



**Australian Government**  
**Department of Health and Ageing**



Australia and New Zealand Horizon Scanning Network

**ANZHSN**

AN INITIATIVE OF THE NATIONAL, STATE AND  
TERRITORY GOVERNMENTS OF AUSTRALIA  
AND THE GOVERNMENT OF NEW ZEALAND

# **Horizon scanning technology prioritising summary**

## **RhinoChill™ intra-nasal cooling system**



**November 2010**

Australian  
Safety  
and Efficacy  
Register  
of New  
Interventional  
Procedures -  
Surgical

© Commonwealth of Australia 2010

ISBN

Publications Approval Number:

This work is copyright. You may download, display, print and reproduce this material in unaltered form only (retaining this notice) for your personal, non-commercial use or use within your organisation. Apart from any use as permitted under the *Copyright Act 1968*, all other rights are reserved. Requests and inquiries concerning reproduction and rights should be addressed to Commonwealth Copyright Administration, Attorney General's Department, Robert Garran Offices, National Circuit, Canberra ACT 2600 or posted at <http://www.ag.gov.au/cca>

Electronic copies can be obtained from <http://www.horizonscanning.gov.au>

Enquiries about the content of the report should be directed to:

HealthPACT Secretariat  
Department of Health and Ageing  
MDP 106  
GPO Box 9848  
Canberra ACT 2606  
AUSTRALIA

**DISCLAIMER:** This report is based on information available at the time of research cannot be expected to cover any developments arising from subsequent improvements health technologies. This report is based on a limited literature search and is not a definitive statement on the safety, effectiveness or cost-effectiveness of the health technology covered.

The Commonwealth does not guarantee the accuracy, currency or completeness of the information in this report. This report is not intended to be used as medical advice and intended to be used to diagnose, treat, cure or prevent any disease, nor should it be used therapeutic purposes or as a substitute for a health professional's advice. The Commonwealth does not accept any liability for any injury, loss or damage incurred by use of or reliance the information.

The production of these Horizon scanning prioritising summaries was overseen by the Health Policy Advisory Committee on Technology (HealthPACT). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by Dr Meegan Vandepeer and Mrs Deanne Forel from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

# PRIORITISING SUMMARY

**REGISTER ID** S000127

**NAME OF TECHNOLOGY** RHINOCHILL™ INTRA-NASAL COOLING SYSTEM

**PURPOSE AND TARGET GROUP** PORTABLE SYSTEM FOR COOLING THE BRAIN FOLLOWING CARDIAC ARREST TO PREVENT PERMANENT NEUROLOGIC INJURY

## STAGE OF DEVELOPMENT (IN AUSTRALIA)

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established  |
| <input type="checkbox"/> Experimental             | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational          | <input type="checkbox"/> Should be taken out of use   |
| <input type="checkbox"/> Nearly established       |   |

## AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- |   |             |    |
|---|-------------|----|
| <input type="checkbox"/> Yes            | ARTG number | NA |
| <input checked="" type="checkbox"/> No  |             |    |
| <input type="checkbox"/> Not applicable |             |    |

## INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials underway or completed	Limited use	Widely diffused
Belgium	✓		
Czech Republic	✓		
Germany	✓		
Italy	✓		
Sweden	✓		

## IMPACT SUMMARY

BeneChill provides the RhinoChill™ Intra-Nasal Cooling System with the aim of cooling the brain following cardiac arrest, to protect it from permanent neurological injury. RhinoChill uses a nasal catheter that sprays a rapidly evaporating coolant liquid into the nasal cavity. The device is portable and battery-operated and nonspecialised medical personnel can begin the brain cooling therapy intra-arrest, before the return of spontaneous circulation. The device has also been tested in-hospital after successful cardiac arrest resuscitation.

## **BACKGROUND**

Cardiac arrest is the failure of the heart to contract effectively, leading to the cessation of normal circulation and lack of oxygen supply to the brain. Prolonged or untreated cardiac arrest results in brain injury or death; therefore, to improve the likelihood of survival and neurological recovery, immediate resuscitation (within five minutes) is vital. Traditional treatment is cardiopulmonary resuscitation to provide circulatory support, followed by defibrillation if a shockable rhythm is present. In the United States, the median rate of survival to hospital discharge after cardiac arrest is only about 8% (Busch et al 2010).

