

## Long-term Follow-up and Outcome of Extremely-low-birth-weight (ELBW) Infants

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### Abstract

**Introduction:** Modern day obstetric and neonatal care has dramatically increased the survival of the extremely-low-birth-weight (ELBW) neonates. As the limits of viability decrease, it is of paramount importance to have reliable data on long-term morbidity. Long-term follow-up of these high-risk survivors is thus becoming an integral part of neonatal intensive care units. **Methods:** Detailed Medline search and review of leading journal articles were done to assess the current data on long-term outcome of ELBW infants. **Results:** The developmental outcome of the ELBW infant is determined by a complex interaction of medical and environmental factors acting on a developmentally vulnerable premature brain. In early childhood, 13% to 37% of ELBW survivors have a significant delay in cognitive function while 7% to 17% have neurosensory impairment viz. cerebral palsy. Advances have been made in measuring functional outcome to assess the impact of ELBW births on long-term quality of life and skills for independent living. Measuring school age outcome is an important landmark in the longitudinal follow-up of ELBW infants and most reports show high rates of cognitive impairment as well as increased incidence of learning disability and school difficulties as well as behavioural problems. The ELBW adolescent and young adult continue to lag behind in academic achievement and cognitive score. However, more than half of the ELBW survivors function within the normal range of variability and their self-reported quality of life in adolescence continues to be comparable to that of their peers. **Conclusion:** In managing ELBW infants, a holistic, systematic approach is needed to assess the degree and impact of impairment on their daily function and issues related to quality of life.

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**Key words:** Behavioural disorders, Cerebral palsy, Cognitive skills, Learning disability, Scholastic performance

### Introduction

With the progressive improvement in the survival of premature neonates,<sup>1,2</sup> including those born at the extreme edge of viability,<sup>3</sup> there has been a great degree of interest focused on the functioning of these high-risk survivors and their outcome into childhood<sup>4-6</sup> and recently up to adolescence<sup>7,8</sup> and early adulthood.<sup>9</sup> Prospective follow-up programmes have been established by neonatal centres either individually or as part of a regional, national or international network to report in a systematic manner, long-term medical, neurodevelopmental, behavioural and educational outcome. The majority of studies reporting long-term outcome of premature infants in the mid-1990s have given data on follow-up till early childhood or till 8 to 9 years of age. However, as these cohorts continue to be followed up longitudinally, more data are becoming available on follow-up till adolescence and beyond.<sup>7-9</sup>

There is extreme variability in the published data due to marked heterogeneity in the nature of samples studied. Some of the heterogeneity has been attributed to the use of

institutional-based samples, small sample size, high attrition rate and differing exclusion criteria. Marked variation in the assessment tools, non-uniform definitions of disability and school failures as well as poor selection of control groups further increases the heterogeneity.<sup>8,10-12</sup> Thus, the true extent of the effect of prematurity on cognitive and school outcome remains unclear.

Amongst the cohort of preterm infants, those weighing less than 1000 g at birth (ELBW) are at higher risk of adverse long-term outcome compared to preterm infants of greater birth weight.<sup>5,13</sup> Higher incidence of cerebral palsy, blindness, deafness and adverse cognitive and behavioural outcome has been reported in several studies on long-term follow-up of ELBW infants.<sup>5,13-15</sup> Severe disability is common in children born extremely preterm and remains a challenging issue in the coming years.

Though studies which report outcome based on gestational age are extremely vital in helping perinatologists and parents in decision making at the threshold of viability, using birth weight categories for reporting outcome

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continues to be useful as a precise measurement on which analysis may be carried out consistently. Morbidity seems to be inversely related to gestation and birth weight.<sup>3</sup> Valid concerns have thus risen as to whether the rate of developmental disability among survivors would increase with improved survival of ELBW babies. Thus, assessment of long-term outcome is becoming increasingly important in follow-up of premature newborns. Increasing health care costs and ethical debates at limits of viability are other important factors which make long-term follow-up critical and an integral part of neonatal intensive care units.

### **Pathogenesis and Risk Factors of Neurodevelopmental Impairment**

The developmental outcome of the ELBW infant is determined by both biological prenatal and perinatal factors as well as postnatal environmental factors. These factors do not act in isolation, but are closely interrelated and it is often quite difficult to assess precisely the influence of each individual factor on the long-term outcome of the ELBW infant.

