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Dear Editor

Prematurity-associated lung disease: looking beyond bronchopulmonary dysplasia

We are delighted that LRM is promoting high-quality research on preterm-born survivors who had had bronchopulmonary dysplasia (BPD) in infancy[1]. Clearly, BPD has important implications in infancy including increased respiratory symptoms and increased hospitalisation. However, we believe the focus on respiratory outcomes after preterm birth must be much broader than just BPD especially as BPD is a poor predictor of the development of prematurity-associated lung disease (PLD). Gestation and intrauterine growth restriction are more closely associated with development of PLD than BPD[2]. In a preterm cohort, 40% with BPD had low lung function ($FEV_1 \leq 85\%$) but 25% without BPD also had predicted $FEV_1 \leq 85\%$, despite including children born up to 34 weeks' gestation. Redefining BPD will not include this at-risk late preterm group especially as most will not have received any neonatal oxygen therapy. This observation is important as a far greater proportion of births each year occur at 32-36 weeks' gestation (2.7% of annual UK live-births) than those born at ≤28 weeks' gestation (0.5%), considered at high risk of BPD. Risks of prematurity extend beyond respiratory disease including significant neurodevelopmental, cardiovascular and nutritional/growth abnormalities. The focus should be on longitudinal tracking of respiratory symptoms and objective markers such as spirometry and exhaled nitric oxide, which will aid understanding of the underlying mechanisms and develop treatments. Moreover, advanced imaging methods using MRI of the lungs[3] and pulmonary vasculature can provide safe, radiation-free, non-invasive insight into the regional lung structure and function that can be studied longitudinally. Crucially, these patterns of diminished lung function in childhood are likely to track into adulthood leading to significant future morbidity and mortality[4].

As the Editorial states, there is paucity of evidence to treat children with PLD. However, we recently demonstrated that ICS improved lung function in children with PLD but the addition of long-acting bronchodilator (LABA) with ICS was superior to placebo or ICS alone thus providing robust evidence for the first time to manage these children[5]. (LABA alone cannot be assessed given safety concerns.)

In summary, we must investigate preterm-born children beyond just BPD because those who do not develop BPD are also at significant risk of developing PLD. Longitudinal studies of respiratory symptoms, lung function deficits and state of the art cardiopulmonary imaging are urgently needed if evidence-based therapies are to be developed. Since a low FEV_1 is an independent risk for early multisystem morbidity and mortality, studying other organ systems is also essential.

Yours sincerely

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