Abstract of thesis entitled

An Evidence-based Guideline in Inducing Therapeutic Hypothermia to Improve Neurological Outcome of Post Cardiac Arrest Patients in Emergency Department

Submitted by

Wu Ho Ming

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Out of hospital cardiac arrest is an increasing public health concern in developed countries with high mortality, where only about one tenth of patients can survive. Recently, therapeutic hypothermia has been recommended for post cardiac arrest unconscious adult survivors with initial cardiac rhythm of ventricular fibrillation or pulseless ventricular tachycardia. This innovation improves neurological outcome and survival of patients. However, in Emergency Department, it is not common for health care professionals to induce therapeutic hypothermia in post resuscitation care. Therefore, the time to reach target temperature is prolonged after patients who have return of spontaneous circulation after resuscitation. Induced therapeutic hypothermia is to keep target body temperature of 32°C -34°C for 24 hours. It can be simply applied by placing ice packs on head, sides of neck, axillae and groins. Nurses play an important role in this innovation and monitor any complications till safe escort to Intensive Care Unit. The aim of this dissertation is to develop an evidence-based guideline to induce therapeutic hypothermia in post cardiac arrest coma adult survivors with ventricular fibrillation or pulseless ventricular tachycardia from evidence to clinical practice. Existing evidence are reviewed to assess the feasibility and transferability
of implementing the guideline and to develop its implementation and evaluation plan.

Eight randomized controlled trials met the selection criteria and were searched from four electronic databases. These eight journals were demonstrated in the form of tables of evidence with key points shown clearly. The quality of these journals was evaluated and graded by using the critical appraisal checklist for randomized controlled trials developed by Scottish Intercollegiate Guidelines Network (SIGN). By utilizing the good quality and grade among these eight studies, keeping patients with target temperature of 32°C -34°C for 24 hours as soon as possible was shown to support the proposed innovation to achieve more desirable clinical outcomes for post cardiac arrest survivors.

The implementation potential (material costs, cost/benefit ratio, etc.) is assessed before implementation. An evidence-based guideline in inducing therapeutic hypothermia to improve neurological outcome of post cardiac arrest patients in Emergency Department is established and is beneficial. The grade of recommendation is rated from A to D in the guideline.

Communication plans with all stakeholders, including administrators, frontline staff, patients and their significant others, are discussed. Initiating the change, guiding the change and sustaining the change are also discussed. A pilot study is proposed before the full-scale implementation to explore any unexpected problems which may be missed in planning. At last, evaluation plan is developed to assess patient outcomes, health care provider outcomes and system outcomes.
The proposed evidence-based guideline is designed to improve neurological function and survival of post cardiac arrest patients with initial rhythms of ventricular fibrillation or pulseless ventricular tachycardia. It is recommended to adopt this protocol in all Emergency Departments to provide more clinical benefits to post cardiac arrest survivors.
An Evidence-based Guideline in Inducing Therapeutic Hypothermia to Improve Neurological Outcome of Post Cardiac Arrest Patients in Emergency Department

by

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Declaration

I declare that this thesis represents my own work, except where due acknowledgement is made, and that it has not been previously included in a thesis, dissertation or report submitted to this University or to any other institution for a degree, diploma or other qualifications.

Signed

Wu Ho Ming
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<tbody>
<tr>
<td>ACLS</td>
<td>Advanced Cardiovascular Life Support</td>
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<tr>
<td>APN</td>
<td>Advanced Practice Nurse</td>
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<tr>
<td>BP</td>
<td>Blood pressure</td>
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<tr>
<td>CONS</td>
<td>Consultant</td>
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<tr>
<td>CMS</td>
<td>Clinical Management System</td>
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<tr>
<td>CPC</td>
<td>Cerebral Performance Categories</td>
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<td>CPR</td>
<td>Cardiopulmonary resuscitation</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
</tr>
<tr>
<td>COS</td>
<td>Chief of Service</td>
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<tr>
<td>DOM</td>
<td>Department Operations Manager</td>
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<tr>
<td>EBP</td>
<td>Evidence-based practice</td>
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<tr>
<td>EN</td>
<td>Enrolled Nurse</td>
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<tr>
<td>GCS</td>
<td>Glasgow Coma Scale</td>
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<tr>
<td>HA</td>
<td>Hospital Authority</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
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<tr>
<td>MO</td>
<td>Medical Officer</td>
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<tr>
<td>NTWC</td>
<td>New Territories West Cluster</td>
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<tr>
<td>PEA</td>
<td>pulseless electrical activity</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>ROSC</td>
<td>Return of spontaneous circulation</td>
</tr>
<tr>
<td>RN</td>
<td>Registered Nurse</td>
</tr>
<tr>
<td>VF</td>
<td>Ventricular fibrillation</td>
</tr>
<tr>
<td>VT</td>
<td>Ventricular tachycardia</td>
</tr>
<tr>
<td>WM</td>
<td>Ward Manager</td>
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</table>
Chapter 1: Introduction

1.1 Background

In developed countries, sudden cardiac arrest is an important public health problem. Cardiac arrest is the abrupt loss of heart function in a person who may or may not have heart disease. That means the heart stops functioning and the circulation ceases; therefore, no cardiac output supplies blood for whole body, organs and cells. Unconscious survivors of out-of-hospital cardiac arrest are at high risk of death and poor neurologic function.

According to American Heart Association (2013), about 360,000 cases of out-of-hospital cardiac arrest occurred and its overall survival rate is low with 9.5%. Heart disease is the first leading cause of death in United States. In Hong Kong, it is also similar. Cardiac arrest takes over 10,000 lives each year and the number keeps growing every year. According to Department of Health (2013), heart disease, which may lead to sudden cardiac arrest, is the 3rd leading cause of death in Hong Kong.

Patients with heart diseases like coronary heart disease have a higher risk to suffer sudden cardiac death. In cardiac arrest, the brain does not have sufficient blood and oxygen supply, and the patient loses consciousness. If lack of oxygen supply sustains for a few minutes, the brain cells begin to be irreversibly damaged, that lead to brain cell death as the brain cells become anoxic. According to Intensive Care Unit (ICU) in Queen Mary Hospital, it was estimated that inpatients who survived to ICU admission and subsequently died, brain injury was one of the main causes of death, about 68%. If witnessed cardiac arrest occurs and cardiopulmonary resuscitation (CPR) starts early, vigorous chest compressions can move blood containing oxygen supply to the heart and the brain so as to prevent further damage. About one tenth to a third successfully resuscitated patients can leave the hospital and lead their own lives again.
Although most patients who are successfully resuscitated after cardiac arrest and have return of spontaneous circulation (ROSC), parts of them finally die. The death is due to severe neurologic damage such as prolonged brain ischemia during cardiac arrest and the reperfusion injury after ROSC (Oddo et al., 2008).

Therapeutic hypothermia is a relatively new concept for the protection of cerebral neurologic function for post cardiac arrest patients who are in coma after successfully resuscitation by maintaining their body temperature at 32 to 34°C as soon as possible for duration of 12-24 hours (Peberdy et al., 2010).

