Clinical Investigation Report

Comparison of the mOm incubator with a standard incubator for the maintenance of thermal stability in infants (≤6kg)

Short title: mOm Incubator Pilot Study

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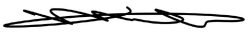
Investigational Device	mOm Essential Incubator (ME1)
Sponsor	Mom Incubators Ltd. Newstead House Pelham Road NG5 1AP www.momincubators.com
Sponsor Representative	Rosalyn Archer Email: rarcher@momincubators.com +44 (0) 7853 633079
CIP	mOm/2018/01
Public Databases	Clinicaltrials.gov: NCT03450668 ISRCTN Registration: ISRCTN14899342
Chief Investigator	Dr Peter Reynolds Neonatal Consultant Email: peter.reynolds1@nhs.net +44 (0) 1932 723499

The study was conducted in compliance with the approved CIP and adhered to the principles outlined in the Declaration of Helsinki, relevant Sponsor's Standard Operating Procedures (SOP)s and study specific procedures, the principles of Good Clinical Practice (ICH-GCP), ISO14155 and any other relevant regulatory requirements.

Report approvals

Approved By	Representative	Signature	Date
Author	Rosalyn Archer		01 Jun 2023
Reviewer	James Roberts		01-Jun-2023
Approver	Peter Reynolds		01.06.2023

NGT	Nasogastric tube
NICU	Neonatal Intensive Care Unit
Obs	Observations
OGT	Orogastric tube
PI	Principal Investigator
PIS	Patient Information Sheet
REC	Research Ethics Committee
S	Standard (control) incubator
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SP	Safety Population
SRB	Serum Bilirubin
TMF	Trial Master File
UT	Ut dictum (as directed)
WR	Ward Round

1. Executive Summary

Title	Comparison of the mOm incubator with a standard incubator for the maintenance of thermal stability in infants (≤6kg)
Short Title	mOm Incubator Pilot study
Locations	**Site 01:** Ashford & St Peter's Hospital, St Peter's Hospitals NHS Foundation Trust, Guildford Rd, Lyne, Chertsey, KT16 0PZ **Site 02:** Royal Hospital for Children, 1345 Govan Road, Glasgow, G51 4TF **Site 03:** Norfolk & Norwich University Hospital, Colney Lane, NR4 7UY
Overview	The mOm Incubator (trade name mOm Essential Incubator) is an infant incubator designed to provide a level of thermoregulation that meets the standards set for conventional incubators whilst being low cost and space-saving.
Purpose	The study compared the level of thermal care delivered to a clinically stable baby in the mOm incubator and a standard (non-humidified) incubator. Staff feedback on the experience of using the mOm incubator was also collected.
Population	Babies at least 30 weeks gestational age (GA) that are clinically stable but require at least 48 hours of thermoregulated incubator care.
Primary Objective	The primary objective of this study was to compare the level of thermal care delivered to a clinically stable baby in the mOm Essential Incubator and a standard (non-humidified) incubator.
Secondary Objectives	The secondary objectives of this study were the assessment of: • Comparability to maintain clinical stability by measurement of physiological parameters. • The mOm incubators' ability to maintain and regulate its temperature to within the appropriate BS standard in clinical practice. • Comparison of between subject incubator cleaning times. • Incubator performance related adverse events. • Staff feedback on the experience of using the mOm incubator (*i.e.*, usability) was also collected.
Summary of Subject Eligibility Criteria	Prospective study participants were identified as requiring treatment for hypothermia but did not require humidification.
Inclusion Criteria	The subject satisfied all the following criteria to be eligible for the study: • Parent/legal guardian was willing and able to give informed written consent for participation of their baby in the study. • Parent/legal guardian was aged 16 years or above. • Subject had spent at least a day (24 hours) in standard incubator care.

