11/15/2023

Dear Participant(s),

Thank you for your involvement in the United States Patent and Trademark Office (USPTO) 2024 National Patent Application Drafting Competition (NPADC). We appreciate your enthusiasm and dedication.

Enclosed, you will find crucial documents that require your attention. The primary document is the invention disclosure statement titled *Invention Disclosure of low-cost incubator/warmer/ cooler for reducing infant mortality*. The invention disclosure statement serves as the hypothetical invention for your tasks, including searching for prior art, preparing a specification, drafting claims, and presenting your reasoning for patentability. You can access a PowerPoint file containing images found in the invention disclosure statement via a separate link on zFairs.

Furthermore, we want to highlight two white papers in the Appendix: *Designing a Low-Cost Multifunctional Incubator* and *Disposable low-cost cardboard incubator for thermoregulation of stable preterm infant - a randomized controlled non-inferiority trial*. While these white papers may appear in your prior art search, it's important to note that, for the purposes of the competition, you should disregard them. Please proceed as if these white papers do not exist.

We wish you the best of luck in the competition. If you have any questions or concerns, please feel free to reach out to us at PatentDraftingCompetition@uspto.gov.

Sincerely,

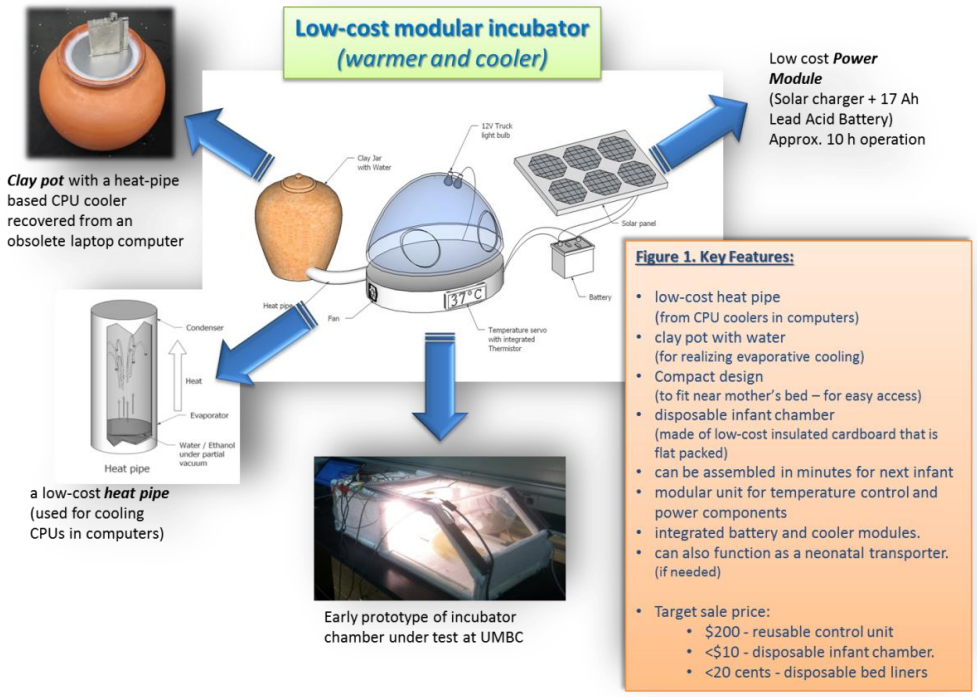
Your USPTO NPADC Team

Attachments:

- Invention Disclosure Statement:
  - *Invention Disclosure of low-cost incubator/warmer/cooler for reducing infant mortality*.
- White Paper Appendix
  - White Paper Document 1: *Designing a Low-Cost Multifunctional Infant Incubator*
  - White Paper Document 2: *Disposable low-cost cardboard incubator for thermoregulation of stable preterm infant - a randomized controlled non-inferiority trial*

Invention Disclosure of low-cost incubator/warmer/cooler for reducing infant mortality.

Section I. We propose to develop and test a novel, and thermodynamically advanced low-cost incubator warmer/ cooler suitable for operation in a low-resource environment. ***Major innovations in our idea are 1. A disposable infant-chamber for infection control 2. Addition of a simple heat pipe-coupled evaporative cooler (water-filled clay pot) that will add controlled cooling functionality. The clay pot includes a temperature sensor for providing audio and/or visual alarms when the pot temperature is above a temperature threshold indicative of pot overheating. 3. Hyper-insulated design with thermal storage will have very low power consumption allowing for off-grid operation with battery backup for several hours. The backup battery includes an electrical power sensor for providing audio and/or visual alarms during battery malfunction or battery failure.***



Compared to adults, newborns are particularly vulnerable to heat loss. Therefore, a well-regulated thermal environment is a critical need for neonatal survival. Although passive, low-cost approaches such as a reflective blanket based system are available for preventing heat loss (e.g., http://embraceglobal.org), they lack user-settable temperature control, cooling capabilities and need regeneration of the thermal material by hot water, which may not be available. In many tropical countries, shade temperatures can reach > 40 °C in the summer and at this point, an incubator warmer can put babies at risk of hyperthermia.

Since many infants serially use the same incubator, having a simple disposable element should greatly assist in infection control. Our modular design supplements the disposable chamber with reusable control modules – leading to a progressively diminishing cost for the device. Sensors (temperature sensors, heart rate sensors, pulse oximetry sensors, etc.) may be coupled to or attached to the chamber or the infant to monitor physiological parameters of the infant. Our device will be suitable for deployment in either home or hospital, and placed right next to the mother thereby permitting normal breast feeding and kangaroo care. We can also add other modules, like a webcam and/or cellphone with camera and modem to enable transmission of infant pictures remotely for telemedicine applications and leverage the local information and communication technology infrastructure. Specifically, evidence for the 3 innovations claimed above is discussed next.

1. The notion of a disposable chamber is based on reports that neonatal hospital acquired (nosocomial) infections are an important cause of infant morbidity and mortality in resource poor countries including parts of India, where some reports of neonatal deaths from sepsis are as high as 30-50% of all neonatal deaths (references available upon request). Consequently, we propose a design where the infant containing chamber is disposable. The chamber includes compact pillow(s) or a pair of straps for securing the infant during transport.
2. With respect to the cooling functionality, we show preliminary data that demonstrate feasibility of this design (Figure 2) in experiments conducted in the lab. The incubator was able to be consistently cooled by 5 degrees- tests were conducted at an ambient temperature of 42 ^{o}C to simulate a hot day in a tropical country.
3. Finally, our design uses insulated panels and a novel thermal bank consisting of water filled pouches (these will be placed just below the baby) that effectively preserve and store heat and greatly reduce power consumption. Preliminary tests in the lab showed a 33% decrease in power consumption by using 6 water filled aluminum soda cans as a thermal bank. Our design goal is to have a power consumption of 20 watts to maintain a 37 ^{o}C incubator temperature at an ambient temperature of 15 ^{o}C. This will permit a standard 12 v 17 Ah sealed lead acid battery to power the device for over 10 hours with no power and a lot longer with intermittent power and/or solar recharging.

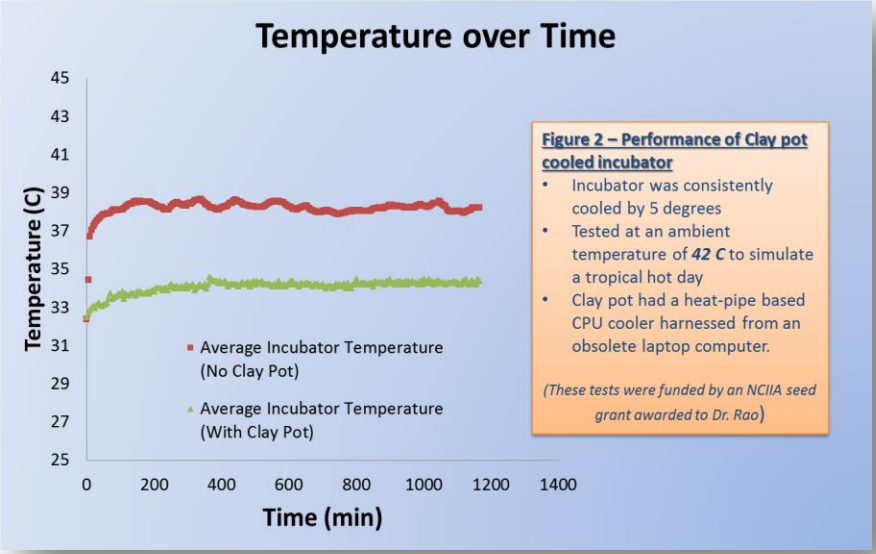


Figure 2 – Performance of Clay pot cooled incubator

- Incubator was consistently cooled by 5 degrees
- Tested at an ambient temperature of ***42 C*** to simulate a tropical hot day
- Clay pot had a heat-pipe based CPU cooler harnessed from an obsolete laptop computer.

(These tests were funded by an NCIIA seed grant awarded to Dr. Rao)

The above contentions are not conjecture. We surveyed target end-users with a field trip on March 20-21, 2013 using seed funds from the National Collegiate Inventors and Innovators Alliance (NCIIA). We visited primary (Karuna Trust) and secondary health care facilities (Vivekananda Tribal Hospital, Karuna Trust) that serve tribal communities in rural Karnataka, India and solicited feedback from health care providers (doctors and nurses) on our incubator design. The consensus was that the most important design features would be the ability to operate without electricity for extended periods of time (up to 8 hours a day), low cost of disposables, and accessibility of the infant. Health care workers favored designs that looked like cribs over other geometries. Many end users would have little technical training, making ease of assembly and use also an important design consideration. Reliability and simple field serviceability were ranked highly, as many current units are in a state of disrepair and not available for use. There was uniform enthusiasm from the end-users about the three major features and a clear excitement to use the device in their settings, with one physician requesting immediate access to the units. In fact, the notion of home use was not ours, but one that was voiced by the nurses who indicated that mothers frequently are pressured to get back home soon and that a device such as this would allow superior infant development (feed and grow) for the critical first few weeks. Other advantages noted were less likely mosquito bites by placing infants in the enclosed chamber. For in-hospital use, nurses noted that the incubator room was distant from the ward where mothers lie and if a unit could be placed right next to the mother, there would be much greater mother-infant bonding and natural care as the mothers would be empowered to have child access whenever needed. Another feature requested was easy conversion from incubator to open bed warmer, which we have implemented in the design. The modular plug-and-play design will also enable facile field service by the end user in the event of malfunctions.

Section II: The component innovations will be prototyped over a period of six months. Phoenix Medical Systems engineers will interactively work with UMBC engineering students/faculty (Drs. Good and Rao) for the design and prototype testing. At Phoenix, Dr. Venkatesan will supervise an engineer from Phoenix R&D. Our team also consists of an infectious disease physician with expertise in infection control (Dr. Ramya Gopinath), whose advice will be sought for the disposable design and assembly protocols. Over the next six months, functional devices will be taken to our proposed pilot study area (various primary and first response centers run by Karuna Trust, Dr. Sudarshan and team) and end-user experience and data will be gathered by our outreach and child care specialist (Mrs. Geetha Ram), which will be fed back into design refinements. Specific data to be gathered include qualitative measures gathered from verbal surveys of ease of use by primary health care worker (ASHA), acceptance by mothers, patterns of behavior of health worker and mothers about reuse of disposable components, quantitative measures of performance in the field including ability to maintain infant temperature for extended periods without electricity, durability of disposable parts, and quantitative measures of outcomes of neonatal health in primary and secondary health care facilities. The goal will be to use the pilot lessons learned during this deployment to scale up to a 12 month scale-up phase. We expect to apply for a transition grant during year 2.