1.2 Affirming the Need

For the health care system in Hong Kong, there is still no guideline or protocol for health care professionals to initiate therapeutic hypothermia in Emergency Department. Only a few hospitals have already tried therapeutic hypothermia for post cardiac arrest patients in Emergency Department. However, a large portion of cardiac arrest patients still are not received therapeutic hypothermia. In recent decade, the practice of inducing hypothermia is a new concept following cardiac arrest because there are a lot of research published that focus on the use of therapeutic hypothermia as the post cardiac arrest care. Yet, inducing therapeutic hypothermia is still seldom used by medical personnel.

In my local setting, it is an acute hospital with Emergency Department service. If the post cardiac arrest case has good prognosis, Intensive Care Unit (ICU) would take over for further intensive management. In current ICU setting, the use of therapeutic hypothermia is already promoted and applied. However, the current clinical practice for post cardiac arrest in Emergency Department is that cooling is not implemented. Therefore, only standard post
cardiac arrest care with no temperature management is applied. Most effort is put on the resuscitation of cardiac arrest patients, rather than on post cardiac arrest care. After ROSC and hemodynamic stabilization of patient, he or she is transferred to Intensive Care Unit (ICU) or medical ward (if ICU does not take over the case) as soon as possible. In the period between ROSC of patient and arrival at ICU, it is possible for nursing staff to start therapeutic hypothermia as quickly as possible for them as American Heart Association (2010) recommended. It can shorten the time of initiation of therapeutic hypothermia and reach the target temperature earlier after ROSC. Actually, inducing therapeutic hypothermia is simple with mild complications only and not complicated to implement. It only requires simple ice packs or cold mattress and even cold crystalloids for intravenous infusion. By utilizing this period of time, it can reduce the time to achieve targeted hypothermic temperature and protect neurologic function early. If the possible outcomes of cooling patients following cardiac arrest with ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) are beneficial, there are no reasons not to induce therapeutic hypothermia in the future clinical practice in emergency department.

In fact, the survival rate from in-hospital and out-of-hospital sudden cardiac arrest is poor. According to the Heart Disease and Stroke Statistics 2013 published by American Heart Association, the survival rate of in-hospital adult patients with cardiac arrest is 23.9%. However, the survival rate from out-of-hospital cardiac arrest is much lower with 9.5% only. Therefore, there is an affirming need to improve the neurological outcome and survival of patients after cardiac arrest.
1.3 Objectives and Significance

1.3.1 Research Question:

In the emergency department, does inducing therapeutic hypothermia to unconscious post cardiac arrest adults with return of spontaneous circulation and initial cardiac rhythm of ventricular fibrillation improve survival and neurological outcome compared with usual standard practice?

By using the PICO format,

Patient/Problem (P): post cardiac arrest and unconscious adult patients with return of spontaneous circulation and initial cardiac rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT)

Intervention (I): inducing therapeutic hypothermia

Comparison (C): standard post cardiac arrest care

Outcome (O): improve survival and neurological outcome

1.3.2 Objectives

1. To systematically review and critique the significance of available literatures about inducing therapeutic hypothermia to post cardiac arrest patients with pulseless VT or VF

2. To review the effectiveness of the use of therapeutic hypothermia in post cardiac arrest patients with pulseless VT or VF on improving neurologic function and survival

3. To assess the implementation potential of applying the proposed guideline of inducing therapeutic hypothermia in Emergency Department

4. To establish an evidence-based guideline of inducing therapeutic hypothermia to post cardiac arrest patients with pulseless VT or VF

5. To develop an implementation plan and evaluation plan of applying the guideline of inducing therapeutic hypothermia to post cardiac arrest patient with pulseless VT or VF
1.3.3 Significance

Nowadays, more patients who suffer from sudden cardiac arrest achieve return of spontaneous circulation. However, the survival rate still remains low (AHA, 2010) even when they are allowed to be admitted to the Intensive Care Unit (ICU) after successful resuscitation. This is due to the cerebral reperfusion establishes again after cardiopulmonary resuscitation. The reperfusion can trigger harmful chemical cascades that include generation of free radicals and other mediators, which results in brain damage as "post-resuscitation syndrome" (Negovsky, 1988).

There is growing evidence to show that mild therapeutic hypothermia in post cardiac arrest survivors can suppress the biosynthesis, release and uptake of several catecholamines and neurotransmitters, which cause tissue damage (D'Cruz, 2002). It reduces the level of Neuron-specific enolase (NSE), which indicates neuronal damage and impairment of blood-brain barrier if serum level is high (Tiainen, Roine, Pettila & Takkunnen, 2003); alleviates the inflammatory cascade of post cardiac arrest syndrome and reduces free radicals (Polderman, 2009). These beneficial effects are proved to be effective with the significant improvement of mortality rate and neurological function in two randomized controlled trials (HACA, 2002 & Bernard et al., 2002).

Inducing therapeutic hypothermia may improve neurological outcome and survival following cardiac arrest with pulseless VT or VF. In Hong Kong's Health care system, it is not common to use therapeutic hypothermia for the treatment of post cardiac arrest patients in Emergency Department. In the American Heart Association (AHA) 2010 guidelines for cardiopulmonary resuscitation (CPR), it is recommended that cooling comatose post cardiac arrest adult patients with return of spontaneous circulation (ROSC) to the target temperature between 32°C and 34°Cis beneficial.
Chapter 2: Critical Appraisal

2.1 Search and Appraisal Strategies

2.1.1 Electronic Databases

The evidenced-based researches were searched and acquired in 3 electronic databases. The following electronic databases - CINAHL Plus, PubMed and MEDLINE were used to search and identify potential journals. The electronic databases were searched via the University of Hong Kong - Libraires. Other sources including Resuscitation via ScienceDirect were searched.

2.1.2 Search Keywords

The keywords used in the searching of relevant researches were "therapeutic hypothermia" or "induced hypothermia" or "targeted temperature management" and "cardiac arrest" or "resuscitation". The key terms used as the same objects were searched by using "OR" and different key terms were linked up by using "AND". The searching was limited to English and human only.

2.1.3 Identification of Studies

The title, keywords and abstract were screened to maximize the selection of the most relevant literatures. For those abstract without sufficient information, most of the content in those journals were reviewed to avoid missing some relevant journal studies. For those selected potential journals, the full texts were read completely to confirm whether those were eligible. The results of other electronic databases were screened for duplication of same papers. Reference lists were searched by screening the titles. If the title was highly relevant, the abstract or/and full text were searched and check for eligibility. The studies which have already been found were excluded. The details of the searching history by using keywords are listed in Appendix 1.
2.1.4 Inclusion Criteria

1. Randomized controlled trials with full text available
2. English language
3. Age of 18 or above
4. Using external cooling methods such as ice packs and cold mattress
5. Post cardiac arrest patients with return of spontaneous circulation
6. Remain unconscious after resuscitation
7. Presumed cause of cardiac origin
8. Initial temperature higher than 30°C

2.1.5 Exclusion Criteria

1. Using invasive methods such as cold intravascular fluid infusion
2. Animal studies
3. Systematic review, meta-analysis, qualitative studies, letters, editorials, news, comments, author's opinion and articles
4. Unwitnessed cardiac arrest with initial rhythm of asystole and pulseless electrical activity
5. Resuscitate more than 60 minutes to ROSC

2.1.6 Data Extraction

Data extraction is shown as tables of evidence in Appendix 2a. Those tables include citation, study type, patients’ characteristics, intervention, comparison, length of follow up, outcome measures and effect size.