Perlman<sup>16</sup> in a recent review has summarised the pathogenesis of the neurobehavioural deficits in the premature very-low-birth-weight (VLBW) infants with a summary of the potential risk factors. One of the principal underlying features is the extreme vulnerability of the developing premature brain to injury secondary to periventricular white matter haemorrhage or ischaemia. Any hypoxic-ischaemic injury during this critical period could result in increased excitatory amino acids, like glutamate, which result in disruption of the organisational events in the brain and damage to the basal ganglia and hippocampus. A recent report<sup>17</sup> comments on the increased vulnerability of hippocampus in the VLBW infant with lower hippocampal volumes resulting in specific deficits in everyday memory and mathematics. Other reports<sup>18,19</sup> using magnetic resonance imaging (MRI) have also demonstrated decrease in whole brain volume, cortical grey matter volume, hippocampal volume, ventricular dilation and thinning of corpus callosum in adolescents who were born very premature.

Superimposed on the pre-existing vulnerability of the premature brain, a variety of clinical risk factors have been implicated in adversely affecting neurodevelopmental outcome. Chronic lung disease (CLD) which is defined as oxygen dependency at 36 weeks has been definitively linked to adverse motor and cognitive outcome<sup>20,21</sup> and is one of the most significant predictors of adverse outcome in the absence of white matter injury. The underlying reasons postulated by Perlman<sup>16</sup> have been recurrent hypoxia, hypercarbia and acidosis associated with CLD as well as poor nutrition and growth and frequent use of

postnatal corticosteroids which increase risk of injury to the basal ganglia and hippocampus. Postnatal corticosteroids, widely used in the management of CLD, are being increasingly associated with adverse long-term outcome in ELBW infants, namely, increasing incidence of cerebral palsy and neurodevelopmental impairment,<sup>20,22</sup> and this adverse outcome is postulated to be due to structural and functional alteration of the developing brain with decreased hippocampal and cortical grey matter volume, as well as altered myelination and brain cell differentiation.<sup>23,24</sup>

Repetitive antenatal steroids have also been implicated in animal and human studies<sup>25,26</sup> to be associated with delayed myelination and decreased brain weight, both of which may have adverse long-term sequelae. Other clinical factors associated with adverse long-term outcome have been hypothyroxinaemia of prematurity,<sup>27</sup> which may result in necrosis, and apoptosis of oligodendrocytes and white matter damage.<sup>28</sup> Hyperbilirubinaemia, which is a nearly universal problem in ELBW infants, may be associated with bilirubin-induced neuronal injury secondary to increased excitotoxic amino acids and the known affinity of bilirubin for basal ganglia and hippocampus.<sup>29,30</sup> Essential fatty acids deficiency which may occur in preterm infants fed formula milk may also affect brain growth and development resulting in hypomyelination<sup>31</sup> and cognitive impairment.<sup>32</sup>

Apart from the clinical factors described above, stressful environmental factors may also play a role in adversely affecting neurodevelopmental outcome. Common among these are loud noise<sup>16,33</sup> and constant bright light,<sup>34</sup> which may alter behavioural response. Social and environmental risk factors after discharge in the form of parental education, race, socioeconomic status, marital status and maternal depression may also have a significant impact on cognitive and behavioural outcome as well as special educational requirements.<sup>35-39</sup>

Thus, there is a complex interaction of medical and environmental factors acting on a developmentally vulnerable premature brain with profound effect on long-term outcome of ELBW infants.

### **Early Childhood Outcome**

In most reports on early childhood outcome of ELBW infants, major neurodevelopmental impairment has been defined as loss or abnormality of function due to presence of severe cerebral palsy, deafness needing hearing aids, blindness and/or cognitive function less than 2 standard deviations below mean.<sup>4,37,40</sup>

ELBW children may present with a wide spectrum of neurological or neurosensory abnormalities ranging from severe cerebral palsy to minor neurological dysfunction.

Cerebral palsy is the most common neurological abnormality and risk increases with decreasing birth weight.<sup>20</sup>

Studies from various countries like the USA, Finland and Australia have reported a prevalence rate of cerebral palsy in ELBW infants ranging from 7% to 17%<sup>15,20,40-42</sup> at 1 to 3 years of age, while prevalence of other severe neurosensory impairment like blindness and deafness ranges from 1% to 6% (Table I).<sup>15,20,41-43</sup>

In Singapore's KK Women's & Children's Hospital, its largest tertiary perinatal centre, there have been 271 (72%) survivors of 373 live-born ELBW infants from 1990 to 1998 and the incidence of cerebral palsy in survivors at 2 years was 10%; blindness, 2.2%; and deafness 1.3%; 24% had Bayley Mental Development Index (MDI) score less than 70 (unpublished data).