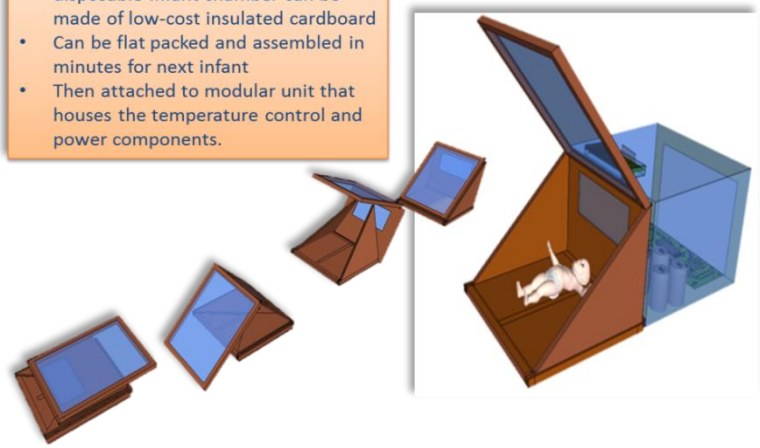
Project Work Plan: The project is planned out in three phases – a design phase where transition to a manufacturable and cost-optimized format is realized, a pilot-phase where production processes are implemented with dissemination in one state and a scale-up phase where production is refined and ramped-up with dissemination extending to 5 states. High-level details are as follows:

Design Phase:(6-8 months)	*Pilot Phase:(6-8 months)*	*Scale-up Phase:(12 months)*
• Design specification • Evaluate & Refine for manufacturability • Bill of Materials optimization • Sourcing & lifecycle management • Design of Molds, Jigs and Fixtures for assembly • Pilot Production - 20 units • Pilot-lot based cost optimization	• Pilot in two centers to test the Incubators • Training pediatric / neonatal Nurses • User feedback collection • Update design based on feedback • Scale-up production to 80 units • Preliminary impact assessment • Validate impact metrics	• Extend to 5 state area • About 40 PHC's roughly 80 incubators • Expand nurses' training • ASHA worker training • Establish service network • Scale-up Impact assessment

Section III: The partners in this proposal are experienced engineers, physicians and outreach specialists. Phoenix Medical Systems is a Chennai, India based company that has been pioneering low-cost affordable health care solutions for over two decades. Phoenix was founded and operates on the principle of bringing neonatal equipment of international quality, within the reach of resource-limited hospitals/clinics all over India and various parts of the world. Along these lines, Phoenix has partnered with various premier institutions leading to disruptive, low-cost products - a recent example being Brilliance Neonatal Phototherapy unit in collaboration with D-Rev. Phoenix's award winning products and innovative approach to technology has led to "Leaders of Tomorrow" award for 2012. Uniquely, Phoenix is committed to developing innovative products that trickle down to low resource settings by setting very modest profit goals for bottom of the pyramid markets.

Figure 3 – Collapsible Modular Design

- Sequential drawings show how the disposable infant chamber can be made of low-cost insulated cardboard
- Can be flat packed and assembled in minutes for next infant
- Then attached to modular unit that houses the temperature control and power components.



The UMBC-CAST team is currently funded by the NCIIA to develop a low-cost incubator. Much of this proposal is based on lessons learned from both technical and end-user perspectives. The NCIIA project enabled a team of CAST personnel to visit India and develop the partnerships with Phoenix and Karuna Trust. CAST is well known for several innovative low cost sensor technologies that have been commercialized for bioprocess monitoring. They are also currently developing neonatal sensors for temperature, glucose and respiratory status with NIH funding.

Karuna Trust believes affordable, ideally free, universal access to health care is a fundamental right of all Indians; such access is a true testimony to the usefulness of all the economic and technological progress India has made. Karuna Trust has pioneered and implemented a successful Public-Private-Partnership model that helps leverage the government's significant investment in public health care infrastructure by complementing it with a socially committed, not-for-profit but professionally competent management team. The Trust today manages 68 Primary Health Care Centers (PHCs) in 8 states – Karnataka, Andhra Pradesh, Orissa, Arunachal Pradesh, Manipur, Maharashtra, Meghalaya and Rajasthan. Through the PHCs it manages, the Trust's 1000+ health care professionals – doctors, nurses & staff – are reaching over 1 million people. Their reach ensures that if this seed grant is successful, we have a vehicle to scale-up immediately. The three partners are committed to the development and deployment of incubator technology that decrease infections and provide operational flexibility in challenging low-resource environments with intermittent power supply. We are eager to work with public/private health care providers and governments to implement this technology in India and other parts of the world that face similar challenges and will pursue policy changes to realize this outcome if the data warrant it. We have proposed an integrated solution that couples technology with demand creation and service delivery. As an example, we note that we had not even considered the use of the incubator for in-home use; this demand came from the frontline workers surveyed. The target sale price of the system is $200 for the incubator, <$10 for the disposable chamber and <$0.20 for disposable bed liners, which we believe will be affordable enough to be a high-volume, low-margin profitable venture (India alone has 26 million births per year). These numbers were arrived at from our survey participants. The eventual purchasers of the incubator are expected to be both governments and NGOs.

White Paper Appendix

Document 1: *Designing a Low-Cost Multifunctional Infant Incubator*

Document 2: *Disposable low-cost cardboard incubator for thermoregulation of stable preterm infant - a randomized controlled non-inferiority trial*

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Designing a Low-Cost Multifunctional Infant Incubator

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Abstract

Every year, an unacceptably large number of infant deaths occur in developing nations, with premature birth and asphyxia being two of the leading causes. A well-regulated thermal environment is critical for neonatal survival. Advanced incubators currently exist, but they are far too expensive to meet the needs of developing nations. We are developing a thermodynamically advanced low-cost incubator suitable for operation in a low-resource environment. Our design features three innovations: (1) a disposable baby chamber to reduce infant mortality due to nosocomial infections, (2) a passive cooling mechanism using low-cost heat pipes and evaporative cooling from locally found clay pots, and (3) insulated panels and a thermal bank consisting of water that effectively preserve and store heat. We developed a prototype incubator and visited and presented our design to our partnership hospital site in Mysore, India. After obtaining feedback, we have determined realistic, nontrivial design requirements and constraints in order to develop a new prototype incubator for clinical trials in hospitals in India.

Keywords

neonatal mortality, incubator, low cost, disposable

Every hour, an estimated 340 babies die in the first week of birth, with preterm birth and asphyxia being two of the leading causes. Ninety-nine percent of these deaths occur in low- and middle-income countries.[1] Compared with adults, newborns are particularly vulnerable to heat loss. Although passive, low-cost approaches such as the Embrace Infant Warmer are available to prevent heat loss, they lack cooling capabilities, temperature control, and need regeneration of thermal material by hot water, which may not be available.[2] In many tropical countries, temperatures in the shade can reach >40 °C in the summer, and at this point, an incubator warmer can put babies at risk of hyperthermia. Advanced incubators exist, but they can cost thousands of dollars. The "Neonurture," a design that takes advantage of locally available replaceable parts of automobiles, is not a viable solution for mass production because it is still too complex and expensive (>$1000) for "bottom of the pyramid" rural users.[3]

In addition to heat loss, nosocomial infections are an important cause of infant morbidity and mortality in resource-poor countries, where reports of neonatal deaths from sepsis reach 29% of all neonatal deaths.[4,5] Preterm birth occurs in 11% of live births globally and accounts for 35% of all newborn deaths.[6] Because preterm newborns have immature innate and adaptive immunity as compared with term babies, mortality due to inadequate immune system response is seen more often in preterm newborns. Routine medical procedures including respiratory support carry an increased risk of infection and associated long-term morbidity in preterm infants.[6] In addition, pediatric respiratory infections appear to contribute to some cases of sudden infant death syndrome.[7]

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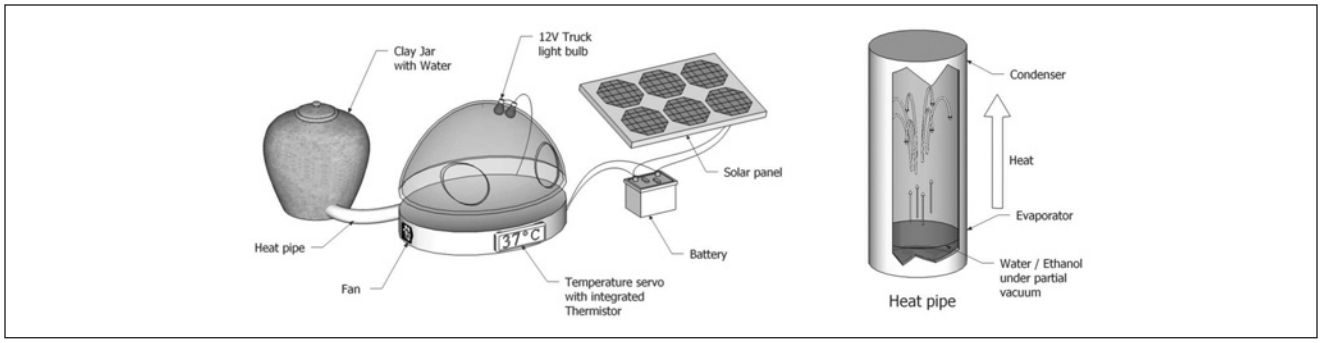

Figure 1. Conceptual design of the proposed multifunctional infant incubator. The unit was designed to be low cost and capable of being heated and cooled and also be able to work off the grid. The insert shows a heat pipe. This is a device that allows efficient heat transfer by using latent heat of evaporation of a fluid in a partially evacuated tube. Heat is transferred from the hot side by fluid that evaporates and condenses on a cold sink. The entire process is repeated until equilibrium. This device is widely used in computers to cool the central processing unit.

We are developing a thermodynamically advanced low-cost incubator suitable for operation in low-resource environments. The incubator features a modular design for multiple purposes. Primarily, this will enable reusable control modules that have low maintenance, decreasing the fixed costs for the device. The incubator features three innovations:

1. a disposable infant chamber that will aid in infection control,
2. a clay pot filled with water coupled with a low-cost heat pipe to passively cool the incubator, and
3. incorporation of insulated panels and a novel thermal bank using water to effectively preserve and store heat, greatly reducing power consumption. This will permit a standard 12 V 17 Ah sealed lead acid battery to power the incubator for more than 10 h.

These innovative contentions are not conjecture. The proposed solution, shown in **Figure 1**, focused on simplicity, high thermal capacity, high visibility, and a low-cost evaporative cooling method. A prototype was developed, refined, and brought to various parts of India to survey target end users. Nurses, doctors, parents, and nongovernment organizations such as Karuna Trust and Swami Vivekananda Youth Movement were surveyed from primary and secondary health care facilities.[8,9] The goal of the survey was to obtain feedback on design features of the prototype. Surprisingly, the surveys indicated that the 360° visibility was not necessary as caregivers would be monitoring the infants often and cooling was not a high priority for the doctors, at least at this location. The most desired design features were the ability to operate without electricity for extended periods of time and low cost of the incubator. To incorporate all of the feedback, two major changes were made. First, the clay pot–coupled heat pipe was made to be an optional module that can be attached when needed. Second, the baby chamber materials were changed from clear plastic to materials with more heat insulation.

Discussions with a partnering incubator manufacturer in India, Phoenix Medical Systems, led to further innovations in the incubator's design. To address neonatal death due to infection control issues, the main infant chamber was redesigned to be completely disposable. Three additional goals were incorporated in the design of the incubator: biodegradability, local manufacturability, and flat pack ability. As a result of the valuable feedback from the target end users of the incubator, the prototype design was redesigned into the conceptual design displayed in **Figure 2**. The total desired cost of the incubator is less than $200, with the disposable baby chamber being less than $10.

Methods

To measure performance of the design, EI1034 temperature probes from Electronic Innovations Corp connected to a LabJack (U3,U12) data acquisition board were used to record all data continuously. The probe features a waterproof stainless-steel probe, 16-bit resolution, and an accuracy of ±0.56 °C at room temperature. The heat supplied to the testing vessels, ranging from 0 to 200 W, was generated using silicone rubber heat strips attached to a heat sink, controlled by a variac. Standard 5 V, 0.18 A, 120 × 120 × 10 mm computer fans were used to circulate air inside of the testing vessels. Temperature and humidity were regulated. Low ambient temperature and high humidity were initially tested to optimize and design safety precautions to the prototype.