The primary outcome measures of the dissertation were the overall survival. The
secondary outcome measures were neurologic outcome and hypothermia-induced complications.

2.1.7 Appraisal Strategies

The appraisal tool used in this dissertation was the Methodology Checklist 2: Randomized Controlled Trials of Scottish Intercollegiate Guidelines Network (SIGN). This checklist consisted of two sections: 1. internal validity and 2. overall assessment of the study. According to the checklists, the selected journals were reviewed in terms of whether they were worth progressing by rating the majority of criteria met. The overall methodological quality of the study was rated as High quality (++), Acceptable (+) and Low quality (0).

2.2 Results

2.2.1 Date of Search

The period of searching related studies was performed from 21st March 2014 to 30th July 2014.

2.2.2 Search History

The relevant literatures were searched from 4 electronic databases: 1. PubMed, 2. CINAHL Plus, 3. MEDLINE & 4. Resuscitation via ScienceDirect. The specific keywords used in the searching were "therapeutic hypothermia", "induced hypothermia", "targeted temperature management"; "cardiac arrest" and "resuscitation". All keywords mentioned above were used to search individually and search in various combinations. The intervention of "therapeutic hypothermia", "induced hypothermia", "targeted temperature management" were used "or" to link together to maximize available results. After applying all the keywords into searching, the numbers of studies in Pubmed, CINAHL Plus, Medline and Resuscitation were 939, 32 380 and 87 respectively. All the titles and abstracts of those studies were
screened at first to find out which were more appropriate. Then full texts of remaining studies were reviewed, including searching from reference lists of those useful studies. After removal of duplicates and only inclusion of randomized controlled trials, total of 8 RCTs were found to be highly eligible. The overall flow list of search history from four electronic databases of was shown in Appendix 2a. The overall search flow diagram was shown as PRISMA (2009) flow diagram in Appendix 2b.

2.2.3 Table of Evidence

The 8 RCT journals extracted from electronic databases were demonstrated specifically in the form of tables of evidence, which could make that journal easier to follow and show the key points clearly for reference. The table includes eight elements: citation, study type, patient characteristics, intervention, comparison, length of follow-up, outcome measures and effect size. The details of the tables of evidence related to the 8 RCTs are shown in Appendix 3.

2.2.4 Study Characteristics

Those studies were published from 2001 to 2013. All of the 8 selected studies were randomized controlled trials.

2.2.4.1 Trial Locations

Four of them were multicenter and they were carried in Australia (Bernard et al., 2002), 9 centers in 5 European countries (HACA, 2002), Europe & Australia (Nielsen et al., 2013) and United States (Heard et al., 2011). Others were carried in Belgium (Hachimi-Idrissi et al., 2001), 2 hospitals in France (Laurent et al., 2005), German (Pittl et al., 2013) and United Kingdom (Tiainen, Roine, Pettila & Takkunen, 2003).
2.2.4.2 Demographic Characteristics

The characteristics of recruited subjects were similar in general. The patients characteristics are out-of-hospital cardiac arrest, unconscious after resuscitation with return of spontaneous circulation, adult aged 18 or above, presumed cause of cardiac origin, hemodynamic stable and no pregnancy, no terminal illness, no coagulation disorder, no traumatic brain injury.

2.2.4.3 Mode of Intervention

Most of the intervention was the use of external cooling devices to induce therapeutic hypothermia and the control groups were the use of normothermia, except Pittl et al. (2013) and Heard et al. (2011). In the study of Pittl et al. (2013), the intervention group was the use of intravenous ice-cold fluids via invasive endovascular catheter and the control group was the use of external cooling pads. In the study of Heart et al. (2011), the intervention group was the use of Arctic Sun (a temperature management system with energy transfer pads) and the control group was standard cooling by using two cooling blankets and applying ice bags. In addition, the remaining control groups in those RCTs were normothermia, which meant no temperature control; however, Nielsen et al. (2013) maintained target temperature of 36°C in control group, which was totally different from others which allows patients with no intervention for temperature control (HACA, 2002; Bernard et al., 2002; Hachimi-Idrissi et al., 2001; Laurent et al., 2005 & Tiainen et al., 2003).

2.2.4.4 Blinding

All of the studies by health care professionals involving in the care of patients were aware of the intervention assignment as this was difficult for the staff involved to be blinded; however, the physicians, at last, who performed the evaluation of patients' neurological functions, were unaware of the intervention assignments at follow-up.
2.2.4.5 Outcome Measures

The major outcome measures were survival or mortality and neurological outcome (HACA, 2002; Bernard et al., 2002; Hachimi-Idrissi et al., 2001; Laurent et al., 2005; Pittl et al., 2013; Heard et al., 2011 & Tiainen et al., 2003).

For the measurement of neurological function, most of the studies used cerebral performance category (CPC) as a standard, valid and reliable way to indicate cerebral function (HACA, 2002; Bernard et al., 2002; Nielsen et al., 2013; Heard et al., 2010; Pittl et al., 2013; Laurent et al., 2005; Tiainen et al., 2003). Hachimi-Idrissi (2001) used overall performance category (OPC) to indicate cerebral function.

To achieve statistical significance of outcome measures, the effect size of the form of p-value must be less than 0.05 or in the confidence interval of 95%.

2.2.4.6 Post Cardiac Arrest Care

All patients receiving induced hypothermia in those studies were under sedation and paralysis to facilitate mechanical ventilation and to prevent shivering, according to their institutional post cardiac arrest protocols or guidelines.

2.2.4.7 Three Phases of Induced Therapeutic Hypothermia

1. Induction phase - to get the target temperature down to 32 - 34°C within two to six hours after ROSC.
2. Maintenance phase - to keep temperature between 32-34°C for 12 hours (Bernard et al., 2002), 24 hours (HACA, 2002) or 28 hours (Nielsen et al., 2013).
3. Rewarming phase - to slow warm temperature to around 37°C passively, except one for active rewarming with the rate of 0.5°C per hour (Nielsen et al, 2002).
Most of the intervention of inducing therapeutic hypothermia was implemented as quickly as possible after ROSC in Emergency Department and then to be continued in ICU.

2.2.5 Methodological Issues

As mentioned in the part of appraisal strategies, those selected 8 RCTs were appraised by using the Methodology Checklist 2: Randomized Controlled Trials of Scottish Intercollegiate Guidelines Network (SIGN). The details of critical appraisal checklists of the 8 RCTs are shown in Appendix 4.

In the 8 selected studies, the appropriate and clearly focused question was all well covered. The subjects in all journals were randomized into treatment group and control group. Randomization was mainly generated by computer with stratification with sealed envelope, except Bernard et al. (2002) using the method of odd and even days for randomization. Informed or written consent was obtained by next-of-kin or waived. The staff caring for the patients during resuscitation could not be blinded with the treatment assignments. For the follow up of neurological evaluation, physicians, who did not know the patients’ treatment assignment, were blinded, except Heard et al. (2010) that the personnel were aware of the intervention assignment. The subjects were unconscious so it was not applicable to blind them. Most of the treatment and control groups were similar at the start of the trial. All relevant outcomes were measured by standardized, valid and reliable scale such as CPC or OPC. The drop-out rate of all studies was low. All studies were based on the major intention-to-treat principle. Although there were 5 studies with multicenter trials (HACA, 2002; Bernard et al., 2002; Nielsen et al.; Laurent et al., 2005; Heard et al., 2011), there was no comparison of results among all sites.
2.2.5.1 Summary of Level of Evidence

Besides the quality of the studies, Melnyk & Fineout-Overholt (2005) provided a hierarchy of evidence to differentiate the level of the studies based on the design of the studies. There are Level I to Level VII in which the highest level indicates the highest is the evidence. As the eight studies were all well-designed randomized controlled trials, they were all rated as Level II (Evidence from at least one well-designed RCT). The hierarchy of evidence table is shown as Appendix 5.