Significant cognitive delay as defined by psychometric score of MDI <70 is reported in 13% to 37% of ELBW infants.<sup>20,43,44</sup> Prevalence of delayed cognitive function is commoner than the prevalence of neurosensory impairment. Within the ELBW group, neurodevelopmental outcome is expectedly better for larger infants weighing >750 g compared to those between 500 and 750 g.<sup>5,20</sup> Neurodevelopmental outcome for the extremely tiny baby <500 g has been reported to be comparatively poorer.<sup>45</sup>

Over time, in spite of improving survival of ELBW infants born in the late 1980s and early 1990s, the rates of neurodevelopmental impairment in North America have remained largely unaltered,<sup>13,15</sup> or worsened as reported by

Emsley in the UK.<sup>46</sup> The Australian Victorian Infant Study Group<sup>44</sup> studied ELBW infants born in the State of Victoria over 3 time periods between 1979 and 1992. They reported improved outcome for survivors born in 1985 to 1987 compared to 1979 to 1980, but no further improvement into the 1990s.

## Functional Outcome

Advances have been made in recent years in measuring functional skills in mobility, self-care and communication. Earlier studies did not routinely assess functional disability of the preterm VLBW cohort. Severity of cerebral palsy has been measured using the number of limbs involved and using gross and fine motor performance milestones. A functional measure commonly used is Gross Motor Functional Classification System (GMFCS)<sup>47</sup> which evaluates a child's skills in rolling, sitting, crawling, walking and running. Msall and Tremont<sup>48</sup> have illustrated that as neuromotor impairment involves more limbs, ambulation potential is progressively reduced and associated sensory and developmental disability in the field of communication, cognitive skills, epilepsy and learning disorders increase. In infants with cerebral palsy, hemiplegia, head righting by 9 months, sitting balance at 2 years and crawling at 30 months, have been used as prognostic indicators to predict ambulation.<sup>49,50</sup> Studies have documented that 100% of children with hemiplegia walked, and 75% to 90% of those with spastic diplegia attained ambulation, in contrast to 0% to 33% of those with quadriplegia.<sup>51-53</sup>

In order to assess long-term quality of life and skills for

TABLE I: NEURODEVELOPMENTAL HANDICAP AT 18 MONTHS TO 3 YEARS IN ELBW INFANTS IN THE 1990s

| Country (centre)                                | Year of birth | Birth weight (g) | No. of survivors/<br>No. of total live births (%) | No. examined | Cerebral palsy (%) | Blindness (%) | Deafness (%) | MDI <70  | Severe handicap* |
|-------------------------------------------------|---------------|------------------|---------------------------------------------------|--------------|--------------------|---------------|--------------|----------|------------------|
| USA (single centre <sup>15</sup> )              | 1990-1992     | 500-750          | 49/114 (43)                                       | 49           | 5/49 (10)          | 1 (2)         | 3 (6)        | 9 (20)   | 15 (31)          |
| NICHD, USA (49) (multi-centre <sup>20</sup> )   | 1993-1994     | 401-1000         | 1527/2498 (63)                                    | 1157         | 187 (17)           | 36 (3)        | 38 (3)       | 392 (37) | 553/1122         |
| Victoria, Australia (regional <sup>40</sup> )   | 1991-1992     | 500-999          | 241/429 (56)                                      | 237          | 22 (9)             | 5 (2)         | 2 (0.8)      | 29 (12)  | 16 (6.8)         |
| Finland (national <sup>41</sup> )               | 1996-1997     | <1000            | 211/351 (62)                                      | 208          | 23 (11)            | 3 (1.5)       | 6 (3)        | —        | 18               |
| KKWCH, S'pore (single centre, unpublished data) | 1990-1998     | <1000            | 270/372 (72)                                      | 248          | 24 (10)            | 6 (2.4)       | 4 (1.6)      | 60 (24)  | 24               |

\* Definition of severe handicap:

Ref. 15: Mental Developmental Index (MDI) <70 and/or cerebral palsy, blindness, deafness;

Ref. 20: Cerebral palsy, abnormal neurologic examination, blindness, deafness, MDI <70 or PDI <70;

Ref. 40: bilateral blindness, non-ambulant severe cerebral palsy, MDI <70 or -2 SD below mean in alternative test;

Ref. 41: blindness, hearing impairment, cerebral palsy or convulsions;

KKWCH: MDI <70, non-ambulant cerebral palsy, bilateral blindness, deafness.

