Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Franklin D, Babl FE, Schlapbach LJ, et al. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis. N Engl J Med 2018;378:1121-31. DOI: 10.1056/NEJMoa1714855

SUPPLEMENTARY APPENDIX

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1 List of Co-Investigators

1.1 PCCRG Co-Investigators (Pediatric Critical Care Research Group)

Australia: Trang Pham, Melanie Kennedy, Kate McEnery, Lee O'Malley and Geraldine Corcoran, Paediatric Critical Care Research Group, Lady Cilento Children's Hospital & Mater Research Institute, Brisbane, Queensland; John Gavranich, Ipswich Hospital, Ipswich, Queensland; Sue Moloney, Gold Coast University Hospital, Southport, Queensland; Prasanna Shirkhedkar, Caboolture Hospital, Caboolture, Queensland; Tom Hurley, Nambour Hospital, Nambour, Queensland; Marlon Radcliffe, Redcliffe Hospital, Redcliffe, Queensland; Vishal Kapoor, Redland Hospital, Redland, Queensland; David McMaster, The Tweed Hospital, Tweed Heads, New South Wales; Colin Myers, The Prince Charles Hospital, Brisbane, Queensland; Jan Cullen, Logan Hospital, Brisbane, Queensland; John Coghlan, Toowoomba Hospital, Toowoomba, Queensland; David Levitt, Lady Cilento Children's Hospital, Brisbane, Queensland; Natalie Phillips, Lady Cilento Children's Hospital, Brisbane, Queensland; Kristen Gibbons, Mater Research Institute – The University of Queensland.
United Kingdom: Vijay Gc (BHCM, MPH), University of East Anglia, United Kingdom; Under the guidance of Jennifer Whitty, Vijay Gc assisted in the economic evaluation.

1.2 PREDICT Co-Investigators (Paediatric Research in Emergency Departments International Collaborative)

Australia: Susan Montgomery, Townsville Hospital, Queensland; Amanda Williams, Royal Children's Hospital, Melbourne, Victoria; Cate Wilson, Royal Children's Hospital, Melbourne, Victoria; Chantelle Cabral, Monash Health, Victoria; Kam Sinn, The Canberra

Hospital, Australian Capital Territory; Karen Brown, The Canberra Hospital, Australian Capital Territory.

New Zealand: Shirley Lawrence, KidzFirst Middlemore Hospital, Auckland; Megan Bonisch, Starship Children's Health, Auckland.

1.3 Funding

The study was funded by the National Health and Medical Research Council (NHMRC) Australia and the Queensland Emergency Medical Research Foundation and several local hospital funds. The high-flow equipment and consumables for the study were provided free of charge by Fisher & Paykel Healthcare(Auckland, New Zealand), who had no involvement in design, conduct, and analysis of the study.

1.4 Steering Committee:

The trial was overseen by a steering committee that presented information regarding the progression and monitoring of the study during 3 monthly collaborative teleconferences between members of the Paediatric Critical Care Research Group (PCCRG, representing all sites in Queensland) and the Paediatric Research in Emergency Department International Collaborative (PREDICT[1], representing all other sites).

A. Schibler (Chair), D. Franklin, F.E. Babl, L.J. Schlapbach, S. Dalziel, J.F. Fraser, E. Oakley.

1.5 Statistician:

All data analysis was performed by the study statistician, in accordance with the International Conference on Harmonization and Good Clinical Practice guidelines.

Mark Jones and Kristen Gibbons (Design)

1.6 Health Economist:

Jennifer Whitty and Vijay Gc

2 Contribution to the Study

2.1 Author Contribution

The trial was designed and conducted by the authors. The trial is an investigator-initiated multicenter study led by A. Schibler. D. Franklin and A. Schibler were responsible for identifying the research question, and contributing to drafting of the study protocol. S. Dalziel, F.E. Babl, E. Oakley, S.S. Craig, J.S. Furyk and J. Neutze as members of the PREDICT research network; L.J. Schlapbach, J.F. Fraser and J.A. Whitty have all contributed to the development of the protocol, study design, interpretation of analyses and manuscript preparation. J.A. Whitty undertook the health economy analysis. D. Franklin was responsible for the drafting of this paper, although all authors provided comments on the drafts and have read and approved the final version. D. Franklin and A. Schibler, for the PARIS group, take responsibility for the manuscript as a whole.

3 Independent Data Safety Monitoring Committee Members

We thank the members of the Independent Data Safety Monitoring Committee (DMSC) for their important contribution to the trial: P.H. Sargent[1] (Chair) and S. Burgess[2].

1. Gold Coast University Hospital, Gold Coast, Queensland, Australia.
2. Mater Health Services, Brisbane, Queensland, Australia.

The data safety monitoring board reviewed independently the data after 200 patients enrolled and did recommend continuing the trial. No serious adverse event was observed. The remaining reported adverse events (pneumothorax and apneas, 8 in total) were reported to the DSMC and the ethic committee and every time the adverse event was deemed unrelated to the study intervention.

4 METHODS

The full study protocol has been published

4.1 Methods: Screening

All infants less than 12 months of age presenting with respiratory symptoms to one of the participating hospital's emergency department were screened for inclusion criteria. Patients could meet the inclusion criteria either upon presentation or during their hospital admission. Some patients were randomized following admission to the ward environment as they met the oxygen requirement some hours after admission. An enrolment logbook existed in both the emergency departments and pediatric wards. The staff could randomize in either area once the patient met all inclusion criteria. Each hospital had their own enrolment logbook, which was monitored by the research team daily to weekly, depending on having a local research nurse dedicated to the trial at their center.

