Respiratory Practices to Prevent or Treat Evolving Bronchopulmonary Dysplasia: A European Survey

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Objective To investigate respiratory practices to prevent or treat evolving bronchopulmonary dysplasia in neonatal intensive care units (NICUs) across Europe.

Study design Between March and July 2024, a web-based survey was sent to European NICUs caring for infants born preterm with gestational age <28 weeks.

Results We received replies from 447 of 721 (62%) NICUs across 24 European countries. Almost 16% of NICUs routinely intubate at birth, especially if the gestational age is <24 weeks. During transition most NICUs use continuous positive airway pressure ≥5 cmH_2O and start with an FiO_2 0.3. Volume-targeted ventilation is the primary ventilation mode in 60% of the NICUs. Permissive hypercapnia is a common practice. Higher SpO_2 target limits have been adopted, although alarm settings vary across NICUs. Caffeine is routinely started (96%). Surfactant is used in all NICUs, mostly rescue (74%) via less invasive administration (81%). Prophylactic inhaled nitric oxide is not used. Treatment of patent ductus arteriosus varies; half of NICUs pharmacologically treat patent ductus arteriosus early, based on echocardiographic findings. Ureaplasma screening is done in 22% of NICUs. Most (97%) NICUs use postnatal corticosteroids, with dexamethasone being the preferred drug (65%) and starting 2-3 weeks after birth. Only 5% use corticosteroids prophylactically. After 2-3 weeks, diuretics are used frequently, inhaled corticosteroids/bronchodilators to a much lesser extent.

Conclusions This large survey shows considerable practice variation in preventing and treating evolving bronchopulmonary dysplasia across Europe, especially for interventions with limited evidence. *(J Pediatr 2026;292:115006)*.

BPD	Bronchopulmonary dysplasia
CPAP	Continuous positive airway pressure
DR	Delivery room
GA	Gestational age
HFOV	High-frequency oscillation ventilation
INSURE	Intubation-surfactant-extubation
LISA	Less invasive surfactant administration
NICU	Neonatal intensive care unit
PDA	Persistent ductus arteriosus
RDS	Respiratory distress syndrome
VTV	Volume targeted ventilation

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Bronchopulmonary dysplasia (BPD) has a reported incidence of approximately 50% in infants born extremely preterm (before 28 weeks' gestation).[1] BPD often results in the need for prolonged respiratory support, recurrent respiratory infections during the first years of life, and compromised lung function lasting into adulthood.[2,3] Furthermore, BPD is a major risk factor for neurodevelopmental impairment.[4,5]

The clinical, histological, and radiographic pattern of BPD has changed over time due to increased survival at lower gestational ages (GA) after the introduction of antenatal corticosteroids, surfactant treatment, and less aggressive modes of respiratory support.[6,7] BPD is characterized by an arrest of lung development more than just parenchymal injury.[6,7] BPD is considered a multifactorial disease, in which not only the degree of prematurity, but also factors such as genetic susceptibility, intrauterine growth restriction, sepsis, nutritional deficits, and lung injury due to mechanical ventilation and oxygen toxicity play an important role.[8-11] Strategies to prevent BPD are thus multifaceted, and various interventions to prevent or treat evolving BPD have been studied during the last decades. Not all of these interventions have been proven effective and/or safe, as summarized in several reviews.[12-14] Ideally, evidence should be translated into clinical practice; however, there is a gap between the care that patients should receive based on existing evidence and recommendations and the care they actually receive.[15-19] This results in considerable variation in practice between centers and countries.[20-23] Although some studies investigating respiratory practice variation in different countries and continents are published, there is only one recent study surveying neonatal intensive care units (NICUs) in Europe.[24] Limitations of this study were the inclusion of centers with a relatively low number of annual admissions of extremely premature infants, limited detail on respiratory care practices, and a stronger focus on the management of respiratory distress syndrome (RDS) than on the prevention of BPD.[24] Therefore, the aim of our study was to assess in more detail which interventions for preventing or treating evolving BPD are used in the European NICUs admitting infants below 28 weeks GA and how much practice varied between NICUs.

