

The RhinoChill intranasal cooling system for reducing temperature after cardiac arrest

Medtech innovation briefing

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Summary

Effectiveness <ul style="list-style-type: none">• Three clinical studies were identified in which the RhinoChill system was used as an intervention for cardiac arrest: 1 randomised controlled trial, 1 single-arm observational study and 1 case study.• The randomised controlled trial demonstrated that the RhinoChill system reduced cerebral and core temperatures compared with standard care after cardiac arrest.• Two in-service evaluations of the RhinoChill system (uncontrolled observational studies) are being carried out in the NHS.	Adverse events and safety <ul style="list-style-type: none">• Serious adverse events reported were cold-related tissue damage, epistaxis, hypertension and hypoxia.• In the randomised controlled trial, nasal whitening was the most common device-related adverse event, occurring in 14% of patients.• Epistaxis occurred in 3 treated patients and was serious in 1 patient with an underlying coagulopathy secondary to hepatic failure. This was the only device-related serious adverse event in the single-arm observational study.
Costs and resource use <ul style="list-style-type: none">• The average cost of consumables per RhinoChill treatment is £1440.• No published evidence was found on the NHS costs of adopting the technology or resource consequences.	Technical factors <ul style="list-style-type: none">• The RhinoChill system is intended for starting and continuing temperature reduction in patients until systematic cooling methods can be used. It is an adjunct to systemic temperature control systems that maintain and reverse hypothermia.

Key points

The RhinoChill intranasal cooling system (BeneChill) is intended for starting and continuing temperature reduction in patients until systematic cooling methods can be used. The system is designed to cool the brain through evaporation and direct conduction at the

base of the skull when there is no circulation. When spontaneous circulation returns, the brain and body are additionally cooled through indirect convection, because the cooled blood removes heat through normal circulation.

Evidence from 2 studies (1 randomised controlled trial and 1 case series) indicates that the RhinoChill system is efficacious in statistically significantly reducing cerebral and core temperatures in patients after cardiac arrest. No published evidence on resource consequences was identified. However, because the system is intended for use as an adjunct to systemic temperature control systems, it is an additional procedure in the emergency care pathway and therefore likely to incur costs to the NHS. No studies have yet demonstrated improved survival rates or improved neurological outcomes from using the RhinoChill system after cardiac arrest.

Introduction

Cardiac arrest leads to loss of consciousness and death unless emergency resuscitation is given and the heart can be restarted. The abnormal cardiac rhythms most commonly associated with cardiac arrest are asystole, pulseless electrical activity, ventricular fibrillation and pulseless ventricular tachycardia. Brain injury after cardiac arrest may be prevented by early cardiopulmonary resuscitation, including defibrillation to treat ventricular fibrillation and pulseless ventricular tachycardia rhythms. Drugs such as adrenaline are also commonly needed ([Therapeutic hypothermia following cardiac arrest](#) [NICE interventional procedure guidance 386]).

Treatment of unconscious survivors after cardiac arrest accounted for 5.6% of the total UK adult general intensive care unit bed days in the Intensive Care National Audit and Research Centre Case Mix Programme Database (ICNARC CMPD), which shows the impact of the condition on NHS resources (Nolan et al. 2007).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The RhinoChill system was CE marked for post-mark clinical investigations in December 2007 and for commercial use in April 2011. At the time of publication of this briefing, the manufacturer has also released other CE-marked devices for use with the RhinoChill system – an MRI-compatible catheter, and a low flow adapter for maintenance cooling (for post-market clinical investigations only). Each of these has separate instructions for use.

Intended use

The RhinoChill system is intended for starting and continuing temperature reduction in patients until systematic cooling methods can be used. General warnings in the instructions for use state that the system should be used as an adjunct to systemic temperature control systems that maintain and reverse hypothermia. The patient must have a protected airway (for example, an endotracheal tube or supraglottic device) and be sedated before intranasal cooling.

Setting and intended user

The RhinoChill system may be administered by any healthcare professional qualified by training and experience, such as physicians, nurses and paramedics, in the pre-hospital, emergency department or intensive care settings.

Description

The RhinoChill system is a Class IIb medical device under the European Medical Devices Directive. It provides emergency therapeutic cooling by using an intranasal evaporative catheter to deliver a mist of perfluorohexane coolant and air or oxygen to the surface of the nasal cavity at ambient temperature. The coolant–gas mixture rapidly evaporates on contact with the nasal cavity, which acts as a rapid heat exchanger, cooling the base of the skull through evaporation and the brain through direct conduction at the base of the skull. When spontaneous circulation returns, the brain and body are cooled through indirect convection, because the cooled blood removes heat through normal circulation. With the RhinoChill intranasal cooling system, systemic cooling will also occur during cardiopulmonary resuscitation before return of spontaneous circulation.

The manufacturer claims that the RhinoChill system is a minimally invasive device, because the only elements of the system in contact with the patient are the proximal end of the catheter, which is inserted into the nose, and the coolant–gas mixture.

The system is intended to be compact and portable, and consists of:

- A modular control unit which controls the flow of the coolant–gas mixture and monitors system status.
- A sterile, single-use intranasal evaporative cooling catheter that connects to the control unit and delivers a pressurised coolant–gas mixture to the patient.
- An inert liquid coolant (perfluorohexane).

The control unit is powered from an internal, rechargeable battery providing 4 hours of operation, an external 12V DC vehicle or AC mains supply. The 1 litre coolant bottle provides therapy for between 20 and 50 minutes, depending on the flow rate selected. Coolant is mixed with medical grade oxygen or breathing air from an external source or optional rear panel tank via a gas hose connected to a side panel connector. Three settings are provided for low (25 litres/min), medium (40 litres/min) and high (60 litres/min) coolant–gas delivery rates.

Once the nasal cannulae are in position, cooling can be started at the desired flow rate setting. During operation, the control unit monitors coolant bottle presence, coolant level, catheter connection, inlet gas pressure, vertical tilt angle, external power source, battery charge level and outlet gas pressure. Front panel indicators show the status of each system component, with warnings (for example, when battery or coolant levels become low) or an alarm (for example, when coolant or gas runs out) which stops gas flow until corrected.

Alternative NHS options

The Resuscitation Council UK 2010 guidelines state that, for unwitnessed out-of-hospital cardiac arrest, emergency medical services personnel should provide an appropriate combination of cardiopulmonary resuscitation and cardiac defibrillation. Tracheal intubation or the use of supraglottic airway devices to provide and maintain a clear and secure airway during cardiac arrest and cardiopulmonary resuscitation are optional (Jewkes and Nolan 2010). The adult advanced life support chapter of the 2010 guidelines states, in post-resuscitation care, that the use of therapeutic hypothermia includes

comatose survivors of cardiac arrest associated initially with non-shockable rhythms as well as shockable rhythms. The lower level of evidence for use after cardiac arrest from non-shockable rhythms is acknowledged (Deakin et al. 2010).