	• Subject was considered clinically stable from a cardio-respiratory point of view. • Subject required thermo-regulated care but not additional humidification. • Subject required thermo-regulated care for at least 48 hours. • Subject was less than or equal to 6kg in weight.
Exclusion Criteria	The subject was not entered into the study if, in the opinion of the Investigator, or delegee taking consent, ANY of the following applied: • Parent/legal guardian with learning disabilities or mental illness and was considered unable to give informed consent. • Parent/legal guardian is a prisoner or young offender. • Parent/legal guardian was considered to have a particularly dependent relationship with the investigator(s). • Parent/legal guardian was deemed to belong to a vulnerable group. • Subject has major congenital abnormalities. • Subject had temperature instability, defined as being outside of a normal range based on each infant's individual characteristics. The attending clinician and/or nursing had a concern regarding the clinical stability of the infant (*e.g*., infection suspected).
Method/Design	The study had a prospective, multi-centre, randomised controlled, cross-over design. Approximately 40 subjects were enrolled to provide 36 evaluable. In total 43 were consented and provided a per protocol population of 37 subjects. See study flow chart (Figure 1). There were two arms to the research. The first arm consisted of mOm incubator care for 24 hours, followed by a further 24 hours where the subject was transferred to a standard incubator for care. The second arm consisted of 24 hours care in a standard incubator followed by 24 hours care in a mOm incubator. Each baby therefore acted as its own control. The care of the baby (subject) was mostly unchanged from standard incubator care, but observations were recorded more frequently (*i.e.,* hourly) such as incubator displayed temperatures and some other physiological measures of clinical stability which would normally be collected every three hours in routine care for this type of clinically stable baby of at least 30 weeks. No additional blood tests or any other invasive testing or monitoring were required. The clinical research team had full control and responsibility for the baby's care, with the ability to withdraw the baby from the study at any time for any reason if they felt the baby was clinically unstable or was adversely affected by their environment. The order of incubator type in which the baby was cared for in (*i.e*., which arm of the study) before being crossed over to the alternative incubator type was assigned at random at the point of written consent being gained and the subject therefore having been officially recruited. The primary objective of this study was to compare the level of thermal care delivered to a clinically stable baby in the mOm Essential Incubator and a standard (non-humidified) incubator. This calculation was based on the ability to maintain normothermia; the core/skin temperature of is expected to fluctuate but remain within normal temperature limits (36.5 to 37.5°C). It is expected that these babies' temperatures will fluctuate by around one degree Celsius, and this is normal. Thus, the analysis explored whether fluctuations for each baby kept within this bound. A 95% confidence interval was calculated around the mean of these fluctuations within each

	baby for each of the two incubators. Data from 36 babies allows such a confidence interval to be calculated to within plus or minus 0.33 of a degree if the actual mean fluctuations are around one degree (*i.e.*, as normally expected) and assuming a two-sided confidence interval. A paired t-test was utilised for this calculation using the control (standard incubator) mean temperature minus the test (mOm incubator) mean temperature for each baby as a self-controlled pairing for each subject (baby). Baseline demographic factors of the study subjects were summarised. For continuous variables, such as weight, the mean, standard deviation, median and range will be presented. For categorical variables, such as gender, the proportion of subjects in each category will be presented.
Results	Approximately 100 patients were screened and identified as eligible for participation in this study over a period from 1st November 2021 (first site opened for enrolment) until 4th August 2022 (last subject recruited) at the three study sites. Forty-three were consented, three had their consent withdrawn. After these were removed along with three others which only had temperatures recorded in the mOm incubator, the remaining subjects met the target of achieving 36 evaluable for statistical validity, giving a per protocol population of 37 and a Safety Population (Full Analysis set) of 42. **Summary of demographics at study inclusion:**

Parameter	**Analysis Population**	
	Safety Population (FAS)	**Per Protocol Population**
N (%)	42 (100%)	37 (88.1%)
Gender: Female Male	 20 (47.6%) 22 (52.4%)	 20 (54.1%) 17 (45.9%)
Weight (g): Mean ± SD Range	 1280 ± 274 709 to 1860	 1272 ± 292 709 to 1860
Length (cm): Mean ± SD Range	 38 ± 3 31 to 46	 38 ± 3 31 to 46
Gestational Age (wk + days): Mean ± SD Range	 32+1 ± 1+5 30+0 to 36+0	 32+1 ± 1+4 30+0 to 36+0

The **Primary Endpoin**t of the study was to compare the level of thermal care delivered to a clinically stable baby in the mOm incubator and a standard (non-humidified) incubator. No significant difference was found in their performance to deliver thermal care and maintain infant normothermia to a 95% confidence limit, calculated using both the per protocol population with imputation of missing or data gathered where the skin temperature probe was not well attached, and using the axilla temperatures giving p-values of 0.13 and 0.30 respectively. Note that because the mean data differences between incubator types and standard deviations are narrow (*i.e.*, 0.07±0.23°C and -0.005±0.03°C), the result is small standard deviations which in turn tends to inflate the p-value.