4.2 Methods: Inclusion and Exclusion Criteria

For the purpose of this trial we defined apnea as an unexplained episode of cessation of breathing for 20 seconds or longer, or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, and/or marked hypotonia[2], **and** assisted ventilation mechanical ventilation. Any infant with a severe apnea and requiring immediate respiratory intervention were excluded.

4.3 Methods: Deferred (Retrospective) Consent

The human research ethics committee at the lead center (for Australia: Children's Health Queensland Ethics Committee, Brisbane, Queensland, HREC/13/QRCH/93 and for New Zealand: Central Health and Disability Ethics Committee, HDEC15/CEN/46) approved a retrospective and prospective consent process. At the time of the study period the use of high-flow therapy was considered normal standard practice in the participating study centers, therefore the ethics committee was comfortable to allow and accept the deferred consent process. Eligible infants could be randomized as soon as they met eligibility criteria and their parent/guardian was then approached as soon as possible once the infant had stabilized and the parent/guardian had time to adjust to the emergency or ward environment. The human research ethics committee did not specify a time limit within which to gain the retrospective consent after the time of randomization, however the staff were educated to obtain within 24-48 hours following randomization and the parent/guardian given options of providing consent for their infant to remain in the trial, or withdrawing them. The data of patients with declined consent was not analyzed but study records were kept for legal purposes. High-flow therapy was routinely used as a management for infants with respiratory illness prior to the initiation of the study, as was standard-oxygen therapy and the consent sought from the parent/guardian was to obtain the data on the infant.

4.4 Methods: Statistical Analysis

The sample size calculation of the study was based on pre existing data from 478 eligible infants with bronchiolitis admitted to 4 of the participating hospitals. Eighty of these infants received escalation and transfer to higher level of care (16.7%). Assuming a more conservative baseline rate of failure of standard-oxygen therapy of 10%, and a 50% relative

reduction to 5% with a power of 90% and type I error of 0.05, 582 participants per group were required, resulting in a total sample size of 1164 patients. An attrition rate of approximately 10-20% was estimated, which indicated an overall sample size of 1400. The primary and secondary outcomes were analyzed based on the assigned treatment group. Data were analyzed first for all infants having received escalation of care. Data were then analyzed for all infants receiving escalation of care who were independently confirmed to meet three of the four clinical criteria. For this purpose, three research nurses reviewed the accuracy and validity of the outcome variables and clinician's decision to escalate care. Each research nurse independently, and on separate occasions reviewed the hospital medical notes and early warning tools; if there was disagreement a third nurse made the final decision. Descriptive statistics were used to report on the baseline characteristics of the total study cohort stratified by treatment group. The primary outcome measure investigating escalation of care and treatment failure was analyzed using a chi-squared test, and reported as relative risk, 95% confidence interval and p-value, as well as risk difference with 95% confidence interval. The continuous outcome measure hospital length of stay was approximately normally distributed hence independent samples t-test was used as suggested by the Journal. Analyses of secondary outcomes were based on chi-square test for proportions and independent samples t-test for continuous measures.

Pre-specified sub-groups included; ex-preterm infants, infants with congenital heart defect, infants less than 3 months and less than 6 months of age (corrected for prematurity), infants presenting to hospitals with and without an on-site intensive care unit. The Breslow-Day test for homogeneity of odds ratios was used for all subgroup analysis. For all but one subgroup analysis there was no evidence of heterogeneity therefore the overall odds ratio was assumed for these subgroups. Exploratory analyses were conducted on the subset of patients who received escalation of treatment. These are conditional analyses that are not based on

comparing complete randomized groups hence caution is needed when interpreting the results. Statistical significance was set at the 0.05 level. Statistical analysis was conducted using SAS, version 9.4 for Windows (SAS Institute Inc., Cary, NC, USA). Independent data and safety monitoring was performed and reported to the Data Safety Monitoring Board after 200 infants were enrolled and every time an adverse event was reported.

4.5 Methods: Extended Baseline Characteristics and Entry Criteria using different saturation thresholds (Supplementary Table S1a, S1b and S1c)

There were 17 participating hospitals in this study with six tertiary hospitals having a lower saturation threshold of <92% prior to applying oxygen to the infant. The rationale for this was due to individual hospitals remaining within their current standard practice and to maintain familiar practice. The other 11 centers had a saturation threshold of <94% prior to applying oxygen to an infant. The two differing saturations thresholds in different centers were accepted in this study as it was balanced through randomization across all sites.

