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Preterm outcomes and evidence synthesis

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Evidence synthesis has become big business. The systematic review has become the highest form of evidence, despite many studies using different methodologies, drug preparations or interventions. Putting a disparate group of studies together may increase confusion rather than clarify outcomes. In putting studies together great care needs to be taken to compare like with like, insofar as is possible.

In 1989, Lesley Mutch and colleagues identified some principles to assist in carrying out and reporting follow up studies, and subsequent suggestions were made for the classification of cerebral palsy and disability. The purpose of these initiatives was to bring a measure of conformity to early studies in the area, as it was acknowledged that researchers would make comparisons. Since then we have a range of initiatives to bring consistency to definitions, for example using the Gross Motor Function Classification System or the Surveillance of Cerebral Palsy in Europe classification of cerebral palsy, and for definitions of populations born at extremely low gestational ages.

The (mis-)perception of disability and its value in counselling parents about outcomes has now assumed importance. In this issue of DMCN, Pascal and colleagues present an evidence synthesis of outcome reports for very preterm children born since 2006.[1] Their stated aims are to provide parents with robust prognoses and for benchmarking.

Estimating such outcomes is challenging. Firstly, because the background mortality rate is a key issue. This is poorly described in most studies, which fail to report the proportion of births for whom there was active intervention. Put simply, the elephant in the delivery room is the self-fulfilling prophesy of death if no action is undertaken for births at 24 weeks of gestation and below.[2] Without knowing this, counselling and benchmarking are impossible.

Describing outcomes is likewise challenging. Probably the easiest is cerebral palsy, where we have recommended classifications and can simply grade function as a descriptive measure, although this too misses the subtlety of the pervasive effect of cerebral palsy on the social functioning and inclusion for an individual. Cerebral palsy is also probably the easiest major adverse outcome to predict from neuroimaging and clinical assessment in this group.

A greater challenge is in the evaluation of 'cognitive' impairment, the commonest and most problematic sequel of very preterm birth. Over the past 20 years we have developed a reliance on developmental test scores that I find somewhat challenging. Professional consensus suggested we use scores below -3 standard deviations (and severe cerebral palsy) to counsel parents, as these were cut-offs that were likely to have major implications for individuals throughout their lives. In all groups, these are the least numerous outcomes. For example, in EPICure2 (2006 births) three quarters of babies surviving birth at 22-23 weeks of gestation did NOT have severe impairment at follow up.[3] Over time there has been a trend to use -2SD as a cut off but this is poorly predictive of later learning problems, certainly among 2-year-old toddlers. There are major issues in comparing studies around the test used, the age of the test norms and the edition of the test, which have been discussed elsewhere.[4]

Finally, studies have different mixes of gestational ages and sex distributions, both of which are closely related to test scores, and different proportions with fetal growth restriction and socio-economic status. Combining studies of births <32 weeks and <27 weeks, without at least correcting for gestational age and infant sex, and providing confidence intervals, makes interpretation rather challenging.

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Neonatologists need to understand the data estimates they use for counselling, how they have been collected and their likely import. Such data must be used wisely in appropriate settings to avoid what Wilkinson has described as a 'let die mistake'.[5] Most very (and extremely) preterm babies do well, this message must not be lost.

References

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