After cardiac arrest, comatose patients whose spontaneous circulation returns can be cooled to a core temperature of 32–34°C with the aim of reducing brain injury and improving neurological outcome. As soon as possible after the cardiac arrest, mild hypothermia is induced using surface techniques (for example, heat exchange cooling pads, cooling blankets, ice packs), internal techniques (for example, an endovascular cooling device) or a combination of cooling methods. Core body temperature is maintained at 32–34°C for 12–24 hours from the start of cooling and is monitored using a bladder temperature probe. Controlled re-warming is usually done over a number of hours. In addition to cooling, patients generally receive standard critical care interventions, together with intravenous sedation and muscle relaxants (to prevent shivering) ([NICE interventional procedure guidance 386](#)). These are systemic temperature control systems that induce, maintain and reverse hypothermia and do not target the brain for cooling.

A recent health technology assessment has described non-invasive head cooling methods and devices that target the brain in adults (Harris et al. 2012):

- Heat loss from the upper airways by convection with gas or fluid flow or by conduction with nasal or pharyngeal balloons. The RhinoChill system is described in this category.
- Heat loss through the skull by convection (fanning, hoods or caps delivering cold air or water) or by conduction (active, for example liquid cooling, or passive, for example ice, gel caps). Some of the devices also have a neck band, which, theoretically, may help cool the brain by reducing the temperature of the carotid blood supply.

The frequency of use of non-invasive head cooling methods and devices in the NHS is unknown.

A number of ambulance services in the UK currently use various methods to start the cooling process before the patient arrives at hospital, such as cold saline drips and cooling pads. However, these methods do not directly target the brain and instead rely on cooling the whole body and blood to achieve an effect.

NICE is not aware of other CE-marked devices that have a similar function to the RhinoChill system.

Costs and use of the technology

The list prices of the RhinoChill system components, excluding VAT, are:

- Durable unit, control unit packaged with tank holder – £7595
- Durable unit, control unit packaged – £7350
- Consumables, coolant bottle, 1 litre – £395
- Consumables, intranasal evaporative cooling catheter – £395
- Mounting options, mini dock – £1100
- Mounting options, docking station – £1100
- Tank holder – £295
- Oxygen/air hose adapter, hose, oxygen, British/BOC, 0.3 m – £110
- Oxygen/air hose adapter, hose, air, British/BOC, 0.3 m – £110

There is no initial maintenance cost to start using the RhinoChill system and no calibration is needed. Ongoing maintenance costs are subject to change and are not included in the above price list. The manufacturer recommends that the control unit is serviced yearly.

The intranasal catheter and coolant bottle are single-use items. The manufacturer states that cooling with the RhinoChill system should continue until standard systemic cooling methods have been implemented in hospital. Thus the cost per patient of a pre-hospital RhinoChill treatment will vary according to the number of coolant bottles used, with additional costs arising from the capital investment in the device, running and maintenance costs. In the PRINCE randomised controlled trial (Castrén et al. 2010), the average amount of coolant used was 1100 ml, needing 2 bottles of coolant. This suggests that the average cost of consumables per RhinoChill treatment is £1440 (including VAT).

Likely place in therapy

The RhinoChill system is intended to be administered before hospital admission and in hospital by any healthcare professional qualified by training and experience. In the NHS, it appears that the introduction of the RhinoChill system for out-of-hospital use would be an additional procedure, with no direct alternative. The RhinoChill system is intended for use

as a precursor to systemic temperature control systems that maintain and reverse therapeutic hypothermia. The portable nature of the RhinoChill system offers the potential advantage of being able to start brain cooling and neuroprotection out of hospital rather than the current systemic cooling on arrival at hospital. The patient must have a protected airway (for example, endotracheal tube or supraglottic device) and be sedated before intranasal cooling.

Specialist commentator comments

Cooling during the intra-arrest or very early post-arrest period, as provided by the RhinoChill system, might be beneficial compared with later post-resuscitation (conventional) cooling.

In an emergency setting the RhinoChill system was effective at reducing temperature and although there is limited UK clinical experience with the RhinoChill system, no complications have been identified.

The system has the advantage that it is compact and portable, and, unlike other cooling methods, can feasibly be used in a pre-hospital setting.

Evidence review

Clinical and technical evidence

Three clinical studies in which the RhinoChill system was used as an intervention for cardiac arrest were identified from the literature search. These were a randomised controlled trial, the PRINCE trial (Castrén et al. 2010); a single-arm observational study (case series; Busch et al. 2010); and a case study (Gordic et al. 2013).

The PRINCE trial was conducted in a pre-hospital emergency setting (before resuscitation) in 200 patients who had a cardiac arrest (Castrén et al. 2010). The primary outcomes were return of spontaneous circulation, survival until discharge (of those admitted to hospital alive), and survival neurologically intact (of those admitted to hospital alive). None of these outcomes were found to be significantly improved by the intervention. However, in patients whose spontaneous circulation returned within 10 minutes, and who were admitted to hospital alive, post hoc subgroup analysis showed that the intervention was associated

with a statistically significant increase in survival compared with control (56.5% compared with 29.4%, $p=0.04$) and neurologically intact survival (43.5% compared with 17.6% $p=0.03$). For secondary intermediate outcomes, the intervention was found to have a statistically significant cooling effect on arrival at hospital as measured by tympanic membrane temperature (34.2°C compared with 35.5°C, $p=0.001$) and core temperature (35.1°C compared with 35.8°C, $p=0.01$). Adverse events are reported in table 1.

The case series recruited 84 patients whose spontaneous circulation had returned (Busch et al. 2010). After using the intervention for 1 hour, the median temperature reduction was 2.3°C (tympanic membrane temperature) and 1.1°C (core temperature). Thirty-four of 84 patients (40%) survived until discharge, with 76% of these (26/34) having a favourable neurological outcome. However, without a comparator group it is not possible to fully attribute these effects to the intervention. Adverse events are listed in table 2.

A single case report (Gordic et al. 2013) did not provide usable efficacy or safety data, but included the observation that after migration into the pharynx and paranasal sinuses the RhinoChill coolant appears as a hyperdense liquid (resembling contrast media) in whole-body CT. In the case reported, this confused emergency physicians, anaesthetists and radiologists and led to a delay in patient treatment.