Hospitals with <92% threshold

- Six tertiary level hospitals

Hospitals with <94% threshold

- Ten regional level hospitals
- One tertiary level hospital

Extended Baseline Characteristics of study patients

Table.S1a Baseline Characteristics of Infants with Bronchiolitis

Characteristic	Standard-oxygen group N=733	High-flow group N=739
Age (months)	6.10±3.44	5.76±3.54
≤ 3 months no. (%)	186 (25.4)	211 (28.6)
> 3 to 6 months no. (%)	170 (23.2)	187 (25.3)
> 6 months no. (%)	377 (51.4)	341 (46.1)
Weight (kg)	7.60±2.21	7.27±2.25
Sex female no. (%)	262 (35.7)	285 (38.6)
Ethnicity		
Caucasian no. (%)	379 (51.7)	390 (52.8)
Aboriginal/Torres Strait Islander no. (%)	31 (4.2)	28 (3.8)
Maori/Pacific Islander no. (%)	217 (29.6)	199 (26.9)
Other/unknown no. (%)	106 (14.5)	122 (16.5)
Prematurity <37 weeks ¶ no (%)	128 (17.5)	137 (18.6)
Need for neonatal respiratory support no. (%)	101 (13.9)	116 (15.7)
Oxygen only no. (%)	37 (5.0)	30 (4.1)
Non-invasive ventilation no. (%)	70 (9.5)	76 (10.3)
Invasive ventilation no. (%)	20 (2.7)	28 (3.8)
Previous hospital admissions for respiratory disease postnatal ¶ no (%)	225 (30.7)	187 (25.3)
Intensive care admission for respiratory support no. (%)	45 (6.2)	27 (3.7)
Invasive ventilation no. (%)	7 (1.0)	4 (0.5)
Non-invasive ventilation no. (%)	6 (0.8)	2 (0.3)
High-flow therapy no. (%)	34 (4.6)	20 (2.7)
Chronic Lung Disease no. (%)	13 (1.8)	16 (2.2)
Congenital Heart Disease no. (%)	16 (2.2)	8 (1.1)
Patient history of wheeze no. (%)	176 (24.1)	160 (21.8)
Family history of asthma no. (%)	361 (50.0)	328 (45.4)
Family history of allergy no. (%)	162 (22.5)	133 (18.4)
Currently attending child care no. (%)	92 (13.0)	96 (13.5)
Viral etiology*	N=584	N=610
Respiratory syncytial virus	322 (55.1)	334 (54.8)
Other viruses	201 (34.4)	177 (29.0)
Multiple viruses	110 (15.0)	102 (13.8)
No virus detected on nasopharyngeal aspirate	112 (19.2)	146 (23.9)
Severity Pre-enrollment		
Heart rate beats/min	159.4 ±28.8	160.9±27.6
Respiratory rate breaths/min	52.0±13.3	53.1±12.8
SpO2 %	88.5±7.4	87.9±7.80
Median time of onset of illness to presentation in days (IQR)	3 (2, 4)	3 (2, 4)

Legend to Table S1a

Plus-minus value denotes means and ±SD, medium interquartile range (IQR).
*Viral testing was not mandated with lower number of tests overall obtained.

Supplementary Table S1b and S1c

Table S1b Baseline Characteristics of Infants with Bronchiolitis for Hospitals with Saturation Threshold of ≥ 92%			
Characteristic		**Standard-oxygen group N=349**	**High-flow group N=340**
Age (months)			
≤ 3 months no. (%)		85 (24.4)	95 (27.9)
> 3 to 6 months no. (%)		87 (24.9)	92 (27.1)
> 6 months no. (%)		177 (50.7)	153 (45.0)
Weight (kg)		7.61 ± 2.18	7.27 ±2.17
Sex Female no. (%)		116 (33.2)	129 (37.9)
Risk Factors	**Prematurity <37 weeks** no. (%)	65 (18.6)	60 (17.7)
	Previous hospital admissions for respiratory disease postnatal[¶]	120 (34.4)	90 (26.5)
	Chronic Lung Disease no. (%)	8 (2.3)	9 (2.7)
	Congenital Heart Disease no. (%)	11 (3.2)	3 (0.9)
	Patient history of wheeze no. (%)	87 (25.1)	72 (21.4)
	Family history of asthma no. (%)	174 (50.9)	149 (45.0)
	Family history of allergy no. (%)	86 (25.2)	75 (22.7)
	Currently attending child care? no. (%)	31 (9.1)	32 (9.7)
Viral etiology[*]	Number tested	N=210	N=220
	Respiratory syncytial virus no. (%)	107 (51.0)	116 (52.7)
	Other viruses no. (%)	83 (39.5)	72 (32.7)
	Multiple viruses no. (%)	69 (19.8)	73 (21.5)
Severity Pre-enrolment	Heart rate beats/min	166.3 ± 27.0	167.4 ± 24.4
	Respiratory rate breaths/min	55.6 ± 13.9	56.0 ± 12.6
	SpO2 %	87.7 ± 6.79	87.0 ±6.87
Severity at escalation	Heart rate beats/min	164.7 ± 20.8	165.8 ± 21.3
	Respiratory rate breaths/min	56.3 ± 12.4	63.7 ± 15.4
	SpO2 %	96.4 ± 2.91	96.4 ± 3.10

Table S1c Baseline Characteristics of Infants with Bronchiolitis for Hospitals with Saturation Threshold ≥ 94%			
Characteristic		**Standard-oxygen group N=384**	**High-flow group N=399**
Age (months)			
≤ **3 months** no. (%)		101 (26.3)	116 (29.1)
> **3 to 6 months** no. (%)		83 (21.6)	95 (23.8)
> **6 months** no. (%)		200 (52.1)	188 (47.1)
Weight (kg)		7.59 ± 2.24	7.26 ± 2.31
Sex Female no. (%)		146 (38.0)	156 (39.1)
Risk Factors	**Prematurity <37 weeks** no. (%)	63 (16.4)	77 (19.4)
	Previous hospital admissions for respiratory disease postnatal¶	105 (27.3)	97 (24.4)
	Chronic Lung Disease no. (%)	5 (1.3)	7 (1.8)
	Congenital Heart Disease no. (%)	5 (1.3)	5 (1.3)
	Patient history of wheeze no. (%)	89 (23.3)	88 (22.2)
	Family history of asthma no. (%)	187 (49.2)	179 (45.8)
	Family history of allergy no. (%)	76 (20.1)	58 (14.8)
	Currently attending child care no. (%)	61 (16.6)	64 (16.8)
Viral etiology*	Number tested	N= 374	N=390
	Respiratory syncytial virus no. (%)	215 (57.5)	218 (55.9)
	Other viruses no. (%)	67 (17.9)	58 (14.9)
	Multiple viruses no. (%)	41 (11.0)	29 (7.3)
Severity Pre-enrolment	Heart rate beats/min	153.1 ± 29.0	155.3 ± 28.9
	Respiratory rate breaths/min	48.7 ± 11.8	50.7 ± 12.5
	SpO2 %	89.2 ± 7.90	88.7 ± 8.44
Severity at escalation	Heart rate beats/min	163.5 ± 19.1	157.4 ± 19.4
	Respiratory rate breaths/min	53.0 ±12.4	60.9 ± 14.8
	SpO2 %	96.4 ± 3.67	96.2 ± 2.85

Legend to Table S1b and S1c

Plus-minus value denotes means and ±SD, medium interquartile range (IQR).