Cooling a patient with restored circulation (but not consciousness) following cardiac arrest may also improve prognosis; this is known as therapeutic hypothermia. Therapeutic hypothermia for patients resuscitated from cardiac arrest has been shown to save lives; however, current cooling modalities are suboptimal (Castrén et al 2010). Traditionally, therapeutic hypothermia is instituted after return of spontaneous circulation, usually upon arrival at the emergency department; however, there is a lack of evidence in regards to how early cooling should be initiated and which cooling method is most effective in achieving optimal patient survival (Becker 2010).

RhinoChill (BeneChill, Inc, San Diego, California) is a new device for delivery of therapeutic hypothermia, novel in that it attempts to cool the brain during cardiac arrest (intra-arrest) whilst cardiopulmonary resuscitation is taking place (Becker 2010). The RhinoChill device may also be used after successful resuscitation from cardiac arrest. Cooling the brain in cardiac arrest patients slows the process of cell death; when blood supply is interrupted and brain cells are deprived of oxygen, toxic compounds overwhelm the organs and result in long-term brain injury. Therapeutic hypothermia slows the body's production of these compounds, reducing the risk of brain injury.

The RhinoChill device (Figure 1) includes a disposable nasal catheter and a 2 litre bottle of coolant. The tubing delivers a mix of coolant via a 10 centimetre nasal catheter with spray ports on the dorsal surface which is fully inserted through the nostril along the base of the nasal cavity; the coolant is nebulised by close contact with oxygen at the spray ports (Busch et al 2010). Coolant evaporation absorbs tissue heat and rapidly cools the nasal cavity to approximately 2°C (Castrén et al 2010). The cooling rate can be controlled and automatically cuts out when the pressure in the nasal cavity exceeds 60 centimetre H<sub>2</sub>O (Castrén et al 2010).

**Figure 1: RhinoChill cooling device (Source: BeneChill 2010).**



The advantages of the RhinoChill device are cited as: ease of handling, rapid administration (30 to 60 seconds to connect components at which point the device is ready to use) and brief training requirements (advanced life support crew had a 2-hour training session) (Castrén et al 2010).

#### **CLINICAL NEED AND BURDEN OF DISEASE**

As previously mentioned, the RhinoChill cooling device has been tested to cool the brain during resuscitation after witnessed cardiac arrest or following successful resuscitation from cardiac arrest, with an aim to prevent permanent neurological damage.

Coronary heart disease is the leading cause of sudden cardiac arrest, with approximately 60% to 70% of sudden cardiac arrests being related to coronary heart disease. Coronary heart disease is the leading cause of death in Australia, with 26,521 deaths reported in the year 2000 (Mathur 2002). This condition is also responsible for significant illness, disability, poor quality of life and premature death in many Australians, and the associated direct healthcare costs exceed those of any other disease (Mathur 2002).

#### **DIFFUSION**

The use of mild therapeutic hypothermia in a hospital setting has been recommended since the publication of two sentinel reports in 2002 which demonstrated significant improvements in neurologically intact survival for comatose patients with ventricular fibrillation or ventricular tachycardia, even when cooling was performed hours after spontaneous circulation was achieved (Bernard et al 2002; The Hypothermia After Cardiac Arrest Study Group 2010). This led to increased use of and recommendation for the use of mild therapeutic hypothermia in international guidelines (Castrén et al 2010).

Trials have been completed that enrolled patients in Belgium, the Czech Republic, Germany, Italy and Sweden. According to the manufacturer's (BeneChill Inc) website,

RhinoChill has received CE mark approval (0086) for use throughout Europe but is not available for sale in the United States (BeneChill 2010).

### **COMPARATORS**

The RhinoChill device enables intra-arrest cooling. Intra-arrest cooling is novel because it attempts to cool the brain during the cardiac arrest in the midst of cardiopulmonary resuscitation. Currently most patients are cooled only on arrival at the emergency department or hospital and often hours later in the intensive care unit (Becker 2010). Only rarely are patients cooled in an ambulance (Becker 2010). Thus, there is no direct comparator for RhinoChill.