In addition to the published studies, a number of clinical trials of the RhinoChill system for cardiac arrest, stroke, traumatic brain injury and other clinical applications were highlighted by the manufacturer. At the time of publication of this briefing, 2 studies are complete and pending results, 5 studies are currently recruiting and a further 6 studies are in development. The ongoing Prehospital Resuscitation Intra Nasal Cooling Effectiveness Survival Study (PRINCESS) will report on neurologically intact survival as the primary outcome measure.

The manufacturer has also provided information on 2 in-service evaluations of the RhinoChill system:

- London's Air Ambulance Service (a charity that provides advanced trauma services to critically injured people in London) studied the RhinoChill system for cardiac arrest. Starting in May 2012, the device was carried in the Physician Response Unit, to start therapeutic hypothermia during active resuscitation and before return of a pulse. The aim of the pilot study, on 20 patients, was to assess the feasibility of using the RhinoChill system before arrival in hospital in the UK (Lyon et al. in press).

- The South East Coast Ambulance Service NHS Foundation Trust, with the Accident and Emergency Department of the Royal Sussex County Hospital, have begun an in-service evaluation of the RhinoChill system, and have treated 4 patients up to June 2013. A planned total of 25 patients with cardiac arrest will start on the RhinoChill system as soon as they have been resuscitated and when treatment has been started by a critical care paramedic. Brain cooling with the system will be maintained from when patients arrive at hospital until they are transferred to the intensive care unit. The evaluation will assess the ease of use of the RhinoChill system in an ambulance, the time it takes to reduce the patient's brain temperature to the optimal range of 32–34°C, the number of days the patient spends in intensive care, the percentage of patients surviving to discharge from hospital and the neurological status of surviving patients at their discharge.

The manufacturer has made available a statement of reported adverse events related to the RhinoChill system, on which the following summary is based.

Risks associated with the use of the RhinoChill intranasal cooling system include those related to the use of the device as well as those related to systemic hypothermia. The following device- or procedure-related adverse events were reported in the 213 patients in whom the RhinoChill has been used:

Serious adverse events

- Cold-related tissue damage: n=1 (0.47%). The patient was in irreversible cardiogenic shock when enrolled and cooled with the RhinoChill system. Tissue discoloration appeared approximately 2 hours after RhinoChill cooling was halted following an 80-minute cooling period. The patient died from persistent cardiogenic shock approximately 36 hours after RhinoChill use without resolution of tissue discoloration.
- Epistaxis: n=1 (0.47%). The patient was enrolled under emergency conditions during resuscitation from cardiac arrest with an undiagnosed coagulopathy. Bleeding began 16 minutes after RhinoChill cooling was started. Cooling was halted, and resuscitation efforts persisted for 8 more minutes. The patient did not regain spontaneous circulation despite 40 minutes of basic and advanced cardiac life support efforts. It was learned that the patient was in late stage hepatic failure at the time of cardiac arrest.

- Hypertension: n=1 (0.47%). The patient presented unconscious with no apparent need for additional sedation. Mean arterial pressure rose from 75 to 94 [mmHg] within the first 15 minutes of RhinoChill cooling. An oral anti-hypertensive was administered. No reduction in pressure was observed over the subsequent 15-minute period of RhinoChill cooling. Cooling was then halted, an intravenous line was placed, and the patient was sedated; mean arterial pressure normalised within 30 minutes.
- Hypoxia: n=1 (0.47%). A loss of airway protection was noted during RhinoChill cooling with a ventilation setting of 50% inspired oxygen when the pulse oximetry reading fell to 94%. Airway protection was re-established and cooling was halted per protocol 15 minutes later. Arterial oxygen saturation fell to 85% over the ensuing 2-hour period. Inspired oxygen was then increased to 100% and positive end-expiratory pressure was increased. Arterial oxygen saturation rose from 85 to 97% over the subsequent 30 minutes. Arterial saturation was maintained at 98% on 50% oxygen within 2 hours.

Non-serious adverse events

- Discoloration of the nasal tissue – approximately 10%
- Epistaxis – approximately 5%
- Peri-orbital emphysema – approximately 1%

Additional potential risks exist that have not been attributed to the use of the RhinoChill in past patient series. These include:

- Acute myocardial infarction
- Barotrauma to the nasal cavity/nasopharynx
- Cardiac rhythm disturbances including ventricular fibrillation
- Death
- Emphysema, pulmonary
- Haemorrhage (not epistaxis)
- Infection
- Pneumonia

- Pulmonary embolism
- Sepsis

Post-marketing experience

The manufacturer states that the following non-serious adverse events have been reported since marketing the RhinoChill system:

- Possible device-related mechanical trauma to intranasal surface; this could have been a result of inserting the RhinoChill catheter or other devices into the nasal cavity (n=1).
- Device-related pneumocephalus, which resolved without medical intervention and without sequelae to the patient (n=1).

Table 1 Summary of the PRINCE trial: Castrén et al. (2010)

Study component	Description
Objectives/ hypotheses	To determine the safety and feasibility of transnasal evaporative cooling by pre-hospital EMS personnel during ongoing resuscitation before achieving ROSC
Study design	Randomised controlled trial
Setting	Pre-hospital setting
Inclusion/ exclusion criteria	Inclusion criteria: adults aged ≥ 18 years, with witnessed cardiac arrest, eligible for advanced cardiac life support irrespective of cardiac rhythm, when cardiopulmonary resuscitation was initiated by EMS within 20 minutes of collapse Exclusion criteria: patients with trauma, drug overdose, cerebrovascular accident, known coagulopathy, asphyxia or known requirement for supplemental oxygen, electrocution, very cold temperature on arrival of EMS personnel, those in whom successful ROSC was achieved before randomisation and those with a do-not-attempt resuscitation order or intranasal obstruction
Primary outcomes	All adverse events within 24 hours, serious adverse events within 7 days, neurological outcome via the CPC score