The thermal conductivity describes the rate of heat transfer across a material. Materials with high thermal conductivity transfer heat with higher rates. Thus, in this application, materials with lower heat conductivity are desired to retain heat better. **Table 1** summarizes the thermal conductivities of the materials studied.[10]

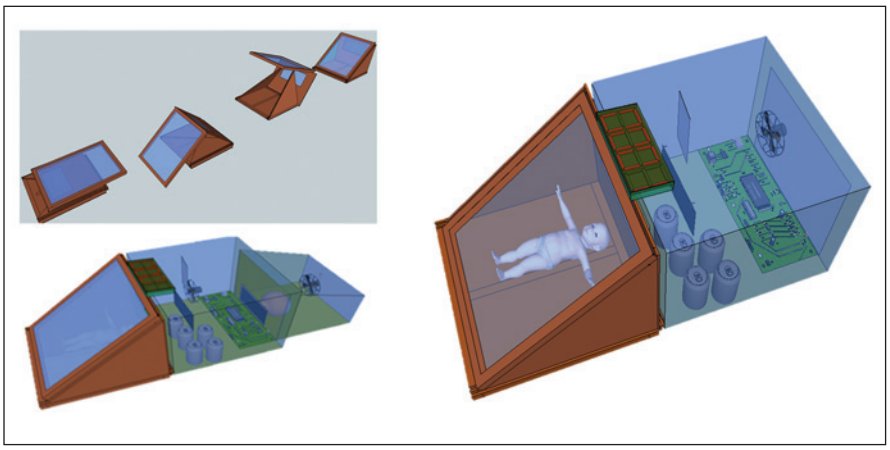

Figure 2. Sequential drawings show how the disposable infant chamber can be made of low-cost insulated cardboard that is flat packed and can be assembled in minutes (top left). The infant chamber can be attached to the modular unit that houses temperature control and power components (right). An optional cooling unit module can be added to the modular power unit (bottom left).

Table 1. Thermal Conductivities of Materials Tested.[8]

Material	Thermal Conductivity (W/m°C)
Corrugated cardboard	0.078
Air	0.026
Polyethylene	0.33
Polystyrene	0.13
Polyethylene terephthalate (polyester)	0.4
Polyvinylchloride	0.12

Insulation

Insulation capabilities of the incubator materials were identified as a critical factor of design. A study of thermally insulating materials was conducted to determine the optimum configuration for minimal heat transfer. Various materials and configurations of double-paned corrugated cardboard were studied as potential incubator lid materials and side wall materials, respectively.

The effectiveness of a double-pane wall (filled with air) versus a solid wall was studied as potential configurations for a transparent lid. In addition, the effectiveness of varying thicknesses of air inside the lid was briefly studied to determine the design of the lid.

Sixteen watts of heat was consistently supplied to the testing vessel at all times. The heat insulation of the materials was evaluated by comparing the steady-state temperatures and temperature differences between the inside of the incubator and outside ambient temperature.

Thermal Bank

Using a small, cheap 12 V lead battery as a reference power source, the available off-grid power would be about 17 to 20 Ah. This limits the total maximum power of the incubator to about 14 W of consistent power when off the grid for 16 h.

To decrease the total power needed to operate the incubator when off the grid, a thermal bank was designed to effectively preserve and store heat. Water was chosen as the heat storage medium because of its high heat capacity of 4.16 J/g°C.

The effectiveness of the thermal bank was tested by observing how quickly heat was lost with and without a thermal bank once the incubator reached a steady-state temperature of 37 °C. The rate of temperature drop with the thermal bank present compared with when the thermal bank was absent was analyzed.

Cooling

The goal is to achieve passive, natural cooling down to the optimal temperature for infants of 37 °C by using the evaporative cooling properties of a clay pot, coupled with the efficient heat transfer of a heat pipe. The clay pot used for experiments had a height of 165.1 mm and a diameter of 101.6 mm. A fan is required to circulate air or provide additional cooling, but the clay pot itself requires no energy input. A heat pipe was chosen because of its ability to transfer heat efficiently, as it combines the principles of thermal conductivity along with those of phase transition.[11]

A simple heat pipe was obtained from a central processing unit cooler of a commercial first-generation Dell XPS Inspiron 9100. The heat pipe consists of three aluminum-plated copper pipes measuring 2 mm in diameter and 50 mm in length and coupled to two heat sinks on each end. Each copper pipe has a grooved wicked structure and uses distilled water as a working fluid. The heat pipe was attached and water sealed to the clay pot using silicone-based caulk. The heat pipe was oriented such that one end of the heat pipe was inside of the clay pot while the other was inserted into the incubator. Small fans direct the air inside of the baby chamber toward the heat sink of the heat pipe. The cooling capacity was determined by the temperature differential between the clay pot and ambient temperature. A heat load of 43 W was supplied to the incubator, and the internal steady-state temperature of the incubator with and without the clay pot was compared. The goal of the experiment is to determine the cooling capacity of the heat pipe–clay pot–coupled apparatus.

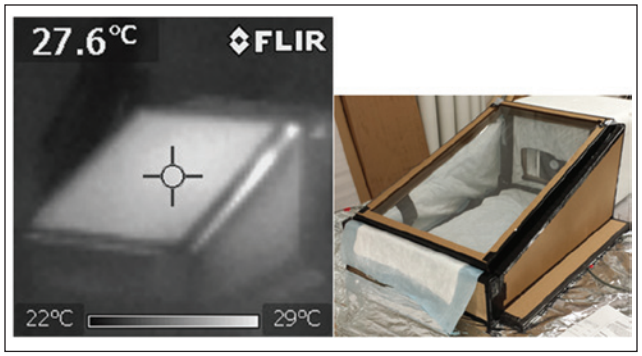

Figure 3. Diagram of controlled environmental chamber that mimics different temperatures and humidity levels of various climates.

Table 2. Lid Material Insulation Experiment Using Controlled Testing Vessel Styrofoam with Different Sheets of Material.

Material	Average Steady-State Temperature Difference from Environment (°C) (Ambient of 22 °C ± 0.5 °C)
Polyvinylchloride	28.0 ± 1.0
Polystyrene	24.5 ± 0.7
Polyethylene	21.0 ± 0.5
Window insulation film	21.2 ± 0.2

Results/Discussion

The theoretical total power needed to keep the incubator at 37 °C based off of heat loss through conduction, convection, and radiation based on the geometry of the incubator at an ambient temperature of 22 °C was calculated to be about 25 W, compared with the measured power consumption of 30 W. It was confirmed that the discrepancy in theoretical versus actual power values was due to small leaks in the incubator at the lid interface. A visual thermal image of this is shown in **Figure 3**.

Insulation

Based on insulation tests, triple-pane clear polyvinylchloride (PVC) film fitted to a corrugated cardboard frame provided the least amount of heat loss. **Table 2** summarizes the insulation experiments conducted on different clear plastic films. Unpaired T-statistical tests were performed to compare the PVC film against every other lid material. The PVC was shown to have greater insulation than any other tested material with 95% confidence.

From the tests, as the air wall thickness is increased, the heat retention is increased. However, tripling the wall thickness from 12.7 mm to 38.1 mm does not result in a large difference in heat retention. Thus, to simplify the design and increase the flat-pack ability and manufacturability of the design, 12.7 mm walls were chosen for the final prototype.

Thermal Bank

The results of the thermal bank tests show little improvement in heat retention. A cutoff point of 35 °C was chosen because that is a dangerously low temperature for a baby. Without the thermal bank, the incubator would drop from the operating temperature of 37.5 °C to below 35 °C in an average of about 5 min versus 8 min with the thermal bank, slowing the loss of heat in the critical temperature range by about 60%. Other insulating materials are being investigated to improve this effect. Although it is not effective enough as a life saver, it was discovered that the thermal bank acts as a dampener allowing for tighter control of the incubator temperature. The thermal bank effectively acts as a thermal buffer that helps keep the temperature within ±0.5 °C, instead of using a more expensive servo controller.

Cooling

The results of the cooling experiments are shown in **Figure 4**.

A heat load of 43 W was supplied to the incubator to simulate many parts of the world where summer temperatures can regularly exceed 42 °C. It should be noted that our tests were conducted at 90% humidity, which is an unfavorable condition and worst-case scenario for evaporative cooling. It can be seen from **Figure 4** that the clay pot is able to consistently maintain an 8 °C temperature differential from the environment.

As can be seen in **Figure 4**, the heat pipe–coupled clay pot was able to lower the incubator temperature by 3.5 °C. A temperature gradient within the incubator and limitations in heat transfer between the incubator and the clay pot cause this decrease to be smaller than what the clay pot could theoretically provide. Therefore, improving the heat transfer between the pot and the incubator would improve the overall efficiency of the cooling system.

Material Cost Analysis

The disposable infant chamber frame is composed entirely of corrugated cardboard. **Table 3** displays the breakdown cost of the materials used to construct the entire incubator. The total projected cost is $93.57, which includes the cooling unit. All prices reported are based on single as opposed to bulk purchase rates. It should also be noted that the total cost of the incubator reflects raw material costs only.

Conclusion

Based on the survey results from India and Ethiopia, cost reduction and infection control were concerns that took priority over cooling. For this reason, design and experiments

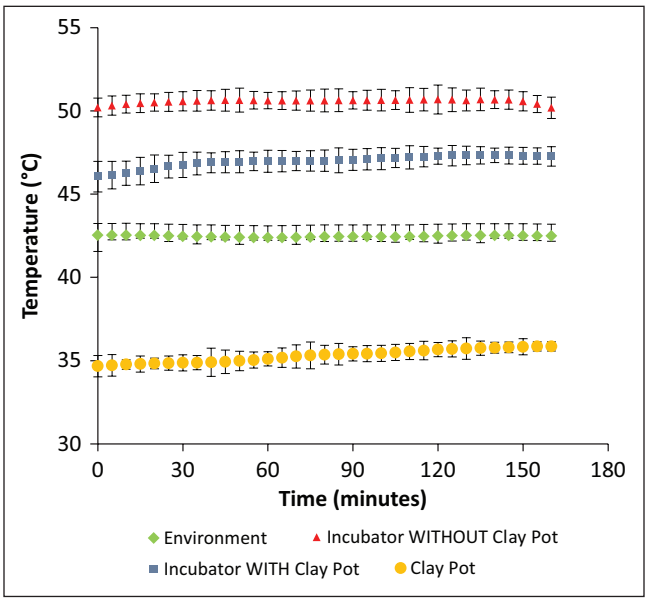

Figure 4. Performance of a passive cooling mechanism made of a clay pot coupled with a heat pipe. The environment outside the incubator was held at 43 °C (diamonds). The inside of the incubator was continuously supplied with 43 W of heat and reached a steady-state temperature (triangles). When the clay pot was added, the temperature inside the incubator dropped (squares). The temperature of the clay pot (circles) was significantly lower than the external environment because of evaporative cooling. Error bars represent the standard deviation of five independent measurements.

Table 3. Rough Outline of Cost.

Material	Cost ($)
Disposable infant chamber	
Corrugated cardboard	4.00
Adhesive	2.00
Disposable bed lining	0.32
Polyvinyl plastic film	2.25
Permanent heating unit	
Heating component	20.00
Fan	10.00
Styrofoam box	20.00
Temperature control unit	
Temperature sensor and microcontroller	20.00
Cooling unit (optional)	
Clay pot	(5.00)
Heat pipe	(10.00)
Total cost	78.57 (93.57)

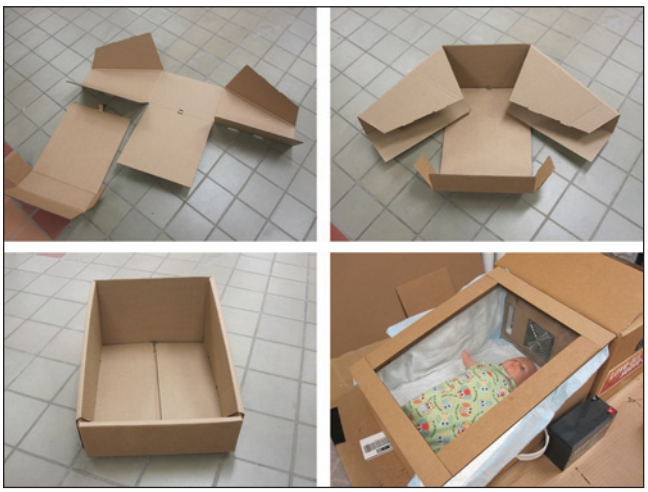

Figure 5. Sequential pictures of the flat-packable infant chamber leading to the scaled-down model of the low-cost disposable incubator prototype.

revolved around constructing a suitable infant incubator using low-cost disposable materials with high insulating properties while consuming minimal power. The current prototype design features double-paned cardboard walls with a thickness of 12.7 mm to increase the flat-pack ability. This effectively increases manufacturing and shipping efficiency. The lid was made from triple-paned clear PVC film sheets for increased visibility and insulation. To make the baby chamber entirely biodegradable, alternative materials to PVC such as cellulose acetate plastic sheets are being researched.

