TABLE 1. Summary of studies for interventions and management of respiratory disease

Study, country	Level of evidence; research design	Population	Total n	Ages	Intervention	Comparison
Airway clearance techniques (7 papers, 6 studies)						
Fitzgerald et al. (2014), US	IV Prospective case series	Neurological impairment; 2 or more LRTI requiring O_2 and hospitalization in previous 12mo	22 (15 with CP)	M 9y 7mo	HFCWC delivered by The Vest® Airway Clearance System at home 20min 2x/day for 12mo, increased to 4x/day for LRTI with increased O_2 reqt; 70% adherence reqd.	Routine care (may incl Cough Assist, Suctioning, Anti-reflux, Anti-seizure, other medications) before Tx.
Garuti et al. (2016), Italy	IV Prospective case series	CP, non-ambulant, spastic tetraparesis; >3 resp exacerbations/y. At least 1 AB course or access to ER in 6 mo before study	8	1-14y, M 8y 3mo	Free-Aspire, an "electromedical machine for removing broncho-alveolar secretions"; passive use at home 20min at least 2x/day, for 18 mo.	Before Tx.
Maher et al. (2006), US	IV Retrospective review	CP SQ in long-term residential care; Hx healthcare-associated pneumonia.	6	[unknown]	Vest therapy in residential care facility for 1y.	Routine care before Tx.
Siriwat et al. (2018), Thailand	II RCT	CP SQ, admitted to hospital with acute respiratory infection.	22	7mo-12y, (Md 6y 5mo)	Mechanical insufflation-exsufflation using a Cough Assist in hospital, 20-30 min (guided by subject fatigue and comfort) 3x/day for several days	Conventional chest PT (chest percussion, vibration, postural drainage, & manual assisted cough). In ptcts with atelectasis nebulization via EzPAP+bronchodilators if required.
Yuan et al. (2010),(Yuan et al., 2010) US	II RCT	CP SQ, dependent for ADL, GOR.	9 with CP (out of 28)	M 12y 11 mo	HFCWC 12 min 2x/day at home for M 5/12	Chest PT 12 min 3x/day for M 5/12
Plioplys et al. (2002), Plioplys et al. (2003), US	IV Retrospective review	CP, quadriplegia, most with frequent pulmonary infections.	11	1-28y (Md 17y)	20 min Vest Therapy (in 1 or 2 sessions) plus every 8 hours as needed in residential care facilities; mCPT 3x/d or as needed.	Routine care before Tx.
Exercise (3 papers)						
Hutzler (1998), US	III NonRCT	CP. Ambulant (n=40).	46	5-7y (M 5y 8mo)	2 x 30 min swimming/w + 1 x 30min gym/w + 2 Bobath/w for 6 mo	4 x 30min/w Bobath for 6 mo
Shin & Kim (2017),(Shin & Kim, 2017) Korea	III NonRCT	CP	15	M 9y 5 mo	Upper extremity resistance exercise with elastic bands (theraband) 20–30min sessions, concurrent with 30min neurodevelopment treatment, 2x/w for 8w.	Neurodevelopmental treatment 30min 2x/w for 8w.
Lee et al. (2014), Korea	II RCT	CP	22	6-12y (M = 9y 6mo)	Feedback respiratory training using a Spirotiger™ 15min feedback respiratory training and 30min conventional rehabilitation (gross motor activities), with 10min break in between, 3d/w for 3w.	Conventional therapy - gross motor activities 20min, 3x/w for 3w