*Viral testing was not mandated with lower number of tests overall obtained.

¶Multiple options possible

4.6 Methods: Analysis of outcome of infants who met ≥ 3 out of the 4 clinical criteria and reason for treatment failure (Supplementary Figure S1)

The primary outcome was defined in the study protocol as treatment failure if ≥ 3 out of the 4 clinical criteria were met and escalation of care or level of care was received. Clinicians were allowed within the protocol to escalate therapy with their best clinical judgment. A chart review by three research nurses showed a lower number of infants reaching ≥3 out of the 4 criteria according to the medical notes and hospital early warning tools. In the standard-oxygen group 31.1% met less than 3 criteria and in the high flow group 39.1% met less than 3 criteria on a retrospective chart review. However, the clinician's judgment and decision was at this time to escalate care.

Supplementary Figure S1

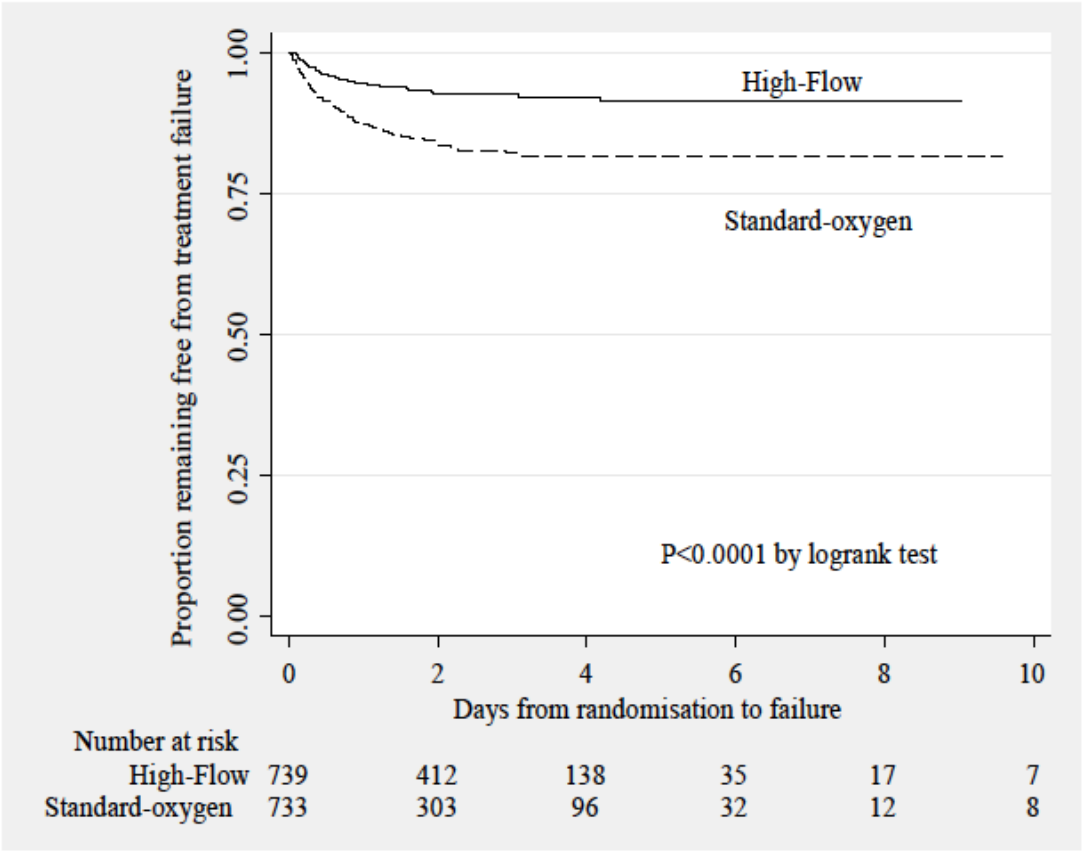

Figure S1. Kaplan Meier Plot of infants who met meeting ≥ 3 out of 4 clinical criteria remaining free of treatment failure.

4.7 Analysis of outcome of infants who met ≥ 3 out of the 4 clinical criteria and reason for treatment failure

The primary outcome was defined in the study protocol as treatment failure if ≥ 3 out of the 4 clinical criteria were met and escalation of care or level of care was received. Clinicians were allowed within the protocol to escalate therapy with their best clinical judgment. A chart review by three research nurses showed a lower number of infants reaching ≥3 out of the 4 criteria according to the medical notes and hospital early warning tools. In the standard-oxygen group 31.1% met less than 3 criteria and in the high flow group 39.1% met less than 3 criteria on a retrospective chart review. However, the clinician's judgment and decision was at this time to escalate care.

4.8 Methods: Proportion of Escalation Criteria met in onsite ICU and no onsite ICU Hospital (Supplementary Table S2)

There were eight hospitals (tertiary and regional) who had access to an onsite Intensive Care Unit (ICU) – some of these centers were stand alone pediatric ICU's and some were mixed adult and pediatric ICU's. Hospitals with no onsite ICU included nine regional centers. When these centers required a higher of level of care or intensive care services for a child they requested a referral and retrieval by the tertiary facility for their state to collect and transfer the child to a hospital with an onsite ICU. Analysis was performed to investigate if a similar proportion of infants with bronchiolitis met the clinical criteria in hospitals with and without onsite ICU.

