Falling through the cracks: what happens to survivors of preterm birth?

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To the Editor:

Premature birth has consequences across the course of life, including reduced life-expectancy, and the most prematurely born have the worst outcomes [1, 2]. Survivors of prematurity have increased respiratory morbidity and mortality, airflow obstruction, asthma-like symptoms and COPD, and cardiovascular disease [1–4]. A history of prematurity is often not sought in adult clinics [5]. We hypothesised that the long-term consequences of prematurity are insufficiently appreciated, likely with detriment to patient care.

We used an online survey developed by a panel of neonatologists, paediatricians, allergologists and pulmonologists. The survey included 21 items addressing four main topics: 1) awareness level among respiratory care providers regarding the long-term respiratory risks of premature birth; 2) communication of neonatal information between different medical specialties; 3) healthcare journey of preterm babies to paediatricians and other respiratory care providers; 4) the knowledge gaps and potential solutions. The survey was customised to each specialty: seven items were for neonatologists only; three for paediatricians; one each for allergologists and respiratory consultants; five for paediatricians, allergologists, and respiratory consultants; and four for all specialties.

We invited 14 651 neonatologists, paediatricians, allergologists and respiratory consultants from Australia, France, Germany, Italy, Spain, the UK, and the USA to participate, excluding physicians with less than 2 years' experience; 1002 (7%) responded. A web link was emailed from listings extracted from Chiesi Farmaceutici S.p.A and from proprietary databases of external healthcare providers. All had previously consented to email contact. Two email reminders were sent and incomplete surveys were rejected.

Sample size was opportunistic in the absence of data enabling a power calculation. The survey results were analysed using Microsoft Excel and Microsoft Power BI. All items involved categorical answers, and absolute and relative frequencies were calculated. All frequencies were treated descriptively. No geographical comparisons were performed due to sample size limitations. The questionnaire is available on request from the corresponding author.

Results are summarised in figure 1. Of the 1002 respondents, 91% had been in practice for more than 5 years, and 62% were practising in an outpatient facility. In terms of specialities, 282 (28%) were neonatologists, 183 (18%) paediatricians, 290 (30%) allergologists, and 247 (24%) were respiratory consultants. Figure 1a shows that neonatologists regarded the presence of respiratory symptoms as being most important in the decision to refer. By contrast, for paediatricians, birth weight was the most important factor, irrespective of respiratory symptoms (figure 1b). All specialists highlighted that the most important gap was lack of clear recommendations for follow-up (figure 1c) and the need for continuing medical education programmes (figure 1d). Most (96%) respondents considered prematurity and bronchopulmonary dysplasia (BPD) risk factors for lung diseases in adulthood. Nevertheless, 74% of respondents perceived only moderate to very low awareness among colleagues. Adult pulmonologists perceived the lowest level (85%) of awareness among the specialties surveyed.

Most (77%) paediatricians "always" took a perinatal history, compared with allergologists (34%) and pulmonologists (21%). Irrespective of specialty, the proportion who always took this history increased with increasing years of clinical experience. Most (95%) neonatologists shared information on gestational age,