Statistical methods	Continuous variables that were not normally distributed reported as median and IQR. Categorical variables reported as counts and percentages. Primary analyses for the efficacy end points were conducted with Pearson chi-squared tests and comparison of binomial proportions. Relative risks (expressed as treatment divided by control) were computed to further characterise the effect sizes. Other analyses were performed with 2-group t tests or Wilcoxon rank sum tests for continuous variables and Pearson chi-squared tests for categorical variables. All probability values were 2-sided, with values less than 0.05 regarded as statistically significant. No statistical adjustments were made to account for multiple comparisons		
Participants	n=200 (6 lost during follow-up, 3 from each group)		
Results	There was no increase in serious adverse events within 7 days in the treatment group. Among device-related adverse events, nasal whitening was the most common event, occurring in 14% of patients. It resolved spontaneously in all resuscitated patients. Epistaxis occurred in 3 treated patients and was serious in 1 patient with an underlying coagulopathy secondary to hepatic failure. This was the only device-related serious adverse event		
Conclusions	Pre-hospital intra-arrest transnasal evaporative cooling is feasible and safe. Early use of cooling is associated with a significant improvement in the time interval required to cool patients. No improvement in the rate of ROSC was observed for the intra-arrest cooled group		
	RhinoChill + advanced cardiac life support	Advanced cardiac life support only	Analysis
Randomised	n=93	n=101	Not applicable
Efficacy			
Primary outcome: ROSC achieved	35 (37.6%) (n=93)	43 (42.6%) (n=101)	p=0.48

Primary outcome: Survival until discharge (of those admitted to hospital alive)	14 (43.8%) (n=32)	13 (31.0%) (n=42)	p=0.26
Primary outcome: Favourable neurological outcome (of those admitted to hospital alive) (CPC=1, CPC=2)	11 (34.4%) (n=32)	9 (21.4%) (n=42)	p=0.21
Selected secondary outcomes:			
Mean (SD) tympanic temperature at ROSC, °C	35.5 (0.9) (n=93)	35.8 (1.5) (n=101)	p=0.40
Mean (SD) tympanic temperature at arrival at hospital, °C	34.2 (1.5) (n=93)	35.5 (0.9) (n=101)	p<0.001
Time to tympanic temperature of 34°C, median [IQR], minutes	102 [81:155] (n=93)	291 [183:416] (n=101)	p=0.03

The RhinoChill intranasal cooling system for reducing temperature after cardiac arrest (MIB4)

Mean (SD) core temperature, °C	35.1 (1.3) (n=93)	35.8 (0.9) (n=101)	p=0.01
Time to core temperature of 34°C, median [IQR], minutes	155 [124:315] (n=93)	284 [174:471] (n=101)	p=0.13
Safety: Adverse events within 24 hours (all patients)	n=93	n=101	
Nasal whitening	14.0% (13/93)	0% (0/101)	Not reported
Epistaxis	3.2% (3/93)	0% (0/101)	Not reported
Peri-orbital emphysema	1.1% (1/93)	0% (1/101)	Not reported
Safety: In-hospital data (those admitted to hospital alive)	n=32	n=42	
Cardiogenic shock cause of death	9.4% (3/32)	26.2% (11/42)	p=NS
Length of hospitalisation, days	24.1	26	p=NS
Length of ICU stay, days	8	11	p=NS

The RhinoChill intranasal cooling system for reducing temperature after cardiac arrest (MIB4)

Time on ventilator, days	4.2	8.8	p=NS
Patients reporting serious adverse events (within 7 days)	22% (7/32)	33.3% (14/42)	p=0.23
Acidosis	0% (0/32)	4.8% (2/42)	Not reported
Acute myocardial infarction (non-fatal)	0% (0/32)	2.4% (1/42)	Not reported
Bleed (device-related epistaxis in patient with an underlying coagulopathy)	3.1% (1/32)	2.4% (1/42)	Not reported
Cardiac arrest (new)	9.4% (3/32)	4.8% (2/42)	Not reported
Convulsions	3.1% (1/32)	2.4% (1/42)	Not reported
Lethal/long-lasting arrhythmia	3.1% (1/32)	4.8% (2/42)	Not reported
Renal failure	3.1% (1/32)	4.8% (2/42)	Not reported
Sepsis/multi-organ failure	0% (0/32)	7.1% (3/42)	Not reported

Abbreviations: CPC, cerebral performance category; EMS, emergency medical services; IQR, interquartile range; n, number of patients; NS, not significant; ROSC, return of spontaneous circulation; SD, standard deviation.

Table 2 Summary of the case series: Busch et al. (2010)

Study component	Description
Objectives/hypotheses	Primary aim to demonstrate safety, feasibility and cooling effectiveness of nasopharyngeal evaporative cooling in comatose patients after successful resuscitation from cardiac arrest
Study design	Case series
Setting	11 European intensive care units and emergency departments
Inclusion/exclusion criteria	Inclusion criteria: patients aged over 18 years, who did not obey any verbal command at any time after ROSC or if received chest compressions for any duration, tympanic temperature >34°C, oxygen saturation >95% on 50% oxygen Exclusion criteria: if trauma or severe bleeding occurred subsequent to cardiac arrest, existence of terminal disease, pregnancy, known coagulopathy, or a barrier inhibiting placement of the intranasal catheter (for example septum deviation, skull base fracture)
Primary outcomes	Cooling rate, time needed to achieve mild hypothermia (34°C), time needed to achieve target temperature (33°C), side effects of evaporative cooling in the nasopharynx and elsewhere occurring between enrolment and discharge, neurological outcome via the CPC score
Statistical methods	Descriptive statistics were performed. Continuous variables presented as median and IQR. Binary variables presented as number and percentage
Participants	n=84

Results	The RhinoChill device effectively lowered tympanic and core temperatures in patients after cardiac arrest. The device proved feasible in an emergency department setting, and safe during 1 hour's use, with the exception of persistent tissue damage in 1 patient at the high oxygen flow rate of 60–80 litres/min. At the lower oxygen flow rate of 40–50 litres/min, no persistent cold-related tissue damage was observed. The reduction in flow rate from 60–80 litres/min to 40–50 litres/min did not affect the cooling rate. Essential safety measures that prevent tissue damage include uncovering the face and keeping the mouth open during cooling, so that coolant vapour can escape from mouth and nostrils. No evidence was obtained that the coolant might have caused lung damage following aspiration. Smell tests demonstrated that cooling via the nasal cavity did not affect the olfactory epithelium. The mortality rate of 60% was not unexpected for this unselected patient population, and good neurologic recovery was observed in a comparably high percentage
Conclusions	Nasopharyngeal cooling for 1 hour using the RhinoChill device is effective in reducing core temperature in cardiac arrest survivors. The device is safe at oxygen flow rates of 40–50 litres/min
	RhinoChill
Randomised	Not applicable
Efficacy	
Duration of cooling (median [IQR], [min–max] minutes)	60 [50:90], (25–195) (n=84)
Tympanic cooling rate in 1 hour of cooling (median [IQR] °C)	2.3 [1.6:3.0] (n=82)

