Supplementary material

European Respiratory Society guideline on long term management of children with bronchopulmonary dysplasia.

Supplementary Methods

The first kick-off meeting with European Respiratory Society (ERS) Task Force members was held in April, 2016, at the Erasmus University Medical Center Rotterdam, The Netherlands, to define strict goals, methodology of assessing evidence, formation of subgroups and tasks, and determine time-lines for a relevant paper. After formulation of the topics and questions, we aimed to identify systematic reviews of randomized trials, randomized controlled trials, and retrospective or prospective cohort studies published from 1999 ('new' BPD defined) until July 2016 through Embase.com, Medline Ovid, Cochrane Central Registry of Trials, and Web of Science Core Collections and where appropriate add relevant individual studies or expert based opinions. A first broad literature search was performed using scripts defined by a librarian according to the research questions. Thereafter, the Task Force members selected the relevant studies themselves. A minimum of 2 independent PICO working group members were required to review the articles to minimize potential bias. Inclusion criteria were the study population of children in whom BPD had been established and were discharged from the hospital, or who were older than 36 weeks of PMA, studying the specifically defined monitoring and treatment tools in relation to the defined outcomes of interest. Exclusion criteria were incorrect population under study (no children, no BPD only as second best), incorrect monitoring or treatment intervention, study focused on prevention instead of monitoring or treatment of BPD, outcomes of interest not reported, no abstract or full text available, no English text available. When no articles for the PICO directly fulfilled these criteria, indirect articles that indirectly fulfilled these criteria were included using a less favourable study design, preterm born children (as opposed to children with BPD) or the old form of BPD (as opposed to the new form of BPD). When also no indirect articles for the PICO were found, experience of local, regional or national management of Task Force members was asked, summarized, and discussed if relevant. When there was no consensus on whether to include one of the identified articles, this was discussed between the independent PICO working group. Initial results of the literature search were discussed during a meeting at the ERS Congress, London, in September, 2016.

Thereafter, finalisation of the rating of the importance of outcomes and final study selection were performed. Because of extended duration of the Task Force, an update of the literature search was performed on July 11th, 2018. No additional relevant articles were observed. During a meeting at the ERS Congress, Paris, in September, 2018, draft recommendations were discussed.

Supplementary Table S1. Scripts used in the first phase of the literature search strategy.

	Database			
	Embase	**Medline Ovid**	**Cochrane**	**Web of Science**
Lung imaging (n=2,120)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('imaging'/exp OR 'radiodiagnosis'/exp OR 'nuclear magnetic resonance imaging'/exp OR 'nuclear magnetic resonance'/exp OR (imag* OR radiodiagnos* OR (comput* NEAR/3 tomography*) OR (magnetic NEAR/3 resonance) OR mri OR radiogra* OR x-ray*):ab,ti) (n=795)	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND (exp "Diagnostic Imaging"/ OR "radiodiagnosis"/ OR (imag* OR radiodiagnos* OR (comput* ADJ3 tomography*) OR (magnetic ADJ3 resonance) OR mri OR radiogra* OR x-ray*).ab,ti.) (n=923)	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((imag* OR radiodiagnos* OR (comput* NEAR/3 tomography*) OR (magnetic NEAR/3 resonance) OR mri OR radiogra* OR x-ray*):ab,ti) (n=35)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND ((imag* OR radiodiagnos* OR (comput* NEAR/3 tomography*) OR (magnetic NEAR/2 resonance) OR mri OR radiogra* OR x-ray*))) AND DT=(article) AND LA=(english) (n=367)
Lung function (n=2,301)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('lung function'/exp OR 'lung clearance'/de OR 'lung diffusion'/de OR 'body plethysmography'/de OR plethysmography/de OR 'airway resistance'/de OR (((lung OR pulmonar*) NEAR/3 function*) OR (cardiopulmon* NEAR/3 exercis*	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND ("Respiratory Function Tests"/ OR "Plethysmography, Whole Body"/ OR Plethysmography/ OR "Airway	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((((lung OR pulmonar*) NEAR/3 function*) OR (cardiopulmon* NEAR/3 exercis* NEAR/3 test*) OR ((nitrogen* OR breath*) NEAR/3 (washout* OR test*)) OR spirometr* OR ((lung OR pulmonar*) NEAR/3 (clearance* OR diffusion*)) OR plethysmogra* OR	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age"))) AND DT=(article) AND LA=(english) AND TS=((((lung OR pulmonar*) NEAR/2 function*) OR (cardiopulmon* NEAR/2 exercis* NEAR/2 test*) OR ((nitrogen* OR breath*) NEAR/2 (washout* OR test*)) OR spirometr* OR ((lung OR pulmonar*) NEAR/2 (clearance* OR diffusion*)) OR plethysmogra* OR (forced NEAR/2 oscillat*) OR rint OR (airway NEAR/2 resistance*))) (n=659)