Methods

This study was initiated by the European Society for Pediatric Research Pulmonary Research Consortium. The following 24 countries were represented in the consortium by at least one national principal investigator (PI): Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Lithuania, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. Formal approval by local ethics committees was not pursued as this study only collected information on policies and did not include patient data. No funds were received to conduct this study. We followed the checklist for reporting results of Internet E-surveys (CHERRIES).[25]

We conducted a web-based survey on respiratory practices in preterm infants with GA below 28 weeks. The survey contained 85 questions covering five themes: (1) general information about the participating NICUs; (2) practice in guiding transition at birth; (3) respiratory support strategies, (4) apnea management, and (5) other therapies for prevention and treatment of (evolving) BPD and is available in the appendix. Data on apnea management are reported separately.[26] Three members (M.L., W.O., and A.K.) of the consortium created the first draft of the survey, which was then distributed for feedback to an additional group of five members (A.L., C.H., C.K., J.H., and R.S.). Following three rounds of corrections, the final version was accepted in March 2024. All questions were mandatory, but the number of questions respondents answered varied, due to adaptive questioning. Respondents could go back to previous questions and change their answers until finalizing the survey. The survey was created with Google Forms, written in English, and mostly included closed questions, some with yes/no answers, and others with multiple-choice options. Neonatologists tested the survey in five centers to improve clarity of content and design. The estimated time to complete the survey was 10-15 minutes. The survey was headed by a brief description of the consortium as well as the aim of the study. There was a clear instruction that only one neonatologist in each NICU should complete the survey. Participants' consent was sought to store the data, which were accessible only to the research team. Participation was voluntary and no incentive was offered to complete the survey.

Responses were collected between March 2024 and July 2024. National PI's were responsible for identifying NICUs in their country that treated preterm infants less than 28 weeks' GA, and for sending out a survey link to a neonatologist at each of these units. The PI recorded the number of NICUs that were approached, and that responded. Up to four reminders were sent to maximize the number of included units.

Completed surveys were initially stored online in a Google spreadsheet and after the deadline for completing the survey had passed, the data were moved to a local server for further analysis. Only descriptive data are presented, and no comparative analyses were performed. Quantitative variables were presented as medians and IQRs, and qualitative variables as frequencies or percentages.

Results

The survey was distributed to neonatologists at a total of 721 NICUs in 24 countries. Of 465 completed surveys, 447 (62%) were included in this report (14 were double entries and 4 units did not treat infants <28 weeks GA). The median (IQR) response rate per country was 81% (49-100%). The participating NICUs reported having a median (IQR) of 13[9-20] beds and admitting median (IQR) 30[20-50] infants with a GA below 28 weeks annually. The median lower GA limit of initiating active treatment was 23 (IQR 22-23) weeks, with 38% of the NICUs reporting a lower limit of 22 weeks, 43% of 23 weeks, and 18% of 24 weeks.

Table I. Respiratory support strategies in the delivery room and the NICU to prevent BPD

Respiratory support strategies in the delivery room	
Routine endotracheal intubation	
	71 (15.9)
<24 wks	42 (60.0)
24-25 wks	19 (27.1)
26-27 wks	9 (12.9)
Initial FiO_2 used	
Dependent on GA	63 (14.1)
0.21	22 (5.0)
0.21-0.30	88 (19.7)
0.30	266 (59.5)
>0.30	8 (1.8)
CPAP pressure used	
No CPAP available	3 (0.7)
Dependent on GA	16 (3.6)
<5 cm H_2O	8 (1.8)
≥5 cm H_2O	420 (94.0)
Sustained inflation*	
No SI used	338 (75.6)
Dependent on GA	13 (2.9)
Routinely in all patients	37 (8.3)
Used if breathing inadequate/bradycardia	59 (13.2)
Primary mode of support during transport to NICU	
Dependent on GA	101 (22.6)
Low flow	0 (0.0)
High flow	1 (0.2)
nCPAP	254 (56.8)
NIPPV	83 (18.6)
IMV	8 (1.7)
Respiratory support strategies in the NICU	
Primary mode of invasive ventilation	
Volume targeted ventilation	266 (59.5)
Pressure targeted ventilation	117 (26.2)
High frequency oscillation	43 (9.6)
Proportional assist ventilation	8 (1.8)
Neurally adjusted ventilatory assist	5 (1.1)
Multiple modalities	8 (1.8)
Allowing permissive hypercapnia	
On IMV ≤2 wks PNA	267 (59.7)
On non-invasive support ≤2 wks PNA	354 (79.2)
On IMV >2 wks PNA	362 (81.0)
On non-invasive support >2 wks PNA	402 (89.9)
SpO_2 alarm limits†	
SpO_2 alarm limit low	89 (88-90)
SpO_2 alarm limit high	95 (95-96)
SpO_2 alarm limit low‡	
<85%	9 (2.0)
85-87%	88 (19.7)
88-90%	309 (69.1)
>90%	24 (5.4)
SpO_2 alarm limit high‡	
<90%	4 (0.9)
90-95%	300 (67.1)
>95%	126 (28.2)

