respond to	Thank you for your comment. The recommendations
	developmental outcomes for children born very preterm and their caregivers?	these comments from the	were based on clinical expert consensus due to the
		reviewer.	lack of available direct evidence for the format and
	This was an extensive, well conducted review, which Identified multiple risk factors for adverse		type of reviews recommended. The guideline
	outcome. 15,324 studies screened, 1105 full text studies assessed for eligibility, 129 studies included in		recommends that all children born <32 weeks should
	the review. However, it is not entirely clear to me what the purpose of this review was in relation to		receive access to follow-up regardless of risk factors.
	the proposed guidelines. Although the review identified multiple risk factors for adverse outcome in		The purpose of identifying risk factors may guide the
	children born preterm, the findings were not presented in a manner that provided an understanding of		intensity of the follow-up (i.e. more than the minimum
	relative risk of adverse outcome. For example, it was identified that gestational age was associated		set of contacts) and the mode of delivery (telehealth
	with increased risk of neurodevelopmental impairment, but no information was provided about risk for		vs. face to face).
1	different gestational age groups (e.g. for children born <28 weeks compared with children born 28 to		
	<32 weeks). Based on consensus opinion, it was deemed that because children born very preterm may		Additionally future research priorities will be needed
1	have multiple risk factors, stratifying access to follow-up based on risk was not appropriate (although		to assess the effectiveness of surveillance
	data on which this decision was based was not provided).		implementation will be needed once this guideline is
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	Instead, the group acknowledged that information gained from follow-up visits at younger ages would provide more insight into the follow-up requirements at older ages, specifically alternative modes to in- person reviews and assessments (e.g., telehealth, screening questionnaires) for children identified as having lower risk for growth, health and developmental difficulties. However, subsequent guidelines are quite prescriptive, including recommendation for "minimum" set of contacts and need for formal developmental assessment at 2 and 4-5 years for all participants.		launched. No amendment was made in response to this comment.
7	 (Reviewer was asked: Have the risks and potential harms of recommendations been fully considered in the context of clinical practice, including any medico-legal implications that you may be aware of?) Based on consensus opinion, the authors have indicated (on p.54) that the desirable effects of offering structured follow-up care would be at least moderate and likely large for some families and undesirable effects are likely to be small. While I agree that follow-up is likely to be beneficial for individual children and their families, I think that there are some additional considerations that should be addressed. These may have medico-legal implications for services providing follow-up if these guidelines are implemented in their current form and services are not offered or provided to a child who subsequently receives a delayed diagnosis of a developmental problem. 1. Cost The formal developmental assessment at 2 and 5 years are likely to have a significant cost implication for the approximately 3000 children/year born <32 weeks gestation in Australia who are likely to fulfill requirements for follow-up. As cost of formal assessment per child is of the order of \$1000-\$2000 per child per assessment, provision of these services is likely to cost in the order of 3-6 million dollars. These services are not currently available for many of the preterm children who are the focus of these recommendations. Currently many services provide the support recommended for children born less than 28 weeks up to two years; however, the recommendations proposed in this guideline include extending this formal follow-up including formal developmental assessment is required at least 5-fold and has significant funding and staffing implications. While these services may be ideal, the lack of strong evidence supporting the value of systematic follow-up may make funding difficult, resulting in difficulties providing the recommended services. Recommend: it would be helpful if the aut	Please consider and respond to the comments and recommendations from the reviewer.	The guideline development group thanks reviewer 2 for their comment. No economic evaluations of different clinical follow-up models were identified in the systematic review of the literature related to Question 1. Using GRADE guidance, the steering committee elected not to consider resource use in forming recommendations, given the lack of reliable data. No amendment was made in response to this comment.