	NEAR/3 test*) OR ((nitrogen* OR breath*) NEAR/3 (washout* OR test*)) OR spirometr* OR ((lung OR pulmonar*) NEAR/3 (clearance* OR diffusion*)) OR plethysmogra* OR (forced NEAR/3 oscillat*) OR rint OR (airway NEAR/3 resistance*)):ab,ti) (n=936)	Resistance"/ OR (((lung OR pulmonar*) ADJ3 function*) OR (cardiopulmon* ADJ3 exercis* ADJ3 test*) OR ((nitrogen* OR breath*) ADJ3 (washout* OR test*)) OR spirometr* OR ((lung OR pulmonar*) ADJ3 (clearance* OR diffusion*)) OR plethysmogra* OR (forced ADJ3 oscillat*) OR rint OR (airway ADJ3 resistance*)).ab,ti.) (n=633)	(forced NEAR/3 oscillat*) OR rint OR (airway NEAR/3 resistance*)):ab,ti) (n=74)	
Daycare attendance (n=197)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('day care'/de OR 'child care'/de OR 'kindergarten'/de OR ('day care' OR daycare OR kindergarten* OR 'child care' OR 'childcare' OR 'centre care' OR 'center care'):ab,ti) (n=108)	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND ("Child Day Care Centers"/ OR "child care"/ OR ("day care" OR daycare OR kindergarten* OR "child care" OR "childcare" OR "centre care" OR "center care").ab,ti.) (n=16)	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND (('day care' OR daycare OR kindergarten* OR 'child care' OR 'childcare' OR 'centre care' OR 'center care'):ab,ti) (n=57)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND (("day care" OR daycare OR kindergarten* OR "child care" OR "childcare"))) AND DT=(article) AND LA=(english) (n=19)
Inhaled bronchodilators (n=902)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('bronchodilating agent'/exp OR 'beta adrenergic stimulation'/de OR 'beta adrenergic receptor stimulating agent'/exp OR (bronchodilat* OR	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND (exp "Bronchodilator	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((bronchodilat* OR beta2mimetic* OR betamimetic* OR salbutamol OR terbutaline OR ipratropium-bromide OR formoterol OR beta-2-agonist* OR beta-adrenerg*-stimulat*):ab,ti)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND ((bronchodilat* OR beta2mimetic* OR betamimetic* OR salbutamol OR terbutaline OR ipratropium-bromide OR formoterol OR beta-2-agonist* OR beta-adrenerg*-stimulat*))) AND DT=(article) AND LA=(english) (n=100)

	beta2mimetic* OR betamimetic* OR salbutamol OR terbutaline OR ipratropium-bromide OR formoterol OR beta-2-agonist* OR beta-adrenerg*-stimulat*):ab,ti) (n=447)	Agents"/ OR exp "Adrenergic beta-Agonists"/ OR (bronchodilat* OR beta2mimetic* OR betamimetic* OR salbutamol OR terbutaline OR ipratropium-bromide OR formoterol OR beta-2-agonist* OR beta-adrenerg*-stimulat*).ab,ti.) (n=337)	(n=18)	
Inhaled/systemic corticosteroids (n=4,329)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('corticosteroid'/exp OR (corticosteroid* OR adrenal-cort*-hormone* OR adrenocort*-hormone* OR steroid* OR fluticasone OR beclomethasone OR budesonide OR prednisolon* OR prednison* OR glucocorticoid* OR dexamethason* OR hydrocortison*):ab,ti) (n=1,806)	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND (exp "Adrenal Cortex Hormones"/ OR (corticosteroid* OR adrenal-cort*-hormone* OR adrenocort*-hormone* OR steroid* OR fluticasone OR beclomethasone OR budesonide OR prednisolon* OR prednison* OR glucocorticoid* OR dexamethason* OR hydrocortison*).ab,ti.) (n=1,148)	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((corticosteroid* OR adrenal-cort*-hormone* OR adrenocort*-hormone* OR steroid* OR fluticasone OR beclomethasone OR budesonide OR prednisolon* OR prednison* OR glucocorticoid* OR dexamethason* OR hydrocortison*):ab,ti) (n=231)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND ((corticosteroid* OR adrenal-cort*-hormone* OR adrenocort*-hormone* OR steroid* OR fluticasone OR beclomethasone OR budesonide OR prednisolon* OR prednison* OR glucocorticoid* OR dexamethason* OR hydrocortison*))) AND DT=(article) AND LA=(english) (n=1,144)
Diuretics (n=670)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('diuretic agent'/exp OR (diuretic* OR chlorothiazide OR hydrochlorothiazide OR furosemide OR bumetanide OR triamterene OR	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND (exp "diuretics"/ OR	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((diuretic* OR chlorothiazide OR hydrochlorothiazide OR furosemide OR bumetanide OR triamterene OR spironolactone):ab,ti) (n=29)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND ((diuretic* OR chlorothiazide OR hydrochlorothiazide OR furosemide OR bumetanide OR triamterene OR spironolactone))) AND DT=(article) AND LA=(english)