FiO_2, fraction of inspired oxygen; *IMV*, invasive mechanical ventilation; *NIPPV*, nasal intermittent positive pressure ventilation; *PNA*, postnatal age; *SI*, sustained inflation; *SpO_2*, oxygen saturation.
Data are n (%), unless stated.
*Sustained inflation is defined as applying a peak inflating pressure for > 5 s.
†Median (IQR).
‡Because of missing values 100% not reached.

Respiratory Support Strategies in the Delivery Room and the NICU to Prevent BPD

Ninety-four percent of NICUs reported starting with nasal continuous positive airway pressure (CPAP) level ≥5 cmH_2O at birth in the delivery room (DR) (Table I). Most (60%) start with a fraction of inspired oxygen (FiO_2) of 0.3, and sustained inflations are not commonly used. Preterm infants <28 weeks GA are routinely intubated shortly after birth at 16% of NICUs; 60% of the NICUs that routinely intubate do this only in infants with a GA <24 weeks (Table I). After stabilization in the DR, the primary mode of respiratory support during transfer to the NICU is either nCPAP (57%), nasal intermittent positive pressure ventilation (19%), or dependent on GA (23%) (Table II). For infants who are mechanically ventilated, volume targeted ventilation (VTV) is the most commonly used primary mode of support (60%), followed by pressure targeted ventilation (26%), and high-frequency oscillation ventilation (HFOV) (10%) (Table I). The percentage of NICUs using a permissive hypercapnia strategy (defined as pCO_2 > 55 mmHg or > 7.2 kPa) ranged from 60% to 90%, depending on mode of respiratory support and postnatal age. The median (IQR) lower and upper peripheral oxygen saturation (SpO_2) alarm limit across all NICUs was set at 89 (88-90)% and 95 (95-96)%, respectively. A lower SpO_2 alarm limit below 88% is used at 22% of the NICUs, and 5% use a lower limit above 90%. For the upper limit, 28% of NICUs reported using an SpO_2 of >95%.

Pharmacological Interventions to Prevent or Treat Evolving BPD

Caffeine is started routinely in 96% of the NICUs, independent of mode of respiratory support (Table III). All NICUs use exogenous surfactant for the treatment of RDS. Surfactant is administered as rescue treatment in 74% of NICUs, prophylactically in 12% of the units, and in 14% of NICUs the timing depends on GA, with increasing use of prophylactic surfactant in infants with a lower GA (Table II). Forty-seven percent of NICUs report the use of multiple surfactant administration techniques, most commonly the less invasive surfactant administration (LISA) method (in 81% of the NICUs) and the intubation-surfactant-extubation (INSURE) method (in 41% of the NICUs). Only 25 (6%) NICUs use neither LISA nor INSURE but only give surfactant via endotracheal tube during mechanical ventilation. Although inhaled nitric oxide is available in 94% of the NICUs, none report using it prophylactically to prevent BPD (Table III). Early pharmacological treatment of persistent ductus arteriosus (PDA) based on echocardiographic findings is reported at 50% of the NICUs; 46% report later pharmacological treatment of infants with clinical signs of compromised lung function. Only 5% of NICUs report that they rarely, if ever, treat a PDA. Infants are screened for ureaplasma at 22% of centers, and 71% of the units performing screening subsequently treat patients with a positive culture with antibiotics. Inhaled corticosteroids and bronchodilators are used at 30-40% of NICUs, usually started depending on clinical picture after 2-3 weeks of life (Table III). Diuretics are used at most (75%) of NICUs, mostly after the third week of life and in infants with signs of fluid retention or impaired lung function.