8	2. Access to formal developmental assessment. The formal assessments are by necessity face-to-face specialised assessments, which may result in greater difficulty of access for children who live in remote locations or are from families with additional needs. These families have been identified in Section 1.6 (p22), with a comment that services should ensure adequate resources are available to engage groups less likely to access follow-up care; however, the recommendation for formal development assessment for the entire cohort may add extra complexity to the service provision for these vulnerable families.	Please consider and respond to the comments and recommendations from the reviewer.	The guideline development group thanks reviewer 2 for this comment. It is not recommended that all children return to a tertiary service to complete formal developmental and cognitive assessments and the guideline promotes a flexible approach to delivery of follow-up based on the needs of children, their families and the abilities of the clinical service.
	3. Lack of focus on children with highest risk The requirement to provide assessments for a high volume of children, without any screening of risk, may dilute the time available for clinical management of children with significant developmental issues. These children and their families often need more extensive support to assist with accessing services and greater time commitments by follow-up clinicians to provide this support.		The guideline development group chose not to recommend a two-tiered approach but instead provided options for a flexible approach which ensures that all assessments did not need to occur in a tertiary setting and could instead be conducted at a local or community health service, or by telehealth. No
	Recommend: As there is lack of evidence for improved outcome with structured assessment of the entire preterm cohort at both 2 years and 4-5 years, the authors may consider providing an option for a two-tier approach. For example, this could include screening of all children through parental report or by local child health services, with referral to tertiary services that can provide formal developmental and cognitive assessments for children who are identified at higher risk for developmental delay or cognitive impairment on a screening assessment. The specific time points for assessment may also need to be more flexible, (e.g. recommend assessment at 2-3 years, rather than "2 years").		amendment was made in response to this comment.
9	(Reviewer was asked: Are there relevant international or well referenced guidelines	Please consider and respond to	Thank you to the reviewer for their comment. A
	(recommendations) on the same topic that conflict with this guideline? If so, is this acknowledged and justified in the guideline?)	reference to the	assessments at 4-5 years of age for the entire cohort
	The International Guidelines referred to in the current proposed guideline provide similar	recommendation that clearer	has been added to the guideline in Chapter 1, Section
	recommendations for assessment of a broad range of issues, including growth, health, sensory,	justification for the inclusion of	1.4 Summary of narrative review (pg. 44) and reads:
	developmental, and behavioural issues. I am not aware of any additional major international guidelines that have not been considered by the authors.	formal assessments at 4-5 years for the entire cohort be included.	<i>"Formal cognitive assessment shortly before the start of formal schooling at 4-5 years corrected age is a</i>
	The Australian guidelines being recommended do not conflict with international guidelines but differ regarding the extent of formal assessments proposed.		common practice and can be utilised for planning future education needs. Early assessments of cognitive development using scales such as he Bayleys may not
	1. UK NICE Guideline (ref: National Institute for Health and Care Excellence, Developmental follow-up of		be indicative of later cognition [80], while assessments
	children and young people born preterm [NICE Guideline No. 72]. 2017:		at 4-5 years are robust and reliable [81] and have the
	www.nice.org.uk/guidance/ng72) is the most extensive and specific international guideline available.		potential to become a major timepoint for the planning
	weeks, and for a subgroup of high risk children born at 30-36 weeks with brain injury/infection/HIE etc.		of education needs."
	The UK guideline recommends assessment at 2 years of medical/developmental/behavioural problems,		
	with development screening (PARCA- Parent Report of Children's Abilities). This assessment can be		