Analysis of paired data for mean fluctuations from normothermia

Parameter	mOm Incubator (B)			Standard Incubator (A)	
	PPP with no imputed data	PPP with imputed data*	Axilla Temperatures	PPP data	Axilla Temperatures
n	37	37	37	37	37
Mean	-0.17	-0.13	0.002	-0.06	-0.01
SD	0.29	0.27	0.034	0.105	0.01

	Mean differences of A-B		
Parameter	PPP with no imputed data**	PPP with imputed data	Axilla Temperatures
n	37	37	37
Mean (95% CI)	0.10 (0.01, 0.19)	0.07 (-0.02, 0.15)	-0.005 (-0.016, 0.005)
SD (95% CI)	0.28 (0.23, 0.37)	0.23 (0.21, 0.34)	0.03 (0.03, 0.04)
Paired T-Test value (p-value)	2.25 (p>0.03)	1.54 (p>0.13)	0.398 (p>0.30)

** Due to problems with the attachment and hence readings from the skin temperature probes provided, where core temperatures were available from the same monitor as used for the standard incubator, these were imputed to provide a more accurate picture of the incubator performance.*

***Results considered untrustworthy due to problems with temperature probe attachment.*

The results showed no significant difference to 95% confidence in the ability of the two incubator types for maintaining the thermal stability of infants ≤6Kg.

Secondary Endpoints

Clinical stability: Comparison of infant health and care in both mOm or standard incubators was similar across both groups in terms of physiological measurements of vital signs.

Incubator performance: Both incubators demonstrated temperature differences between set and actual temperature which were within the allowed limits of the BS EN 60601-2-19 Standard.[5] Both had the same median difference of 0.03°C. With one anomaly excluded for the mOm incubator, the overall mean difference was only 0.04±0.06°C for the mOm compared to 0.03±0.03°C compared for the standard incubator.

During the data collection period the mean length of time the infants underwent care activities with the portholes and/or door open in the mOm and standard incubators was similar for both incubator groups, 15±15 minutes and 15±16 minutes respectively, and were likewise similar when the long periods where the infant was not in the incubator were excluded, 13±10 minutes for the mOm incubator and 13±8 minutes for the standard incubator; both types had a range of <1 to 50 minutes for activities conducted with the infant inside the incubator. The median time for an activity was 10 minutes.

Cleaning of incubators: Although the cleaning times were recorded most of the time for the mOm incubator because they were different and completing the cleaning log was more often remembered, there are approximately twice as many recordings of

cleaning times for the mOm incubator (44(69%)) compared to 20(31%) cleaning times recorded for standard incubators. The analysis of times taken to clean the incubators showed the mOm incubator to be faster to clean based on mean ± SD and median cleaning times which were 23±10 (median 25) minutes and 37±11 (median 40) minutes, respectively.

Adverse Events: Seven AEs were reported (3 hyperthermia, 1 hypothermia, 1 skin irritation, and 2 O_2% desaturation) of which none were considered causally related to either type of incubator. No SAEs or device-related AEs were reported.

Staff user feedback:

Summary of what Staff liked about the mOm Essential Incubator

Item	Number of times mentioned	Comments
Good alternative for special care (SCBU)	9	'Better than a Cot'
Small and compact	17	Parents said easier to see baby and that "baby looked perfect size in incubator" *(parent),* "less invasive looking for parents", "easy to transfer patient"
Easy to move	2	
Easy to store and portable	2	
Easy to position near chair	2	For parents to care for baby
Baby appears comfortable and safe	6	
Good maintenance of temperature even with portholes open	8	
Helpful to have baby's temperature displayed	3	Two parents, one nurse
Overall experience good	2	Two parents
Easy to clean / no problem cleaning	20	
Easy to set/adjust temperature	3	

Summary of what staff disliked about the mOm Essential Incubator:

Item	Number of times mentioned	Comments
Poor visibility through flexible panel & difficult to clean	22	Sticky, difficult to fit, prone to streaking when cleaned, may tear
Poor visibility through top	13	Due to flexible panel and if person tall