Table II. Practices dependent on gestational age

Respiratory support strategies in the delivery room dependent on GA				
Initial FiO_2 used (63 NICUs [14.1% of all responses])		GA<24 wks	GA 24-25 wks	GA 26-27 wks
	0.21	1 (1.6)	3 (4.8)	7 (11.1)
	0.21-0.30	2 (3.2)	8 (12.7)	34 (54.0)
	0.30	32 (50.8)	37 (58.7)	20 (31.7)
	> 0.30	24 (38.1)	14 (22.2)	2 (3.2)
	n/a	4 (6.3)	1 (1.6)	-
CPAP pressure used (16 NICUs [3.6% of all responses])		GA<24 wks	GA 24-25 wks	GA 26-27 wks
	< 5 cm H_2O	5 (31.3)	1 (6.2)	1 (6.2)
	≥ 5 cm H_2O	1 (6.2)	10 (62.5)	15 (93.8)
	n/a	10 (62.5)	5 (31.3)	-
Sustained inflation* (13 NICUs [2.9% of all responses])		GA<24 wks	GA 24-25 wks	GA 26-27 wks
	No SI used	2 (15.4)	1 (7.7)	-
	Routinely in all patients	7 (53.8)	7 (53.8)	2 (15.4)
	Used if breathing inadequate/bradycardia	1 (7.7)	3 (23.1)	10 (76.9)
	n/a	3 (23.1)	2 (15.4)	1 (7.7)
Primary mode of support during transport to NICU		GA<24 wks	GA 24-25 wks	GA 26-27 wks
(101 NICUs [22.6% of all responses])	nCPAP	1 (1.0)	24 (23.8)	68 (67.3)
	NIPPV	14 (13.8)	39 (38.6)	32 (31.7)
	IMV	83 (82.2)	38 (37.6)	1 (1.0)
	n/a	3 (3.0)	-	-
Surfactant indication dependent on GA				
Timing of administration		GA<24 wks	GA 24-25 wks	GA 26-27 wks
(61 NICUs [13.6% of all responses])	Prophylactic administration	57 (1.7)	40 (65.6)	1 (1.6)
	Rescue administration	1 (1.6)	21 (34.4)	60 (98.4)
	n/a	3 (4.9)	-	-

FiO_2, fraction of inspired oxygen; *n/a*, not applicable; *SI*, sustained inflation; *NIPPV*, nasal intermittent positive pressure ventilation; *IMV*, invasive mechanical ventilation.
Data are n (%).
*Sustained inflation is defined as applying a peak inflating pressure for >5 s .

Almost all (97%) NICUs report using postnatal corticosteroids to prevent the development of BPD, with 56% starting treatment in weeks 2 and 3 after birth (Table IV). Of the 22 (5%) units that report using corticosteroids in the first week after birth, 18 (82%) use hydrocortisone. Postnatal corticosteroids are considered only in infants on invasive mechanical ventilation at 48% of NICUs, and 50% of the NICUs start treatment in infants on both invasive and noninvasive respiratory support. The corticosteroid of first choice is dexamethasone in 65% of NICUs and hydrocortisone in 27% of NICUs. In case an alternative corticosteroid, different from the primary drug, is used, most NICUs prescribe hydrocortisone (32%). In 36% of NICUs, no fixed dosing scheme is used. The starting and cumulative doses of dexamethasone used are similar across the NICUs (median [IQR] 0.15 [0.15-0.20] mg/kg/d, and 0.89 [0.89-0.93] mg/kg, respectively), but there is a wider range for median (IQR) starting (3 [1.5] mg/kg/d) and cumulative doses (12 [8.50-65.6] mg/kg) of hydrocortisone. Repeat treatment with corticosteroids was considered in 292 (67%) of the units.

Discussion

This is one of the largest international surveys assessing in detail which interventions for preventing or treating evolving BPD in extremely preterm infants have been implemented in NICUs across European countries. Our study shows that most of the interventions supported by evidence have been implemented in the majority of the European NICUs. However, this survey also shows considerable variation in practice between NICUs, especially regarding interventions with weak or insufficient evidence to support or refute their use.