2.2.5.2 Summary of Quality Assessment

The quality of studies was assessed by the section 2 of Methodology Checklist 2: Randomized Controlled Trials of Scottish Intercollegiate Guidelines Network (SIGN). This quality assessment is based on the overall assessment of the paper in the section 1 of Methodology Checklist 2: Randomized Controlled Trials of SIGN.

In the section of overall assessment of the studies, there were 5 studies rated as "++" (HACA, 2002; Hachimi-Idrissi et al., 2001; Pittl et al., 2013; Heard et al., 2011 & Tiainen et al., 2003) as most of the items in the checklist were well covered. There were 3 studies rated as "+" (Bernard et al., 2002; Nielsen et al., 2013 & Laurent et al., 2005) as more items were adequately addressed. It is certain that most of the overall effect is due to the study intervention, except Nielsen et al. (2013). The results of those studies could be directly applicable to post cardiac arrest patients. More information is shown in Appendix 4.
2.3 Summary and Synthesis

There are four multicenter studies (HACA, 2002; Bernard et al., 2002; Nielsen et al., 2013; Laurent et al., 2005) and two single centers (Hachimi-Idrissi et al., 2001 & Tiainen et al., 2003) that investigated the effectiveness of therapeutic hypothermia to post cardiac arrest patients with return of spontaneous circulation (ROSC) compared with normothermia group.

2.3.1 Survival and Neurological outcome

HACA (2002), Bernard et al. (2002), Laurent et al. (2005) and Tiainen et al. (2003) indicated that induced hypothermia in post cardiac arrest patients resulted in favorable neurological outcome and reduced mortality (p-value<0.05). In contrast, a recent multicenter study of Nielsen et al. (2013) drew the conclusion that TH of 33°C did not have a beneficial effect on survival rate and neurological outcomes as compared with a targeted temperature of 36°C. Hachimi-Idrissi et al. (2001) also had a result that the survival between hypothermia group and normothermia group was not statistically significant (p-value > 0.05).

There was one study that compared inducing therapeutic hypothermia with hemofiltration, using hemofiltration only and providing standard supportive care (Laurent et al., 2005). Although it indicated that therapeutic hypothermia with hemofiltration to post cardiac arrest patients improved survival and decreased the death rate as compared with the group of standard supportive care group, the effect size of hemofiltration group only was also statistically significant. The results might be related to the hemofiltration effect. However, the therapeutic hypothermia effect could not be ruled out as the effect size of therapeutic hypothermia with hemofiltration was statistically significant.
2.3.2 Inclusion Criteria and Exclusion Criteria

Such an extreme difference between Nielsen et al. (2013) and previous significant studies was due to several factors related to the study design, although the sample size was larger. Firstly, the inclusion criteria were broader and exclusion criteria were fewer. The inclusion criteria were the age 18 or above were recruited, e.g. 90 years old; irrespective of the initial cardiac rhythm, whatever asystole or PEA which was associated with poor prognosis as the mortality in non-shockable rhythm was higher. The exclusion criteria were the interval from ROSC to screening of more than 240 minutes. The initiation of therapeutic hypothermia was very slow if the interval was allowed to be as long as 4 hours after ROSC. The delay of initiation of cooling might increase the death rate. These factors might lead to different conclusions when compared with other trials. In the statistically significant studies, more specific inclusion criteria were used. HACA (2002) involved only cardiac arrest patients with VF or pulseless VT as initial cardiac rhythm; age of 18-75 years. Bernard et al. (2002) recruited cardiac arrest patients with VF rhythm only. These criteria were associated with better prognosis because patients with non-VT or non-VF arrest were more likely to have comorbidities and these non-shockable rhythms indicated a longer time of nonperfusion. In addition, patients with pulseless VT or VF might be defibrillated by ambulancemen who used automated emergency defibrillator. This kind of patients would be prone to have better clinical outcome than patients with non-VT or non-VF. These might lead to different conclusions of trials.

For the study of Hachimi-Idrissi et al. (2001), the inclusion criteria for patient selection included only cardiac arrest patients with asystole or pulseless electrical activity (PEA) rhythm were recruited; tympanic temperature at admission over 30°C. This kind of patients had a poor prognosis since the heart stopped functioning and could not pump blood to the whole body and organ. Also, the sample size was small with only 30 patients recruited. This
resulted in the lack of statistical representation of the phenomenon. Therefore, the neurologic outcome and survival of therapeutic hypothermia group were similar to control group. However, it was evidently shown that it was effective to use helmet device for cooling patients.

2.3.3 Duration of Therapeutic Hypothermia

Furthermore, the detail of intervention of inducing therapeutic hypothermia is not similar. The duration of cooling was 12hours (Bernard et al., 2002) and 24 hours (HACA, 2002). On the other hand, the period for cooling was 28 hours in the trial of Nielsen et al. (2013). The prolonged period of therapeutic hypothermia might have adverse effects; for example, increasing the risk of hypothermia-associated complications like hypokalemia and infection, leading to worse clinical outcomes. Hence, cooling survivors between 12 to 24 hours is recommended.

2.3.4 Intervention of Control Groups

In addition, the characteristics of control groups between the two studies with favorable neurological outcomes and one of the studies with poor neurological outcomes were totally different. There was no temperature control in the comparison groups which provided standard post resuscitation treatment (HACA, 2002; Bernard et al., 2002; Laurent et al., 2005; Hachimi-Idrissi et al., 2001; Tiainen et al., 2003). However, in the control group in Nielsen et al. (2013), there was strict temperature control which targeted core temperature to 36°C by using various cooling or warming methods. This temperature management could prevent fever within 72 hours after cardiac arrest and did not allow the evolution of temperature in both groups. This was completely different from previous studies. Therefore, the control group of Nielsen et al. (2013) still had a minor effect of cooling on the patients, although the effect was mild. This might cause different clinical outcomes with previous studies with no
strict temperature control in control groups.

2.3.5 Rewarming after Therapeutic Hypothermia

In the study of Nielsen et al. (2013), active rewarming was too rapid from 33°C to 36°C in 6 hours (increase in 0.5°C per hour). It was faster than all other trials (HACA, 2002; Bernard et al., 2002; Hachimi-Idrissi et al., 2001) in which passive rewarming was utilized.

2.3.6 Complications of Therapeutic Hyperthermia

For the most hypothermia-induced complications, there were no statistical significant differences between induced hypothermia groups and normothermia groups (HACA, 2002; Nielsen et al., 2013; Hachimi-Idrissi et al., 2001). However, hypokalemia was more likely to occur in hypothermia group (Nielsen et al., 2013) as hypothermia promoted the influx of serum potassium into cells. Therefore, it was evidently shown that there was no much harm to induce therapeutic hypothermia.