Core cooling rate during cooling (median [IQR] °C/h)	1.1 [0.7:1.5] (n=84)
Cooling rate for central core temperature measurements from oesophageal and arterial sites (median [IQR] °C/h)	1.4 [0.9:2.0] (n=36)
Cooling rate for peripheral core temperature measurements from bladder and rectal sites (median [IQR] °C/h)	0.9 [0.5:1.2] (n=48)
Time to tympanic temperature 34°C (median [IQR] minutes)	27 [14:58] (n=82)
Time to tympanic temperature 33°C (median [IQR] minutes)	60 [36.5:117.5] (n=82)

Time to core temperature 34°C (median [IQR] minutes)	52 [26:86] (n=36)
Time to core temperature 33°C (median [IQR] minutes)	180 [120:285] (n=36)
Number reaching target tympanic temperature 33°C	55 (66%) (n=76)
Number reaching target core temperature 33°C	16 (19%) (n=80)
Number with favourable neurological outcome (CPC=1, CPC=2)	26 (76%) (n=34)
Safety	
Mortality	50 (59.5%) (n=84)
Total number of adverse events related to device	15 (17.9%) (n=84)
Nasal discoloration	10 (11.9%) (n=84)

Cold-induced tissue damage	1 (1.2%) (n=84)
Epistaxis	2 (2.4%) (n=84)
Coolant in sinus	1 (1.2%) (n=84)
Peri-orbital gas emphysema	1 (1.2%) (n=84)
Patients reporting serious adverse events	n=1 (1.2%)
Unspecified event	After the observation of a severe device-related adverse event at the oxygen flow rate of 60–80 litres/min, the flow rate during cooling was lowered to 40–50 litres/min. After reduction of the flow rate, no more serious device-related adverse events were observed
Abbreviations: CPC, cerebral performance category; IQR, interquartile range; n, number of patients; ROSC, return of spontaneous circulation.	

Costs and resource consequences

The RhinoChill intranasal cooling system is intended for use as an adjunct to systemic temperature control systems and is an additional procedure, and cost, in the emergency care pathway.

The RhinoChill intranasal cooling system has only been used in the NHS to date in clinical trials or in-service evaluations. No published information on the NHS costs of adopting the technology was found.

Other than medical-grade oxygen or breathing air and a power source to charge the control unit, the RhinoChill is a standalone system that does not need any supporting technology to operate.

The only training resources needed for the RhinoChill system are the instructions for use.

The manufacturer states that patient temperature monitoring is needed whenever the device is used. Tympanic or oesophageal, but not nasopharyngeal, thermometers are appropriate for use.

No published evidence on resource consequences was identified.

Strengths and limitations of the evidence

One randomised controlled trial that described the Rhinocill system as the intervention was identified by the literature search. This was the Pre-ROSC IntraNasal Cooling Effectiveness trial (PRINCE trial; Castrén et al. 2010) which recruited 200 patients. Overall, this was a well-conducted trial that set out to investigate the feasibility, safety and efficacy of the intervention in a pre-hospital emergency setting. This was a challenging trial to perform, and there were inevitable practical difficulties that could lead to some forms of selection, performance and detection bias, but which were reasonably well controlled for. Additionally, this was a relatively small trial that was not powered to detect the primary clinical outcomes of achieving successful return of spontaneous circulation, overall survival and discharge without neurological deficit. The clinical outcomes reported in the trial are therefore subject to significant uncertainty and should be viewed with caution. Although the trial failed to conclusively demonstrate any clinical benefit from the device, the intervention significantly reduced cerebral and core temperatures relative to control (standard care).

One case series that described RhinoChill as the intervention was identified by the literature search (Busch et al. 2010). This was a prospective, multicentre, single-arm observational study. A total of 84 patients were recruited into this study, all of whom had suffered a cardiac arrest but had since achieved return of spontaneous circulation (in contrast to the PRINCE trial). Although this study was well conducted it lacked a control group, and consequently was unable to demonstrate the safety or efficacy of the intervention over that of standard care.

Two service evaluations are currently being performed in UK NHS settings. As these are uncontrolled observational studies they are likely to provide low-level evidence for the RhinoChill system.

Relevance to NICE guidance programmes

NICE has issued interventional procedures guidance on [Therapeutic hypothermia following cardiac arrest](#) (NICE interventional procedure guidance 386).

References

[BeneChill website](#) [online; accessed 7 November 2013]

Busch H-J, Eichwede F, Födisch M et al. (2010) [Safety and feasibility of nasopharyngeal evaporative cooling in the emergency department setting in survivors of cardiac arrest](#). Resuscitation 81 (8): 943–9

Castrén M, Nordberg P, Svensson L et al. (2010) [Intra-arrest transnasal evaporative cooling a randomized, prehospital, multicenter study \(PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness\)](#). Circulation 122 (7): 729–36

Deakin CD, Nolan JP, Soar J et al. (2010) [European Resuscitation Council guidelines for resuscitation 2010 section 4. Adult advanced life support](#). Resuscitation 81 (10): 1305–52

Deakin C, Nolan J, Perkins G et al. (2010) [UK Resuscitation Guidelines 2010 section 7. Adult advanced life support](#) [online; accessed 7 November 2013]

European Commission. [Medical Devices Regulatory Framework](#) [online; accessed 7 November 2013]

Gordic S, Gerstl P, Brueesch M et al. (2013) [It is not contrast media: CT imaging appearance of intra-arrest transnasal evaporative cooling](#). American Journal of Emergency Medicine 31 (3): 638.e5–638.e6

Harris B, Andrews PJD, Murray GD et al. (2012) [Systematic review of head cooling in adults after traumatic brain injury and stroke](#). Health Technology Assessment 16 (45): 1–175

Jewkes F, Nolan J (2010) [UK Resuscitation Guidelines 2010 section 4. Pre-hospital cardiac arrest](#) [online; accessed 7 November 2013]

London's Air Ambulance Service. [Trialling brain-cooling device in cardiac arrest patients](#)

[online; accessed 7 November 2013]

Lyon RM, Van Antwerp J, Henderson C, Weaver A, Davies G and Lockey D. Prehospital intranasal evaporative cooling for out-of-hospital cardiac arrest: a pilot, feasibility study. European Journal of Emergency Medicine. In press

National Institute for Health and Clinical Excellence (2011) Therapeutic hypothermia following cardiac arrest. NICE interventional procedure guidance 386

Nolan JP, Laver SR, Welch CA et al. (2007) Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database. Anaesthesia 62: 1207–16

Prehospital Resuscitation Intra Nasal Cooling Effectiveness Survival Study (PRINCESS) protocol. ClinicalTrials.gov identifier NCT01400373 [online; accessed 7 November 2013]

Pre-ROSC Intra-Nasal Cooling Effectiveness (PRINCE) protocol. ClinicalTrials.gov identifier NCT00808236 [online; accessed 7 November 2013]

South East Coast Ambulance Service NHS Foundation Trust. SECAmb looking into benefits of directly cooling brains of cardiac arrest patients [online; accessed 7 November 2013]

Search strategy and evidence selection

Search strategy

The search strategy was peer reviewed by an independent information specialist. The following databases were searched:

- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effectiveness (DARE)
- Embase
- MEDLINE and MEDLINE in Process

- Health Technology Assessment database (HTA).