Supplementary Table S2: Proportion of clinical criteria met in onsite ICU and no on-site ICU hospitals

Table S2: Proportion of escalation criteria met in onsite ICU and non onsite ICU hospitals		
	Standard-oxygen group	**High-Flow group**
	N = 167	**N = 87**
Hospitals with onsite ICU (N=165)		
Persistent Tachycardia no (%)	64/98 (65.3)	39/67 (58.2)
Persistent Tachypnea no (%)	69/98 (70.4)	49/67 (73.1)
Increasing oxygen requirement no (%)	35/98 (35.7)	29/67 (43.3)
Early Warning Tool triggers review and/or clinician directed escalation occurred no (%)	83/98 (84.7)	53/67 (79.1)
Hospitals without onsite ICU (N=89)		
Persistent Tachycardia no (%)	51/69 (73.9)	10/20 (50.0)
Persistent Tachypnea no (%)	59/69 (85.5)	14/20 (70.0)
Increasing oxygen requirement no (%)	15/69 (21.7)	8/20 (40.0)
Early Warning Tool triggers review and/or clinician directed escalation occurred no (%)	46/69 (66.7)	15/20 (75.0)

4.9 Methods: Further Subgroup Analysis for Primary Outcome (Table S3)

Additional subgroup analysis was performed to investigate the impact of i.) previous hospital admission for respiratory disease, ii.) family history of asthma, iii.) prematurity born < 33 weeks post-conceptional age.

Table S3. Primary Outcomes in additional Subgroups as per Escalation

Outcome	Standard-oxygen N=733	High Flow N=739	Relative risk (95%-CI)	Risk Difference (95%-CI)	P Value
Escalation					
Previous hospital admissions for respiratory disease					
Yes no (%)	44/225 (19.6)	21/187 (11.2)	0.57 (0.34-0.95)	-8.3% (-15% to -1.5%)	0.60¶
No no (%)	123/508 (24.2)	66/551 (12.0)	0.50 (0.37-0.66)	-12% (-17% to -7.6%)	
Family history of asthma					
Yes no (%)	88/361 (24.4)	39/328 (11.9)	0.49 (0.34-0.70)	-12% (-18% to -6.8%)	0.52¶
No no (%)	72/361 (19.9)	45/394 (11.4)	0.57 (0.40-0.82)	-8.5% (-14% to -3.3%)	
Prematurity <37 weeks					
Yes no (%)	38/128 (29.7)	27/137 (19.7)	0.66 (0.42-1.05)	-10% (-20% to 0.4%)	0.19¶
No no (%)	129/605 (21.3)	60/601 (10.0)	0.47 (0.35-0.63)	-11% (-15% to -7.3%)	
Prematurity <33 weeks					
Yes no (%)	10/45 (22.2)	9/55 (16.4)	0.74 (0.30, 1.82)	-5.9% (-21%, 9.7%)	0.38¶
No no (%)	157/688 (22.8)	78/683 (11.4)	0.50 (0.39, 0.65)	-11% (-15%, -7.5%)	

¶P-value for all subgroup analyses represents test of interaction between treatment group and subgroups using a log binomial regression model.

4.10 Methods: Predefined Secondary Outcomes (Supplementary Figures S2a and S2b)

Secondary outcomes were defined as (a) the proportion of infants requiring transfer to higher acuity care, which includes admission to an on-site pediatric intensive care or transfer to a tertiary hospital; (b) length of hospital stay, including intensive care length of stay and (c) intubation rates; (d) associated health care costs for respective therapy; (e) length of oxygen therapy and; (f) adverse events.