2.3.6.1 Comparison of Different Methods to Induce Therapeutic Hypothermia

Two RCTs were the comparison of two different methods for inducing therapeutic hypothermia. One was the comparison between invasive cooling and non-invasive cooling (Pittl et al., 2013). Another was the comparison between Arctic Sun cooling and standard cooling (Heard et al., 2011).

2.3.6.2 Invasive Cooling versus Non-Invasive Cooling

Invasive cooling is the administration of intravenous ice-cold fluids via endovascular catheter into femoral vein; non-invasive cooling involves the use of Arctic Sun, which is a temperature control system with hydrogel-coated energy transfer pads applied to the subject's skin (Pittl et al., 2013). In this study, the neurological outcome and overall survival were similar in both groups. For the cooling-associated complications, invasive cooling and
non-invasive cooling were similarly safe. Only bleeding complications in invasive cooling was more frequent than that in non-invasive cooling (Pittl et al., 2013). Therefore, these two interventions were similarly effective in inducing hypothermia to unconscious cardiac arrest with ROSC.

2.3.6.3 Arctic Sun Cooling versus Standard Cooling

Another comparison was Arctic Sun cooling and standard cooling (Heard et al., 2011). Arctic Sun is an accurate temperature management system which provides a higher flow rate of cold fluid and utilizing conductive cold gel pads; standard cooling was the use of two cooling blankets wrapped around patient's upper and lower torso with additional application of ice pads to axillae and groin. It was concluded that both interventions had similar neurological outcome and overall survival. Although Arctic Sun cooled patients more rapidly to target temperature of 34°C than standard cooling blanket, the proportion of subjects reaching target temperature of 34°C by four hours was similar. Thus, both interventions were effective to induce hypothermia for patients after cardiac arrest.

2.3.7 Evidence-Based Recommendations

Based on the review of the eight studies, it is evidently shown that inducing therapeutic hypothermia to keep target temperature of 32°C -34°C for 24 hours to post cardiac arrest patients with ventricular fibrillation or pulseless ventricular tachycardia as initial rhythm improves neurological outcome and survival. The initiation of therapeutic hypothermia by using external cooling methods (e.g. ice packs) should be implemented as soon as possible once return of spontaneous circulation occurs after successful resuscitation. The standard external cooling methods are recommended as they can be applied more conveniently, economically and easily in Emergency Department with similar efficacy when compared to Arctic Sun and invasive cooling.
The target group is the post cardiac arrest patients with return of spontaneous circulation and with initial cardiac rhythm of ventricular fibrillation or pulseless ventricular tachycardia. The reason why the survivors with other initial rhythms such as asystole or pulseless electrical activity are not chosen is that there is less evidence which shows that inducing therapeutic hypothermia can improve neurological function and survival for them.
Chapter 3: Translation and Application

As discussed in the previous section, there is a necessity to develop an evidence-based clinical protocol or guideline of inducing therapeutic hypothermia to post cardiac arrest patient in Emergency Department (ED) so as to maximize the patients' outcomes and facilitate the staff to perform this innovative practice efficiently. Therefore, the implementation potential should be well analyzed before the application of this protocol or guideline into clinical practice (Polit & Beck, 2004).

In this chapter, there are two main parts. In the first part of implementation potential, the transferability, feasibility and cost/benefit ratio of the innovation are well assessed. In the second part of evidence-based practice protocol, the objectives, target group and recommendations supported by evidence are well discussed.

After affirming the needs of translating the evidence into the best practice, an innovation will be proposed as an evidence-based guideline with literature support.
3.1 Implementation Potential

3.1.1 Transferability of the findings

3.1.1.1 Target setting

In the review of those studies, they were all conducted in Western countries and the transportation time from incident site of cardiac arrest to Emergency Department (ED) was relatively longer than that in Hong Kong. It was due to long distance. Besides that, there was not much difference between them. Both medical settings are similar. The patient with sudden cardiac arrest occurred in out-of-hospital setting and was transported to ED by paramedic to continue resuscitation. According to the research noted above, those hospitals conducted contained ED and Intensive Care Unit (ICU) which were same as Hong Kong health care setting. The initiation of therapeutic hypothermia is applied as early as possible.

3.1.1.2 Target population

The target population in the research and that in Hong Kong are not much different except the ethnicity in Hong Kong is mainly Chinese. Both are focused on out-of-hospital sudden cardiac arrest adults (age 18 or above) with return of spontaneous circulation and hemodynamically stable. The target population in those researches was varied, including initial rhythm of ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), pulseless electrical activity (PEA) and asystole; however, the target population in the new setting is focused on shockable rhythm of VF and pulseless VT only.
3.1.1.3 Philosophy of care

According to Hospital Authority (2014), the people-centered care is one of the main values - "this concept extends beyond providing patients with the best-possible services ". In addition, in the Guidelines for Specialty Nursing Services - Accident & Emergency Care from Hospital Authority (2012), the philosophy of emergency nursing "provides timely care to patient suffering from life-threatening conditions and those urgently in need of medical and nursing interventions". The emergency nurse plays an important role in ED to provide high quality care after resuscitation to maximize the patient's benefit.

Aim of the proposed innovation

The proposed innovation aims at delivering the evidence-based post resuscitation care to post cardiac arrest patients so as to improve their survival and neurological outcome. Thus, this innovation is in line with the philosophy of care of the practice setting.

3.1.1.4 Benefit to target clients

The innovation could benefit post cardiac arrest patients who have initial cardiac rhythm with VF or pulseless VT in the practice setting. With reference to all non-traumatic out-of-hospital cardiac arrest from 1 January 2011 to 31 December 2012 in the New Territories West Cluster (NTWC), there were totally 1252 cases with 20.3% of the cases were shockable cardiac rhythm including VF or pulseless VT. According to Heart Disease and Stroke Statistics (2014) released by American Heart Association, 23% out of cardiac arrest had an initial rhythm of VF or pulseless VT. These were very similar. Although the number of patients who could benefit from the innovation was not high and difficult to
estimate, this innovation proved to become effective for those critically ill clients with good evidence as the survival rate of cardiac arrest was low. It is estimated that around 125 cases will benefit from the new innovation in two EDs in NTWC annually.

3.1.1.5 Time for implementation and evaluation

It will take around four months for the innovation to be implemented. It takes one month to purchase necessary equipment - extra ice packs and for three trainers (1 APN and 2 RNs) to attend one day course for therapeutic hypothermia simultaneously. It takes one month to establish a one-hour training workshop by three trainers for other nursing staff, around twenty staff; three months for the implementation trial. If there are no enough suitable victims, the implementation trial can be extended for one to three more months so as to recruit more patients for better evaluation.

For the evaluation of nursing staff, it takes one week for return demonstration of the innovation.

For the evaluation of the innovation for patients' outcome, it will take six months to assess as the rehabilitation progress is slow for the cardiac arrest survivors and the survival and neurological outcome of them can be better assessed as suggested (HACA, 2002; Laurent et al., 2005; Nielsen et al., 2013).
3.1.2 Feasibility

3.1.2.1 Nurse's autonomy

With reference to Guidelines for Specialty Nursing Services - Accident and Emergency Care released by Hospital Authority (2012), the practice standard stated that "patients are provided with effective and efficient advanced life support intervention during and after resuscitation" and "to initiate advanced life support interventions according to protocols". ED nurses have the autonomy to initiate therapeutic hypothermia after resuscitation in the target setting if all criteria are met in the protocol and terminate the innovation if patient’s condition is considered undesirable.