MEDLINE, MEDLINE in Process and Embase were searched using the OvidSP interface. All other databases were searched using the Cochrane Library interface. The search strategies for each of the 6 literature databases are presented below (A1 to A6).

A1: Source: MEDLINE In-Process & Other Non-indexed Citations and Ovid MEDLINE 1946 to Present. Search date: 22/10/13

1 exp Heart Arrest/ 33667

2 exp Cardiopulmonary Resuscitation/ 11375

3 ((heart* or cardiac* or cardiopulmonary* or cardio-pulmonar* or circulat*) adj5 arrest*).ti,ab. 29159

4 ((heart* or cardiac* or cardiopulmonary* or cardio-pulmonar* or circulat*) adj5 (resuscita* or life support*)).ti,ab. 13961

5 (sudden cardiac death* or SCD or SCA).ti,ab. 18686

6 or/1-5 71829

7 exp Cerebrovascular Disorders/ 275909

8 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain vascul* or cerebral vascul* or cva* or apoplexy* or SAH).ti,ab. 196056

9 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemisphere* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior circulation or posterior circulation or basal gangli*) adj5 (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*)).ti,ab. 88408

10 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) adj5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)).ti,ab. 49562

11 or/7-10 394509

12 exp Craniocerebral Trauma/ 120439

13 Brain Edema/ 12285

14 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemisphere*) adj5 (injur* or trauma* or damage* or wound* or fracture* or contusion*)).ti,ab. 114180

15 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemisphere*) adj5 (edem* or oedem* or swell*)).ti,ab. 14905

16 (TBI or diffuse axonal injur*).ti,ab. 13767

17 or/12-16 202435

18 6 or 11 or 17 610402

19 Hypothermia, Induced/ 16514

20 Cryotherapy/ 3715

21 Hypothermia/ 8604

22 Cold Temperature/ 42038

23 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherapy* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*).ti,ab. 164801

24 ((low or lower* or reduc*) adj5 temperature*).ti,ab. 65380

25 or/19-24 236682

26 Administration, Intranasal/ 11505

27 exp Nose/ 71246

28 exp Nasopharynx/ 9445

29 (nasal* or intranasal* or transnasal* or nasopharynx* or naso-pharynx* or rhinopharynx* or rhino-pharynx* or nose or noses or nostril*).ti,ab. 143015

30 or/26-29 181289

31 18 and 25 and 30 251

32 (rhinochill* or rhino chill* or benechill* or bene chill*).ti,ab. 8

33 ((nasal* or intranasal* or transnasal* or nasopharynx* or naso-pharynx* or rhinopharynx* or rhino-pharynx* or nose or noses or nostril*) adj5 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherapy* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*)).ti,ab. 588

34 or/31-33 765

35 exp animals/ not humans/ 4050087

36 34 not 35 648

37 limit 36 to (english language and yr="2008 -Current") 129

A.2: Source: Database of Abstracts of Reviews of Effectiveness (DARE) - Issue 3 of 4, Jul 2013. Search date: 23/10/13

#1 MeSH descriptor: [Heart Arrest] explode all trees 1080

#2 MeSH descriptor: [Cardiopulmonary Resuscitation] explode all trees 525

#3 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/ 5 arrest*) 2040

#4 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/ 5 (resuscita* or life support*)) 1062

#5 (sudden next cardiac next death* or SCD or SCA) 820

#6 #1 or #2 or #3 or #4 or #5 3451

#7 MeSH descriptor: [Cerebrovascular Disorders] explode all trees 8578

#8 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain next vasc* or cerebral next vasc* or cva* or apoplex* or SAH) 31807

#9 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemispher* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior next circulation or posterior next circulation or basal next gangli*) near/5 (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*)) 5794

#10 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) 4056

#11 #7 or #8 or #9 or #10 35341

#12 MeSH descriptor: [Craniocerebral Trauma] explode all trees 1740

#13 MeSH descriptor: [Brain Edema] this term only 124

#14 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (injur* or trauma* or damag* or wound* or fracture* or contusion*)) 4257

#15 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (edem* or oedem* or swell*)) 483

#16 (TBI or diffuse next axonal next injur*) 592

#17 #12 or #13 or #14 or #15 or #16 5226

#18 #6 or #11 or #17 41518

#19 MeSH descriptor: [Hypothermia, Induced] this term only 674

#20 MeSH descriptor: [Cryotherapy] this term only 415

#21 MeSH descriptor: [Hypothermia] this term only 301

#22 MeSH descriptor: [Cold Temperature] this term only 1030

#23 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*) 9773

#24 ((low or lower* or reduc*) near/5 temperature*) 979

#25 #19 or #20 or #21 or #22 or #23 or #24 10302

#26 #18 and #25 1463

#27 (rhinochill* or rhino next chill* or benechill* or bene next chill*) 6

#28 ((nasal* or intranasal* or transnasal* or nasopharyn* or naso-pharyn* or rhinopharyn* or rhino-pharyn* or nose or noses or nostril*) near/5 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*)) 210

#29 #26 or #27 or #28 from 2008 to 2013, in Other Reviews 32

A.3: Source: Health Technology Assessment database (HTA) - Issue 3 of 4 Jul 2013.