Resuscitation guidelines recommend that pulmonary transition in preterm infants should be assisted noninvasively with CPAP with an initial FiO_2 of 0.21 to 0.30. Sustained inflations (>5 seconds) are not recommended.[27,28] Our survey shows that the majority of NICUs across Europe adhere to these recommendations. At the minority of NICUs that routinely intubate in the DR, this strategy is mainly used in preterm infants <24 weeks GA. Poor respiratory drive, compromised lung function and underrepresentation of these infants in the studies that showed feasibility and efficacy of DR CPAP may explain this finding. Still, several studies do suggest that a strategy using noninvasive support during pulmonary transition after birth is feasible in at least part of preterm infants with a very low GA.[20,29-33] Despite the existing evidence that VTV reduces the rate of death or BPD compared with pressure targeted ventilation in preterm infants[34], only 60% of NICUs in Europe use VTV as the primary mode in infants requiring invasive mechanical ventilation. It is unclear why in a quarter of the NICUs, pressure targeted ventilation is still the preferred mode of ventilation. One of the possible explanations could be that some NICUs use older ventilators that do not support VTV and that few extremely preterm infants are included in the studies investigating VTV.[30] HFOV is used as the primary mode in almost 10% of the NICUs. This limited use of primary HFOV may be due to a modest and inconsistent benefit to HFOV across trials[35], although centers often use HFOV as a secondary (rescue) mode when conventional modes fail or require high settings. Neurally adjusted ventilatory assist,

Table III. Pharmacological interventions to prevent or treat evolving BPD

Surfactant and other drug therapies	
Caffeine	
Started routinely	429 (96.0)
Started only on noninvasive support	18 (4.0)
Surfactant	
Indication	
No surfactant available	0 (0.0)
Dependent on GA	61 (13.6)
Prophylactic administration*	54 (12.1)
Rescue administration	332 (74.3)
Route of administration†	
Via LISA procedure	361 (80.8)
Via endotracheal tube on IMV	214 (47.9)
Via endotracheal tube INSURE procedure	183 (40.9)
Via LMA	1 (0.2)
iNO administration prophylactically	
No iNO available	29 (6.5)
Not used prophylactically	415 (92.8)
Used routinely in all infants	0 (0.0)
Used only in specific infants	3 (0.7)
PDA policy	
Early treatment based on echocardiographic findings	222 (49.7)
Treatment if (serious) compromised lung function	204 (45.6)
PDA is not/hardly ever treated	21 (4.7)
Ureaplasma	
Routine screening	100 (22.4)
Treatment for all Ureaplasma positive cultures‡	71 (71.0)
Treatment only in certain clinical conditions‡	29 (29.0)
Inhalation corticosteroids	180 (40.3)
Timing start	
Week 1	16 (8.9)
Week 2-3	53 (29.4)
After week 3	102 (56.7)
Other	9 (5.0)
Indication	
Routinely if high risk of BPD	43 (23.9)
In infants with evolving BPD	122 (67.8)
Other	15 (8.3)
Diuretics	334 (74.7)
Timing start	
Week 1	5 (1.5)
Week 2-3	84 (25.1)
After week 3	220 (65.9)
Other	24 (7.2)
Indication	
Routinely	39 (11.7)
If fluid retention and/or lung function impairment	258 (77.2)
Only occasionally in infants with evolving BPD	33 (9.9)
Other	4 (1.2)
Bronchodilators	137 (30.6)
Timing start	
Week 1	0 (0.0)
Week 2-3	25 (18.2)
After week 3	103 (75.2)
Other	8 (5.8)
Indication	
Routinely in infants with evolving BPD	6 (23.4)
If bronchoconstriction/lung function impairment	97 (70.8)
Only occasionally in infants with evolving BPD	32 (4.4)
Other	0 (0.0)

IMV, invasive mechanical ventilation; *iNO*, inhaled nitric oxide; *LMA*, laryngeal mask airway; *PDA*, patent ductus arteriosus.
Data are n (%).
*Prophylactic administration of surfactant is defined as administration < 30 minutes after birth to all infants with GA < 28 weeks.
†Multiple routes of administration per NICU possible.
‡Percentage related to number of NICUs screening for Ureaplasma.