3.1.2.2 Interference with current staff functions

The implementation of the therapeutic hypothermia only interferes mildly with the current staff functions. This is because it simply requires ice packs to be applied on head, side of neck, axillae and groins after return of spontaneous circulation (ROSC) and changes ice pack every 30 minutes. This nursing intervention is also within the time of ICU consultation, so it will not interfere much and safe to implement.

3.1.2.3 Administration support and organizational climate

These years, the target department updated and renewed most of the guidelines and protocols in ED as nursing became more professional than in the past decades. Most nursing practices are evidenced-based nowadays. Also, the administration well supports innovation
including Department Operations Manager, Ward Manager and Advanced Nursing Practitioner of ED. For instance, the nurse-initiated prescription of medications, such as Paracetamol in triage based on the endorsed protocol, can give antipyretic as early as possible before doctor consultation. Moreover, the target hospital is relatively new and still developing. The organizational climate is welcomed for any innovation if it would provide effective evidence-based nursing care to patients.

3.1.2.4 Consensus among staff and administrators

Lift-saving is the top priority among ED nursing. If the implementation of therapeutic hypothermia will improve the survival rate and neurological function (HACA, 2002 & Bernard et al., 2002), staff and administrators are keen on reaching a consensus to provide quality care for patients. Hence, there is no major resistance or uncooperativeness for nursing staff to implement or evaluate the innovation.

3.1.2.5 Possible friction within organization and support from other department

This may produce a possible friction to frontline staff, though the innovation is just simple. Resuscitation is already energy-demanding and implementing the new innovation increases the extra burden.

In Hong Kong's health care system, most of the ICUs have already been promoted to initiate therapeutic hypothermia based on the evidence-based systematic reviews and
meta-analysis. There is a great support from the Department of Intensive Care Unit so as to initiate therapeutic hypothermia as soon as possible to maximize patient's neurological outcome and survival. This could shorten the time to achieve the target temperature of mild hypothermia when arriving in ICU.

3.1.2.6 Necessary skills for innovation

The necessary skill is a simple nursing procedure which places ice packs at the head, sides of the neck, axillae and groins and change packs every 30 minutes. Besides, monitoring any complications such as shivering, cold burn and arrhythmias are also important.

3.1.2.7 Equipment and facilities

The equipment for the implementation is ice packs, which are simple disposable ice bags. To facilitate the utilization of the innovation, posters with brief protocol of therapeutic hypothermia should be posted on wall for reminder.

To organize a teaching workshop, a conference room with projector is required, which already exists.
3.1.2.8 Staff development

In ED, all nurses are required to take the course of Advanced Cardiovascular Life Support (ACLS); therefore, the advantages of therapeutic hypothermia are well introduced. Three trainers are sponsored to attend a one day course of therapeutic hypothermia course organized by the Hong Kong College of Emergency Medicine when the course is available. Also, a one-hour workshop is arranged to all nursing staff in ED by the three trainers and handouts are given so as to educate and reinforce them what the rationale is, how and when to implement the protocol of therapeutic hypothermia. Moreover, educating nurses to observe any complications during therapeutic hypothermia is important. It is vital for nursing staff to understand that the innovation is evidenced-based and the targeted clients can clinically benefit from it.

3.1.2.9 Evaluation of the innovation

After the training workshop, all nurses are required to complete a questionnaire (Appendix 6) about the understanding and satisfaction of the innovation and workshop respectively. In addition, all nursing staff is required to perform return demonstration for audit so as to reconfirm their understanding. In clinical situation, feedback will be given by resuscitation nurse-in-charge for any improvement.

For evaluation of nursing care of implementing therapeutic hypothermia, one month is needed for any feedback and any improvement.
For evaluation of and neurological outcome of patients, the Cerebral Performance Categories (CPC) scale (Appendix 7) is widely used (Bernard et al., 2002, HACA, 2002, Hachimi-Idrissi et al., 2001, Laurent et al., 2005 & Nielsen et al., 2013) and easy to measure for the survived patients after six months to grades them response to CPR on a scale of 1 to 5. CPC1 and CPC2 which indicate good cerebral performance and moderate cerebral disability respectively are accepted for good neurological outcomes after cardiac arrest as they are independent for daily lives (HACA, 2002 & Bernard et al., 2002). The survival is also an outcome indicator. It is defined as patients remaining alive to be sent home, to hospital discharge or to rehabilitation hospital and is measured at six months.

3.1.3 Cost/Benefit ratio of the innovation

3.1.3.1 Risks of innovation to patients

Applying cold packs on body directly would cause possible cold burn to targeted patients. Shivering is a common body response to coldness and is effectively solved by sedations and muscle relaxants. Adverse events such as pneumonia, infection, hyperglycemia, hypokalemia, and arrhythmia may occur; however, there was no significant difference in serious complications between hypothermia and normothermia groups (Bernard et al., 2002; HACA, 2002; Hachimi-Idrissi et al., 2001& Nielsen et al., 2013).

3.1.3.2 Potential benefits of innovation

Implementation the guideline for therapeutic hypothermia in Emergency Department results in better survival rate and neurological outcomes of post cardiac arrest patients with
ROSC. With reference to the statistic of non-traumatic out-of-hospital cardiac arrest between 2011 and 2012, the survival-to-discharge rate (only 1.9%) was very low, even if ROSC can be achieved (26.1%). It is important to apply the innovation to suppress inflammatory response, reduce reactive oxygen radicals and reduce brain metabolism so as to save patients' lives with good neurological function upon discharge.

### 3.1.3.3 Risks of maintaining current practices

Maintaining current practices without therapeutic hypothermia cause post-cardiac arrest syndrome to be persisted. The adverse effect such as anoxic brain injury and systemic ischemia and reperfusion response cannot be reduced. Hence, the mortality rate of post cardiac arrest patients will remain high and their neurological function will become low. Brain injury is one of the main causes of death after out-of-hospital cardiac arrest.

### 3.1.3.4 Material costs of implementation of innovation

The material cost is minimal as only disposable ice packs and course for training three trainers (1 APN & 2 RNs) are needed. Thus, most of the expenditure is the staff pay of one-hour training workshop as all nursing staff are required to attend it. The summary of material costs in the short term and long term are shown in Appendix 8.
For the short term cost, posters, training course for three trainers, organizing a one-hour training workshop for ED nursing staff and evaluation are required. It is estimated to cost about $14833.

For the annual long term cost, disposable ice packs, printing of protocol and checklist, organizing one-hour refreshment training workshop for new nursing staff and evaluation for nursing staff and patients are needed. It is estimated to cost about $5120.

3.1.3.5 Material costs of no implementation of innovation

If there is no implementation of therapeutic hypothermia, the period of hospital stay would be shortened because of high mortality rate. However, this is not ethical. Life-saving is the highest priority however high the cost is. Thus, implementing the innovation will raise the material cost.