	spironolactone):ab,ti) (n=407)	(diuretic* OR chlorothiazide OR hydrochlorothiazide OR furosemide OR bumetanide OR triamterene OR spironolactone).ab,ti.) (n=151)		(n=83)
Oxygen duration (n=1,815)	('lung dysplasia'/de OR 'chronic lung disease'/de OR 'chronic respiratory tract disease'/de OR 'lung disease'/de OR (((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ('prematurity'/de OR 'premature labor'/de OR 'extremely low birth weight'/de OR 'very low birth weight'/de OR 'gestational age'/de OR (((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND [english]/lim NOT [Conference Abstract]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('oxygen therapy'/de OR 'home oxygen therapy'/de OR (((oxygen OR o2 OR o-2) NEAR/3 (therap* OR treat*))):ab,ti) (n=902)	("Bronchopulmonary Dysplasia"/ OR "Lung Diseases"/ OR (((lung OR bronchopulmon* OR pulmon*) ADJ3 dysplasi*) OR ((lung OR pulmonar*) ADJ3 (disease*)) OR bpd OR (oxygen ADJ3 dependen*)).ab,ti.) AND (exp "Infant, Premature"/ OR exp "Obstetric Labor, Premature"/ OR exp "Infant, Very Low Birth Weight"/ OR "Gestational Age"/ OR (((prematur* OR pre-matur*) ADJ3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) ADJ3 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age").ab,ti.) AND english.la. NOT (exp animals/ NOT humans/) AND ("Oxygen Inhalation Therapy"/ OR (((oxygen OR o2 OR o-2) ADJ3 (therap* OR treat*))).ab,ti.) (n=578)	((((lung OR bronchopulmon* OR pulmon*) NEAR/3 dysplasi*) OR ((lung OR pulmonar*) NEAR/3 (disease*)) OR bpd OR (oxygen NEAR/3 dependen*)):ab,ti) AND ((((prematur* OR pre-matur*) NEAR/3 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/3 (birth-weight OR birthweight)) OR elbw OR vlbw OR 'gestational age'):ab,ti) AND ((((oxygen OR o2 OR o-2) NEAR/3 (therap* OR treat*))):ab,ti) (n=55)	TS=(((((lung OR bronchopulmon* OR pulmon*) NEAR/2 dysplasi*) OR ((lung OR pulmonar*) NEAR/2 (disease*)) OR bpd OR (oxygen NEAR/2 dependen*))) AND ((((prematur* OR pre-matur*) NEAR/2 (birth* OR child* OR born OR newborn OR neonat* OR infan* OR labor)) OR preterm* OR pre-term* OR ((extreme* OR very) NEAR/2 (birth-weight OR birthweight)) OR elbw OR vlbw OR "gestational age")) AND ((((oxygen OR o2 OR o-2) NEAR/3 (therap* OR treat*))))) AND DT=(article) AND LA=(english) (n=280)

Rows represent the topic of the research question ('What is the evidence for *lung imaging* to monitor patients to reduce morbidity and related outcomes?', 'What is the evidence for *lung function testing* to monitor patients to reduce morbidity and related outcomes?', 'What is the evidence for *discouragement of daycare attendance* to reduce morbidity and related outcomes?', What is the evidence for *the use of inhaled bronchodilators* to reduce morbidity and related outcomes?", 'What is the evidence for *the use of inhaled or systemic corticosteroids* to reduce morbidity and related outcomes?', 'What is the evidence for *the use of systemic diuretics* to reduce morbidity and related outcomes?', and 'What is the evidence for *oxygen use* to reduce morbidity and related outcomes?'. Columns represent the data base in which the literature search was performed. Cells represent the used scripts.

Supplementary Table S3. Evidence profiles of monitoring and treatment for children with BPD.

Table S3.1. Evidence for children with BPD if monitoring with *lung imaging* versus no lung imaging affect important and critical defined outcomes.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Impaired lung function									
2 [1,2]	observational studies	serious [a]	not serious	serious [b]	serious [c]	none	In 21 schoolchildren with a history of new BPD (mild, n = 9; moderate, n = 4; and severe, n = 8) with a mean age of 12.7 years (range: 8.7-16.7). HRCT scores were inversely related to FEV1 (β -4.23; 95% CI -6.97 to -1.49, p = 0.004) and MMEF (β -3.45; 95% CI -6.10 to -0.80, p = 0.013) but not to DLCO. In a retrospective review of 41 very low birthweight infants with BPD, who had exacerbations in the last 6 months at a mean age of 16 months, underwent HRCT scans and lung function tests. Forced expiration (VmaxFRC) and functional residual capacity (FRC) was measured by the squeeze technique. CT abnormalities such as an increased number of triangular subpleural opacities and of limited linear opacities were associated with a lower FRC (r -0.426 and -0.421 (p-value for both <0.02), respectively), but not VmaxFRC.	⊕◯◯◯ VERY LOW	IMPORTANT
Prolonged duration of supplemental oxygen need									
2 [3,4]	observational studies	serious [d]	not serious	serious [e]	serious [f]	none	No association between oxygen supplementation and chest CT during their first year of life among children with moderate to severe BPD. No association between neonatal or 40-month chest X-ray severity scores and duration of oxygen therapy. Infants who remained oxygen dependent at a post-conceptional age of 36 weeks had significantly higher scores (median 9, range 7 to 20) than those not chronically oxygen dependent (median 3, range 0 to 13); p<0.05	⊕◯◯◯ VERY LOW	IMPORTANT
Adverse growth, reduced physical exercise capacity, adverse neurodevelopment, , and side effects									
							These outcomes were assessed as important, however no articles were found.	-	IMPORTANT
Number and severity of respiratory symptoms, hospital admissions, decreased quality of life, and mortality									
							These outcomes were assessed as critical, however no articles were found.	-	CRITICAL

CI: Confidence interval

Explanations

a. In the second study (Mahut et al), correlations between CT abnormalities and lung function was measured only, and there was no adjustment for confounders.

b. Cross-sectional measures of lung imaging and lung function. Prognostic/longitudinal value cannot be determined.

c. Low number of patients for each BPD severity group (Ronkainen et al)

d. Retrospective data collection

e. Indirect study population

f. Not enough numerical data reported to be able to judge imprecision

References

1. Ronkainen E, Perhomaa M,Mattila L,Hallman M,Dunder T. Structural Pulmonary Abnormalities Still Evident in Schoolchildren with New Bronchopulmonary Dysplasia. Neonatology; 2018.