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Positioning (2 papers)						
Lephart & Kaplan (2015), US	IV SSRD	CP, GMFCS V.	1	19y	Custom moulded chair for 10 sessions over 10w.	Original chair for 10w baseline, 5w follow-up.
Littleton et al. (2011), US	IV SSRD	CP, GMFCS V; recurrent bronchitis, pneumonias.	3 within age range (out of 5)	17, 22 & 25y	Variation in positioning (supine, sitting, side-lying) over 12 sessions.	Supine position before and after intervention phase for 5 sessions each.
Mealtime management (3 papers, 2 studies)						
Adams (2009) Adams et al. (2012), Bangladesh	IV Prospective case series	CP, spastic (n=17), hypertonic (n=3), athetoid (n=1), mixed (n=1); GMFCS III (n=3), IV (n=3), V (n=16); feeding difficulties.	22	1y 7mo-5y 9mo (M = 3y 11mo)	Assessment and advice followed by training about dietary intake (texture & nutritional modifications) and ease and efficiency of feeding.	Before intervention.
Romero et al. (2017), Spain	IV Retrospective review	Children referred for videofluoroscopy (66% of whom had neurological involvement: CP and hypotonia)	61	[unknown]	Multidisciplinary mgt including videofluoroscopy and mealtime mgt	Before Tx.
Salivary gland BoNT-A (4 papers)						
Kim et al. (2006), US	V Case study	CP, SQ; multiple respiratory hospital admissions.	2	2y & 5y	BoNT-A into submandibular glands bilaterally + SEMLC.	Before Tx.
Meece et al. (2010), US	IV Retrospective parent interview	"Mostly CP" who had received 1 or more BTA salivary gland injections in 2y	14	2-17y	30 units BoNT-A injected into each parotid gland & 200 units BoNT-A into each submandibular gland; 1-2 injections over 3y.	Before Tx.
Cheng et al. (2014), UK	V Case study	CP, severe SQ with dysphagia, epilepsy & mod-severe UAO.	1	2y 6mo	BoNT-A injected into rt thyroarytenoid & rt lateral cricoarytenoid mm (4x in 8mo) + PEG inserted	Nebulized adrenaline + intravenous steroids, then endotracheal intubation, then extubated with recurrent O_2 supplementation.
Faria et al. (2015), US	IV Retrospective review	CP + GDD (n=2), CP + HIE (n=1) with $\geq$1 inpatient hospitalization for respiratory distress.	3 CP (out of 13)	4, 18 & 21y	35 units BoNT-A injected into each submandibular gland, and 15 units into each parotid gland, 1x.	Before Tx.
Salivary gland surgery (3 papers)						
Vijayeskaran et al. (2007), US	IV Retrospective chart review	CP undergoing SG surgery for chronic aspiration.	13 CP (out of 62)	7mo-23y (M 5y 8mo)	Salivary gland surgery, 1x.	Before Tx.

Study, country	Level of evidence; research design	Population	Total n	Ages	Intervention	Comparison
Manrique & Sato (2009), Brazil	IV Retrospective cohort	CP, undergoing SMGE, ≥4 LRTI needing AB in y before surgery.	29	18mo-9y	SMGE bilatterally ± bilateral parotid ducts ligation , 1x.	Before Tx.
Noonan et al. (2014), Australia	IV Retrospective chart review	CP undergoing SMGE, GMFCS V (n=7) IV (n=1) & II (n=1); had PEG (n=8); tracheostomy (n=5); fundoplication (n=5); previous hospital admissions for LRTI (n=5).	9 CP (out of 12)	3-21y (M 11y 5mo)	Bilateral SMGE + bilateral PDL, 1x.	Before Tx.
Upper airway management (6 papers)						
Denbar (1998), US	V Case study	Severe CP, non-ambulant with sleep apnoea unable to use CPAP.	1	12y	Adjustable mandibular advancing device (Thornton adjustable Positioner)	Before Tx.
Preciado (2014), US	IV Prospective case series	CP with UAO.	4 CP (out of 5)	2y 0mo – 3y 2mo (M 2y 9mo)	Mandibular distraction osteogenesis, 1x.	Before Tx.
Hartzell et al. (2013), US	IV Retrospective chart review	CP, who had surgery for OSA + pre-op and post-op PSB	14	1-16y (M 6y)	TBS surgery + T&A + UPPP, 1x.	T&A + UPPP.
Myatt & Beckenham (2000), UK	IV Prospective cohort	CP with UAO requiring CPAP but unable to tolerate it.	4 CP (out of 20)	2-13y (M 7y 3mo)	UVPP (n=2), tonsillectomy + CO_2 laser supraglottoplasty (n=1), T&A + CO_2 laser supraglottoplasty (n=1), following sleep nasendoscopy	Before Tx.
Hsiao & Nixon, (2008), New Zealand	IV Retrospective parental report	Dev problems or SQ CP, GMFCS V with OSA.	19	3-18y (M 12y 8mo)	Adenotonsillectomy or Continuous positive airway pressure	Before Tx.
Worley (2003), US	V Case study	CP, dystonia, inspiratory stridor secondary to laryngeal dystonia	1	4y 5mo	BoNT-A into vocalis muscle every 3-4mo	Surgical resection of left aryepiglottic fold & tissues over left cuneiform cartilage + removal of left cuneiform cartilage
Antibiotics (1 paper)						
Plioplys (2011), US	IV Case series	Severe CP with recurrent hospital admissions for pneumonia.	2 with CP (out of 3)	13y & 24y	300 mg nebulized tobramycin in 5 ml vial, 2x/d, passively by facemask for 15 min. Daily for 28d, discontinued 28d, then repeated 28d.	Before nebulized tobramycin.