is only used in a few NICUs in Europe, probably because there is a lack of evidence on its efficacy and safety, additional costs of consumables and availability limited to 1 ventilator.[36] Though several randomized controlled trials in ventilated infants up until 14 days after birth failed to show a positive effect of permissive hypercapnia on BPD prevention, this strategy is routinely used in many NICUs, not only in patients on invasive respiratory support and also beyond 2 weeks of life.[37] This strategy is likely applied to avoid intubation and mechanical ventilation. Future trials should establish whether this policy reduces the risk of BPD without any adverse effects. Studies have shown that targeting an SpO2 between 91 and 95% reduces the risk of mortality and necrotizing enterocolitis, but increases the risk of retinopathy of prematurity and BPD compared with a range between 85 and 89%.[38] Our survey shows that most NICUs in Europe have adopted the higher alarm limits. However, a concerningly high number of NICUs in this survey (almost 30%) use an upper alarm limit of >95%, yet 22% use a lower alarm limit <88%. It is important to emphasize that we collected survey data on alarm and not target limits, which may explain why some units recorded the alarm limits to be set outside the target range of 91-95%.

There is strong evidence that caffeine to treat apnea of prematurity reduces the risk of BPD, explaining its routine use in all NICUs.[39,40] The use of surfactant for preterm infants with RDS is also an undisputed intervention in neonatal care, although the timing and route of surfactant administration impact its treatment effect.[41,42] Studies have shown that prophylactic surfactant treatment combined with intubation and mechanical ventilation has no benefits over rescue treatment of infants on nCPAP with signs of RDS[43], accordingly, only 12% of the NICUs still use prophylactic surfactant. Recent studies have shown that LISA reduces the risk of mortality and BPD, when compared with other administration techniques.[41,44-46] Most European centers (80%) have implemented LISA as routine care and its use seems to be increasing over time, as a 2022 survey reported the use of LISA in only 52% of the units.[24] The fact that around 40% of the NICUs still use other techniques such as INSURE might be explained by lack of experience with LISA and the fact that not all infants can be managed on nCPAP due to insufficient respiratory drive. The results of the large clinical trial examining the benefit of prophylactic surfactant via LISA remain pending.[47] Inhaled nitric oxide is rarely used in Europe as a prophylactic treatment to prevent BPD, which is consistent with the reported lack of efficacy and safety.[48] There is ongoing debate whether a PDA should be treated to reduce the risk of associated morbidity, including BPD[49]; almost half of the NICUs currently screen and treat PDA early based on echocardiographic findings, and the other half only treat if there are (serious) clinical signs of compromised lung function. Two recent trials and a meta-analysis have shown no benefit or even harm of early treatment of a PDA compared with expectant management.[50-52]

Table IV. Pharmacological interventions to prevent or treat evolving BPD

Postnatal systemic corticosteroids	
Use of postnatal systemic corticosteroids	434 (97.1)
Timing	
Week 1	22 (4.9)
Week 2-3	251 (56.2)
After week 3	149 (33.3)
Other	11 (2.5)
Mode of support to consider PNS	
Only on IMV	213 (47.7)
On both IMV and noninvasive respiratory support	221 (49.4)
Type of corticosteroid, first choice	
Dexamethasone	289 (64.7)
Hydrocortisone	119 (26.6)
Betamethasone	22 (4.9)
Prednisone/Prednisolone	4 (0.9)
Type of corticosteroid, alternative	
Dexamethasone	71 (15.9)
Hydrocortisone	141 (31.5)
Betamethasone	33 (7.4)
Prednisone/Prednisolone	37 (8.3)
Repeat corticosteroid course	292 (67.3)

Corticosteroid dose*†			
Type of corticosteroid	Starting dose (mg/kg/d)	Cumulative dose (mg/kg)	Duration (days)
Dexamethasone	0.15 (0.15-0.20)	0.89 (0.89-0.93)	10 (9-10)
Hydrocortisone	3 (1-5)	12 (8.50-65.6)	10 (7-13.5)
Betamethasone	0.3 (0.13-0.32)	0.83 (0.50-1.32)	5,75 (3-8.63)
Prednisone/ Prednisolone	2 (2-4.25)	10.5 (7.25-12.8)	3 (3-6)

IMV, invasive mechanical ventilation; *PNS*, postnatal corticosteroid.
Data are n (%), unless stated.
†Median (IQR).
*35.6% of NICUs do not have a fixed dosing scheme.