At laboratory temperatures of about 22 °C, the incubator was able to achieve a steady 37.5 °C using 30 W of power on average. In India, where the average temperature is much higher, the power consumption will be significantly reduced, making a small battery more than sufficient to power the device. The worst-case scenario was also considered, in which ambient temperatures can reach as low as 15 °C. Studies at different temperatures and humidity are ongoing. Operating the incubator at lower ambient temperatures can be easily achieved with larger batteries that will be able to provide enough power for this application. Alternatively, increasing the number of batteries or using recharging methods such as solar power are possible.

The incubator is also equipped with a cotton bed liner that covers all sides of the interior and will be changed as needed. This serves as an additional line of defense against infection as well as a layer of heat insulation. The incubator lid is being redesigned to incorporate an optional mosquito screen to prevent vector-borne diseases. In addition, we are also exploring an open-air radiant warmer option for the incubator. The incubator design was originally intended for hospital use only, but after surveying end target users, it has been determined that the incubator can be extended to home use because of its low maintenance.

At this stage, the prototype is being finalized for clinical trials for the partnership hospital in Mysore, India. Sequential pictures leading to the construction of the flat-packable, scaled-down incubator prototype can be seen in **Figure 5**. This will be the first-generation unit, and the design will undoubtedly evolve based on end-user experience and feedback.

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Disposable low-cost cardboard incubator for thermoregulation of stable preterm infant – a randomized controlled non-inferiority trial

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ABSTRACT

Background: Incubators and radiant warmers are essential equipment in neonatal care, but the typical 1,500 to 35,000 USD cost per device makes it unaffordable for many units in low and middle-income countries. We aimed to determine whether stable preterm infants could maintain thermoregulation for 48 h in a low-cost incubator (LCI).

Methods: The LCI was constructed using a servo-heater costing 200 USD and cardboard infant-chamber. We conducted this open-labeled non-inferiority randomized controlled trial in a tertiary level teaching hospital in India from May 2017 to March 2018. Preterm infants on full feeds and receiving incubator or radiant warmer care were enrolled at 32 to 36 weeks post-menstrual age. We enrolled 96 infants in two strata (Strata-1< 33 weeks, Strata-2 ≥ 33 weeks at birth). Infants were randomized to LCI or standard single-wall incubator (SSI) after negative incubator cultures and monitored for 48 h in air-mode along with kangaroo mother care. The incubator temperature was adjusted manually to maintain skin and axillary temperatures between 36.5 °C and 37.5 °C. During post-infant period after 48 h, SSI and LCI worked for 5 days and incubator temperatures were measured. The primary outcome was maintenance of skin and axillary temperatures with a non-inferiority margin of 0.2 °C. Failed thermoregulation was defined as abnormal axillary temperature (< 36.5 °C or >37.5 °C) for > 30 continuous-minutes. Secondary outcomes were incidence of hypothermia and required incubator temperature. Trial registration details: Clinical Trial Registry - India (CTRI/2015/10/006316).

Findings: Prior to enrollment 79(82%) infants were in radiant warmer and 17(18%) infants were in incubator care. Median weight at enrollment in Strata-1 and Strata-2 for SSI vs. LCI was 1355(IQR 1250–1468) vs. 1415 (IQR 1280–1582) and 1993(IQR 1595–2160) vs. 1995(IQR 1632–2237) grams. Mean skin temperature in Strata-1 and Strata-2 for SSI vs. LCI was 36.8 °C ± 0.2 vs. 36.7 °C ± 0.18 and 36.8 °C ± 0.22 vs. 36.7 °C ± 0.19. Mean axillary temperature in Strata-1 and Strata-2 for SSI vs. LCI was 36.9 °C ± 0.19 vs. 36.8 °C ± 0.16 and 36.8 °C ± 0.2 vs. 36.8 °C ± 0.19. Mixed-effect model done for repeated measures of skin and axillary temperatures showed the estimates were within the non-inferiority limit; -0.07 °C (95% CI -0.11 to -0.04) and -0.06 °C (95% CI -0.095 to -0.02), respectively. Failed thermoregulation did not occur in any infants. Mild hypothermia occurred in 11 of 48(23%) of SSI and 16 of 48(33%) of LCI, OR 1.28 (95%CI 0.85 to 1.91). Incubator temperature in LCI was higher by 0.7 °C (95%CI 0.52 to 0.91). In the post-infant period SSI and LCI had excellent reliability to maintain set-temperature with intra-class correlation coefficient of 0.93 (95%CI 0.92 to 0.94) and 0.96 (95%CI 0.96 to 0.97), respectively.

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Interpretation: Maintenance of skin and axillary temperature of stable preterm infants in LCI along with kangaroo mother care was non-inferior to SSI, but at a higher incubator temperature by 0.7 °C. No adverse events occurred and LCI had excellent reliability to maintained set-temperature.
Funding: Food and Drug Administration (Award number P50FD004895)

Research in Context

Evidence before this study

Infant incubators and radiant warmers are essential equipment in neonatal intensive care unit. But, the typical cost of 1500 to 35,000 USD per device leads to shortage of these equipment, over-crowding and neonatal deaths in low and middle-income countries. We searched PubMed on January 11, 2016 for original articles published in English done in humans with age limit infant (birth to 23 months) using search terms "infant incubator", "infant warmer", "thermoregulation equipment", "low cost" and "cost effective" in various combinations. Meta-analyses prove the benefits of kangaroo mother care in stable low birth weight infants. Low cost equipment for thermoregulation in neonates were conductive thermal mattress, recycled incubators, solar powered radiant warmers, solar powered room heating system and prototype cardboard incubator. Feasibility of thermoregulation for low birth weight infants in conductive thermal mattress and solar-powered room-heating-system is demonstrated in trials. Details of thermoregulation were not provided in other studies. We therefore planned this study to assess thermoregulation of stable preterm infants using a low cost disposable cardboard incubator (LCI) with the estimated cost of 200 USD.

Added value of this study

This non-inferiority trial done in stable preterm infants at post-menstrual age 32 to 36 weeks and weight 1250 to 2250 gs demonstrated, that thermoregulation of these infants in LCI along with kangaroo care was non-inferior to standard single-wall incubator. Skin temperature and axillary temperature of infants monitored in LCI was within the pres-specified non-inferiority margin of 0.2 °C. LCI required a higher incubator temperature by 0.7 °C and no adverse events occurred. 'Measured temperature' and 'set-temperature' of LCI had excellent agreement.

Implications of all the available evidence

Our LCI does not have the disadvantages of other low cost thermoregulation equipment. Conductive thermal mattress provides only a fixed amount of latent heat and requires recharging every 4 h, whereas LCI can be readily used at different set-temperatures. High ambient room temperatures in servo-controlled room would be uncomfortable for health care providers. Hence LCI could serve as thermoregulation source for stable preterm infants when not on kangaroo care. LCI require further validation for use in high risk preterm infants.

1. Introduction

Incubators and radiant warmers have a significant role in providing a thermo-neutral environment for preterm infants and are essential in any neonatal intensive care unit (NICU) [1–6]. However, many hospitals in low-and middle-income countries cannot afford high capital and maintenance costs of currently available thermoregulation equipment [7–12], and hence affordable high-quality equipment is needed. Some low-cost solutions tried in preterm infants are conductive thermal-mattress [13], servo-controlled rooms [14], recycled infant incubators [15], solar-powered warmers [16], cardboard incubators [17] and life-raft incubators [9]. Non-availability of affordable thermoregulation equipment leads to > 100% bed occupancy rates of NICUs in low-and middle-income countries [6,8,18]. Use of hot water bottles, high wattage bulbs, electric room heater and electric stove coils for thermoregulation in infants can cause life-threatening complications [9,10,15,19]. The capital cost for available incubators ranges from 1500 USD to 35,000 USD [9,20], while that of low-cost incubator (LCI) used in the present study is around 200 USD.

Maintaining normothermia (36.5 to 37.5 °C) in neonates from delivery room till discharge, and ensuring thermoregulation at discharge is recommended by the World Health Organization (WHO) and other organizations [2,21,22]. Hypothermia increases the risk of respiratory distress, hypoglycemia, sepsis and pulmonary hemorrhage in preterm infants [23–27]. Despite providing respiratory support and surfactant, prolonged hypothermia in preterm infants increases the mortality for respiratory distress syndrome [26]. Although observational studies show admission-hypothermia as risk factor for mortality in preterm infants [28–30], meta-analyses of interventions to decrease admission-hypothermia did not show improved survival [23]. Preventing admission-hypothermia is a key-driver to improve survival of preterm infants in quality improvement studies [27,31,32].

Preterm infant deaths account for a significant proportion of under-5 mortality (16%) [33,34]. Adequate thermal support in low-risk and high-risk preterm infants could avert 20% and 40% of preterm related deaths, respectively [25,26]. Only a few low-cost thermoregulation devices have been evaluated in clinical trials, hence we did this trial to fulfill a knowledge gap [9,13,17]. Any new thermoregulation device should demonstrate the ability to maintain infant's temperature and the ability to perform in a clinical setting. Being a first trial in this low-cost incubator, we enrolled stable preterm infants, who required radiant warmer or incubator at post-menstrual age 32 to 36 weeks. We aimed to determine whether thermoregulation for 48-hour time-period along with kangaroo mother care (KMC) for stable preterm infants in LCI is comparable to standard single wall incubator (SSI).

2. Methods

2.1. Study design and participants

This trial was conducted in a tertiary level teaching hospital in India from May 2017 to March 2018, and the protocol is available as online Appendix-1. This is an open-labeled non-inferiority trial using stratified block randomization of variable size blocks with a 1:1 allocation. Preterm infants who required radiant warmer or incubator for thermoregulation were enrolled at 32 to 36 weeks post-menstrual age, if they weighed 1250 to 2250 gs. Enrolled infants were on full enteral nutrition and received no intravenous therapy. Infants born before 33 weeks had an apnea-free period for 7 days prior to enrollment, and infants born after 33 weeks had no respiratory distress for 6 h from the time of birth. Infants who had major congenital anomalies or temperature instability within 24 h-period prior to enrollment,

and those requiring phototherapy were excluded. Maternal details, demographic details, neonatal variables, details of KMC duration prior to enrollment and details of thermoregulation prior to enrollment were recorded.

2.2. Ethics and trial registration

Institutional ethical committee of Sri Ramachandra University gave approval for the final study protocol of the study (reference number IEC/15/SEP/119/08). The study protocol was in accordance with the guidelines for Good Clinical Practices and Indian Council of Medical Research Schedule-Y guidelines. An information sheet and study brochure was given to parents of eligible infants, followed by verbal discussion with parents to address their queries and written informed consent was obtained from the parents. Audio-video recording of the informed consent process was acquired for each enrolled infant. The trial was registered at Clinical Trial Registry – India with registration details CTRI/2015/10/006,316.