	completed by local child health services or by parental report as it does not require formal developmental assessment unless concerns are identified through screening.		
	The assessment at 4 years includes a formal cognitive assessment (eg WPPSI), but is confined to a higher risk group born <28 weeks, so applies to a smaller cohort of children.		
	2. Guidelines from New Zealand (ref: de Vries, N.K., et al., <i>New Zealand Newborn Clinical Network:</i> <i>Practice recommendations for 2-year follow-up of infants, at high risk of developmental disability.</i> 2022.) recommend comprehensive follow-up on multiple occasions over the first 2 years of life for children identified at high risk of developmental disability including <28 weeks gestation, encephalopathy, severe growth restriction, neonatal surgery, home oxygen, brain infections and chromosomal abnormalities.		
	Standardised assessments for early detection of cerebral palsy (eg GM, HINE assessments) and multidisciplinary developmental support is recommended. A formal developmental assessment using the Bayley or Griffiths assessment is recommended at 2-3 years for all children born <28 weeks gestation. Several other assessments are discussed, although it is not clear if all assessments are utilised for all children.		
	The Australian Guidelines as presented in this draft would lead the world in its recommendation for follow-up for all children <32 weeks gestation to 4-5 years, including formal cognitive assessment at 4-5 years. This is a worthy recommendation; but has not been clearly justified in this draft guideline.		
	Recommend: As implementation may be difficult for some services, the authors should provide clearer justification for the inclusion of formal assessments at 4-5 years for the entire cohort. Alternatively, clinical practice points should emphasise that the children with the highest needs should be prioritised for formal assessment if services are not available for all children.		
	Reviewer Three (Canada)	NHMRC Comment	Developer response
10	(Reviewer was asked: Has the appropriate evidence been identified and reviewed in line with the scope and clinical questions posed by this guideline?)	Please review comments and consider if a definition of very preterm should be included in	The guideline development group thanks Reviewer Three for their comment. The definition of very preterm (less than 32 weeks) has been added to the
	The appropriate evidence has been identified and reviewed in line with the scope and clinical questions posed by this guideline.	the Plain Language Summary.	Plain Language Summary in the Guideline Document on page 10.
	The definition of very preterm (<32 weeks) is not easily determined in the Plain Language Summary and should be considered. The systematic search and quality assessment employed well recognized framework PICOT and GRADE.		
	As an aside, in identification of risk and resilience factors the positive influence of structured childcare and addressing parental mental health concerns on child development seemed under identified, although the risk of ACEs was noted. Recognizing the limitations associated with evidence reviews,		

	Section 5.4 p 63, and 6.0 p 65 are well stated, aligned with the evidence and offer incentive to better understand protective factors		
11	(Reviewer was asked: Have the risks and potential harms of recommendations been fully considered in the context of clinical practice, including any medico-legal implications that you may be aware of?) This is not my area of expertise, however, the potential risks of follow up have been articulated, and linked to the quality of evidence (eg. Low quality evidence about adverse outcomes associated with follow up). As noted, families will still have agency over engaging with follow up.	For noting.	Comment noted.
12	(Reviewer was asked: Are there relevant international or well referenced guidelines (recommendations) on the same topic that conflict with this guideline? If so, is this acknowledged and justified in the guideline?) To my knowledge, there are no relevant international or well referenced guidelines (recommendations)	For noting.	Comment noted.
	on the same topic that conflict with this guideline.		
13	Other commentsThe document is well prepared and addresses contemporary issues associate birth <32 weeks gestational age. The guidelines encouraging routine follow up and assessment align with evidence and clinical practice objectives to optimize outcomes for infants at risk. Implementation of these guidelines will be of value to the population.Emerging evidence from longitudinal studies/cohorts/ offers some insight into protective factors for preterm children. These include access to early intervention, structured childcare, language supports, parenting practices &competency, parenting supports and supportive environments and addressing mental health concerns. Recognizing the challenges of RCT approaches to understanding protective factors, perhaps some of these can be evaluated for inclusion in documents that enable clinicians and families to discuss 'what to do' as concerns emerge. Addressing concerns early can enhance 'readiness for school' among this population with limited risk of harm, ultimately, alleviating suffering and improving outcomes for children and families.The committee is to be commended for addressing this issue with contemporary guideline.	Please consider these comments and whether reference to protective factors would enhance the guideline.	The guideline development group thanks reviewer three for this comment. The group feels that this is best addresses as an implementation tool developed with experts alongside consumer groups that might facilitation discussions with clinicians and families. This will be considered in the development of the dissemination and implementation plan.
	Reviewer Four (United Kingdom)	NHMRC Comment	Developer response
14	These are well written guidelines in easily accessible language. I am impressed by the sensitivity to families who have additional or different needs and may less likely access follow-up services. These groups are outlined on p. 22. The Chairs, Steering Committee and project team have been sensitive to include a wide range of stakeholders in the Guideline development group and to have consulted widely in Australia.	For noting.	Comment noted.
15	 The synthesis of evidence is mostly comprehensive and competently carried out and written up in accessible language. However, there are a few points that I would want to raise where I am not sure how the evidence was obtained or why evidence was not sought. a) P.46 – in the recommendation 1 it is stated "Corrected age should be used when considering a child's growth, health, and development". There is consensus in the literature to correct for 	Please consider and respond to each of these comments from the reviewer.	a) Thank you to the reviewer for their comment. Recent evidence (Gould, et al. 2021) suggests that the magnitude of difference between corrected and uncorrected cognitive scores diminishes after 3 years. The magnitude of difference is present but less than motor scores. However, growth disparity