This recent evidence on PDA treatment strategies has probably not reached all European NICUs yet and will likely lead to a change in practices in the near future. Studies on the association between colonization or infection with Ureaplasma species and the development of BPD provided controversial results, and the studies investigating treatment of this infection did not show benefits in the long term.[53-57] Accordingly, only 22% of units screen for Ureaplasma, even fewer treat positive infants.

Of the participating NICUs, 40% indicate the use of inhalation corticosteroids in preterm infants. Although inhaled corticosteroids initiated early (<7 days after birth) probably modestly reduce the incidence of BPD, long-term benefits are uncertain and there are concerns about increased mortality.[58,59] This is consistent with our finding that the majority of NICUs only consider inhaled corticosteroids after the third week of life in infants with already evolving BPD. Interestingly, the evidence to support this late use of inhaled corticosteroids is limited and inconclusive.[60] Bronchodilators are prescribed in one third of NICUs participating in the survey, mostly in infants with evolving BPD with bronchoconstriction and/or lung function impairment after 3 weeks of life. Indeed, studies have shown that bronchodilators may improve pulmonary mechanics in infants with established BPD although the number of studies is limited and the results are not consistent.[61,62] Evidence that bronchodilators prevent BPD is missing.[63] This relatively high use of bronchodilators in absence of solid evidence has also been reported by other studies.[64,65] Diuretics are prescribed in preterm infants with GA <28 weeks with evolving BPD in 75% of the NICUs, mostly after the third week of life and in infants with fluid retention and lung function impairment. However, the widespread use of diuretics is not supported by available evidence.[66-68]

Systemic postnatal corticosteroids have been shown to reduce the risk of BPD but the efficacy and safety strongly depend on the type, dose, and timing of administration.[60,69-71] Our survey showed that only 5% of the NICUs use systemic corticosteroids prophylactically, probably reflecting the concern of long-term neurodevelopmental impairment after early (<7 days after birth) dexamethasone treatment.[69] The majority of NICUs (56%) start systemic postnatal steroids between 7 and 21 days after birth, and a third of the NICUs delay the start of dexamethasone treatment to >3 weeks of life. Although evidence on optimal timing is still not conclusive, there are reports suggesting that reducing inflammation earlier in the course of the disease may result in more effective reduction of BPD.[13,72,73] The median dose of dexamethasone used in the NICUs is relatively low (cumulative 0.89 mg/kg over 10 days), equivalent with the DART regime tested in a randomized placebo-controlled trial.[74] It is important to acknowledge that this small trial did not show a reduction in BPD, and that there is growing evidence that a cumulative dose <2 mg/kg may

not affect the risk of BPD.[71,75] The alternative drug hydrocortisone is prescribed as first-line corticosteroid in 27% of the NICUs. Since only 5% of the European NICUs are prescribing systemic corticosteroid prophylaxis, this means that hydrocortisone is mainly used as a targeted treatment after the first week of life. However, two large trials have shown that targeted hydrocortisone treatment does not reduce the risk of BPD.[76,77] Other types of steroids, such as betamethasone, prednisone, and prednisolone are rarely used as first choice and are not supported by evidence. Interestingly, about two-thirds of NICUs prescribe repeat courses of systemic corticosteroids in case of insufficient or nonlasting effect. Although very few trials investigate systemic postnatal corticosteroid treatment of patients on noninvasive respiratory support[13], almost half of the participating NICUs consider both infants on invasive and noninvasive respiratory support for treatment with systemic postnatal corticosteroids. This information might be valuable when designing future corticosteroid trials.

In the past 10 years, other surveys on evidence-based strategies and interventions to prevent BPD have been published from several continents.[22,23,78-81] Most of these studies comprised only some of the possible respiratory and pharmacological treatments to prevent BPD. To our knowledge, only one international survey on respiratory practices including pharmacological interventions in NICUs in Europe has been published.[24] However, the primary emphasis of that survey was on the treatment of RDS, and to a lesser extent on BPD. Overall, the results were in line with our findings, showing considerable differences between hospitals, especially regarding interventions that lack sufficient evidence on efficacy and/or safety. In our view, one of the main contributors to this practice variation is the lack of an international European guideline on the prevention of BPD. The only existing European guideline is on the long-term management of children with established BPD.[82] Besides this, some guidelines address parts of what can be seen as prevention of BPD. The European Society for Paediatric Research and the Union of European Neonatal and Perinatal Societies endorsed a consensus guideline on the management of RDS[83], and the National Institute for Health and Care Excellence issued a guideline on 'Specialist neonatal respiratory care for babies born preterm.'[84] This lack of a European guideline on the prevention of BPD might contribute to the delay of implementing existing and new evidence into practice.