2.3. Preparation of incubators

A prototype cardboard incubator comprised of disposable cardboard infant chamber and modular heating unit was developed at the centre for Advanced Sensor Technology, University of Maryland Baltimore County, Maryland, USA [17]. The LCI used in this trial was redesigned from this prototype, and its components included a disposable cardboard infant chamber (DCIC), servo-controlled heater, air temperature sensor, skin temperature sensor, two connecting ducts and infant trolley. The construction of LCI is explained in Fig. 2 and Appendix-2 Figure 1. DCICs were of size 0.8 m length, 0.35 m breath and 0.35 m height was made using insulated corrugated cardboard. DCICs had windows on its top, fixed side and head end, which were covered by transparent biodegradable cellulose acetate sheet for good visibility of infants. The openable side of DCIC had two ports through which infant can be accessed. DCIC units were packed separately after aerosolized propanol and quaternary ammonium salt sterilization. Electronic components namely the servo-controlled heater, air temperature sensor and skin temperature thermistor sensors in the LCI were identical to those in SSI and comply with IEC60601−1 standards. An air sensor was screwed to the fixed side of DCIC and skin sensor entered DCIC through a small aperture in the foot end of DCIC. During assembly DCIC and servo-controlled heater were kept in upper and lower rack of the infant trolley, respectively. The foot end of DCIC was connected with servo-controlled heaters by food-grade steel-wired clear plastic ducts of size 7.5 and 5 cm which were inflow and outflow air-ducts, respectively. The SSI used in this trial 'INC100' infant incubator and the parts of LCI were supplied by Phoenix Medical Systems, who had no role in design or conduct of the trial. The SSI is ISO13485 certified.

After disinfection, SSIs and LCIs were assembled and started in the step-down nursery with a set-temperature of 35 °C. Two surface cultures were collected by swabbing two 10 by 10 cm areas in crisscross pattern from any two inner corners of canopy in SSI and DCIC in LCI, using moistened sterile swab-sticks. Incubators were ready for enrollment, if both cultures exhibited no growth after 48 h of incubation in thioglycollate broth at Microbiology laboratory. Four SSI and four servo-controlled heaters for LCI were available. A minimum of one SSI and one LCI was kept ready for enrollment throughout the study period.

2.4. Randomization

A web-based randomization program (www.sealedenvelope.com) was used to assign equal number of infants to either SSI or LCI in varying block sizes of 2, 4, 6 or 8 by two strata. Strata-1 included infants born before 33 weeks, and Strata-2 included infants born after 33 completed weeks of gestation. Allocation concealment was achieved by using sequentially numbered opaque sealed envelopes; and infants were assigned to one of the study group by a nursing coordinator, who had no role in rest of the trial. In view of obvious differences between SSI and LCI masking was not done.

2.5. Intervention

Our unit policy is to use air-servo mode for incubators, skin-servo mode for radiant warmers, and KMC initiation after 30 weeks post-menstrual age, if infants have hemodynamic stability. Infants are weaned from incubator to radiant warmer if the incubator temperature required is below 32 °C. Stable infants in radiant warmers are weaned to co-bedding with the mother in a sleep-pouch after 34 weeks post-menstrual age, if no heater output is required for a 24 h-period with adequate clothing. SSI and LCI were used in air-servo mode during this trial. Daily surface disinfection of SSI and LCI was as per hospital policy. During the process of disinfection, infants were swaddled in pre-warmed baby cotton sheets and held in hands by another nurse.

Incubator temperature of SSIs or LCIs were adjusted as per standard guidelines based on weight and postnatal age [35]. After attaining the required incubator temperature for 15 min, infants were dressed in nappy and cotton hats, and shifted to the respective incubators. Infants were monitored in incubators for 48 h in the step-down nursery or KMC ward with 1:1 nurse to infant ratio. Vitals were monitored using pulse-oximeter, and axillary temperature was measured every 4 h using a digital thermometer. Skin temperature was measured by the thermistor sensor of the incubator placed on the infant's abdomen, which was repositioned every 6 h or whenever displaced. Alarm limits for skin temperature namely, 'skin-alarm low' and 'skin-alarm high' were set at 36.5 °C and 37.5 °C, respectively. Whenever skin-alarms got activated, skin sensor attachment was confirmed. If skin sensor was properly attached, incubator temperature was increased and decreased manually by 0.5 °C for skin-alarm low and skin-alarm high, respectively; and axillary temperature was measured. Subsequent manual adjustments of incubator temperature were guided by axillary temperature measured every 15 min, till the infant's temperature normalized (36.5 °C to 37.5 °C).[2] The thermoregulation protocol is depicted in Appendix-2 Figure 2. Room temperature, room humidity and incubator humidity were measured using a digital thermo-hygrometer (HTC 288-CTH™, India) every 4 h. Incubator temperature was measured by an air-sensor attached in the fixed side of DCIC in LCI or in the canopy of SSI and manually entered by a study-nurse every 4 h. KMC, nursing care, screening for retinopathy of prematurity or hearing, breastfeeding or any other care requiring infants out of the incubator was allowed. Axillary temperatures were measured before taking outside and after repositioning the infant inside the incubator.

Details of the infant's hourly skin temperature, axillary temperature, room temperature, room humidity, incubator temperature, incubator humidity and vitals of baby were manually entered by a study-nurse in a data log sheet. Skin-alarm or abnormal axillary temperature events (< 36.5 °C or >37.5 °C) were manually entered in 'event-1 log sheet'. Event-1 log sheet had details of heart rate, respiratory rate, saturations and skin temperature recorded every 10 min and axillary temperature recordings every 15 min till infant's temperature was normal (36.5 °C to 37.5 °C). Event-2 log sheet had manually entered axillary temperature measurements while taking infants out of incubators, and the duration out of incubator.

A Wi-Fi module in the servo-controlled heater component of both the SSI and LCI transferred data of skin temperature, incubator temperature and heater output data every 2−3 min to an internet cloud-server through an internet router [36]. Upon completion of 48-hour time period, infants were taken out of study incubators and managed in accordance to our unit policy; and two surface-cultures from

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incubators were sent. Incubators continued to work in step-down nursery with last set-temperature for 5 days in post-infant monitoring period. Incubators were disinfected daily and surface-cultures were repeated on Days 3 and 5. The details of room temperature, incubator temperature, room humidity and incubator humidity were manually entered every 6 h during the post-infant monitoring period. Subsequently the incubators were cleaned after disassembly, air-ducts were gas sterilized and the DCIC was discarded. Study-nurse feedback was collected after each 8 hourly shift on a 10-point Likert scale regarding the ease of assembly of incubators, the ease of shifting infants in and out of incubators, the ease of nursing care and the ease of paladai feeding while infants were inside incubator. Paladai is a traditional cup-like infant feeding utensil used in India.

2.6. Primary and secondary outcomes

The primary outcome was the efficacy of incubators to maintain skin and axillary temperature for 48 h. 'Failed thermoregulation' was defined as abnormal axillary temperature (< 36.5 °C or >37.5 °C) for more than 30 continuous-minutes. 'Successful thermoregulation' was defined as normal axillary temperature (36.5 °C to 37.5 °C) for 48 h or if abnormal, the duration was less than 30 continuous-minutes.[2] Secondary outcomes were the incidence of mild hypothermia, moderate hypothermia and hyperthermia defined as axillary temperatures 36–36.4 °C, 32–35.9 °C and > 37.5 °C respectively.[2] Incubator temperature, number of adjustments in incubator temperature and nurses' feedback were other secondary outcomes; additional outcomes were incubator surface-culture and ability to maintain set-temperature during the post-infant monitoring period . Additional infant outcomes assessed were weight gain, duration of hospital stay, discharge outcome and occurrence of clinical sepsis prior to discharge. Incubator outcomes assessed were surface-culture and ability to maintain set-temperature during post-infant monitoring period. Adverse events considered were failed thermoregulation, tachycardia for more than 30 continuous minutes, apnea, tachypnea, feed intolerance or any other clinical deterioration. If adverse events occurred, infants were shifted out of trial incubators permanently and managed as per unit protocol.

2.7. Sample size calculation and statistical analyses

A total of 96 infants (48 per group) that would have evaluated 2304 infant-hours in each incubator group was required at 95% confidence interval (CI), to have 90% power for a test of non-inferiority with a margin of 0.2 °C and standard deviation (SD) of 0.33 °C [37] for axillary temperature measured by digital thermometer. A non-inferiority margin of 0.2 °C was clinically pertinent, as we tried to maintain normothermia.[2] IBM SPSS statistics 24 was used for analysis and intention-to-treat principle was followed. All tests were 2-tailed and P value of < 0.05 was considered significant. Dichotomous data were expressed as number and percentage, and analyzed using chi-square or Fisher's exact test. Continuous data were expressed as mean (SD) or median (inter-quartile range, IQR), and based on whether parametric or non-parametric distribution analyzed by *t*-test or Mann-Whiney U test. Line graph were constructed using mean and 95% CI. In view of repeated measures, axillary temperature and skin temperature was analyzed using mixed models compound symmetry structure, restricted maximum likelihood estimates; using incubator type, time, strata as fixed factor, and study location (step-down nursery or KMC ward) as random factor. Skin temperature and incubator temperature from internet cloud-server data [36] and the corresponding manually entered study-nurses' data log were compared using intra-class-correlation coefficient (ICC) and Bland-Altman plot. Set-incubator temperature and measured-incubator temperature recorded in post-infant period was compared using intra-class-correlation coefficient (ICC) and Bland-Altman plot. The statistician was masked regarding group allocation.

2.8. Role of funding

The study was funded by Food and Drug Administration, and the funders had no involvement in the study design, conduct of the study, data collection, and data interpretation or publication process. The corresponding author had final responsibility for decision to submit the paper for publication.

3. Results

During the study period from May 2017 to March 2018, among the 172 eligible infants, 96 infants were enrolled and 48 infants were randomly assigned to each group (Fig. 1). We enrolled 44 infants in the step-down nursery and 52 infants in the KMC ward based on space availability and to ensure internet router connectivity for the Wi-Fi module. Median (IQR) postnatal age and weight at enrollment in Strata-1 and Strata-2 were 15 (10–26) and 2 (1–5) days; 1390 (1250–1550) gs and 1990 (1692–2200) gs, respectively. Strata-1 regained birth weight at a median (IQR) age of 12 (10–14) and 12 (9–15) days, $P = 0.89$, in SSI and LCI, respectively. Baseline characteristics did not differ statistically between LCI and SSI groups (Table 1). Prior to enrollment, incubators worked in step down nursery in a room temperature and room humidity of mean (SD) 28.2 (2.6) °C and 52 (6)%, respectively. The median (IQR) heater-output required to maintain a 35 °C incubator temperature in SSI and LCI did not differ-15% (10–40%) and 20% (10–50%), $P = 0.42$, respectively.

Hourly skin temperatures recorded by nurses in SSIs and LCIs are shown in Fig. 3. Mean (SD) skin temperature of infants in Strata-1 and Strata-2 for SSI vs. LCI was 36.8 (0.2) °C vs. 36.7 (0.18) °C, $P<0.001$ and 36.8 (0.22) °C vs. 36.7 (0.19) °C, $P<0.001$, respectively. Skin temperature in LCI crossed non-inferiority limit in the first 4 h, but subsequent mean differences (95% CI) were within the non-inferiority margin of 0.2 °C (Appendix-2 Figure 3). Mixed models showed the skin temperature was lower in LCI and the estimate −0.07 (95%CI −0.11 to −0.04) was within the non-inferiority margin.

Axillary temperatures measured every 4 h in SSIs and LCIs are shown in Fig. 4a. Mean (SD) axillary temperature of infants in Strata-1 and Strata-2 for SSI vs. LCI was 36.9 (0.19) °C vs. 36.8 (0.16) °C, $P<0.001$ and 36.8 (0.2) °C vs. 36.8 (0.19) °C, $P = 0.007$, respectively. The mean differences (95% CI) of axillary temperatures in LCI were within the non-inferiority margin of 0.2 °C during the entire 48 hour period (Appendix-2 Figure 4). Mixed models showed axillary temperature was lower in LCI and the estimate −0.06 (95% CI −0.095 to −0.021) was within the non-inferiority margin.

In the SSI group 13 of 48 (27%) infants and 28 of 48 (58%) infants in the LCI group had skin-alarm low, odds ratio (OR 2.1, 95% CI 1.2 to 3.6). Overall there were 61 and 81 skin-alarm low events in SSI and LCI, respectively. Median (range) of skin temperature vs. corresponding axillary temperature during these events were 36.3 °C (36–36.4) vs. 36.7 °C (36.3–37.0) and 36.3 °C (35.8–36.4) vs. 36.7 °C (35.8–37.1) in SSI and LCI, respectively. Strata-1 had longer duration of skin temperature < 36.5 °C in LCI than SSI, the median (IQR) was 12 min (0–20) vs. 0 min (0–0), $P = 0.08$ (Table 2). Duration of skin temperature < 36.5 °C in LCI and SSI did not differ in strata-2, and the median (IQR) was 10 min (0–30) and 0 min (0–20), $P = 0.14$, respectively (Table 2).

