

The WHEAT Pilot Trial

WithHolding Enteral feeds Around packed red cell Transfusion to prevent necrotising enterocolitis in preterm neonates: a multi-centre, electronic patient record (EPR), randomised controlled point-of-care pilot trial

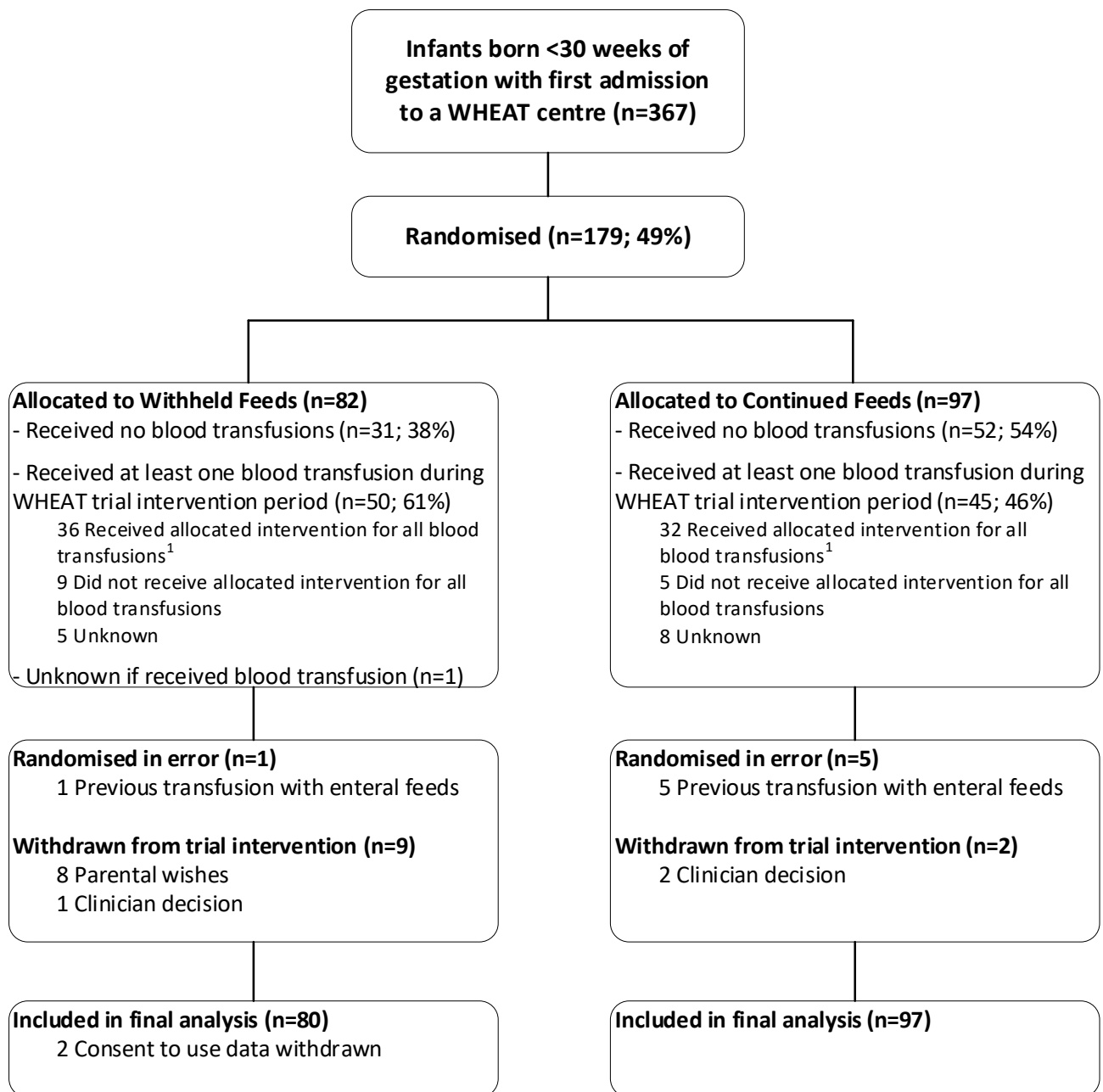
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ISRCTN: 62501859

IRAS ID: 154432

REC reference: 18/LO/0900

Participant Flow:



¹ Infants receiving nil-by-mouth for clinical reasons are included as compliant with protocol

Baseline Characteristics: A tabular summary showing baseline demographic (age and gender) and clinical characteristics of the participants.