### **SAFETY AND EFFECTIVENESS ISSUES**

Two studies were eligible for inclusion in the review: one randomised controlled trial (RCT) PRINCE (**P**re-**R**eturn of spontaneous circulation **I**ntra**N**asal **C**ooling **E**ffectiveness) which aimed primarily to determine the safety and feasibility of trans-nasal evaporative cooling by pre-hospital rescuers during ongoing resuscitation before achievement of return to spontaneous circulation (Castrén et al 2010), and a multicentre case series study that examined the cooling effectivity, safety and feasibility of nasopharyngeal cooling with RhinoChill induction of therapeutic hypothermia (Busch et al 2010).

#### *Study profiles*

Castrén et al (2010) conducted an RCT between November 2008 and June 2009 at 15 sites in five European countries. Included were adult patients ( $\geq 18$  years) who had suffered a witnessed cardiac arrest with treatment initiated by emergency medical personnel within 20 minutes. Patients were randomised to intra-arrest cooling with RhinoChill or standard care. Both groups were cooled after hospital arrival. The final analysis included 93 versus 101 patients, respectively. There were no significant differences in baseline characteristics between the treatment groups. The study was primarily focussed on safety and feasibility. Clinical outcomes included return of spontaneous circulation rate, survival to discharge and neurologically intact survival, although the study was not powered to detect changes in these outcomes.

Busch et al (2010) reported the outcomes of a European multicentre observational study in intensive care units and emergency departments (n=11) investigating the safety, feasibility and cooling effect of one hour of nasopharyngeal evaporative cooling in comatose patients (n=84) after they had been successfully resuscitated after cardiac arrest. Primary endpoints were cooling rate, time needed to achieve mild hypothermia (34°C) and target temperature (33°C), and neurologic outcome at hospital discharge using cerebral performance categories (CPC: 1=normal to 5=dead), as well as adverse events (AEs). Included, if investigators trained on the device were on duty, were patients  $\geq 18$  years of age who did not obey any verbal command at any time after return of spontaneous circulation and prior to initiation of cooling.

### *Safety*

In the RCT by Castrén et al (2010), nasal whitening occurred in 14% patients (13/93) but resolved in all five who were resuscitated, and epistaxis occurred in 3% (3/93). The only device-related serious AE was serious epistaxis in a patient in hepatic failure. Periorbital emphysema occurred 75 minutes into treatment in one patient and resolved spontaneously within 24 hours. The total number of serious AEs that occurred within 7 days of cardiac arrest was seven in the treatment group and 14 in the control group. There were no significant differences between groups in regards to hemodynamic, oxygen saturation or chest radiograph abnormalities on admission.

Busch et al (2010) reported device-related AEs in 16% (15/84) of patients (Table 1). A patient with cardiogenic shock experienced tissue damage of the nose and cheeks due to freezing. Signs of aspiration on chest x-ray were evident in nine patients. Intra-cooling death occurred in one patient; however, autopsy found that infarct was responsible for the death and the AE was rated as ‘probably not device related’. Post-discharge olfactory function was measured in those patients with favourable neurological recovery who were willing to cooperate (n=11) and all scored within the normal range for smell identification for age and gender.

**Table 1: Device-related adverse events reported in Busch et al (2010)**

	<b>Total incidence (%)</b>	<b>Resolved (%)</b>	<b>Sequelae (%)</b>
Nasal discolouration	10/84 (11)	10/10 (100)	0/10 (0)
Cold-induced tissue damage	1/84 (1)	0/1 (0)	1/1 (100)
Epistaxis	2/84 (2)	2/2 (100)	0/2 (0)
Coolant in sinus	1/84 (1)	1/1 (100)	0/1 (0)
Periorbital gas emphysema	1/84 (1)	1/1 (100)	0/1 (0)
Total	15/84 (16)	14 (93)	1 (7)

\*percentage values were taken directed from Busch et al (2010).

### *Effectiveness*

In the RCT by Castrén et al (2010) mean tympanic temperature was significantly lower in the treatment group (34.2°C) compared with the control group (35.5°C) upon arrival at the hospital ( $P<0.001$ ), as was mean core temperature (35.1 °C versus 35.8°C;  $P=0.01$ ). Tympanic temperature of 34°C was achieved in a median of 102 minutes in the treatment group compared with 291 minutes for the control group ( $P=0.03$ ). Median time to target core temperature (34°C) was 155 minutes in the treatment group and 284 minutes in the control group.