Study, country	Level of evidence; research design	Population	Total n	Ages	Intervention	Comparison
Gastro-intestinal interventions (7 papers, 6 studies)						
Bozkurt et al. (2004), Turkey	IV Case series	CP SQ (n=19) or SH (n=9) with GORD.	28	3mo-12y (M=5y 0mo)	2mg/kg cisapride 4x/d for 3mo (+ 6mg/kg ranitidine 2x/d for those with reflux index > 10%). (Note: Cisapride has been withdrawn.)	Before cisapride.
Miyazawa et al. (2008), Japan	IV Prospective crossover	CP using nasogastric tube.	18	M 11y 8mo	Enteral formula with high pectin (viscosity 3,000+50 mPa. s) or low pectin (viscosity 1,200+40 mPa. s) for 4w.	No pectin enteral formula for 4w.
Sullivan et al. (2005), Sullivan et al. (2006), UK	IV Prospective case series	CP with gastrostomy clinically indicated by severe oral-motor dysfunction compromising nutritional status + clinical signs of undernutrition;	57	5mo to 17 y (Md 4y 4mo)	Gastrostomy placement±fundoplication	Before Tx.
Cheung et al. (2006), China	IV Prospective cohort	Severe CP with GORD, who had used nasogastric tube for at least 1y.	11 (out of 20)	3y 7mo-14y 5mo (M=8y 6mo)	Nissen fundoplication by open or laparoscopic technique.	Before Tx.
O'Loughlin et al. (2013), Australia	IV Retrospective parent report	Children with NI who had undergone Nissen fundoplication, 92% GMFCS V, 78% with recurrent chest infections.	122 (incl 77 SQ CP)	2-10y (Md = 6y)	Nissen fundoplication by open or laparoscopic technique	Before Tx.
Ishimaru (2017), Japan	IV Retrospective review and carer report	Individuals with NI who had undergone laparoscopic fundoplication.	31 (incl 17 CP)	7mo-40y (Md = 13y)	Laparoscopic Nissen fundoplication	Before Tx.
Spinal surgery (1 study)						
Keskinen et al. (2015), Finland	IV Retrospective chart review	CP who had undergone surgery for scoliosis; 15 non-ambulatory.	17 CP (out of 42)	M=15y 2mo	Scoliosis surgery.	Before Tx.

AB, antibiotics; ADL, activities of daily living; BoNT-A, Botulinum Toxin-A; CO_2, Carbon dioxide; CP, cerebral palsy; CPAP, continuous positive airway pressure; Ctrl, control; d, day; DD, developmental delay; Dev, developmental; gp, group; ER, Emergency Room; GORD, gastro-oesophageal reflux disease; HFCWC, high frequency chest wall compression; HIE, hypoxic ischemic encephalopathy; Hx, medical history; incl, including; LM, laryngomalacia; LRTI, lower respiratory tract infection; M, mean; mCPT, manual chest physical therapy; Md, median; mgt, management; min, minutes; ml, millilitres; mm, muscle; mo, months; mod, moderate; N, number of participants for whom results are available; NI, neurological impairment; O_2, oxygen; PEG, percutaneous endoscopic gastrostomy; PDL, parotid duct ligation; rt, right; post-op, post-operational; pre-op, pre-operational; PSB, polysomnogram; PT, physiotherapy; RCT, randomized controlled trial; reqd, required; reqt, requirement; SEMLC, single event multi-level chemoneurolysis; SG, salivary gland; SGP, supraglottoplasty; SMGE, submandibular gland excision; SQ, spastic quadriplegia; SSRD, Single subject research design; T&A, tonsillectomy and adenoidectomy; TBS, tongue base suspension; Tx, treatment; UAO, upper airway obstruction; URTI, upper respiratory tract infection; UVPP, uvulopalatopharyngoplasty; w, weeks; x, times.

TABLE 2. Conduct of Group Design Studies (levels I, II, and III evidence only)

Study	Level/Quality	1	2	3	4	5	6	7
Siriwat et al. (2018)	II-S (6/7)	✓	✓	✓		✓	✓	✓
Yuan et al. (2010)	II-W (3/7)	✓	✓	✓				
Hutzler (1998)	III-W (2/7)			✓			✓	
Shin & Kim (2017)(Shin & Kim, 2017)	III-W (3/7)	✓		✓			✓	
Lee et al. (2014)	II-S (6/7)	✓	✓	✓	✓		✓	✓

The conduct of an individual study will be judged as S (strong, if 6-7 of the questions are rated "yes"), M (moderate, if 4 or 5 questions are rated "yes") or W (weak, if less than 0-3 questions are rated "yes"). AACPDM conduct questions: 1. Were inclusion and exclusion criteria of the study population well described and followed? 2. Was the intervention well described and was there adherence to the intervention assignment? (for 2-group designs, was the control exposure also well described?) Both parts of the question need to be met to score 'yes'. 3. Were the measures used clearly described, valid and reliable for measuring the outcomes of interest? 4. Was the outcome assessor unaware of the intervention status of the participants (i.e., were the assessors masked)? 5. Did the authors conduct and report appropriate statistical evaluation including power calculations? Both parts of the question need to be met to score 'yes'. 6. Were dropout/loss to follow-up reported and less than 20%? For 2-group designs, was dropout balanced? 7. Considering the potential within the study design, were appropriate methods for controlling confounding variables and limiting potential biases used?