Search date: 23/10/13

#1 MeSH descriptor: [Heart Arrest] explode all trees 1080

#2 MeSH descriptor: [Cardiopulmonary Resuscitation] explode all trees 525

#3 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/5 arrest*) 2040

#4 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/5 (resuscita* or life support*)) 1062

#5 (sudden next cardiac next death* or SCD or SCA) 820

#6 #1 or #2 or #3 or #4 or #5 3451

#7 MeSH descriptor: [Cerebrovascular Disorders] explode all trees 8578

#8 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain next vasc* or cerebral next vasc* or cva* or apoplex* or SAH) 31807

#9 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemispher* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior next circulation or posterior next circulation or basal next gangli*) near/5 (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*)) 5794

#10 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) 4056

#11 #7 or #8 or #9 or #10 35341

#12 MeSH descriptor: [Craniocerebral Trauma] explode all trees 1740

#13 MeSH descriptor: [Brain Edema] this term only 124

#14 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (injur* or trauma* or damag* or wound* or fracture* or contusion*)) 4257

#15 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (edem* or oedem* or swell*)) 483

#16 (TBI or diffuse next axonal next injur*) 592

#17 #12 or #13 or #14 or #15 or #16 5226

#18 #6 or #11 or #17 41518

#19 MeSH descriptor: [Hypothermia, Induced] this term only 674

#20 MeSH descriptor: [Cryotherapy] this term only 415

#21 MeSH descriptor: [Hypothermia] this term only 301

#22 MeSH descriptor: [Cold Temperature] this term only 1030

#23 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*) 9773

#24 ((low or lower* or reduc*) near/5 temperature*) 979

#25 #19 or #20 or #21 or #22 or #23 or #24 10302

#26 #18 and #25 1463

#27 (rhinochill* or rhino next chill* or benechill* or bene next chill*) 6

#28 ((nasal* or intranasal* or transnasal* or nasopharyn* or naso-pharyn* or rhinopharyn* or rhino-pharyn* or nose or noses or nostril*) near/5 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*)) 210

#29 #26 or #27 or #28 from 2008 to 2013, in Technology Assessments 13

A.4: Source: Cochrane Central Register of Controlled Trials (CENTRAL) - Issue 3 of 4 Jul 2013. Search date: 22/10/13

#1 MeSH descriptor: [Heart Arrest] explode all trees 1080

#2 MeSH descriptor: [Cardiopulmonary Resuscitation] explode all trees 525

#3 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/

5 arrest*) 2040

#4 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/5 (resuscita* or life support*)) 1062

#5 (sudden next cardiac next death* or SCD or SCA) 820

#6 #1 or #2 or #3 or #4 or #5 3451

#7 MeSH descriptor: [Cerebrovascular Disorders] explode all trees 8578

#8 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain next vasc* or cerebral next vasc* or cva* or apoplex* or SAH) 31807

#9 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemispher* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior next circulation or posterior next circulation or basal next gangli*) near/5 (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*)) 5794

#10 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) 4056

#11 #7 or #8 or #9 or #10 35341

#12 MeSH descriptor: [Craniocerebral Trauma] explode all trees 1740

#13 MeSH descriptor: [Brain Edema] this term only 124

#14 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (injur* or trauma* or damag* or wound* or fracture* or contusion*)) 4257

#15 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (edem* or oedem* or swell*)) 483

#16 (TBI or diffuse next axonal next injur*) 592

#17 #12 or #13 or #14 or #15 or #16 5226

#18 #6 or #11 or #17 41518

#19 MeSH descriptor: [Hypothermia, Induced] this term only 674

#20 MeSH descriptor: [Cryotherapy] this term only 415

#21 MeSH descriptor: [Hypothermia] this term only 301

#22 MeSH descriptor: [Cold Temperature] this term only 1030

#23 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*) 9773

#24 ((low or lower* or reduc*) near/5 temperature*) 979

#25 #19 or #20 or #21 or #22 or #23 or #24 10302

#26 MeSH descriptor: [Administration, Intranasal] this term only 1941

#27 MeSH descriptor: [Nose] explode all trees 1944

#28 MeSH descriptor: [Nasopharynx] explode all trees 291

#29 (nasal* or intranasal* or transnasal* or nasopharyn* or naso-pharyn* or rhinopharyn* or rhino-pharyn* or nose or noses or nostril*) 13189

#30 #26 or #27 or #28 or #29 13474

#31 #18 and #25 and #30 143

#32 (rhinochill* or rhino next chill* or benechill* or bene next chill*) 6

#33 ((nasal* or intranasal* or transnasal* or nasopharyn* or naso-pharyn* or rhinopharyn* or rhino-pharyn* or nose or noses or nostril*) near/5 (cool* or chill* or cold* or hypotherm*

or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*)) 210

#34 #31 or #32 or #33 from 2008 to 2013, in Trials 19

A.5: Source: Cochrane Database of Systematic Reviews (CDSR). Search date: 23/10/13

#1 MeSH descriptor: [Heart Arrest] explode all trees 1080

#2 MeSH descriptor: [Cardiopulmonary Resuscitation] explode all trees 525

#3 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/5 arrest*):ti,ab,kw 1733

#4 ((heart* or cardiac* or cardiopulmonar* or cardio-pulmonar* or circulat*) near/5 (resuscita* or life support*)):ti,ab,kw 943

#5 (sudden next cardiac next death* or SCD or SCA):ti,ab,kw 653

#6 #1 or #2 or #3 or #4 or #5 2987

#7 MeSH descriptor: [Cerebrovascular Disorders] explode all trees 8578

#8 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain next vasc* or cerebral next vasc* or cva* or apoplex* or SAH):ti,ab,kw 22589

#9 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemispher* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior next circulation or posterior next circulation or basal next gangli*) near/5 (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*)):ti,ab,kw 4919

#10 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)):ti,ab,kw 3177

#11 #7 or #8 or #9 or #10 27884

#12 MeSH descriptor: [Craniocerebral Trauma] explode all trees 1740

#13 MeSH descriptor: [Brain Edema] this term only 124

#14 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (injur* or trauma* or damag* or wound* or fracture* or contusion*)):ti,ab,kw 3372

#15 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemispher*) near/5 (edem* or oedem* or swell*)):ti,ab,kw 343

#16 (TBI or diffuse next axonal next injur*):ti,ab,kw 501

#17 #12 or #13 or #14 or #15 or #16 4252

#18 #6 or #11 or #17 33634

#19 MeSH descriptor: [Hypothermia, Induced] this term only 674

#20 MeSH descriptor: [Cryotherapy] this term only 415

#21 MeSH descriptor: [Hypothermia] this term only 301

#22 MeSH descriptor: [Cold Temperature] this term only 1030

#23 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*):ti,ab,kw 8043

#24 ((low or lower* or reduc*) near/5 temperature*):ti,ab,kw 869

#25 #19 or #20 or #21 or #22 or #23 or #24 8528

#26 #18 and #25 976

#27 (rhinochill* or rhino next chill* or benechill* or bene next chill*):ti,ab,kw 6