gestational age in the first two years of life but assessments at later age (e.g. 4-5 years of age) are in many follow-up studies scheduled at chronological age. Just using simulation of comparing corrected with chronological age measurement (e.g. growth or cognitive scores) indicate that the lower the gestation of the child at birth the larger the difference in outcome score and these are detectable into school age (purely numerically) but the clinical significance reduces with advancing age. The issue is: should corrected age assessment be done at the assessment just before school age although the chronological age (and cut-off dates) in most countries is used to decide on school entry? Maybe Australia is different and all VPT have delayed school entry? Teachers and parents assess their child to peers of the same chronological age rather than corrected age. Is there evidence that correcting for age beyond, let's say 2-3 years has higher predictive validity than chronological age assessment? Maybe, both measures should be reported (even if assessment scheduled according to post conception age).

b) As outlined in the tables (no table numbers are given – maybe should be numbered) from p. 41 onwards, relationships with others, i.e. not just with parents but also siblings in the family and with peers are important in child development. No friends, poor peer relationships or being a victim of bullying has been shown in dozens of follow-up studies to have adverse effects on mental and physical health. In general population studies the evidence is strong and of high quality. In contrast there are only very few studies of those born very preterm – mainly because this is not part of routine follow-up or research follow-up studies with very few exceptions. Other guidelines mostly recommend assessment of parent and other relationships.

Considering the strong evidence that social relationships with parents, siblings and peers matter for child development and outcome, I am surprised that these are not included in the literature reviews and in the Follow-up schedule (p. 49f.). The behaviour measures suggested (e.g. SDQ, CBCL) have some questions about peer relationships but none about sibling relationships or information about parenting.

c) Parenting. It is acknowledged that parenting is important. However, the reviews do not include parenting as a potential "resilience factor" (I prefer to call it a protective factor). Parent wellbeing or depression are considered but that is quite different from parenting behaviour. Gold standard measures include short observations of e.g. caretaker - child interaction and their ratings. These include observation of cognitive stimulation to sensitivity and reciprocity of caretaker-child relationship. There are also parent report measures of warmth of interaction (e.g. Pianta). Considering that most early interventions post discharge of VPT focus on changing parent – child interaction, I find this a big omission in the follow-up schedule. It is presumably one of the strongest protective factors for at risk children.

d) It is sensibly suggested that for children with complex needs a lead clinician should be determined to coordinate. That is principally a good suggestion. However, in Europe some have adopted an approach of appointing a case manager that does not need to be a clinician with many competing demands. The case manager also helps parents to organise transport, completing claims for social benefits etc.

Please ensure that all tables are numbered in the final draft guideline submitted to NHMRC. continues to be seen even after 2 years. In Australia, children may be held back from commencing school, especially if they were born preterm.