2. Mahut B, de Blic J,Emond S,Benoist MR,Jarreau PH,Lacaze-Masmonteil T,Magny JF,Delacourt C. Chest computed tomography findings in bronchopulmonary dysplasia and correlation with lung function.. Arch Dis Child Fetal Neonatal Ed; 2007.

3. Tonson la Tour A, Spadola L,Sayegh Y,Combescure C,Pfister R,Argiroffo CB,et al. Chest CT in bronchopulmonary dysplasia: clinical and radiological correlations. Pediatr Pulmonol; 2013.

4. Maconochie I, Greenough A,Yuksel B,Page A,Karani J.. A chest radiograph scoring system to predict chronic oxygen dependency in low birth weight infants. Early Hum Dev; 1991.

Table S3.2. Evidence for children with BPD if monitoring with *lung function* versus no lung function affect important and critical defined outcomes.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Number and severity of respiratory symptoms									
2 [1,2]	observational studies	serious [a]	not serious	serious [b]	not serious	none	Lung function was measured at discharge or term age (whichever came first) in 35 children born before 28 weeks gestational age. TEF50/PTEF was lower in the group with respiratory morbidity (defined as need for hospital readmission for respiratory symptoms and/or parental report of treatment with inhaled asthma medication) in the first year of life, than in the group without (73.5 vs 79.9, p-value = 0.03). Other tidal breathing lung function measures did not differ between the two groups. Another prospective cohort among 163 preterm born children measured tidal breathing and performed multiple breath washout measurements during sleep at the age of 44 weeks PMA. After adjustment for confounders, a higher respiratory rate and tidal volume were associated with a decreased and increased risk of wheeze in the first year of life (OR (95% CI): 0.69 (0.50, 0.96) and 1.40 (1.04, 1.90), respectively). Other measures, such as FRC and LCI showed no associations with wheeze. The additional value of lung function tests was tested by adding them to prediction models for wheezing in the first year of life based on BPD classification, the clinical risk index for babies (CRIB) score, or clinical standard predictors such as sex, PMA and days of mechanical ventilation. Adding lung function to either of the three models however did not improve prediction of wheeze (AUC (likelihood ratio test p-value) 0.63 vs 0.54 (0.15), 0.62 vs 0.52 (0.08) and 0.71 vs 0.68 (0.12)).	⊕◯◯◯ VERY LOW	CRITICAL
Use of bronchodilators									
1 [2]	observational studies	not serious	not serious	serious [b]	not serious	none	In the cohort among 163 preterm born children, a higher tPTEF/tE was associated with a decreased risk of β2-agonist inhalation therapy during the first year of life after adjustment for confounders (OR (95% CI): 0.56 (0.35, 0.89)).	⊕◯◯◯ VERY LOW	IMPORTANT
Hospital admissions									
1 [2]	observational studies	not serious	not serious	serious [b]	not serious	none	In the cohort among 163 children born preterm, a higher moment 1 ratio from multiple breath washout was associated with a decreased risk of re-hospitalization in the first year of life after adjustment for confounders (OR (95% CI): 0.15 (0.02, 0.96)).	⊕◯◯◯ VERY LOW	CRITICAL
Prolonged duration of supplemental oxygen need									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
1 [2]	observational studies	not serious	not serious	serious [b]	not serious	none	In the cohort among 163 children born preterm, none of the tidal breathing measurements, nor multiple breath washout measurements were associated with home oxygen therapy.	⊕◯◯◯ VERY LOW	IMPORTANT
Reduced physical exercise capacity, and decreased quality of life									
							These outcomes were assessed as critical, however no articles were found.	-	CRITICAL
Adverse growth, CT abnormalities, use of inhaled/systemic corticosteroids, use of diuretics, side effects, adverse neurodevelopment, and mortality									
							These outcomes were assessed as important, however no articles were found.	-	IMPORTANT

CI: Confidence interval

Explanations

a. Difference in lung function measurement was assesed by t-test and no adjustment for confounders (Bentsen). No group where lung function was not measured (Bentsen and Proietti).

b. Indirect population (preterm born children, not specifically BPD)

References

1. Bentsen MH, Markestad T,Oymar K,Halvorsen T. Lung function at term in extremely preterm-born infants: a regional prospective cohort study. BMJ Open; 2017.

2. Proietti E, Riedel T,Fuchs O,Pramana I,Singer F,Schmidt A,Kuehni C,Latzin P,Frey U. Can infant lung function predict respiratory morbidity during the first year of life in preterm infants?. Eur Respir J; 2014.

Table S3.3. Evidence for children with BPD if treatment with *inhaled/systemic corticosteroids* versus no inhaled/systemic corticosteroids affect important and critical defined outcomes.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Number and severity of respiratory symptoms									
1 [1]	randomised trials	serious [a]	not serious	serious [b]	not serious	none	The difference in symptom score (cough, wheeze), was 59 points (confidence interval ranging from 24.1 to 92.9), in favour of treatment, which is a 37% improvement.	⊕⊕◯◯ LOW	CRITICAL
Impaired lung function									
1 [1]	randomised trials	serious [a]	not serious	serious [b]	not serious	none	During the active period, FRC increased significantly (30 vs 36 ml/kg, p < 0.002), while there was no change in FRC during the placebo treatment period (31 vs 32 ml/kg).	⊕⊕◯◯ LOW	IMPORTANT
Hospital admission, mortality, decreased quality of life, reduced physical exercise capacity, neurodevelopment and pulmonary hypertension									
							These outcomes were assessed as critical, however no articles were found.	-	CRITICAL
Prolonged duration of supplemental oxygen and adverse growth									
							These outcomes were assessed as important, however no articles were found.	-	IMPORTANT

CI: Confidence interval

Explanations a. High loss to follow up; possible bias. b. Indirect study population (preterm born children, not within 'new' BPD era)

References 1. B Yuksel, A Greenough. Randomised trial of inhaled steroids in preterm infants with respiratory symptoms at follow up. Thorax; 1992.