3.1.3.6 Potential nonmaterial costs of innovation to organization

Extra time on preparation is required for three trainers. They will need to spend much time on the implementation of therapeutic hypothermia into clinical situation. It includes making a proposal, holding a meeting with medical staff to discuss the feasibility, organizing a training working and attending the course for therapeutic hypothermia. Also, frontline nursing staff may be under stress as it takes time for nursing staff to accept the new concept of innovation and adapt the new practice for post cardiac arrest patients. Although the
implementation of innovation increases the workload during resuscitation, it is estimated that not many patients would be required to induce therapeutic hypothermia as only 23% out of cardiac arrest cases with VF or pulseless VT. Hence, staff morale will not be affected much by the workload.

3.1.3.7 Potential nonmaterial benefits of innovation to organization

If the targeted patient could be discharged with good neurological outcome, the staff morale would be improved. Moreover, job satisfaction will be higher as they are pleased with their professional performance and they help patient to have better quality of life. Upon the implementation of evidence-based protocol, nurse's professionalism becomes higher as nurse can have greater autonomy to improve quality care.
3.2 Evidence-Based Practice Protocol

After assessing the implementation potential of the proposed innovation, an evidence-based protocol of inducing therapeutic hypothermia to post cardiac arrest patients with initial rhythm of VF or pulseless VT is established. In this chapter, the evidence-based practice protocol is established based on the grades of recommendations which are in accordance with the levels of evidence by Scottish Intercollegiate Guidelines Network (SIGN, 2012). The grades of recommendations is graded from A to D (Appendix 9) and the levels of evidence is rated from 1++ to 4 (Appendix 5). The detail of the proposed guideline is attached in Appendix 10.

To conclude, the innovation can be implemented because of its transferability, feasibility and high cost/benefit ratio.
Chapter 4: Implementation Plan

After the demonstration of the implementation potential and evidence-based guideline, the implementation plan for inducing therapeutic hypothermia to post cardiac arrest adults with VF or pulseless VT is discussed, including communication plan with all stakeholders and pilot testing. Lastly, the evaluation plan for the guideline is analyzed.

4.1 Communication Plan

4.1.1 Identification of stakeholders

A stakeholder is "someone who is affected by the proposed changes or anticipated results of the proposed innovation" (Melnyk & Fineout-Overholt, 2005). Chief of Service (COS), Consultant, Department Operational Manager (DOM), Ward Manager (WM) are the key stakeholders and the administrators for the approval of the innovation. They have the authority to consider an innovated clinical change to be advocated. In addition, they can allocate resources (i.e. manpower, funding and equipment), to support the implementation of new evidence-based guideline in the target setting so as to improve patients' clinical outcomes.

Doctors (Senior Medical Officers and Medical Officers), and nurses (including Advance Practice Nurses/Nursing Officers, Registered Nurses and Enrolled Nurses) are also the important stakeholders and frontline staffs to implement the innovated practice in the target setting. Doctors are the team leaders during resuscitation and post resuscitation. The final decision of continuing or withholding the innovated treatment is owned by the doctors and they need to keep patients relatively stable after resuscitation. They, then, proceed patients to post resuscitation care smoothly to facilitate the effect of therapeutic hypothermia, for instance, giving sedatives to prevent shivering.
Nurses, who are the main operators of carrying out the proposed treatment during post resuscitation, need to assess patients' general conditions, monitor patients' core temperature and responsible for applying ice packs on patients' body correctly and observing any cold burns. Therefore, their opinions are important for promoting this innovation.

Advance Practice Nurses are important as they are the main trainers for all frontline nurses and the nursing leader to monitor the quality, safety and clinical outcome of the implementation of innovation.

The last stakeholder is the patients and their significant others. As the mortality rate and neurological damage of post cardiac arrest are very high, they can benefit from the implementation of proposed innovation. Patients can have a better chance to survive and better neurological function after recovery.

4.1.2 The Process of the Communication Plan

The communication team includes WM, one MO, two APNs and two RNs. The communication sequence is vital for gaining support from all stakeholders. The sequence should start from the administrative level to the frontlines staff who involved in the change.

Before beginning the communication with administrators, the proposer should gain the support from APNs and RNs by explaining the inadequacy of our current practice of post cardiac arrest care and introducing the importance of inducing therapeutic hypothermia to those patients based on literature reviews and evidence-based research. APNs also play the role of using up-to-date knowledge on innovated clinical practice to improve quality of patient care. Their clinical experience and feedback are beneficial for the promotion of innovation. After the discussion and modification of the innovation, these can help gain
support from frontline nursing staff for promoting the innovation.

WM should be the first one of the stakeholders to be communicated with. He plays the key communication role among COS, DOM, doctors and nurses. The disadvantage of continuing current practice and advantage of using innovated practice are presented to him with the critical review of literature. The details of the guideline and equipment needed are explained to get his recommendation and approval.

DOM is the second stakeholder to be approached. A formal nursing meeting with DOM is arranged by WM for communication team to present the evidence-based innovated practice to her. DOM has the authority in making decision for implementing the evidence-based nursing practice in the Emergency Department. Funding and resources need to be approved by DOM to facilitate the commencement of the new practice.

After approval from WM and DOM, the next stakeholders who should be communicated with are COS and Consultant. A formal department meeting is needed for introducing the innovation. The details of the proposed innovated practice are explained through a presentation, including the objectives, statistics measurement, cost-benefit ratio, pros, cons, literature support, transferability and feasibility from foreign hospitals. The differences between the current and the new practice are compared to show the significance of the need in Emergency Department, so as to gain their great support and medical recommendation.

After all approval from administrative level, the next stakeholders who are all frontline nursing staffs and doctors need to be communicated with. As nurses are the main coordinators to implement the innovation, their workload will be increased. Hence, gaining their support is the most important. A training session will be held for the nursing staff and doctors about the proper use of guideline on implementing therapeutic hypothermia to post
cardiac arrest patients. In the session, the clinical issue, the inadequacy of current practice and the benefit of the innovated change for patient and the need for change based on the evidence-based literature support. At the end of the session, nurses and doctors will be encouraged to express what they are concerned about and their opinions. After the training workshop, they will have better understanding of applying the innovation and it is easy to implement. Prior to implementation of therapeutic hypothermia in clinical situation, frontline MO need to counter-check with a RN to make sure that all selection criteria are fulfilled and patients are suitable for the intervention of therapeutic hypothermia.

4.1.3 Initiating the change

It takes about six weeks to initiate the change. At the beginning, a core team is formed for proposing the innovation, including 2 APNs and 4 RNs who are the trainers for staff teaching. Strong evidence is required to support the innovation and to convince the stakeholders, including administrators and frontline staffs, to gain their support. There is sound evidence from the literature that current practice is not good enough to help patients get better quality of life. It is shown that the patients' neurological outcome and survival can be improved by inducing therapeutic hypothermia for post cardiac arrest patients. Thus, to have a clear vision for the change, the core team members should show that the high mortality rate and poor neurological outcome are correlated to no temperature control for post cardiac arrest patients based on evidence based literature. To facilitate the change, it is necessary to show that good neurological function and survival rate will be accomplished if implementing the evidence-based guideline of inducing therapeutic hypothermia. To gain as much as support from stakeholders as possible, the training workshop for frontline nursing staffs need to include the background, objectives, rationale, advantages of the guideline, the intervention of the practice and how to implement it. Moreover, the core team will play an important role on evaluating their understanding of implementing the guideline, dealing with
their enquiry and allocating information i.e. posters over the staff notice board about the promotion of innovation for target patients. It ends with the approval of the proposed innovation from the stakeholders.