Reference: Gould et al., 2021 https://journals.plos.org/plosone/article/ citation?id=10.1371/journal.pone.0256824

b) All tables have been numbered. The guideline development group acknowledges that social relationships with parents, siblings and peers' matter for child development and outcome and these were thought to be included under mental health, with assessment of parent-child attachment listed as a footnote in the follow-up schedule and resources and information needs present at each timepoint of the follow-up schedule. It is anticipated these resources and information needs follow-up should include information about parenting and social relationships should the need arise. The follow-up schedule is not intended to replace clinical judgement and individual clinicians should be guided in their follow-up by the needs of the children and their families, as described in the clinical practice points.

c) The guideline development group acknowledges the importance of parenting in the development of children born VPT. Parent-child attachment is encouraged to be included in mental health of the family unit in all follow-up timepoints as denoted by the footnote g in the follow-up schedule.

d) The guideline development group thanks reviewer 2 for this comment. The guideline development group felt as there was not enough evidence to support different follow-up structures, such as an additional case manager, which would pose additional implementation barriers to incorporating the followup recommendations. However, children with complex needs should be referred to relevant follow-up services which may or may not include case coordination services.

16	 e) In the recommended follow-up schedule, I cannot see anywhere a structured assessment of the socio-economic (SES) background of the family (education, household income, housing, social benefits etc.). As the evidence shows SES and ACES are strongly associated with developmental outcome, that is an omission. Or do "Resources/information" in the table refer to it – if yes than please clarify. As clinicians are poorly trained to assess SES, ACES – this should be explicitly included in the guidelines. f) I wonder why it is not explicitly stated that structured follow-up is necessary for quality monitoring of the NICU's in Australia and information should be feedback in regular audits. This is highly relevant to improve the quality of care and identify units of excellence or those that may need improvement. It also allows to detect whether there are trends in quality of survival and not just in survival. For example, the EFCNI guidelines strongly advocate this. I strongly agree with the future research priorities a) to investigate the impact of structured, preterm specific follow-up programmes; b) further research on risk and in particular resilience factors (although I would call them protective or promotive factors as resilience is a process not a factor). (Reviewer was asked have the risks and potential harms of recommendations been fully considered in the context of clinical practice, including any medico-legal implications that you may be aware of?) As outlined in the guidelines there is very little empirical evidence (just 1 study) of how structured follow-up is necessary and helpful to plan medical, social and academic pathways. There may be medico-legal implications if it is detected that children of a particular NICU or region may do worse than those from others (but 1 am not a lawyer). Ethically, it is correct that potential issues are identified through structured follow-up to improve the care of all IVPT children to allow for equity. Five assessment points a	Please review these comments and consider whether the reviewer's comments about implementation challenges and resource issues should be addressed in the implementation plan.	 e) The guideline development group thanks reviewer 2 for this comment. SES and ACES are important factors to assess and should be included in the resources/information follow-up. A footnote to the follow-up schedule has been added in response to this comment. "Consider socio-economic background assessment of family when considering information needs". f) The guideline development group thanks reviewer 2 for this comment. Auditing and feedback to NICUs around Australia occurs for the infants born before <28 weeks by the Australian and New Zealand Neonatal Network. Additional audit and feedback for children born between 28 and 32 weeks and their families is outside the scope of resources of the guideline. The guideline development group thanks reviewer four for their comment. The implementation challenges and resources issues mentioned have been addressed in the implementation plan in the development of additional resources such as examples of guideline implementation barriers and mitigation strategies in Table 7, pg. 15-16 of the Dissemination and Implementation Plan.
	development of children in the first few years may be challenging to implement in all communities and		
17	may be dependent on resource issues. (Reviewer was asked Are there relevant international or well referenced guidelines	For noting.	Comment noted.
	(recommendations) on the same topic that conflict with this guideline? If so, is this acknowledged		
	and justified in the guideline?) The major English language guidelines are referenced. There are others by national organisations in		
	non-English speaking countries.		
	I do not find conflicts with these Australian Guidelines. However, the here proposed guidelines is wider		
1	or narrower than some others in the areas of assessment, age limited to preschool for follow-up or the		
	group definition. For example, the NICE guideline is narrower (extremely preterm target group) while		
	the EFCNI guidelines include sick children who are not VPT that may require follow-up care.		