Table S3.4. Evidence for children with BPD if treatment with *diuretics* versus no diuretics affect important and critical defined outcomes.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Hospital admissions									
1 [1]	randomised trials	very serious [a]	not serious	serious [b]	serious [c]	none	After discharge until age 1 year of corrected age no difference in number of rehospitalizations for respiratory deterioration (diuretic group 22 of 14 patients vs placebo group 19 of 6 patients)	⊕◯◯◯ VERY LOW	IMPORTANT
Impaired lung function									
1 [1]	randomised trials	very serious [a]	not serious	serious [b]	serious [c]	none	Pulmonary function tests (PFT) were performed at baseline (1), 4 weeks after start RCT (2), 1 and 8 weeks after weaned from oxygen (3,4), and 1 year at corrected age (5). Between PFT 1 and 2, infants in the diuretic group had improvement in dynamic pulmonary compliance (46%; p <0.001) and airway resistance (31%; p<0.05), while the placebo group did not. No changes in TGV or FRC in the groups. No differences in PFT after discontinuation of diurectics/placebo. Comparison within groups but not between groups are given.	⊕◯◯◯ VERY LOW	IMPORTANT
Prolonged duration of supplemental oxygen need									
1 [1]	randomised trials	very serious [a]	not serious	serious [b]	serious [c]	none	No difference in total duration of supplemental oxygen use (diuretic group 133+/-53 days vs. placebo group 147 +/- 71 days)	⊕◯◯◯ VERY LOW	CRITICAL
Side effects									
1 [1]	randomised trials	very serious [a]	not serious	serious [b]	serious [c]	none	No difference in number of infants with nephrocalcinosis (diuretic group 7/22 patients vs placebo group 5/21 patients), supplemental electrolytes (diuretic group 2/22 patients vs placebo group 0/21) or hearing deficit (diuretic group 2/22 patients vs placebo group 1/21 patients). Note: Difference in supplemental furosemide (diuretic group 0/22 patients vs placebo group 5/21 patients, p<0.05)	⊕◯◯◯ VERY LOW	IMPORTANT
Number and severity of respiratory symptoms, pulmonary hypertension, and reduced physical exercise capacity									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
							These outcomes were assessed as important, however no articles were found.	-	IMPORTANT
Adverse neurodevelopment, decreased quality of life, and mortality									
							These outcomes were assessed as critical, however no articles were found.	-	CRITICAL

CI: Confidence interval

Explanations a. Exact method of randomization procedure unclear, not stated whether patients were treated equally except for the intervention (but could be assumed), potential confounders were not taken into account, intention to treat analysis not fully clear, additional furosemide supplementation differed between the groups (diuretic group 0/22 patients vs placebo group 5/21 patients; p-value <0.05). b. Indirect study population of infants with oxygen-dependent BPD after extubation, clinically stable for at least 3 weeks before enrolment (gestational age and definition of BPD not specified). c. Differences between the intervention and placebo groups not examined but changes in lung function per group are described. Number of subjects small.

References 1. Kao LC, Durand DJ,McCrea RC,Birch M,Powers RJ,Nickerson BG.. Randomized trial of long-term diuretic therapy for infants with oxygen-dependent bronchopulmonary dysplasia.. May; 1994.

Supplementary table S4. Evidence to decision tables of monitoring and treatment for children with BPD.

Table S4.1 Evidence to decision tables for children with BPD if monitoring with *lung imaging* versus no lung imaging affect important and critical defined outcomes.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Based on clinical experts opinion it is of relevance to have evidence on monitoring with chest imaging in children with established BPD	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	No direct evidence that would answer this question in an appropriate way was identified. Indirect evidence was provided by four studies that examined the relation of lung imaging with lung function or duration of supplemental oxygen need.. Twenty-one school-children with BPD (mild, n = 9; moderate, n = 4; and severe, n = 8) were offered the opportunity to undergo high-resolution CT (HRCT) scans. The rate of severe BPD was higher compared to those not participating for scanning. Mean age of the children was 12.7 years (range: 8.7-16.7). Higher HRCT scores were related to lower Forced Expiratory Volume in 1 second (FEV1) (β -4.23; 95% CI -6.97 to -1.49, p = 0.004) and Maximal Mid-Expiratory Flow (MMEF) (β -3.45; 95% CI -6.10 to -0.80, p = 0.013), but not to gas exchange as measured by CO diffusion capacity (DLCO). A retrospective study among 19 children with BPD observed that all children at a median age of 14.6 months (range 1.5-53.7) had CT abnormalities, which were not associated with clinical outcomes such as gestational age, type and duration of mechanical ventilation and BPD severity. In a retrospective review, 41 very low birthweight infants with BPD, who had exacerbations in the last 6 months at a mean age, underwent HRCT scans and lung function tests at a mean age of 16 months. Maximal expiratory flow at functional residual capacity (VmaxFRC) and functional residual capacity (FRC) were	

	measured by the squeeze technique. An increased number of triangular subpleural opacities and of limited linear opacities on CT were associated with a lower FRC (r -0.426 and -0.421 (p-value for both <0.02), respectively), but not VmaxFRC. A study among 40 preterm born children (median age 27 weeks (range 24-32 weeks) observed that those remaining oxygen dependent at a post-conceptional age of 36 weeks had significantly higher chest radiograph scores at one of month of age (median 9, range 7 to 20) than those not chronically oxygen dependent (median 3, range 0 to 13); p<0.05.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	Lung imaging with CT or chest X-ray implies the use of radiation.	

Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
● Very low ○ Low ○ Moderate ○ High ○ No included studies		

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Among the presented studies with indirect evidence to use lung imaging as a monitor tool, the study population consisted of children defined with the old form of BPD, the studies used retrospective or cross-sectional data collection with potential risk of bias, or reported not enough numerical data to be able to judge imprecision. Therefore, the evidence was considered very low. In clinical practice, Task Force members agreed that given the low certainty of evidence and potential side effects of radiation, monitoring with lung imaging would be justified only in subgroup of children with severe BPD, severe symptoms, recurrent hospitalizations or equivalent. For example, a chest CT with intravenous contrast could be considered to exclude other diagnoses, which may affect treatment strategies.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know		

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Very low ○ Low ○ Moderate ○ High ● No included studies		

Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies		Not studied.

Equity

What would be the impact on health equity?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know		

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	**Probably yes**	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

The Task Force suggests lung imaging to monitor children with BPD in subgroups only, for example children with severe BPD, severe respiratory symptoms, and/or recurrent hospitalizations (Conditional recommendation based on very low certainty of evidence).

Justification

Among the presented studies with indirect evidence to use lung imaging as a monitor tool, the study population consisted of children defined with the old form of BPD, the studies used retrospective or cross-sectional data collection with potential risk of bias, or reported not enough numerical data to be able to judge imprecision. Therefore, the evidence was considered very low. In clinical practice, Task Force members agreed that given the low certainty of evidence and potential side effects of radiation, monitoring with lung imaging would be justified only in subgroup of children with severe or an atypical course of BPD, severe symptoms, recurrent hospitalizations or equivalent. For example, a chest CT with intravenous contrast could be considered to exclude other diagnoses, which may affect treatment strategies.

Subgroup considerations

The Task Force suggests lung imaging for monitoring in subgroups only, for example children with severe BPD, sever respiratory symptoms, recurrent hospitalization or equivalent.

Implementation considerations

Implementation depends on expert knowledge of the center/country, availability (CT, MRI), and costs.

Monitoring and evaluation

None.

Research priorities

Recently, nonionizing magnetic resonance imaging (MRI) scan protocols for children with BPD have been developed, and a quite-breathing MRI scan independently assessed structural abnormalities of BPD, disease severity, and predicted short term outcomes at discharge from the neonatal intensive care unit. This technique is a promising monitoring tool for long term outcomes. Further studies are warranted to examine the predictive value of lung imaging, preferably non-radiant, on long term outcomes of children with established BPD. Studies using lung imaging such as computer tomography (CT) or MRI in the neonatal phase might be considered to better define the severity of BPD, or to diagnose or exclude other causes of BPD.

Table S4.2 Evidence to decision tables for children with BPD if monitoring with *lung function* versus no lung function affect important and critical defined outcomes.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Based on clinical experts opinion it is of utmost relevance to have evidence on monitoring with lung function in children with established BPD	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	No direct evidence that would answer this question in an appropriate way was identified. Indirect evidence was provided by two studies among preterm born children. The first study showed that among extremely preterm born children, the ratio of tidal expiratory flow at 50% of expired volume to peak tidal expiratory flow (TEF50/PTEF), which reflects airway obstruction, measured by electromagnetic inductance plethysmography predicts respiratory morbidity in the first year of life (Area Under Curve (95% Confidence Interval: 0.723 (0.55, 0.86)). Also, TEF50/PTEF was lower in the group with respiratory morbidity in the first year of life, than in the group without (73.5 vs. 79.9, p-value = 0.03). Other tidal breathing lung function measures did not differ between those with and without respiratory morbidity. Another prospective cohort among 163 preterm born children measured tidal breathing and performed multiple breath washout measurements during sleep at the age of 44 weeks PMA. After adjustment for confounders, a higher respiratory rate and higher tidal volume were associated with a decreased and increased wheeze in the first year of life (OR (95% CI): 0.69 (0.50, 0.96) and 1.40 (1.04, 1.90), respectively), and a higher time to peak	

	tidal expiratory flow expiratory time ratio (*t*PTEF/*t*E) with less bronchodilator inhalation therapy during the first year of life (OR (95% CI): 0.56 (0.35, 0.89)). A higher moment ratio 1 (representing the mean alveolar flow volume distribution) was associated with a decreased risk of re-hospitalization in the first year of life (OR (95% CI): 0.15 (0.02, 0.96)). Other lung function measures such as FRC and lung clearance index (LCI) were not associated with wheeze, inhalation therapy or re-hospitalization, and none of the lung function measures were associated with home oxygen therapy. The additional value of lung function tests was tested by adding them to prediction models for wheezing in the first year of life based on BPD classification, the clinical risk index for babies (CRIB) score, or clinical standard predictors such as sex, PMA and days of mechanical ventilation. Adding lung function to either of the three models however did not improve prediction of wheeze (AUC (likelihood ratio test p-value) 0.63 vs 0.54 (0.15), 0.62 vs 0.52 (0.08) and 0.71 vs 0.68 (0.12)).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	Undesirable effects are not studied, however, since monitoring with lung function is non-invasive and performed often, undesirable effects are most likely small.	

Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Very low ● Low ○ Moderate ○ High ○ No included studies		

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	No studies have been performed that examined the potential beneficial effect of lung function monitoring on important and critical defined outcomes in children with BPD. Among the presented studies with indirect evidence to use lung function as a monitor tool, the study population consisted of preterm born children, not specifically children with BPD, or potential confounders were not taken into account. Therefore, the evidence was considered very low. No evidence was found that monitoring children with BPD with lung function reduces morbidity and related outcomes. However, for clinical practice, Task Force members agreed that monitoring with lung function would be justified despite the lack of evidence. Lung function, specifically spirometry and related bronchodilator response at older ages, is an objective measure, is associated with lung function in adulthood, and with increased risks of morbidity and mortality, has sex, age, height, and ethnicity adjusted reference ranges, and has no potential side effects. Lung function could also act as a potential indicator for the risk of lung- and related vascular diseases in childhood.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know		

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Very low ○ Low ○ Moderate ○ High ● No included studies		

Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know		

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Spirometry seems the most useful method for longitudinal follow up of lung growth and airway obstruction in school-age children with BPD. For preschool children (age <= 4 years) with BPD, the forced oscillation technique and multiple breath washout tests are the most applicable regarding technique and validity. However, reported studies have small sample sizes and limitations, and the success rate in routine clinical practice without sedation is considered low.	

SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	**Probably yes**	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

The Task Force suggests lung function to monitor with BPD (Conditional recommendation based on very low certainty of evidence).

Justification

No direct evidence that would answer this question in an appropriate way was identified. Indirect evidence was provided by two studies among preterm born children. The first study showed that among extremely preterm born children, the ratio of tidal expiratory flow at 50% of expired volume to peak tidal expiratory flow (TEF50/PTEF), which reflects airway obstruction, measured by electromagnetic inductance plethysmography predicts respiratory morbidity in the first year of life (Area Under Curve (95% Confidence Interval: 0.723 (0.55, 0.86)). Also, TEF50/PTEF was lower in the group with respiratory morbidity in the first year of life, than in the group without (73.5 vs. 79.9, p-value = 0.03). Other tidal breathing lung function measures did not differ between those with and without respiratory morbidity. Another prospective cohort among 163 preterm born children measured tidal breathing and performed multiple breath washout measurements during sleep at the age of 44 weeks PMA. After adjustment for confounders, a higher respiratory rate and higher tidal volume were associated with a decreased and increased wheeze in the first year of life (OR (95% CI): 0.69 (0.50, 0.96) and 1.40 (1.04, 1.90), respectively), and a higher time to peak tidal expiratory flow expiratory time ratio (*t*PTEF/*t*E) with less bronchodilator inhalation therapy during the first year of life (OR (95% CI): 0.56 (0.35, 0.89)). A higher moment ratio 1 (representing the mean alveolar flow volume distribution) was associated with a decreased risk of re-hospitalization in the first year of life (OR (95% CI): 0.15 (0.02, 0.96)). Other lung function measures such as FRC and lung clearance index (LCI) were not associated with wheeze, inhalation therapy or re-hospitalization, and none of the lung function measures were associated with home oxygen therapy. The additional value of lung function tests was tested by adding them to prediction models for wheezing in the first year of life based on BPD classification, the clinical risk index for babies (CRIB) score, or clinical standard predictors such as sex, PMA and days of mechanical ventilation. Adding lung function to either of the three models however did not improve prediction of wheeze (AUC (likelihood ratio test p-value) 0.63 vs 0.54 (0.15), 0.62 vs 0.52 (0.08) and 0.71 vs 0.68 (0.12)). No evidence was found that monitoring children in whom BPD has been established and were discharged from the hospital, or who were older than 36 weeks of PMA with lung function reduces morbidity and related outcomes. However, for clinical practice, Task Force members agreed that monitoring with lung function would be justified despite the lack of evidence. Lung function, specifically spirometry and related bronchodilator response at older ages, is an objective measure, is associated with lung function in adulthood, and subsequently increased risks of morbidity and mortality, has sex, age, height, and ethnicity adjusted reference ranges to compare with, and has no potential side effects. Lung function could also act as a potential indicator for the risk of lung- and related vascular diseases in adulthood. Spirometry seems the most useful method to longitudinally examine lung growth and airway obstruction in school-age children with BPD. For preschool children (age <= 4 years) with BPD, the forced oscillation technique and multiple breath washout tests are the most applicable regarding technique and validity. However, reported studies have small sample sizes and limitations, and the success rate in routine clinical practice without sedation is considered low.

Subgroup considerations

None.

Implementation considerations

None.

Monitoring and evaluation

None.

Research priorities

Further studies, observational or RCT, are warranted to examine the predictive value of lung function on long term lung structure and respiratory morbidity of children with established BPD, and its value in monitoring responses to treatment.