	Infant compartment slightly small	13	Not enough room to put safety equipment in incubator (*e.g.*, suction, Neopuff), access for resuscitation	
	Portholes do not stay open & slightly small	29	Portholes swing shut on arms, difficult for care activities and examinations, not practical	
	Portholes & doors only on one side	14	As only on one side, difficult for two person cares and resuscitation. Take whole infant compartment off then lose the heat.	
	Door does not drop away	21	Difficult to reach over for care activities and to put baby in and out of incubator	
	No tilt function	16	Need to raise head up to prevent vomiting	
	Not height adjustable	30	Most said too short, and one person said too tall	
	IV ports very small	5	Difficult for high flow O_2 tubing, plus monitor wires and drug/feed tubing at same time.	
	Incubator temperature does not go below 30°C	5	Needs to go down to at least 28°C. All sites told the CRA they could have recruited more if mOm went down to 28°C.	
	E12 very sensitive	6	Goes off when door open too long (*e.g.*, when first putting baby in incubator when needs to be changed, fed, made comfortable etc).	
	Problems with Skin Temperature probe reading less than axilla temperature	2	Note: skin temperature probes found to be working correctly but more training required in how to attach them affectively.	
	Suggestion to have temperature setting in 0.1°C increments instead of 0.5°C	2	Both comments by same person	

Discussion

Comparison of infant health and care in both mOm or standard incubators was similar across both groups in terms of physiological measurements of vital signs, similar times for care activities where the portholes/door was opened and no device-related adverse events being reported. No significant difference was found in the performance of the incubators to maintain thermal stability of the infants within as would be expected for such CE marked medical devices.

User questionnaires

- A total of 32 clinical staff completed a questionnaire, the majority of which were neonatal nurses and 10 non-clinical staff, who are responsible for cleaning, and setting up, the incubators.
- The usability of the incubator from the staff points of view were mainly positive, the main feature they did not like was the difficulty they experienced when trying to perform procedures inside the incubator due to the portholes not staying open (this was a feature originally added as a safety feature but will be removed) and

	the door not dropping down out of the way, impeding access to the baby in the incubator. • The respondents had some safety concerns for performing resuscitation, as you need to remove the infant compartment to do so and they felt it might be better to instead have a door on the opposite side to the one current door to allow resuscitation to occur within the infant compartment and hence avoid loss of heat. However, 100% of the respondents would allow their own baby to be treated in a mOm Essential incubator. • 85% of the participants thought the mOm was intuitively designed and thought they would be able to set it up without any instructions. • 78% of the Clinical staff thought the mOm would be useful for interdepartmental transfer. 66% thought the mOm could be useful in patient homes to improve rates of early release to the home environment or prevention from needing to be emitted to hospital and 63% thought they would be useful on the hospital ward, or in the delivery suite (56%). • The majority of participants liked the compactness of the mOm and how easy it was to use. • Many participants did not like that the mOm only had portholes and door on one side and said it would be difficult to perform procedures needing two people, or lots of equipment such as babies with complicated health issues who require a lot of wires and thick tubes to be passed through the IV ports. • The main other comment was regarding the trolley not being height adjustable. • The few parents who gave comments that were recorded or mentioned to us anecdotally all said they liked the compact size and look of the mOm Essential incubator as their babies did not look tiny within, they could get closer than in the standard incubator and they liked that the babies temperature was displayed. **Changes to Device Post Clinical Investigation** As a result of findings from this Clinical Investigation the operational Set Temperature range has been changed to 28 to 37°C as the sites felt they could have greatly improved recruitment rate if such was available (*e.g*. Site 01 said they think they would have doubled recruitment numbers as clinically stable infants often need an incubator setting of 28 to 30°C). The alarm label on the device and the Instructions for Use have been updated for the instructions for when an E12 alarm arises. The instruction has been changed to make sure there is no blockage then switch the incubator off and on again. This removes the safety lock, in place to prevent the incubator from continuing to heat when a blockage of the vents is present or the fan is blocked. Should such a blockage be present the alarm would sound again, at which point the user is instructed to take the device out of service and call for repair. Any trolley provided with the incubator will have the option of height adjustability.
Conclusion	The study compared the level of thermal care delivered to a clinically stable baby in the mOm incubator and a standard (non-humidified) incubator. No significant difference was found in their performance to deliver thermal care and maintain infant normothermia. Both incubators demonstrated temperature differences between set and actual temperature which were within the allowed limits of the BS EN 60601-2-19 Standard[5] and the ability to maintain thermal stability of infants within. No device related adverse events were reported during the study.

Figure 1: STUDY FLOW CHART