Supplementary Figures S2a and S2b

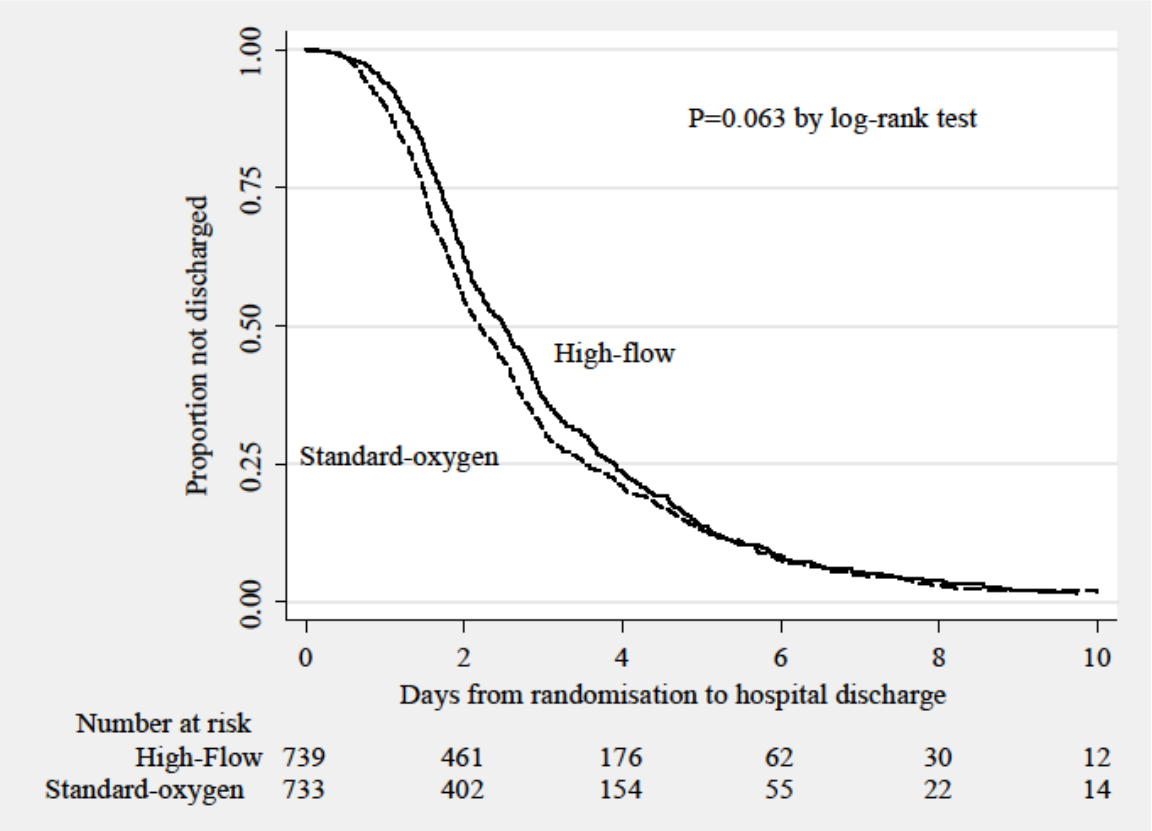

Figure S2a. Length of hospital stay for all infants in standard-oxygen and high-flow group

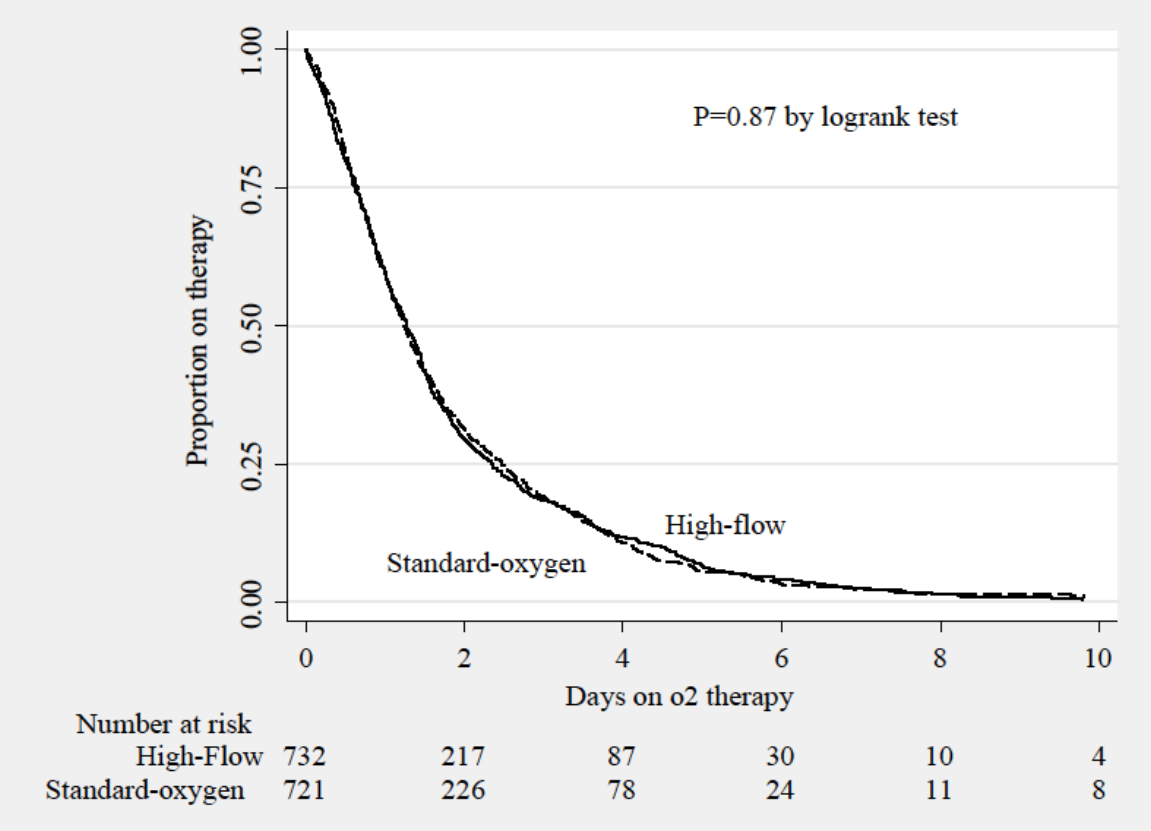

Figure S2b. Length of oxygen therapy for all infants in standard-oxygen and high-flow group

4.11 Methods: Compliance with Study Protocol

All 17 participating centers were provided with the same education and educational materials and resources, which included face-to-face education on both the protocol and equipment used in the study, voice over power-point presentations, lanyards, flowcharts and signage for department and ward areas. The development of troubleshooting guides and frequently asked questions was improved upon over the course of the study and provided to all centers. Prior to the study commencing at each center the medical and nursing staff were both educated in the general pediatric ward and emergency department settings.

The regional centers were educated and monitored for compliance by the central study team. The larger tertiary facilities, which had dedicated research staff, educated their own staff and monitored their own hospital compliance to protocol. The central study team also monitored all hospitals compliance with reviewing and auditing the de-identified early warning tools during the course of recruitment.

Each center had nurse champions who were provided with additional education, including the use of high-flow therapy in infants with bronchiolitis and education regarding the study protocol, research etiquette and the importance of compliance and good documentation.

The central study team visited the regional centers on a two weekly basis throughout the study period and collected clinical research forms (CRF) and de-identified early warning tools.