Characteristics at trial entry		Withheld feeds (n=80)	Continued feeds (n=97)
Gestation at delivery ¹ (weeks)	Median {IQR}	27.9 {26.3, 29.1}	28.0 {26.7, 29.3}
	<28 ⁺⁰ , n (%)	41 (51.3)	46 (47.4)
	28 ⁺⁰ to 29 ⁺⁶ , n (%)	39 (48.8)	51 (52.6)
	Missing, n (%)	0 (0.0)	0 (0.0)
Infant sex ¹	Male, n (%)	47 (58.8)	55 (56.7)
	Missing, n (%)	0 (0.0)	0 (0.0)
Birthweight (g)	Median {IQR}	967 {779, 1,123}	980 {824, 1,199}
	Missing, n (%)	0 (0.0)	0 (0.0)
Multiple births	Twins, n (%)	18 (22.5)	26 (26.8)
	Triplets or higher order, n (%)	3 (3.8)	5 (5.2)
	Missing, n (%)	0 (0.0)	0 (0.0)
Level of delivery unit	Neonatal Intensive Care Unit, n (%)	56 (70.0)	65 (67.0)
	Special Care Baby Unit, n (%)	17 (21.3)	26 (26.8)
	Local Neonatal Unit, n (%)	6 (7.5)	4 (4.1)
	Home or during transfer, n (%)	1 (1.3)	2 (2.1)
	Missing, n (%)	0 (0.0)	0 (0.0)
Mode of delivery	Emergency Caesarean section, n (%)	42 (55.3)	56 (59.0)
	Elective Caesarean section, n (%)	3 (4.0)	3 (3.2)
	Vaginal – instrument assisted, n (%)	0 (0.0)	3 (3.2)
	Vaginal – spontaneous, n (%)	31 (40.8)	33 (34.7)
	Missing, n (%)	4 (5.0)	2 (2.1)
Apgar score at 5 minutes	Median {IQR}	8 {7, 9}	8 {7, 9}
	Missing, n (%)	5 (6.3)	6 (6.2)
Respiratory support at randomisation	None, n (%)	12 (15.2)	11 (11.6)
	Non-invasive ventilation, n (%)	41 (51.9)	57 (60.0)
	Invasive ventilation, n (%)	26 (32.9)	27 (28.4)
	Missing, n (%)	1 (1.3)	2 (2.1)
Early onset sepsis ²	n (%)	1 (1.3)	1 (1.0)
	Missing, n (%)	Unknown ³	Unknown ³
Maternal antenatal steroids	None, n (%)	6 (7.9)	2 (2.1)
	Partial course, n (%)	8 (10.5)	21 (22.3)
	Full course, n (%)	62 (81.6)	71 (75.5)
	Missing, n (%)	4 (5.0)	3 (3.1)
Maternal ethnicity	White, n (%)	38 (64.4)	37 (50.7)
	Asian or Asian British, n (%)	13 (22.0)	19 (26.0)
	Black or Black British, n (%)	3 (5.1)	7 (9.6)
	Mixed, n (%)	0 (0.0)	6 (8.2)
	Other ethnic group, n (%)	5 (8.5)	4 (5.5)
	Missing, n (%)	21 (26.3)	24 (24.7)

¹ Randomisation stratification variables
² Positive culture within 72 hours of birth
³ Can only identify definite cases; cannot confirm definite non-cases
IQR denotes inter-quartile range (25th and 75th percentiles)

Outcome Measures:

Primary outcomes: recruitment, retention, compliance

Outcome	Withheld Feeds n (%)	Continued Feeds n (%)	Groups combined N (%)	95% CI
Overall recruitment ¹	-	-	179/367 (48.8)	(43.6 to 54.0)
Mean (SD) monthly infant recruitment per site	-	-	2.1 (1.3)	(1.2 to 2.9)
Retention ²	80/82 (97.6)	97/97 (100)	177/179 (98.9)	(96.0 to 99.9)
Compliance to allocation for all transfusions received ³	36/45 (80.0)	32/37 (86.5)	68/82 (82.9)	(73.0 to 90.3)
<i>Missing</i>	5	8		