During incubator-stay mild hypothermia (axillary temperature 36 - 36.4 °C) occurred in 2 infants (4 events) and 2 infants (2 events) of SSI and LCI, respectively. During placing the infants after any procedure such as KMC, feeding or nursing care, mild hypothermia occurred in 9 infants (19 events) and 14 infants (19 events) of SSI and LCI, respectively. Overall mild hypothermia occurred in 11 of 48 (23%) of the SSI group and 16 of 48 (33%) of the LCI group (OR 1.28,

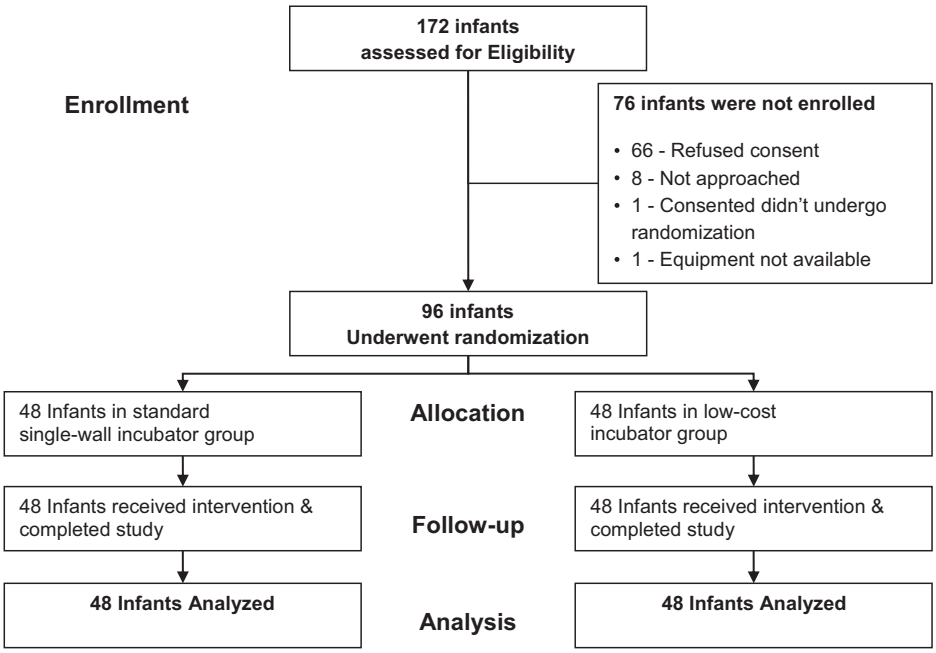

Fig. 1. CONSORT flowchart.

95%CI 0.85 to 1.91) (Table 2). An axillary temperature of 35.8 °C (moderate hypothermia) occurred in one infant of the LCI group. Hyperthermia occurred in 1 infant (1 event) and 2 infants (2 event) in the SSI and LCI respectively. All these hypothermia or hyperthermia events resulted in adjusting incubator temperature, after which axillary temperature normalized at either at the first or second repeat measurement done after 15 or 30 min respectively (Appendix-2 Figure 5 and Appendix-2 Figure 6).

Incubator temperatures measured every 4 h in SSIs and LCIs are shown in Fig. 4b. Strata-1 and Strata-2 had higher incubator temperature at 4 h after enrolment in LCI than SSI, and the mean (SD) was 33.8 (0.51) °C vs. 33.2 (0.63) °C, $P<0.01$ and 33.9 (0.55) °C vs. 33.2 (0.74) °C, $P<0.01$, respectively (Table 2). Subsequent incubator temperatures were higher in LCI and the unadjusted mean difference was 0.7 °C (95% CI 0.6 to 0.78) (Appendix-2 Figure 7). Post-hoc mixed model using incubator type, time, strata and study location (KMC ward or step-down nursery) as fixed factor showed that incubator temperature was higher in LCI with an estimate was 0.7 °C (95%CI 0.52 to 0.91). Ambient room temperature measured every 4 h did not differ in SSI and LCI in both

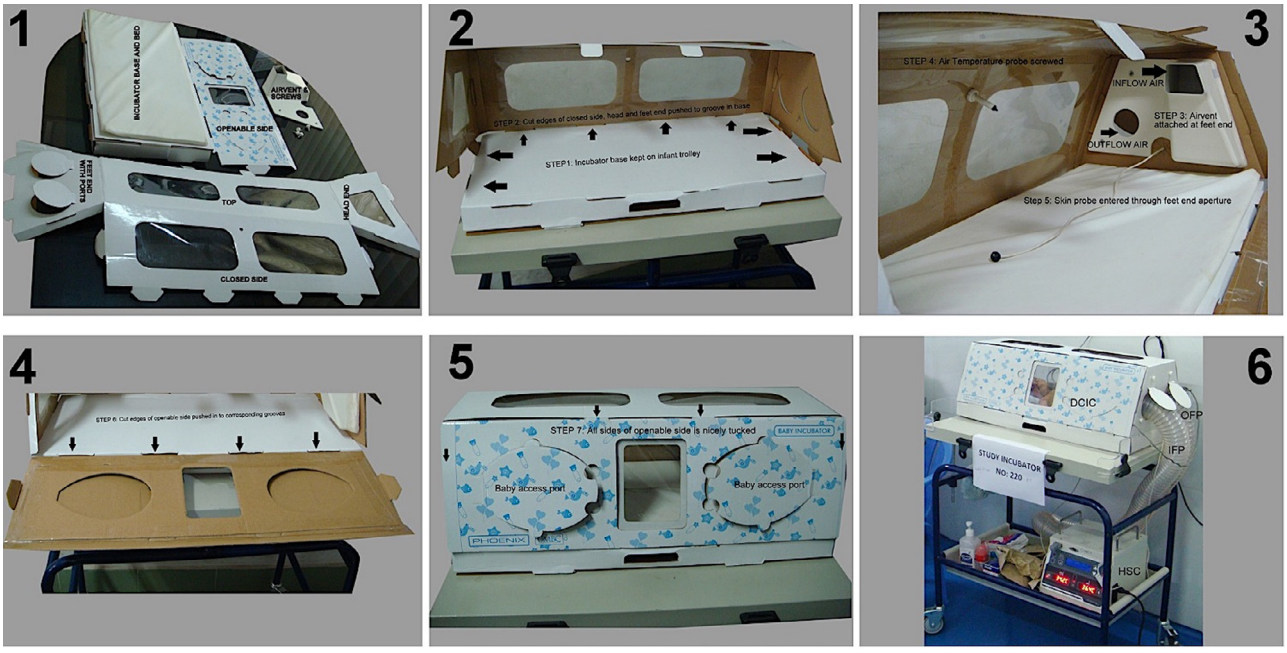

Fig. 2. Assembly of low cost incubator

Part 1 Incubator based, bed, openable side, air-vents and screws, feet end, head end, close side and top side are parts of disposable cardboard infant chamber. **Part 2**- Steps in assembly; Step 1 incubator base kept on baby trolley. Step2: Cut edges of closed side, feet end and hed end pushed to groove in base. **Part 3** - Step3: Air-vent attached to feet end. Step 4: Air temperature probe screwed. Step 5: Skin probe entered through feet end aperture. **Part 4** - Step 6: Cut edges of openable side pushed in corresponding grooves. **Part 5**- step 7: All sides of openable side nicely tucked. **part 6** +- Final assembly of low-cost incubator. DCIC - Disposable Cardboard infant chamber, OFP - Outflow pipe air-duct, IFP- Inflow pipe air-duct, HSC - Servo-Controlled heater.

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Table 1
Baseline Characteristics of participants

Characteristic	Strata -1 Gestational age <33 weeks		Strata-2 Gestational age ≥33 weeks	
	SSI Group (n=24)	LCI Group (n=24)	SSI Group (n=24)	LCI Group (n=24)
Maternal				
Age, mean (SD), year	28.2 (4.5)	29.6 (5.8)	28 (5.2)	27.4 (4.1)
Gravida, median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)	2 (1-3)
Parity, median (IQR)	1 (1-2)	1 (1-3)	1 (1-1)	1 (1-1)
Pregnancy complications, No (%)				
Hypertension or preeclampsia	3 (12.5%)	4 (16.6%)	5 (21%)	6 (25%)
Diabetes	2 (8%)	3 (12.5%)	6 (25%)	3 (12.5%)
Hypothyroid	3 (12.5%)	2 (8%)	3 (12.5%)	4 (16.6%)
Delivery by section, No (%)	22 (92.6%)	21 (87.5%)	21 (87.5%)	20 (83.3%)
Antenatal Steroids, No (%)	21 (97.5%)	23 (96%)	12 (50%)	13 (54%)
Infant				
Gestational age, Mean (SD), week	29.7 (1.6)	29.6 (1.5)	34.5 (1.1)	34.1 (1.2)
Female, No (%)	8 (33%)	9 (37.5%)	11 (46%)	10 (41.5%)
Birth weight, Median (IQR), gram	1220 (960-1425)	1310 (973-1500)	2045 (1770-2218)	2120 (1895-2240)
Small for gestation, No (%)	4 (16.6%)	5 (21%)	8 (33%)	3 (12.5%)
Head circumference, Mean (SD), cm	27.8 (2.2)	27.5 (2.3)	31.4 (2.3)	31.5 (1.5)
Apgar score 1 minute, Median (IQR)	6 (4-7)	6 (4-7)	8 (7-8)	8 (6-8)
Apgar score 5 minute, Median (IQR)	8 (7-9)	8 (7-9)	9 (9-9)	9 (8-9)
Need for PPV at delivery, No (%)	6 (25%)	7 (29%)	3 (12.5%)	6 (25%)
Need for respiratory support, No (%)	24 (100%)	21 (87.5%)	8 (33%)	7 (29%)
Surfactant given, No (%)	7 (29%)	8 (33%)	0	1 (4%)
Respiratory support duration, Median (IQR), day	5 (2-9)	3 (2-13)	0 (0-2)	0 (0-1)
Full feeds reached, Median (IQR), day	7 (6-8)	7.5 (6-9)	3 (2-4)	4 (2.5-4.5)
Feed intolerance, No (%)	3 (12.5%)	3 (12.5%)	1 (4%)	0
Culture proven sepsis, No (%)	1 (4%)	3(12.5%)	0	0
Antibiotic duration, Median (IQR), day	3 (2-5)	4 (3-8)	0 (0-2)	0 (0-2)
Patent ductus arteriosus treated, No (%)	4 (16.6%)	3 (12.5%)	0	0
Anemia transfused, No (%)	6 (25%)	9 (37.5%)	0	0
Retinopathy of prematurity, No (%)	2 (8%)	6 (25%)	2 (8%)	2 (8%)
KMC duration, Median (IQR) hour / day	4.3 (3.5-4.9)	4.5 (3.5-5.2)	1.5 (0-3)	2.5 (0-3)
Hypoglycemia, No (%)	5 (21%)	1 (4%)	6 (25%)	5 (21%)
Infant at enrollment				
Postnatal age, Median (IQR), day	15.5 (10-26)	15 (10-31)	1.5 (1-5)	2 (1-5)
Weight, Median (IQR), gram	1355 (1250 - 1468)	1415 (1280-1582)	1993 (1595 - 2160)	1995 (1632 -2237)
Head circumference, Median (IQR), cm	29.5 (28.1-30.4)	29.8 (28.5-30.4)	32 (30-33)	31.5 (31-32.8)
Place of study step-down nursery, No (%)	16 (66.7%)	12 (50%)	7 (29%)	9 (37.5%)
Axillary temperature, Mean (SD), °C	36.8 (0.15)	36.8 (0.2)	36.8 (0.2)	36.8 (0.2)
Skin temperature, Mean (SD), °C	36.7 (0.2)	36.6 (0.14)	36.6 (0.15)	36.7 (0.22)
Radiant warmer care No (%)	14 (58%)	18 (75%)	23 (96%)	24 (100%)
Radiant warmer heater output, Median (IQR), %[a]	35 (30-40)	30 (30-40)	30 (30-30)	30 (30-40)
Incubator care No (%)	10 (42%)	6 (25%)	1 (4%)	0
Incubator temperature, Median (IQR), °C[b]	33 (33-34)	33.5 (33-34)	33	-

SD – Standard deviation, IQR – Interquartile range, No (%) – Number (Percentage)
PPV – positive pressure ventilation, KMC –kangaroo mother care
[a] - Data from 32 infants in strata-1 and 47 infants in strata-2
[b] - Data from 16 infants in strata-1 and 1 infant in strata-2

Strata-1 and Strata-2, with mean (SD) of 29.4 (2.6) °C vs 29.7 (2.5) °C, P = 0.09, respectively (Table 2).