ELBW: extremely low birth weight; KKWCH: KK Women's and Children's Hospital; NICHD: National Institute of Child Health and Development

independent living, it is critical to assess functional outcome, as it will impact on literacy, social competency and interaction and participation in the community. Measurement of functional status links neurological impairments, physical health, developmental skills and family socioeconomic means, and this provides a more complete understanding of the child's current abilities and needs of the child and family. Healthcare providers can also then prioritise health care resources. Commonly used tools to measure the functional outcome include Vineland Adaptive Behaviour Scale (VABS),<sup>54</sup> the Functional Independence Measure for Children (WeeFIM)<sup>55</sup> and Batelle Developmental Inventory (BDI).<sup>56</sup>

Msall et al<sup>57</sup> assessed neurodevelopmental and functional status of extremely preterm infants  $\leq 28$  weeks born between 1983 and 1986 at kindergarten entry, 21% of the survivors had neurodevelopmental impairment and 5% had multiple disabilities. The severe functional limitations including inability to walk, talk or perform self-care activities of daily living were present in  $<5\%$  of survivors.

In an assessment of functional outcome of ELBW infants born between 1993 and 1994 in the large National Institute of Child Health and Development (NICHD) network, at 18 to 22 months 70% of the cohort were walking fluently, 86% had a pincer grasp and 80% were feeding independently.

Functional morbidity has been shown to consistently increase with decreased birth weight<sup>4,13,20</sup> and was notably higher in babies  $<500$  g.

### School Age Outcome

Limiting follow-up to the first 2 to 3 years of life is often inadequate and unreliable because of the transient nature of neurological impairments which may improve with time and show motor catch-up.<sup>20,58</sup> Furthermore, developmental delay at 2 years may overestimate intellectual impairment at 8 years.<sup>59</sup> On the other hand, subtle cognitive difficulties, behavioural learning disorders which affect academic achievement may not be evident in the early preschool years. Of the studies reporting outcome of ELBW infants born in the 1980s, only a quarter of them included follow-up up to 5 years or older and a meta-analysis of these studies<sup>60</sup> raised the issue that ELBW infants may have subtle dysfunction not revealed in gross IQ measurements. This indicated that specific deficits reflecting learning disabilities and behavioural and social outcomes need to be studied. Thus, measuring school age outcome is an important landmark in the longitudinal follow-up of ELBW infants. Increasing amounts of data are currently available in the cognitive, educational and behavioural outcome of children born ELBW. These longitudinal studies from birth to school age  $\geq 5$  years have reported ELBW infants experiencing academic difficulties in school with need for additional educational assistance of varying degrees.<sup>4-6,13,14,61-65</sup>

### Cognitive Outcome

Studies on cognitive outcome of ELBW infants at school age showed that the mean IQ scores ranged between 86 and 91<sup>4,13,14</sup> and rates of IQ score  $<70$  ranged between 8% and 18%. The ELBW infants had lower scores than higher birth weight controls even when socio-demographic differences were accounted for. Within the ELBW group, Hack et al<sup>5</sup> reported on a regional cohort of  $<750$  g birth weight children and showed that they had a mean score of  $87 \pm 15$  with subnormal scores  $<70$  in 20% of the children. This was in comparison with a score of  $93 \pm 14$  in children weighing 750 to 1499 g and  $100 \pm 13$  for children born at term.

Another study from New Zealand<sup>61</sup> reported outcome on a national cohort of 298 VLBW survivors at 7 to 8 years in comparison to 1000 historical controls in a general population, and demonstrated that VLBW infants and ELBW infants in particular had significantly higher levels of cognitive impairment. The authors reported that after adjusting for socio-demographic and perinatal co-variables, 36% of ELBW children had WISC-R full IQ score  $<85$  compared to 24% of VLBW children and 10.7% of the controls. Apart from cognitive impairment, the ELBW children also demonstrated poorer levels of functioning across all domains namely behaviour, school achievement and need for special education.

In a recent meta-analysis<sup>62</sup> looking at the outcome of school-aged children born preterm, the authors concluded that preterm births were associated with lower cognitive scores and increased risk for Attention Deficit Hyperactivity Disorder (ADHD) at school age, compared to term controls. Fifteen case control studies were included in this meta-analysis and a lower cognitive score was noted in the cases with cognitive scores being directly proportional to the birth weight and gestational age. The authors further concluded that a mean difference of 10.9 points between the cognitive scores of the cases and controls was clinically significant and would have an impact on the educational requirement of the preterm births and affect their future socio-economic potential.