¹ n (%) infants born <30 weeks of gestation with first admission to a WHEAT centre who were randomised; recruitment rate by trial arm was not available as total eligible babies were only recorded at the aggregate level and not by trial arm

² n (%) randomised infants who completed follow-up to 40⁺⁰ weeks of gestation or discharge from the neonatal unit, whichever occurred first (including those who died)

³ Infants who were nil-by-mouth for clinical reasons at the time of transfusion are included as protocol compliant

Primary outcomes – data accuracy (all participants)

Outcome	True positives	False positives	True negatives ¹	False negatives ¹
	Cases correctly identified in NNRD	Cases incorrectly identified in NNRD	Non-cases correctly identified in NNRD	Non-cases incorrectly identified in NNRD
Severe necrotising enterocolitis, n (%)	10/12 (83.3)	4/165 (2.4)	61/61 (100)	0/61 (0.0)
Spontaneous intestinal perforation, n (%)	6/6 (100)	0/171 (0.0)		
All-cause mortality, n (%)	13/13 (100)	2/164 (1.2)		
Central line associated blood stream infections, n (%)	7/8 (87.5)	4/169 (2.4)		

¹ In all infants with any non-severe NEC and a 25% sample of infants without necrotising enterocolitis recorded in NNRD
NNRD denotes National Neonatal Research Database

Primary outcome – opt-out rate: Data describing opt-out rate was not available as these parents did not consent for their baby's data to be included in the study

Data completeness: This is presented below in secondary outcomes for the key clinical items

Secondary outcomes

Outcome ¹		Withheld feeds (n=80)	Continued feeds (n=97)
Severe necrotising enterocolitis ²	n (%)	7 (8.8)	5 (5.2)
	<i>Missing, n (%)</i>	0 (0.0)	0 (0.0)
Spontaneous intestinal perforation	n (%)	4 (5.0)	2 (2.1)
	<i>Missing, n (%)</i>	<i>Unknown⁴</i>	<i>Unknown⁴</i>
All-cause mortality	n (%)	5 (6.3)	8 (8.3)
	<i>Missing, n (%)</i>	0 (0.0)	0 (0.0)
Central line associated blood stream infections	n (%)	5 (6.3)	3 (3.1)
	<i>Missing, n (%)</i>	<i>Unknown⁴</i>	<i>Unknown⁴</i>
Duration of neonatal care (days)	Median {IQR}	57.5 {43, 86}	57 {42, 78}
	<i>Missing, n (%)</i>	6 (7.5)	2 (2.1)
Duration of any parenteral nutrition (days)	Median {IQR}	6.5 {2, 14}	5 {1, 13}
	<i>Missing, n (%)</i>	6 (7.5)	8 (8.2)
Central venous line in situ (days)	Median {IQR}	6 {0, 13}	5 {0, 10}
	<i>Missing, n (%)</i>	9 (11.3)	9 (9.3)
Weight standard deviation scores ⁵	Mean change (SD)	-1.10 (0.93)	-0.96 (0.79)
	<i>Missing, n (%)</i>	13 (16.3)	14 (14.4)
Head circumference standard deviation scores ⁵	Mean change (SD)	-0.79 (1.62)	-0.68 (1.63)
	<i>Missing, n (%)</i>	53 (66.3)	72 (74.2)

¹ Outcomes recorded between delivery and 40 weeks of gestation or final neonatal unit discharge (whichever occurred sooner)

² Confirmed at surgery or reported as the cause of death on the death certificate

⁴ Can only identify definite cases; cannot confirm definite non-cases

⁵ Change in weight and head circumference from birth to 40 weeks of gestation or final neonatal unit discharge standard deviation score (standardised for gestational age and sex)

IQR denotes inter-quartile range (25th and 75th percentiles); SD denotes standard deviation

Adverse Events

Allocation	Details	Intensity	Related to study intervention	Outcome	Expected
Withheld feeds	Extravasation second cannula for TPN	Moderate	Definitely	Full recovery	Yes
Withheld feeds	Baby died due to severe metabolic acidosis	Severe	Not related	Fatal	Yes

There were no other adverse events