Incubator humidity was lower in LCI than SSI in both Strata-1 and Strata-2, and the mean (SD) was 45.6 (10.4)% vs. 49.8 (10.9)%, P<0.01 and 46.3 (8.5)% vs. 48.7 (9.1)%, P<0.01, respectively (Table 2). Post-hoc mixed model using incubator type, time, strata and study location (KMC ward or step-down nursery) as fixed factor showed incubator humidity was lower in LCI and the estimate was −3.3 (95%CI -6.7 to 0.16). Ambient room humidity measured every 4 h did not differ in SSI and LCI in both Strata-1 and Strata-2, and the mean (SD) was 52.1 (11.1)% vs 52.7 (11.2)%, P = 0.46 and 58.2 (12.5)% vs 59.6 (10.3)%, P = 0.15, respectively (Table 2).

Among Strata-1 median KMC hours per day prior enrollment, during study incubator and after study incubator stay did not differ; 4.5 (3.5–5.2), 4 (3.5–5) and 4 (4–5) hours, P = 0.81, respectively. Among Strata-2 median KMC hours per day were lower prior to enrollment compared with during study incubator and after study incubator stays; 1.75 (0–3), 3 (1.75–3.5) and 3.3 (3–4.2) hours, P<0.01, respectively. Median (IQR) weight gain of infants during incubator and post-incubator stay in Strata-1 did not differ; 10.8 (8.5–13) gm/kg/day and 11 (9–12.5) gm/kg/day, P = 0.49, respectively. In Strata-2 median (IQR) weight gain during incubator stay was lower than in post-incubator stay; −20 (−34 to −2.8) g/kg/day and 5 (0.8–10.7) g/kg/day, P<0.01, respectively. No adverse events occurred in either SSI or LCI group. All study infants had uneventful post-incubator stay and were discharged. Study-nurses' feedback showed that ease of paladai feeding in SSI was better than LCI for both Strata-1 and Strata-2, and median (IQR) score was 8 (7–9) vs. 7(6–8) and 8 (8–9) vs. 6 (5–7), P<0.01, respectively (Table 2).

Data from 45 infants (24 SSI and 21 LCI group infants) were transferred to the cloud-server. Skin temperature recorded by study-nurses and skin temperature captured in the cloud data had good reliability, ICC 0.85 (95%CI 0.83 to 0.86), and the Bland-Altman plot showed mean difference (95% limits) of 0.02 °C (0.32 to −0.27) (Appendix-2 Figure 8). Cloud- server skin temperature recorded every 15 min from infants in the SSI and LCI had a mean (SD) of 36.77 (0.21) °C and 36.67 (0.17) °C respectively, and the mean difference −0.1 °C (95% CI −0.11 to −0.09) was within the non-inferiority margin. Incubator temperatures from the nurses' log and cloud-server data had excellent reliability, ICC 0.99 (95%CI 0.98 to 0.99), and the Bland-Altman plot showed mean difference (95% limits) of 0.03 °C (0.34 to −0.29) (Appendix-2 figure 9). Positive incubator surface

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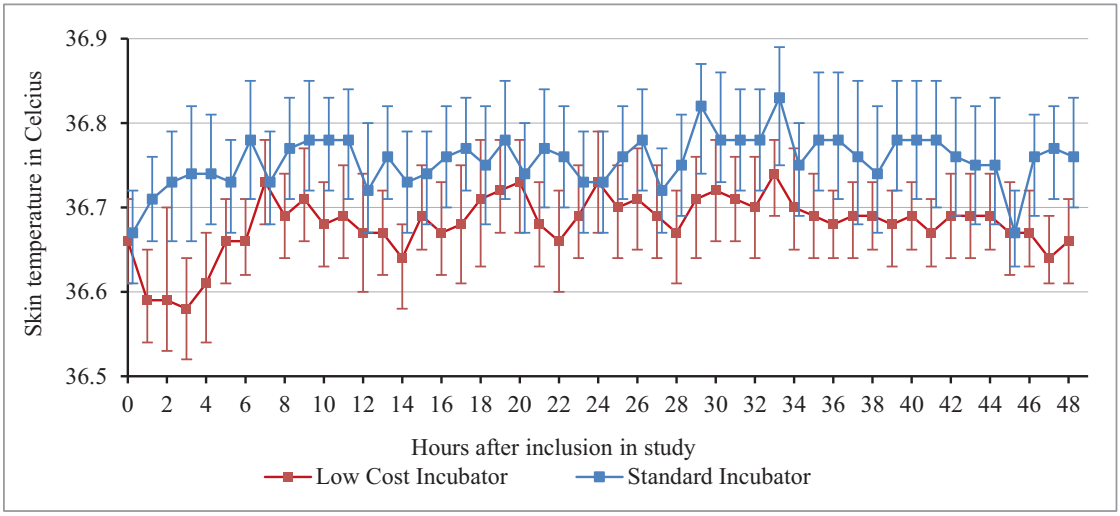

Fig. 3. Skin temperature of infants during 48 h in incubators

Points plotted show mean skin temperature and whiskers show 95% CI error bars of all infants in low-cost incubator group and standard single-wall incubator group. Skin temperature was lower in low-cost incubator and crossed non-inferority limit (0.2 °C) during 1–4 hour period, subsequently during 5–48 hour period was skin temperature in low-cost incubator was within non-inferiority limit.

cultures after infant-stay occurred in 2 of 48 of SSI (*Klebsiella pneumonia* 1, *Coagulase-negative Staphylococcus aureus* 1), while none of 48 of LCI.

During the post-infant monitoring period, both SSI and LCI had excellent reliability to maintain set-temperature of the incubator and the corresponding ICC was 0.93 (95%CI 0.92 to 0.94) and 0.96 (95%CI 0.96 to 0.97), respectively. The corresponding Bland-Altman plot for measured-temperature and set-temperature of incubators in SSI and LCI groups showed a mean difference (95% limits) of −0.06 (−0.55 to 0.43) and −0.02(−0.47 to 0.44) respectively (Appendix-2 Figure 10 and Appendix-2 Figure 11). During the post-infant monitoring period mean (SD) incubator humidity in SSI was higher than LCI, 53.2 (12.9)% vs 51.6 (13.3)%, $P = 0.01$ and mixed models for repeated measures using incubator type and time as fixed factor showed incubator humidity was higher in SSI by an estimate of 4.9 (95% CI −0.08 to 10.7). Mean (SD) room temperature and room humidity during post-infant monitoring period did not differ between SSI and LCI, 28.6 (1.8) °C vs. 28.7 (1.7) °C, $P = 0.16$ and 59 (13.3)% vs. 58 (13.2)%, $P = 0.06$, respectively.

4. Discussion

Among stable preterm infants at risk for hypothermia, thermoregulation for 48 h in LCI along with KMC was non-inferior to thermoregulation in SSI and no adverse events occurred. The estimates of mixed models for skin and axillary temperatures recorded by study-nurses were −0.07°C (−0.11 to −0.04) and −0.06°C (−0.095 to −0.02), respectively; both were within pre-specified non-inferiority margin of 0.2°C. The mean difference from cloud-server transferred data for skin temperature −0.1°C (95%CI −0.11 to −0.09) was also within 0.2°C. The duration of skin temperature < 36.5°C was more in LCI during initial 4-hour period. But, after LCI temperature increased by 0.7°C (95%CI 0.52 to 0.91), the duration of skin temperature below 36.5°C did not differ between LCI and SSI in 4-hour to 48-hour period.

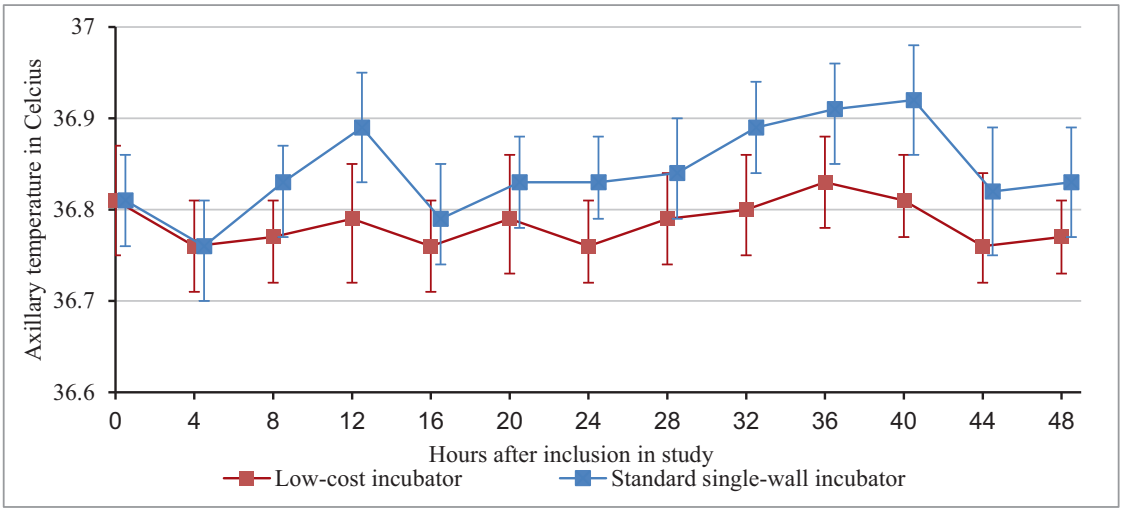

Fig. 4a. Axillary temperature of infants during 48 h in incubators

Points plotted show mean axillary temperature and whiskers show 95% CI error bars of all infants in low-cost incubator group and standard single-wall incubator group. Axillary temperature was lower in low-cost incubator but was within non-inferiority limit (0.2 °C) during the entire 48 hour period.

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Table 2
Secondary outcomes and other hospital outcomes