Our study has several limitations. First, a survey collects information on what policies clinicians should practice according to local protocols, but it does not necessarily reflect what is done in actual practice. Obtaining data on actual practice requires a European prospective cross-sectional study that collects information on care provided and outcomes in actual patients. Second, the response rate per country differed. The characteristics of the nonresponding NICUs remain unknown, which might have influenced the results. However, the strength of this study is the structured and conditional questionnaire developed by experts in the field of BPD prevention and treatment, and the comprehensive overview of possible treatments for the prevention of developing BPD.

In conclusion, we found considerable practice variation between NICUs in the prevention and management of BPD, particularly for those interventions that lack sufficient evidence. This emphasizes the need for well-performed, multicenter, randomized clinical trials to resolve these gaps in knowledge. Furthermore, an international guideline summarizing the existing evidence and providing recommendations on which interventions should and should not be implemented for the prevention of BPD could reduce practice variation. Whether this will improve neonatal outcomes remains to be determined. ■

CRediT authorship contribution statement

Moniek van de Loo: Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Wes Onland:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jeroen Hutten:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Anna Lavizzari:** Writing – review & editing, Resources, Methodology, Investigation, Conceptualization. **Christian Heiring:** Writing – review & editing, Resources, Methodology, Investigation, Conceptualization. **Victoria Aldecoa-Bilbao:** Writing – review & editing, Resources, Investigation. **Harald Ehrhardt:** Writing – review & editing, Resources, Investigation. **Merih Cetinkaya:** Writing – review & editing, Resources, Investigation. **Tomasz Szczapa:** Writing – review & editing, Resources, Investigation. **Victor Sartorius:** Writing – review & editing, Resources, Investigation. **Gustavo Rocha:** Writing – review & editing, Resources, Investigation. **Tobias Werther:** Writing – review & editing, Resources, Investigation. **Hanna Soukka:** Writing – review & editing, Resources, Investigation. **Olivier Danhaive:** Writing – review & editing, Resources, Investigation. **Charles Roehr:** Writing – review & editing, Resources, Investigation. **Manuela Cucerea:** Writing – review & editing, Resources, Investigation. **Andrea Calkovska:** Writing – review & editing, Resources, Investigation. **Gabriel Dimitriou:** Writing – review & editing, Resources, Investigation. **Bernard Barzilay:** Writing – review & editing, Resources, Investigation. **Boris Filipovic-Grcic:** Writing – review & editing, Resources, Investigation. **Roland Hentschel:** Writing – review & editing, Resources, Investigation. **Ulrich Thome:** Writing – review & editing, Resources, Investigation. **Kajsa Bohlin:** Writing – review & editing, Resources, Investigation. **Gianluca Lista:** Writing – review & editing, Resources, Investigation. **Sven Schulzke:** Writing – review & editing, Resources, Investigation. **Richard Plavka:** Writing – review & editing, Resources, Investigation. **Rasa Tameliene:** Writing – review & editing, Resources, Investigation. **Colm P.F. O'Donnell:** Writing – review & editing, Resources, Investigation. **Claus Klingenberg:** Writing – review & editing,

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Declaration of Competing Interest

A.L. has been a consultant for Chiesi S.p.A, Vyaire Medical, and ZOLL. C.H. has received honoraria from Chiesi as a member of the board for the Nordic Neonatal Meeting. C.R. has received speakers' honoraria from Chiesi Pharma Italy. T.S. is the president of the Polish Neonatal Society and has received speakers' honoraria from the following companies: Masimo, Medtronic, AstraZeneca, and Sanofi. H.S. received honoraria from Getinge. B.F.G has received speaker's honoraria from ThermoFisher Scientific and Baxter International. All other authors have no conflicts of interest to declare.

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