With respect to clinical outcomes, there were no significant differences between groups, although the study was not adequately powered to detect changes in these outcomes. The values for treated versus control were:

- rate of return of spontaneous circulation: 38% versus 43%;  $P=0.48$
- overall survival of those admitted alive: 44% versus 31%;  $P=0.26$
- neurologically intact survival at discharge, i.e. Pittsburgh cerebral performance category scale 1 to 2: 34% versus 21%;  $P=0.21$ .

No significant differences were seen between groups in relation to cardiogenic shock as the cause of death, length of hospitalisation, days in the intensive care unit and days on a ventilator.

The purpose of the case series study by Busch et al (2010) was to determine whether use of the device in primary cardiac arrest survivors was feasible and safe in a hospital setting. As the study was not comparative, no relative advantage can be determined. However, the researchers reported that 40% of patients survived (34/84), 76% (26/34) of which with favourable neurological outcomes at discharge. Of all patients treated with RhinoChill, the rate of neurologically intact survival at discharge was 31% (26/84).

#### **COST IMPACT**

No economic studies were identified.

#### **ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS**

No issues were identified in the retrieved material.

#### **OTHER ISSUES**

BeneChill Inc., the makers of RhinoChill, supported the participating centres in the case series study by Busch et al (2010) with respect to medical supplies and personnel for data processing. Three of the 17 authors received some form of financial support from BeneChill Inc. Two of these authors were also involved in the Castrén et al (2010) RCT.

#### **SUMMARY OF FINDINGS**

From the limited literature available, use of the RhinoChill device in witnessed pre-hospital arrest situations or in-hospital post-arrest situations appears to be safe and feasible. Enduring device-related adverse events were rare. The rate of neurologically intact survival at discharge was 31% and 34% of patients in the two included studies, although the RCT did not show a benefit for the RhinoChill group. Further high-quality studies are required.

#### **HEALTHPACT ASSESSMENT**

RhinoChill may not become available for use in Australia in the near future and further research is required, therefore it is recommended that no further assessment of this technology be carried out at this time.

- |  |  |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input type="checkbox"/> Monitor                 | <input checked="" type="checkbox"/> Archive                |

#### **HEALTHPACT ACTION**

#### **NUMBER OF STUDIES INCLUDED**

Total number of studies	2
Level II evidence	1
Level IV evidence	1

## REFERENCES

Becker LB. Cooling heads and hearts versus cooling our heels. *Circulation* 2010; 122(7): 679-681.

BeneChill 2010. Last Updated 2010. <http://www.benechill.com/> [Accessed September 2010].

Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *New England Journal of Medicine* 2002; 346: 557–563.

Busch HJ, Eichwede F, Födisch M, Taccone FS, Wöbker G, Schwab T, Hopf HB, Tonner P, Hachimi-Idrissi S, Martens P, Fritz H, Bode Ch, Vincent JL, Inderbitzen B, Barbut D, Sterz F, Janata A. Safety and feasibility of nasopharyngeal evaporative cooling in the emergency department setting in survivors of cardiac arrest. *Resuscitation* 2010; 81(8): 943-949.

Castrén M, Nordberg P, Svensson L, Taccone F, Vincent JL, Desruelles D, Eichwede F, Mols P, Schwab T, Vergnion M, Storm C, Pesenti A, Pachl J, Guérisse F, Elste T, Roessler M, Fritz H, Durnez P, Busch HJ, Inderbitzen B, Barbut D. Intra-arrest transnasal evaporative cooling: a randomized, prehospital, multicenter study (PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness). *Circulation* 2010; **122**(7): 729-736.

Mathur S 2002. Epidemic of coronary heart disease and its treatment in Australia. Cardiovascular disease series no. 20. AIHW cat no. CVD 21. Canberra: Australian Institute of Health and Welfare.

The Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *New England Journal of Medicine* 2002; 346: 549 –556.

## SOURCES OF FURTHER INFORMATION

-

## SEARCH CRITERIA TO BE USED

RhinoChill

BeneChill

Intra nasal cooling system

## HEALTH PACT DECISION

- |  |  |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input type="checkbox"/> Monitor                 | <input type="checkbox"/> Archive                           |
| <input type="checkbox"/> Refer                   | <input type="checkbox"/> Decision pending                  |

**PRIORITY RATING**

**High**

**Medium**

**Low**