Table S4.3 Evidence to decision tables for children with BPD if treatment with *corticosteroids* versus no corticosteroids affect important and critical defined outcomes.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	No direct evidence that would answer this question in an appropriate way was identified. Indirect evidence was obtained from one study, a crossover RCT that recruited eighteen children born premature (mean gestational age 28 weeks) at the age of 10.5 months, who had symptoms that were not controlled despite regular use of bronchodilators. Children received either 200 µg of beclomethasone dipropionate or placebo twice daily for two six week periods, separated by a two-week washout period. During the active period, as compared to the placebo period, respiratory symptoms decreased (37% improvement in symptom score, p-value <0.001). During the active period, FRC increased significantly (30 vs 36 ml/kg, $p < 0.002$), while there was no change in FRC during the placebo treatment period (31 vs 32 ml/kg).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know	Side-effects are not specifically studied. One study mentions that none of the children developed oral candidiasis, but also mentions that there might be side effects and therefore monitoring is needed during treatment.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Very low ● Low ○ Moderate ○ High ○ No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Important uncertainty or variability		

● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Only one study was available and not specifically performed in children with the new form of BPD. Additionally, loss to follow up was of methodological concern. Last, the use of corticosteroids may have side effects and/or can lead to adverse events, which need to be outweighed by the possible benefits. Therefore, the evidence was considered low. Since the use of corticosteroids may lead to side effects, the Task Force did not deem it justified to recommend treatment with inhaled corticosteroids.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know		

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Very low ○ Low ○ Moderate ○ High ● No included studies		

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know		

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know		

SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	**Don't know**
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

CONCLUSIONS

Recommendation

The Task Force suggests not to treat with inhaled or systemic corticosteroids for children with BPD (conditional recommendation based on low certainty of evidence). If the treating physician considers it of additional value, the effects of treatment with inhaled/systemic corticosteroids should be carefully monitored by symptoms, lung function, if applicable, or of hospitalizations or emergency visits before chronically applied.

Justification

Only one study was available and not specifically performed in children with the new form of BPD. Additionally, loss to follow up was of methodological concern. Last, the use of corticosteroids may have side effects and/or can lead to adverse events, which need to be outweighed by the possible benefits. Therefore, the evidence was considered low. Since the use of corticosteroids may lead to side effects, the Task Force did not deem it justified to recommend treatment with inhaled corticosteroids.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

If the treating physician considers it of additional value, the effects of treatment with inhaled/systemic corticosteroids should be carefully monitored by symptoms, lung function, if applicable, or reduction of number of hospitalizations or emergency visits before chronically applied.

Research priorities

Further studies are urgently needed to examine the use of inhaled or systemic corticosteroids for children with BPD.

Table S4.4. Evidence to decision tables for children with BPD if treatment with *diuretics* versus no diuretics affect important and critical defined outcomes.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Based on clinical experts opinion it is of utmost relevance to have evidence on diuretic use in children with established BPD	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	No direct evidence that would answer this question in an appropriate way was identified. Indirect evidence was provided by one study. A randomized trial showed that, among infants with oxygen-dependent BPD-who were clinically stable, there were no differences in number of rehospitalizations for respiratory deterioration (diuretic group 22 of 14 patients vs placebo group 19 of 6 patients), pulmonary function tests, or total duration of supplemental oxygen use (diuretic group 133+/-53 days vs. placebo group 147 +/- 71 days) after 36 weeks of PMA Only FRC measured between 9 weeks after weaned from oxygen and diuretics and 1 year of corrected gestational age was increased in the diuretics group. At 1 year of corrected age, the FRC/TGV had improved in both the diuretic group (0.98±0.18) and the placebo group (0.97±0.11).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	The above mentioned randomized trial found no differences in side effects including nephrocalcinosis, supplemental electrolytes or hearing deficits between the groups.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
● Very low ○ Low ○ Moderate ○ High ○ No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	*RESEARCH EVIDENCE*	*ADDITIONAL CONSIDERATIONS*
○ Important uncertainty or variability		

○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	No intervention studies examined the potential beneficial effect of diuretics on important and critical defined outcomes in children in whom BPD has been established and were discharged from the hospital, or who were older than 36 weeks of PMA. In the presented study, the exact method of randomization procedure was unclear, potential confounders were not taken into account, the intention to treat analysis was not fully clear, and additional furosemide supplementation differed between the groups (diuretic group 0/22 patients vs placebo group 5/21 patients; p-value <0.05). They study group did not contain children with the new form of BPD. Therefore, the evidence was considered very low.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know		

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Very low ○ Low ○ Moderate ○ High ● No included studies		

Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies		

Equity What would be the impact on health equity?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know		

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know		

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	***RESEARCH EVIDENCE***	***ADDITIONAL CONSIDERATIONS***
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	**Probably yes**	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

For those children with BPD who already received treatment with diuretics from the neonatal phase or neonatal intensive care unit onwards, the Task Force suggests natural weaning by the relative decrease in dose with increasing weight gain (conditional recommendation based on very low certainty of evidence). If the treating physician considers the use of diuretics of additional value, for example when clinical sign of fluid retention are present, the effects of treatment with diuretics should be carefully monitored during a trial period before chronically applied.

Justification

No intervention studies examined the potential beneficial effect of diuretics on important and critical defined outcomes in children in whom BPD has been established and were discharged from the hospital, or who were older than 36 weeks of PMA. In the presented study, the exact method of randomization procedure was unclear, potential confounders were not taken into account, the intention to treat analysis was not fully clear, and additional furosemide supplementation differed between the groups (diuretic group 0/22 patients vs placebo group 5/21 patients; p-value <0.05),. The study group did not contain children with the new form of BPD. Therefore, the evidence was considered very low.

Subgroup considerations

None

Implementation considerations

None

Monitoring and evaluation

None

Research priorities

Further studies are urgently needed to examine the use of diuretics in children in whom BPD has been established and were discharged from the hospital, or who were older than 36 weeks of PMA with diuretics to reduce morbidity and related outcomes.