Outcome	Strata-1 Gestation at birth <33 weeks			Strata-2 Gestation at birth ≥33 weeks		
	SSI Group (n=24)	LCI Group (n=24)	P value	SSI Group (n=24)	LCI Group (n=24)	P value
'Skin-alarm low', n (%)	5 (21%)	13 (54%)	0.02	8 (33.3%)	15 (62.5%)	0.04
'Skin-alarm high', n (%)	0	1 (4%)	-	2 (8.3%)	0	-
'Skin-alarm low' n / infant,[a] Median (IQR)	0 (0-0)	2 (0-3)	0.11	0 (0-3)	1 (0-3)	0.15
Duration ST < 36.5°C, min / infant[b]						
Entire 48 hour time-period, Median (IQR)	0 (0-0)	12 (0-20)	0.08	0 (0-20)	10 (0-30)	0.14
Initial 4-hour time-period,[c] Median (IQR)	0 (0-0)	10 (0-18)	0.04	0 (0-0)	0 (0-20)	0.06
4 to 48 hour time-period, Median (IQR)	0 (0-0)	0 (0-8)	0.76	0 (0-15)	0 (0-10)	0.96
Total duration out of SINC, Median (IQR) hours	11 (9-13)	11.8 (9.2-13.8)	0.47	8.2 (6.9-10)	9 (7.5-11.2)	0.26
KMC hours / day, Median (IQR)	4 (3.5-5)	4.5 (3.5-5)	0.60	2.3 (1.6-3)	3 (1.6-3.9)	0.32
AT while taking out procedure[d], Mean (SD) °C	36.8 (0.18)	36.8 (0.19)	0.12	36.8 (0.19)	36.8 (0.17)	0.29
AT after placing back procedure[d], Mean (SD) °C	36.7 (0.22)	36.7 (0.21)	0.54	36.6 (0.19)	36.7 (0.23)	0.21
Mild hypothermia (AT 36 – 36.4°C)[e]						
While inside SINC, n (%)	1 (4%)	2 (8.3%)	0.96	1 (4%)	0	-
While placing back post- procedure, n (%)	6 (25%)	9 (37.5%)	0.35	3 (12.5%)	5 (21%)	0.71
All events, n (%)	7 (25%)	11 (46%)	0.23	4 (16.6%)	5 (21%)	0.92
Ambient environment						
Set IT at enrollment, Mean (SD) °C	33.4 (0.49)	33.4 (0.5)	0.77	33.4 (0.5)	33.6 (0.49)	0.16
Set IT at the end of study, Mean (SD) °C	33.3 (0.4)	33.9 (0.61)	<0.01	33.1 (0.53)	34 (0.53)	<0.01
Measured IT at enrollment, Mean (SD) °C	33.5 (0.42)	33.6 (0.48)	0.34	33.5 (0.5)	33.6 (0.41)	0.41
Measured IT 4 hours after enrollment, Mean (SD) °C	33.2 (0.63)	33.8 (0.51)	<0.01	33.2 (0.74)	33.9 (0.55)	<0.01
N times IT adjusted / infant,[f] Median (IQR)	1 (0-2)	1 (1-3)	0.27	1 (0-3)	1 (0-2)	0.31
Incubator humidity every 4h, Mean (SD) RH %	49.8 (10.9)	45.6 (10.4)	<0.01	48.7 (9.1)	46.3 (8.5)	<0.01
Room temperature every 4h, Mean (SD) °C	29.4 (2.6)	29.7 (2.5)	0.09	29.9 (2.3)	29.6 (1.9)	0.08
Room humidity every 4h, Mean (SD) RH %	52.1 (11.1)	52.7 (11.2)	0.46	58.2 (12.5)	59.6 (10.3)	0.15
Infant outcomes						
WG in 48 hour incubator stay, Median (IQR) gm/kg/day	12 (9-13)	10 (9-13)	0.49	-18 (-30 - -1)	-20 (- 40 - -6)	0.51
WG in post-SINC stay, Median (IQR) gm/kg/day	11.3 (10 - 13)	11 (8.8 – 12)	0.21	5.3 (1-11)	3.5 (-0.7 - 10)	0.43
Post-SINC incubator / warmer days, Median (IQR)	10 (6-12)	9 (7-11)	0.46	4 (3-5)	4 (2.5-5)	0.49
Post-SINC infant hospital stay-days, Median (IQR)	11.5 (9-13)	14 (11-18)	0.85	5 (4-8)	6 (4-8)	0.88
Discharge weight, Median (IQR) gm	1590 (1505 - 1778)	1695 (1573 - 1795)	0.13	1980 (1662 - 2265)	2010 (1807 - 2225)	0.86
Nurses feedback on 10-point 'Likert scale'						
Ease of assembly, Median (IQR)	8 (8-9)	8 (8-9)	0.25	8 (7-9)	8 (8-9)	0.91
Ease of shifting infants, Median (IQR)	9 (8-9)	8 (8-9)	0.35	8 (8-9)	8 (8-9)	0.55
Ease of nursing care, Median (IQR)	8 (7-9)	8 (8-8)	0.80	8 (8-9)	8 (7-9)	0.44
Ease of palady feeding, Median (IQR)	8 (7-9)	7 (6-8)	<0.01	8 (8-9)	6 (5-7)	<0.01

ST – Skin temperature, AT Axillary temperature, IQR – Interquartile range, SD – Standard deviation, SINC – Study incubator, KMC – Kangaroo mother care, RH– Relative Humidity

[a] 'Skin-alarm low' Overall N=142, (Strata-1, SSI n=33, LCI n=43; Strata-2, SSI n=28, LCI n=38)
[b] Skin temperature < 36.5°C during entire 48 hour period (Total infant-minutes: Strata-1, SSI = 215, LCI=350 and Strata-2, SSI =220, LCI =355)
[c] Skin temperature < 36.5°C during initial 4 hour period (Total infant-minutes: Strata-1, SSI =110, LCI=275 and Strata-2, SSI = 75, LCI =240)
[d] Number of events out of incubator (Strata-1, SSI n=155, LCI n=164; Strata-2, SSI n=99, LCI n=106)
[e] Number of mild hypothermia events (Strata-1, SSI n=14, LCI n=13; Strata-2, SSI n=9, LCI n=8)
[f] Number of IT adjustments (Strata-1, SSI n=35, LCI n=38; Strata-2, SSI n=37, LCI n=32)

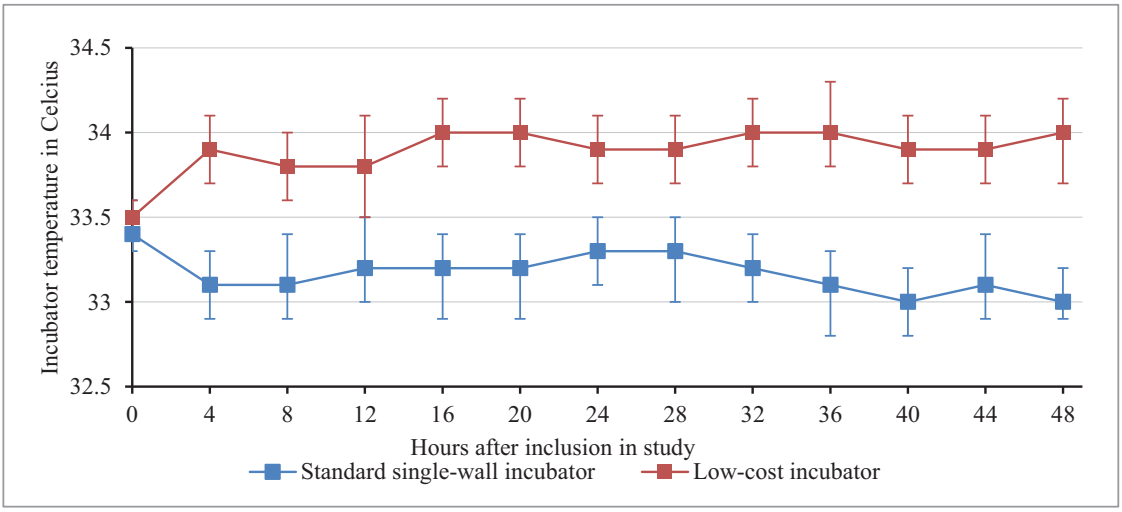

Fig. 4b. Incubator temperature during 48 h - infant's stay
Points plotted show mean incubator temperature and whiskers show 95% CI error bars for all infants in low-cost incubator group and standard single-wall incubator group. Incubator temperature at enrollment was similar, but subsequent incubator temperature was higher in low-cost incubator by 0•7 °C (95% CI 0•6 to 0•78).

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Hypothermia and weight gain did not differ between LCI and SSI. To the best our knowledge LCI is the first low cost thermoregulation equipment, which has been tested for 48-hour time-period.

In conductive-thermal-mattress study, which could provide latent heat Bhat et al., reported higher axillary temperature in study group by 0.11 (SD 0.03) °C when compared to control group [13]. Incubator air temperature in LCI is adjustable and servo-controlled. This mattress needs charging every 4 h and does not need continuous power-supply [13], while the LCI need a continuous 350 watt power source. Power supply is easily available in hospital settings, but availability of electricity in community settings is challenging [38]. LCI has been designed to readily use solar rechargeable batteries. Daga et al., successfully managed 85 preterm infants over 3 years in a solar powered servo-room at a temperature of 34 °C, with minimal cost [14]. But, health-care personnel would be uncomfortable in high room temperature, and incubators or radiant warmers are better options. Thermoregulation details were not provided from other low-cost servo-controlled devices such as recycled incubators and solar powered radiant warmers [15,16].

The mean difference between thermistor probe abdominal skin temperature and digital axillary temperatures during skin-alarm low was −0.4 °C (95% agreement limits −0.73 to 0.06), and using similar methods Schafer et al., reported a difference of −0.3 °C (−1 to 0.4) [39]. Thermal conductivity of corrugated cardboard and canopy is similar, around 0.1 watt/meter/kelvin [17]. However our LCI needed higher incubator temperature for thermoregulation (Figure 4b) possibly due to unavoidable air-leaks in DCIC assembly, whereas canopy is an air-tight compartment. Air-leaks decrease the insulating ability of a compartment [40], and hence temperature may have to be set at least 0.5 °C higher than recommended [35]. while using the LCI and weaning can be attempted at 0.5 °C higher temperature. Lower LCI humidity could be explained by higher incubator temperature and air-leaks [41]. LCI had excellent reliability to maintain set-temperature in post-infant monitoring period.

Despite daily disinfection two SSIs had positive surface cultures in post-infant period, while none in LCI. Corrugated cardboard inhibited growth and bio-film formation of *Escherichia coli, Salmonella enteritidis* and *Listeria monocytogenes* when compared to plastics in food packaging [42]. Incubator contamination by gram-positive and gram-negative organisms could cause outbreaks of infection in NICU [43,44], hence the disposable DCIC may aid in infection control. The present COVID-19 pandemic may favor closed incubators to open-care warmers for neonates [45,46]. Extended KMC was possible in strata-1, but in strata-2 only short KMC was possible as mothers were in initial postnatal days [47]. External devices may not affect KMC duration in the community [48]. The LCI scored less on paladai feeding in study-nurse feedback due to space constraints. Remote collection of data captured by WiFi module had good to excellent reliability with nurse's data [49].

Thermoregulation equipment have improved survival of preterm infants requiring intensive care in the past several decades [3,4]. But, there is shortage of working radiant warmers or infant incubators in low-and middle-income countries worldwide, and further high capital costs for commercially available incubators make these equipment unaffordable for many neonatal units [6,8−20]. In this study, we found thermoregulation of stable preterm infants in the redesigned LCI that costs 200 USD, along with KMC was within non-inferiority limit. LCI has the potential for using up to a week till availability of proper device, as a stop-gap measure in high risk infants.

The merits of our study include microbiological monitoring of incubators, provision of KMC during trial, remote monitoring of thermoregulation data and checking incubators' functioning for 5 days post-infant period in clinical setting. The limitations are that care givers could not be masked due to the nature of intervention, cloud-server transfer of data could be done only in 45 infants due to internet-connectivity issues, and 1:1 nurse to infant ratio for stable preterm might be impractical in clinical setting. Analysis of skin temperatures from cloud-server data showed that the mean difference was within the non-inferiority limits and a good to excellent reliability was there between study-nurses' data and cloud-server data. A 1:1 nurse infant ratio was maintained in study so as to alleviate parents' fear for a new equipment, which is a major reason for poor enrollment in clinical trials from India [50]. The study was done in a tertiary level hospital where room temperature and humidity are relatively high, >25 °C and >50%, respectively. Further studies are needed at different settings, in different high risk population to determine the efficacy of thermoregulation, longer infant-periods to determine weight gain and infection control while using LCI.

In conclusion, stable preterm infants, who needed equipment for thermoregulation, were able to maintain skin and axillary temperatures in LCI, within the non-inferiority margin of 0.2 °C as compared to SSI. Incubator temperature in LCI was higher by 0.7 °C. No infants experienced adverse events and LCI had excellent reliability to maintain set incubator temperature during post-infant monitoring period.

Author contributions

Concept and design: AC, BN, PA, UB, GR, TA, SMSJ, US, GT. Data acquisition and data interpretation: AC, UB, TA, SMSJ, UDR. Manuscript drafting: AC, TA. Manuscript revision and critical review: All authors. Obtained funding: GR, BN. Statistical analysis: GT, AC, TA. Study supervision: BN, PA, UB. Administrative and technical support: UB, AC.

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Declaration of Competing Interest

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Data sharing statement

Deidentified individual participant data regarding the results published in this article and supplementary material will be made available along with the study protocol upon the publication of article. Proposals should be directed to the corresponding author and requesters will need to sign a data access agreement. Deidentified participant datasets and study protocol is also available in Mendeley database (DOI: 10.17632/8m6922 × 96r.2) under a Creative Common Attribution 4.0 International license.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2020.100664.

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