### Neuro-psychological Outcome

#### *Academic Achievement and Learning Disability*

Neuro-psychological tests, which assess reading, spelling, mathematics, perceptive motor performance, memory, perceptual and language skills,<sup>4,14</sup> have consistently revealed poorer performance in ELBW children compared to normal birth weight children.<sup>4,14,66</sup> Learning disabilities are extremely common among ELBW children. Traditionally, learning disability is identified if there is a discrepancy between observed and expected level of achievement.<sup>67</sup> A wide array of neuro-psychological tests have been used to

assess reading, spelling, arithmetic and writing. In an assessment of a national cohort of VLBW babies in New Zealand between 7 and 8 years of age, Horwood et al<sup>61</sup> demonstrated poorer school performance and higher need for special education in comparison to controls from a general population. Whitfield et al<sup>65</sup> assessed 115 ELBW survivors and 50 controls in a regional cohort and found that even ELBW with global IQ >85 scored significantly lower in tests of gross and fine motor control, visual motor integration with lower academic achievement in reading, arithmetic and writing. ELBW survivors were 3 times more likely to have learning disability and 30% to 41% of ELBW with learning disability had multiple areas of learning disabilities.<sup>65,66</sup> Similarly, Hack et al<sup>4</sup> demonstrated that among neurologically normal ELBW children, those with birth weight <750 g performed poorly on tests of mathematics skills. Having difficulties in mathematics, independent of IQ scores, have been reported widely in other reports<sup>64,68</sup> and has long been considered to be a sensitive marker of impairment in the longitudinal studies of VLBW infants.

ELBW children are more likely to experience school difficulties with a higher need for special educational assistance. This need increases progressively with decreasing birth weight.<sup>63,64</sup> Increasing number of studies are also documenting the utilisation of special educational resources by nearly half of ELBW survivors. Studies have shown that at 8 years >50% of ELBW need special assistance in the classroom, 20% need special education, while 20% to 30% exhibit signs of ADHD.<sup>4,38,39,63,65</sup>

This increased need for remedial education in the ELBW cohort needs to be taken into account while calculating the increased educational cost and needs attributable to the low birth weight at the regional and national level. Greater attention needs to be focused on evaluating strategies that would alleviate school difficulties.

### *Behavioural Outcomes*

A growing number of studies have led to an increasing consensus that VLBW infants, at school age, tend to have increased incidence of behavioural and attention related problems, namely, attention deficit and hyperactivity. Hack et al,<sup>4</sup> in a study of outcome of school age children with birth weight <750 g, revealed a significantly higher risk of neurobehaviour dysfunction and poor school performance as measured using the Child Behaviour Checklist. Thirty-seven per cent of the children with birth weight <750 g had abnormal T scores, compared to 21% of 750 to 1499 g birth weight groups.

In a recent meta-analysis, Bhutta et al<sup>62</sup> concluded that preterm children have nearly a 3-fold higher risk for developing ADHD. The tools used to assess behaviour

TABLE II: SUMMARY OF SCHOOL AGE PROBLEMS IN ELBW SURVIVORS

|                                                                   |
|-------------------------------------------------------------------|
| Cognitive outcome                                                 |
| • Lower cognitive scores <sup>4,13,14,61,62</sup>                 |
| Academic achievement/learning disability <sup>4,14,64,65,67</sup> |
| • Poor reading, arithmetic, spelling                              |
| • Poor motor performance                                          |
| • Poor visuo-motor co-ordination                                  |
| • Poor visuo-perceptual and perceptual motor skills               |
| • Poorer expressive and language skills                           |
| • Academic failure, especially in mathematics                     |
| • Poorer memory skills                                            |
| Special educational needs <sup>62,63</sup>                        |
| • Regular class with special assistance                           |
| • Grade repetition                                                |
| • Special school                                                  |
| Behavioural problems <sup>61,62</sup>                             |
| • Attention deficits/hyperactive                                  |
| • Inattention                                                     |
| • Disability                                                      |
| • Impulsivity                                                     |
| • Hyperactivity                                                   |
| • Conduct problems                                                |
| • Aggression                                                      |
| • Destructive behaviour                                           |
| • Oppositional behaviour                                          |
| • Anxiety/withdrawal behaviour                                    |

ELBW: extremely low birth weight

usually include parental and teacher rating of the children's behaviour using various standard questionnaires.<sup>69,70</sup> The behavioural manifestations in this meta-analysis were reported as externalising (hyperactivity, delinquency) or internalising (anxiety, depression, phobias). The basis of the development and underlying possible biological mechanisms of ADHD in the meta-analysis by Bhutta et al, was proposed to be impairment of pre-attentional mechanisms, altered threshold for arousal, poorer attention states as well as poorer information encoding. Stewart et al<sup>18</sup> in a recent MRI study reported that >55% of a cohort of preterm infants <33 weeks had abnormal MRI findings and qualitative behavioural impairment in this cohort was significantly related to structural abnormality seen.