#28 ((nasal* or intranasal* or transnasal* or nasopharynx* or naso-pharynx* or rhinopharynx* or rhino-pharynx* or nose or noses or nostril*) near/5 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherap* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*)):ti,ab,kw 176

#29 #26 or #27 or #28 from 2008 to 2013, in Cochrane Reviews (Reviews and Protocols) 34

A.6: Source: Embase 1974 to 2013 October 22. Search date: 23/10/13

1 exp heart arrest/ 46245

2 resuscitation/ 65875

3 ((heart* or cardiac* or cardiopulmonary* or cardio-pulmonar* or circulat*) adj5 arrest*).ti,ab. 38150

4 ((heart* or cardiac* or cardiopulmonary* or cardio-pulmonar* or circulat*) adj5 (resuscita* or life support*)).ti,ab. 17709

5 (sudden cardiac death* or SCD or SCA).ti,ab. 25836

6 or/1-5 131314

7 exp cerebrovascular disease/ 362327

8 stroke/ 127432

9 stroke patient/ 8900

10 stroke unit/ 1615

11 (stroke or strokes or poststroke or poststrokes or cerebrovasc* or cerebro-vasc* or brain vascul* or cerebral vascul* or cva* or apoplexy* or SAH).ti,ab. 263173

12 ((brain* or cerebr* or cerebell* or cortical or vertebrobasilar or hemisphere* or intracran* or intra-cran* or intracerebral or infratentorial or infra-tentorial or supratentorial or supra-tentorial or MCA or anterior circulation or posterior circulation or basal gangli*))

adj5 (ischemi* or ischaemic* or infarct* or thrombo* or emboli* or occlus* or hypox* or vasospasm*).ti,ab. 115208

13 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or intra-cran* or parenchymal or intraventricular or intra-ventricular or infratentorial or infra-tentorial or supratentorial or supra-tentorial or basal gangli* or subarachnoid) adj5 (haemorrhage* or haemorrhage* or haematoma* or hematoma* or bleed*)).ti,ab. 65266

14 or/7-13 543723

15 exp head injury/ 214002

16 coma/ 22248

17 traumatic epilepsy/ 1334

18 brain edema/ 22925

19 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemisphere*) adj5 (injur* or trauma* or damage* or wound* or fracture* or contusion*)).ti,ab. 144804

20 ((head or heads or forehead* or crani* or intracrani* or intercrani* or cerebr* or intracerebr* or intercerebr* or capitis or brain* or forebrain* or skull* or hemisphere*) adj5 (edem* or oedema* or swell*)).ti,ab. 19204

21 (TBI or diffuse axonal injur*).ti,ab. 19531

22 or/15-21 314018

23 6 or 14 or 22 902350

24 induced hypothermia/ 8670

25 profound induced hypothermia/ 267

26 cryotherapy/ 12102

27 hypothermia/ 25553

28 low temperature/ 10690

29 low temperature procedures/ 1744

30 cold treatment/ 381

31 cooling/ 10724

32 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherapy* or cryo-therap* or cryotreat* or cryo-treat* or cryogen* or cryo-gen* or cryotherm* or cryo-therm*).ti,ab. 198446

33 ((low or lower* or reduc*) adj5 temperature*).ti,ab. 64407

34 or/24-33 269806

35 intranasal drug administration/ 11550

36 exp nose/ 51549

37 exp nasopharynx/ 10303

38 nasopharynx airway/ 35

39 (nasal* or intranasal* or transnasal* or nasopharynx* or naso-pharynx* or rhinopharynx* or rhino-pharynx* or nose or noses or nostril*).ti,ab. 170749

40 or/35-39 193421

41 23 and 34 and 40 356

42 (rhinochill* or rhino chill* or benechill* or bene chill*).af. 31

43 ((nasal* or intranasal* or transnasal* or nasopharynx* or naso-pharynx* or rhinopharynx* or rhino-pharynx* or nose or noses or nostril*) adj5 (cool* or chill* or cold* or hypotherm* or hypo-therm* or cryotherapy* or cryo-therap* or cryotreat* or cryo-treat* or cryogen*

or cryo-gen* or cryotherm* or cryo-therm*))).ti,ab. 714

44 or/41-43 959

45 (animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not human/
3680046

46 44 not 45 857

47 limit 46 to (english language and yr="2008 -Current")

Evidence selection

Initial scoping work on the topic, with NICE, informed the inclusion and exclusion criteria for the final evidence selection. The [BeneChill website](#) indicated that the stroke and traumatic brain injury applications of the RhinoChill system are still in clinical trials. Search terms for these clinical applications were included in the search strategy and relevant papers, when retrieved, confirmed this understanding.

This first sift removed evidence based on the following exclusion criteria:

- articles of poor relevance against search terms
- publication types that were out of scope:
 - non-English language studies
 - conference abstracts
 - review protocols (for example, Cochrane review protocols)
 - articles if neither the abstract nor the full text is freely available online.

A total of 460 records were retrieved from the literature search. After removing duplicated records, 316 remained. An initial 199 records were excluded as being animal studies, studies on children, the wrong population or irrelevant. A total of 117 were considered in more detail and a further 92 records were excluded, comprising: 29 conference abstracts, 2 without English translation, 1 animal study, 17 with an alternative population, 19 in the wrong clinical setting, 7 using alternative devices or technologies, 6 not relevant to cooling, and 10 were not original research (5 reviews, 4 letters/editorials, 1 study protocol),

plus 1 duplicate. Full articles were ordered for the remaining 25 records, with 22 successfully retrieved within the timeframe of production of this briefing.

A second sift of the evidence included relevant primary research addressing the use of the medical technology within the defined indication under review (cardiac arrest). The conventional evidence hierarchy applies and the best available evidence was selected for inclusion within the evidence tables and for critical appraisal.

Included studies in second sift:

- Primary research on the RhinoChill intranasal cooling system for the cardiac arrest application.

During the second sift, 19 records were excluded for the following reasons: 6 did not describe intranasal cooling or the RhinoChill device, 3 pooled data and therefore results were not specific to intranasal cooling, RhinoChill or a cardiac arrest population, 9 were not original research (5 review articles, 2 letters to the editor, 1 editorial, 1 study protocol) and 1 was a non-English language study.

This left 3 articles on the cardiac arrest application of RhinoChill for inclusion in the evidence tables and critical appraisal (1 randomised controlled trial, 1 case series and 1 case report, tables 1 to 3 respectively). The HTA systematic review (Harris et al. 2012) was used to inform the narrative in this briefing for the clinical application of RhinoChill to stroke and traumatic brain injury.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by Newcastle and York External Assessment Centre. The [Interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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