4.12 Methods: Non Study Treatments received

Non-study treatments were medications (excluding oxygen) the infant received during the course of the study which were not prescribed by the study protocol. The use and administration of these medications was at the discretion of the attending clinicians. These

interventions were recorded in the clinical research form (CRF) and included medications such as steroids, antibiotics, antipyretics, bronchodilators and hypertonic saline.

4.13 Supplementary Non Study treatment received Table S4

We recorded for all infants data on non study treatment and medications such as steroids and bronchodilators. Particular attention was given to collect data for sedation medication.

Table S4. Non Study treatment and medication received

Treatment	Standard-oxygen group N=733	High-flow group N=739
Any non-study treatment no (%)	499 (67.5)	520 (70.9)
Steroids no (%)	58 (7.9)	53 (7.2)
Nebulised saline no (%)	77 (10.5)	69 (9.3)
Bronchodilators no (%)	214 (29.2)	182 (24.6)
Adrenaline nebulizations no (%)	2 (0.3)	6 (0.8)
Antibiotics no (%)	120 (16.4)	117 (15.8)
Pain/fever no (%)	273 (37.2)	270 (36.5)
Sedation no (%)	35 (4.8)	49 (6.6)

4.14 Early warning tool example

This chart is an example of one of the early warning tools used in the study for infants less than 12 months of age. This example was used for Queensland, Australia and is known as the “Children’s Early Warning Tool” (CEWT).

Queensland Government

Bronchiolitis High Flow Trial
Children's Early Warning Tool (CEWT®)

LESS THAN 1 YEAR

For tertiary and secondary facilities

Facility:

(Affix identification label here)

URN:

Family name:

Given name(s):

Address:

Date of birth: Sex: ☐M ☐F ☐I

< 1 YEAR

General Instructions

- This form is only for use for children < 1 year on the High Flow Nasal Cannula Treatment for Viral Bronchiolitis Randomised Control Trial *(HREC/13/QRCH/93)*.
- Full CEWT score = Respiratory rate + Respiratory distress + O2 + O2 Saturation + Temperature + Heart rate + Blood pressure + Capillary refill time + Level of consciousness.
- A Full CEWT score and a pain score (p4) must be calculated
  - › on admission
  - › CEWT score of 1 or more
  - › if patient is deteriorating or you are concerned.
- A CEWT score (with BP as clinically indicated) must be calculated at least every 8 hours
- When graphing observations, place a dot (•) in the appropriate box and join to the preceding dot (e.g. ╲). For blood pressure, use the symbols indicated (⁾).
- Any observation outside the range of the graph, you must write the number.
- Score each observation by referring to the CEWT Score Legend or by aligning the dot with the scoring columns on either side of the graph. Add up all observation scores to calculate the Total CEWT score and record this in the Total CEWT score row, even if the score is zero.
- For abnormal observations, you must continue to check until normal.
- Aside from the above, do appropriate observations at an appropriate frequency for the patient's clinical status.

Modifications

Use if *abnormal* observations are tolerated for patient

- Modifications should be made on the basis of chronic abnormal physiology.
- Modifications can only be authorised by SMO / Registrar / PHO (or equivalent).
- Modifications must be assessed and rewritten with each new CEWT chart.

Diagnosis which justifies modification (e.g. cystic fibrosis):

Authorised by (SMO / Registrar / PHO):

Doctor's name (please print): Designation:

Signature: Date / Time: / / :

Write the acceptable range (will score zero) below:

Respiratory Rate	to	breaths/min
O_2 Saturation	to	%
O_2 Flow Rate	to	L/min
Systolic BP	to	mmHg
Heart Rate	to	beats/min

Scoring Note: observations outside the modified range revert to the original score on CEWT

Example: if O_2 saturations > 90% are tolerated (score of zero) and the O_2 saturations drop to 90%, it would score 1

NB: tick modifications box at bottom of page 3 to indicate modifications are in use

Interventions

If an intervention is administered, record here and note letter in *Interventions* row over page in appropriate time column

A
B
C
D
E
F
G

BRONCHIOLITIS HIGH FLOW TRIAL CEWT® LESS THAN 1 YEAR TERTIARY AND SECONDARY

Pain Assessment Chart Instructions

- If you are concerned about the patient's pain but they do not fit the below criteria notify medical officer
- For any score in coloured zone follow instructions in action box
- Note pain relief in table
- **If on opioid / analgesia infusions, use pain infusion chart**

(Affix identification label here)

URN:

Family name:

Given name(s):

Address:

Date of birth: Sex: ☐M ☐F ☐I

< 1 YEAR

Pain Assessment Tools

Select (with tick) appropriate pain assessment tool

☐ **FLACC**

Each category is scored 0–2, resulting in a total score of 0–10

Categories	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position, or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractible	Difficult to console or comfort

Pain Assessment Chart

Actions: Pain Score		Time →
• Urgent registrar review. Consider opioids. Obtain a full CEWT score. • Contact Acute Pain Service if pain remains severe after permitted interventions	10 9 8	
• Administer prescribed analgesia • Consider a full CEWT score • Registrar review if no improvement • Consider referral to Acute Pain Service if interventions ineffective	7 6 5 4	
• Consider analgesia • Ward doctor review to prescribe if required	3 2 1	
• No action	0	
Bolus Indicate if IV bolus given (P)aracetamol (O)pioid (Ot)her		
Enteral (P)aracetamol (O)pioid (N)SAID (Ot)her		

Additional Observations

Date								
Time								
Height (cm) ☐ Weight (kg)								
Other:								