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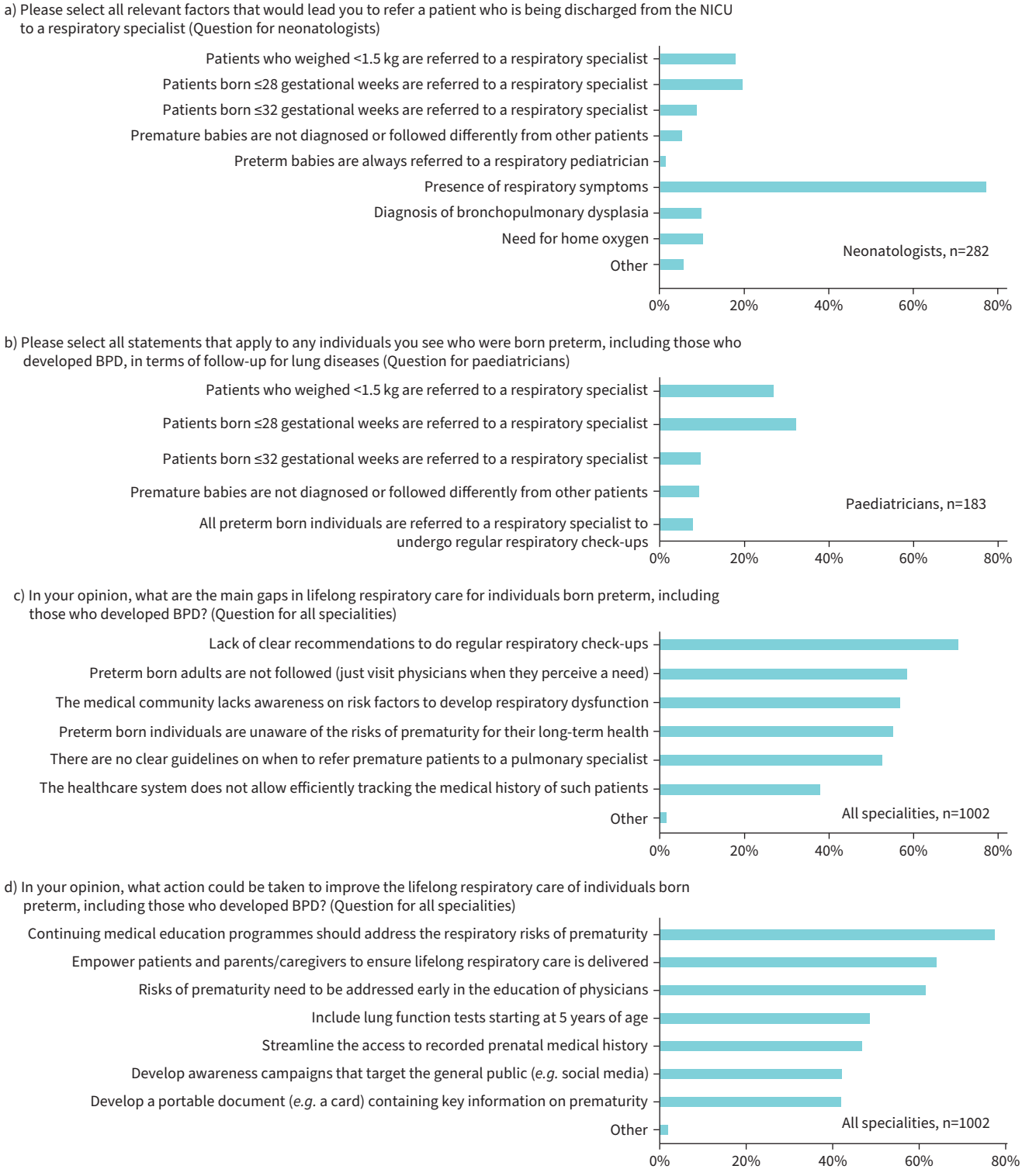

FIGURE 1 Reasons for neonatologists (a) and paediatricians (b) to refer preterm-born patients to a respiratory specialist. The gaps and potential solutions to improve the long-term respiratory care of preterm-born individuals are shown in (c) and (d). The bars show the percentage of participants who selected each option. NICU: neonatal intensive care unit; BPD: bronchopulmonary dysplasia.

birth weight, need for supplemental oxygen and respiratory support, BPD diagnosis and other lung sequelae of prematurity (>80%), and this was consistently reviewed by paediatricians (83%). This information was mainly through medical records (57%) and by oral communication (52%). Allergologists

and respiratory consultants used feedback from other physicians (58% and 37%, respectively) and electronic medical records (43% and 26%, respectively) to gather neonatal information. They reviewed less neonatal information, although BPD diagnosis and lung sequelae were reviewed by 72% and 65% of allergologists and respiratory consultants, respectively.

Most neonatologists (99%) shared information with parents and caregivers, and more than 70% of paediatricians and allergologists received information from the caregivers. Only 59% of adult pulmonologists acknowledged receiving information from parents and caregivers.

Most neonatologists (70%) followed up preterm babies for two years, but 27% for only 1–2 years. Most (>75%) of all those surveyed, believed that premature babies should be followed up lifelong.

Most (>80%) allergologists modified clinical management, at least partially, if they were aware that the patient was born preterm. Only 60% of adult pulmonologists adapted management pathways in preterm survivors.

Most (>60%) respondents considered that preterm-born individuals and their parents and caregivers should be empowered to ensure they receive the best respiratory care. Other suggested initiatives were measuring lung function during follow-up from 5 years of age, streamlining access to the perinatal medical history and the development of a portable record with neonatal information. Going forward, the use of a lifelong electronic patient record, accessible to all who are involved in patient care, would likely greatly facilitate communication between specialist groups.

In summary, there is inadequate awareness of the importance of preterm birth for management across the life course; communication between specialist teams is inadequate; and there is lack of clear guidance as to how to follow-up preterm born survivors.

The European Respiratory Society [6], and the American Thoracic Society [7] have published guidelines with conditional recommendations on low strength evidence. However, the former only covered the follow-up of BPD survivors [6], and the latter were limited to the follow-up of preterm-born children and adolescents with respiratory symptoms [7]. These guidelines are limited, not least because we now know that the risk of compromised lung health later in adulthood exists even for early term born infants [4, 8, 9]. However very few paediatricians actually referred extremely preterm or low birth weight babies to a respiratory specialist. An international consensus on how to structure respiratory follow-up remains an unmet need [1, 10].