A summary of the school age problems seen in ELBW survivors is illustrated in Table II.

### **Outcome at Adolescence/Adolescent Follow-up**

Longitudinal follow-up of ELBW children up to adolescence is important to assess whether the increased morbidity in ELBW children seen in early childhood and school age persists into later years or improves with time.

Saigal<sup>8</sup> has reviewed the data on follow-up to adolescence and concluded that VLBW children continue to lag behind their normal birth weight peers in areas of cognition and scholastic achievement, with higher prevalence of learning difficulties and behaviour problems. Reports from the

USA, Canada and Australia<sup>7,8,71-74</sup> have shown that ELBW children had lower cognitive scores than heavier VLBW children and controls with a difference of 8 to 18 IQ points between ELBW children and controls. Between 11% and 17%<sup>73,74</sup> of ELBW children are seen to have subnormal IQ scores <70 compared to 0% to 7% in controls. Even apparently normal teenagers of ELBW children with IQ >85 score lower than controls.<sup>73</sup> Lower cognitive scores often translate into poorer academic performance and ELBW children are reported to have poorer academic achievement especially in mathematics skills at adolescence.<sup>64,65,68,73,74</sup>

School difficulties, with higher need for educational assistance and grade repetition, have been reported to be extremely common in ELBW teens, with 30% to 58% needing remedial assistance in areas of reading, spelling, mathematics and writing.<sup>68,73,74</sup> Psychometric measures at 8 years seem to be useful in predicting subsequent educational and cognitive outcome in the teenage years.<sup>72,73</sup>

Behavioural and psychiatric disorders are also reported to be significantly commoner in VLBW adolescents than controls, with increased prevalence of ADHD, anxiety and depression.<sup>8,65,75</sup>

### Early Adulthood

On follow-up to 20 years, Hack et al<sup>9</sup> reported fewer VLBW young adults graduated from high school or enrolled in a 4-year college programme compared to normal birth weight young adults. They also had a lower mean IQ score and lower academic achievement scores, reflecting a persistence of poor performance into young adulthood. They were also more likely to have chronic health problems. On a more optimistic note, however, these VLBW survivors also demonstrated similar or lower risk-taking behaviour and criminal activity.

Compared to health professionals, parents and children seem to have a different perspective regarding health status and quality of life.<sup>76</sup> Saigal et al<sup>76,77</sup> reported that, based on direct self-reporting of health status and utility scores, the ELBW adolescents had higher morbidity and poorer quality of life than control teenagers. Nevertheless, the majority of the ELBW cohort viewed their health-related quality of life to be satisfactory.

### Conclusion

There is an emerging consensus that the high-risk premature ELBW neonate continues to be a high-risk child, adolescent and young adult with lower cognitive and scholastic achievement and higher behavioural problems, neurosensory impairment and chronic health problems. It is important to be cognisant of and recognise the increased magnitude of academic problems in ELBW children, in order to ensure early diagnosis and adequate educational assistance. However, even though ELBW survivors

demonstrate a poorer level of functioning in many domains compared to their peers, more than half of them function within the normal range of variability and their self-reported quality of life in adolescence seems to be very satisfactory and comparable to their peers. It is thus vital to conduct systematic well-designed longitudinal follow-up studies using standardised parameters to assess the presence and severity of impairment and disability. Furthermore, a more holistic approach<sup>78</sup> is needed to assess the significance and functional impact of impairment on the child, family and society. It is also important to evaluate the quality of life using well-validated modern instruments.

If prognosis of the extremely high-risk preterm infant needs to be improved, then an increased understanding of the underlying biologic mechanisms which result in damage to the premature brain is important. Use of newer technique like MRI imaging to diagnose structural brain defects is important and attention needs to be focused towards minimising prevalence of these structural brain defects. The close and important interaction between the environmental, social and biological factors needs to be studied so as to optimise the outcome of these vulnerable members of society.

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