Other Charts

☐ Blood Glucose ☐ Neurological ☐ Pain/Epidural/Patient Controlled Analgesia

☐ Fluid Balance ☐ Neurovascular

DO NOT WRITE IN THIS SHADED AREA

TRIAL

DO NOT WRITE IN THIS BINDING MARGIN

v0.10 - 06/2015 - TRIAL

SW595

BRONCHIOLITIS HIGH FLOW TRIAL CEWT®

Less than 1 year old

Parameter	Score	Range	Date / Time	Range	Score
Respiratory rate (breaths / min) Measure for a full minute	3	56–60		56–60	3
	2	51–55		51–55	2
	1	46–50		46–50	1
	0	41–45		41–45	0
		36–40		36–40	
		31–35		31–35	
		26–30		26–30	
		21–25		21–25	
	2	16–20		16–20	2
	3	11–15		11–15	3
	E	≤ 10		≤ 10	E
Respiratory distress	3	Severe		Severe	3
	2	Moderate		Moderate	2
	1	Mild		Mild	1
	0	Nil		Nil	0
Control O_2 (L/min)	2	> 5		> 5	2
	1	1–5		1–5	1
	0	< 1		< 1	0
High Flow (FiO_2)	2	≥ 60 %		≥ 60 %	2
	1	40–60%		40–60%	1
	0	< 40%		< 40%	0
Actual L/min (Control) or FiO_2 (HF) Value					
High Flow L/min on AIRVO$_2$ screen					
O_2 Saturation (%)	0	≥ 94 %		≥ 94 %	0
	1	90–93%		90–93%	1
	2	86–89%		86–89%	2
	3	≤ 85%		≤ 85%	3
Write O_2 saturation value					
Probe change					
Temperature (C)	2	40.5–40.9		40.5–40.9	2
		40–40.4		40–40.4	
		39.5–39.9		39.5–39.9	
		39–39.4		39–39.4	
	1	38.5–38.9		38.5–38.9	1
		38–38.4		38–38.4	
	0	37.5–37.9		37.5–37.9	0
		37–37.4		37–37.4	
		36.5–36.9		36.5–36.9	
		36–36.4		36–36.4	
		35.5–35.9		35.5–35.9	
	2	35–35.4		35–35.4	2
Heart rate (beats / min)	3	190s		190s	3
	2	180s		180s	2
		170s		170s	
	1	160s		160s	1
	0	150s		150s	0
		140s		140s	
		130s		130s	
		120s		120s	
		110s		110s	
	1	100s		100s	1
	2	90s		90s	2
	3	80s		80s	3
		70s		70s	
		60s		60s	
	E	50s		50s	E
Blood pressure (mmHg) Score systolic BP	2	120–124		120–124	2
	0	115–119		115–119	0
		110–114		110–114	
		105–109		105–109	
		100–104		100–104	
		95–99		95–99	
		90–94		90–94	
		85–89		85–89	
		80–84		80–84	
		75–79		75–79	
	1	70–74		70–74	1
		65–69		65–69	
	2	60–64		60–64	2
		55–59		55–59	
	3	50–54		50–54	3
	E	45–49		45–49	E
		40–44		40–44	
Capillary refill time	1	> 2 sec		> 2 sec	1
	0	≤ 2 sec		≤ 2 sec	0
Level of consciousness (If indicated and patient is asleep, ensure they're awake before scoring)	0	Alert		Alert	0
	1	Verbal		Verbal	1
	E	Pain		Pain	E
		Unresp.		Unresp.	
Total CEWT Score				Tick box if modifications in use	
Interventions		e.g. 'A'			
Nurse / Patient ratio					

(Affix identification label here)

URN:

Family name:

Given name(s):

Address:

Date of birth: Sex: ☐M ☐F ☐I

< 1 YEAR

Weight: kg

CEWT Score Legend

- 0 Score 0
- 1 Score 1
- 2 Score 2
- 3 Score 3
- E Emergency call

Actions for Bronchiolitis High Flow Trial CEWT

Total CEWT Score 0
- Minimum 8th hourly CEWT score (with BP as clinically indicated)
- Minimum 24th hourly full CEWT score with BP

Total CEWT Score 1–3
- Obtain a full CEWT score
- Carry out and document appropriate interventions as prescribed
- Consider increasing frequency of observations (minimum 4 hrly)
- Manage anxiety / fever / pain (pain tool overleaf)
- Review oxygen requirement
- Consider informing team leader

Total CEWT Score 4–5
- Obtain a full CEWT score
- Ward doctor to review within 30 minutes
- Notify team leader
- Carry out and document appropriate interventions as prescribed
- Hourly observations (or more frequently if indicated)
- Obtain a full CEWT score after interventions
- If no review within 30 minutes, escalate to registrar review

Total CEWT Score 6–7
- Obtain a full CEWT score
- Registrar to review patient-response within 15 minutes
- Notify team leader
- Carry out and document appropriate interventions as prescribed
- If no review within 15 minutes, or if clinically concerned, initiate emergency call
- Obtain a full CEWT score after interventions
- Record observations at least once every 30 minutes
- Registrar to ensure consultant is notified
- Ward doctor to attend

Total CEWT Score 8+
- Initiate emergency call
- Registrar to attend
- Ensure consultant is notified

Place emergency call if any of the following:
- Airway threat
- Apnoea
- Seizure
- Bleeding (major)
- Any observation in the purple area
- You are worried about the patient

BRONCHIOLITIS HIGH FLOW TRIAL CEWT®

References

1. Babl F, Borland M, Ngo P, et al. Paediatric Research in Emergency Departments International Collaborative (PREDICT): first steps towards the development of an Australian and New Zealand research network. Emerg Med Australas 2006;18:143-7.

2. Committee on F, Newborn. American Academy of P. Apnea, sudden infant death syndrome, and home monitoring. Pediatrics 2003;111:914-7.