Most allergologists (80%) and adult pulmonologists (60%) modified diagnostic pathways and treatment approaches, at least partly, when they were aware the patient was born premature. Lack of appreciation of the implications of prematurity across the life course may lead to wrong treatment being prescribed. For example, school-age wheeze and variable airflow obstruction is common in preterm survivors [11]. Some may respond to treatment with inhaled corticosteroids (ICS) [12] but in others there is no evidence of type 2 inflammation so they should not be treated with ICS [13]. They may have dysanaptic airway growth [14], which is known to be associated with poor outcomes in term-born children [15]. More work is needed to determine disease pathology in preterm survivors and to stimulate new research. Trials to stimulate lung development at birth and control airway inflammation in extremely premature babies are underway with stem cell-based therapies, insulin-like growth factor 1 and intratracheal surfactant/budesonide.

Proposed mitigation strategies to improve the current situation include better continuing medical education. Another is empowering patients and caregivers by supplying accurate information which they can ensure is available to subsequent caregivers, including during transition to adult services.

The main strength of the survey is that it includes >1000 physicians from different specialties and countries. There are some limitations. The overall response rate was relatively low, although similar to the British Thoracic Society survey [5], and there is a risk of selection bias. General practitioners were not invited, and this was a mistake given their role in follow-up care.

In conclusion, we need to increase awareness of the long-term implications of prematurity to ensure optimal follow-up for these babies, and design studies to obtain an evidence base for the development of improved guidelines.

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References

1 Crump C, Sundquist J, Winkleby MA, *et al.* Gestational age at birth and mortality from infancy into mid-adulthood: a national cohort study. *Lancet Child Adolesc Health* 2019; 3: 408–417.
2 Risnes K, Bilsteen JF, Brown P, *et al.* Mortality among young adults born preterm and early term in 4 Nordic nations. *JAMA Netw Open* 2021; 4: e2032779.
3 Simpson SJ, Turkovic L, Wilson AC V, *et al.* Lung function trajectories throughout childhood in survivors of very preterm birth: a longitudinal cohort study. *Lancet Child Adolesc Health* 2018; 2: 350–359.

4 Pulakka A, Risnes K, Metsälä J, *et al.* Preterm birth and asthma and COPD in adulthood: a nationwide register study from two Nordic countries. *Eur Respir J* 2023; 61: 2201763.
5 Bolton CE, Bush A, Hurst JR, *et al.* Are early life factors considered when managing respiratory disease? A British Thoracic Society survey of current practice. *Thorax* 2012; 67: 1110.
6 Duijts L, van Meel ER, Moschino L, *et al.* European Respiratory Society guideline on long-term management of children with bronchopulmonary dysplasia. *Eur Respir J* 2020; 55: 1900788.
7 Cristea AI, Ren CL, Amin R, *et al.* Outpatient respiratory management of infants, children, and adolescents with post-prematurity respiratory disease. *Am J Respir Crit Care Med* 2021; 204: e115–e133.
8 Du Berry C, Nesci C, Cheong JLY, *et al.* Long-term expiratory airflow of infants born moderate-late preterm: A systematic review and meta-analysis. *EClinicalMedicine* 2022; 52: 101597.
9 Kotecha SJ, Watkins WJ, Paranjothy S, *et al.* Effect of late preterm birth on longitudinal lung spirometry in school age children and adolescents. *Thorax* 2012; 67: 54–61.
10 Bonadies L, Cavicchiolo ME, Priante E, *et al.* Prematurity and BPD: what general pediatricians should know. *Eur J Pediatr* 2023; 182: 1505–1516.
11 Lum S, Kirkby J, Welsh L, *et al.* Nature and severity of lung function abnormalities in extremely pre-term children at 11 years of age. *Eur Respir J* 2011; 37: 1199–1207.
12 Goulden N, Cousins M, Hart K, *et al.* Inhaled corticosteroids alone and in combination with long-acting β_2 receptor agonists to treat reduced lung function in preterm-born children: a randomized clinical trial. *JAMA Pediatr* 2022; 176: 133–141.
13 Baraldi E, Bonetto G, Zacchello F, *et al.* Low exhaled nitric oxide in school-age children with bronchopulmonary dysplasia and airflow limitation. *Am J Respir Crit Care Med* 2005; 171: 68–72.
14 Cousins M, Hart K, Kotecha SJ, *et al.* Characterising airway obstructive, dysanaptic and PRISm phenotypes of prematurity-associated lung disease. *Thorax* 2023; 78: 895–903.
15 Forno E, Weiner DJ, Mullen J, *et al.* Obesity and airway dysanapsis in children with and without asthma. *Am J Respir Crit Care Med* 2016; 195: 314–323.