4.1.4 Guiding the change

It takes around four weeks to guide the change. The innovation is guided by the vision mentioned in the initiate phase - to induce therapeutic hypothermia for post cardiac arrest patients with initial rhythm of VF/pulseless VT. The core team will develop a programme to lead the change in practice. They develop and modify the new evidence-based guideline by collecting feedback from administrators and frontline staffs. One APN and one RN are main leaders to communicate with different stakeholders. Their work includes introducing the new practice, conducting the pilot testing and sharing the test result to all stakeholders. Also, training the trainers is one of the important steps for the core team to utilize the evidence-based practice guideline, playing the role models for frontline staffs to learn and acting troubleshooters to help them deal with the hardship.

To obtain the additional support, the guideline can be made easily accessible into a checklist (Appendix 11) and to be used for all frontline nursing staff. Also, putting posters regarding the guideline in resuscitation rooms can remind nursing staff to handle the innovation well. In addition, the guideline manual is kept updated and kept in database of the department guideline. This phase ends when the innovation turns from theory into the start of practice.

4.1.5 Sustaining the change

To maintain the change, sufficient facilitation of the new evidence-based practice will be required. Regular meeting is required to monitor the implementation of the new guideline and
get any feedback from frontline staffs so as to evaluate its effectiveness and assess nurses' compliance with the new guideline by APN of the core team. The quality of implementation is maintained by annual audit (Appendix 12) and return demonstration of each frontline nurse which are evaluated by the core team. Success stories will be shared to all staffs on staff notice board in Emergency Department.

Moreover, monitoring patient clinical outcomes is a good indicator for sustaining the change. Revision to the new guideline will be made based on evidence collected and feedback from staff every two years and refreshment workshop will be organized for frontline staffs for reinforcement of the guideline and pointing out any change if necessary. In this phase, the evidence-based guideline of the innovation will be continuously sustained.

4.2 Pilot Study Plan

Pilot testing is to determine the feasibility of implementing the innovation before the full scale implementation of the innovation. It is a small scale trial running for a short period of time and aims at avoiding unexpected difficulties and limitations. After the pilot study, the proposed evidence-based guideline will be evaluated for any revisions prior to the implementation of the innovation in clinical areas.

4.2.1 Objectives

The main objectives of the pilot study are:

1. to determine the feasibility and cost-effectiveness of the proposed guideline
2. to assess frontline nurses' compliance and competency with the proposed guideline
3. to identify any potential barriers and difficulties met by frontline staffs while implementing the guideline
4. to determine any modification to revise the guideline
4.2.2 Methodology of pilot study

As the number of post cardiac arrest patients with initial rhythm of VF/pulseless VT is unpredictable, the time frame is set to be 3 months. The target sample size of this pilot study is expected to be at least 5 patients by using convenience sampling. The inclusion and exclusion criteria are the same as the guideline mentioned in Chapter 3.2 - Evidence-based practice protocol (Appendix 10). All eligible patients are recruited to take part in the treatment of therapeutic hypothermia. All nurses who participated in this pilot study have completed the training programme about the use of guideline on therapeutic hypothermia. Case MO needs to recheck the therapeutic hypothermia guideline with a RN before implementation of the intervention.

Informed consent is obtained from patients' relatives as patients are unconscious. Inducing therapeutic hypothermia by applying ice packs on head, sides of neck, axillae and groins is initiated after patients have ROSC. In ED, the goal is to initiate the cooling as soon as possible after ROSC. Shivering and cold burn to skin are observed every 10 minutes to prevent adverse effects. The most accurate way to measure core body temperature is to take rectal temperature (Mazerolle et al., 2011). Rectal temperature is taken every 15 minutes to monitor temperature change. Disposable ice packs are changed every 20 minutes to provide maximal cooling effect until arrival to the ICU admission as the remaining parts of therapeutic hypothermia will be continued in intensive care.

4.2.3 Evaluation

At the end of the pilot study, the feasibility and effectiveness of the guideline, nurses' compliance and competence of using the guideline, potential barriers and difficulties encountered are evaluated. The neurological outcome and survival rate of patients are evaluated when discharged and after 180 days of cardiac arrest. The logistics of the workflow
is tested to assess whether the use of new evidence-based guideline is appropriate. Also, the transfer and hand-over of patients under cooling from ED to ICU are evaluated to find out any difficulties and communication problems.

4.2.4 Planning after pilot test

All frontline nurses are required to attend the training workshop for inducing therapeutic hypothermia to post cardiac arrest patients in 2 sessions, as the appropriate use of the guideline requires their understanding and knowledge. Stocking materials are planned to store in two resuscitation rooms as the ice packs need to be stored in a convenient location and to be used immediately after resuscitation.

Annual audit (Appendix 12) can be done to assess nursing staff compliance and competency of using the guideline by return demonstration to the trainers.

A formal meeting will be held regularly for communication team to help make revision of the proposed guideline at the end of the pilot study prior to the full implementation of the innovation.
4.3 Evaluation Plan

An evaluation plan is used to assess the effectiveness of inducing therapeutic hypothermia to post cardiac arrest patients in the setting of Emergency Department. It helps identify patients, healthcare providers and system outcomes and measurements. Also, it provides important information about the nature of clients to be involved and determines the number of clients. Finally, the analyses of data are evaluated.

4.3.1 Identifying outcomes

4.3.1.1 Patient outcomes

It aims at assessing the clinical benefits of the innovation to patients. The primary outcome is survival at 6 months (HACA, 2002, Bernard et al., 2002, Nielsen et al., 2013). This outcome measures are in comparison between inducing therapeutic hypothermia and current practice without temperature control to post cardiac arrest patients with VF/pulseless VT.

The secondary outcome is neurological outcome. Good neurological performance is defined as cerebral performance category (CPC) of 1 and 2, which is a functional status scale to evaluate the normal brain function to severe disability of patients after out-of-hospital cardiac arrest.

4.3.1.2 Healthcare provider outcomes

It mainly targets at assessing the guideline users - frontline nurses. The acceptance and compliance level of using the therapeutic hypothermia guideline in ED are assessed. The guideline is more likely to be followed if it is simple to use and clearly defined. Nurses' satisfaction of using the guideline is also a measure outcome. After the training workshop for frontline staff, the questionnaire for training workshop (Appendix 6) is used for evaluation.
After the implementation, it is measured by using evaluation form for staff (Appendix 13). Regular presentation of cases with good clinical outcomes to frontline staff may increase their outcome expectancy and change their perception of futility. The skill and knowledge of applying therapeutic hypothermia are regarded as important because nurses can meet the goals of the intervention effectively. Hence, these factors can increase the self-efficacy of nurses after attending the training workshop. Those outcome measures can be reassessed by return demonstration and annual audit.

4.3.1.3 System outcomes

It is to measure system effectiveness. The utilization of the innovation, use of materials and human resources and the cost-effectiveness ratio are regarded as the system outcomes. The cost is very low as it only requires disposable ice packs to be ready to use and the effectiveness is the better neurological function and survival of patients. Both outcome measures can be evaluated by comparison with the current records. Neurological outcome is evaluated by CPC scale (Appendix 7).

4.3.2 Period of outcome measurements

Since the recovery period of post cardiac arrest patients is long, the neurological function is difficult to assess in the short term. Then the survival is measured at 2 weeks as short term measurement and it can easily be accessed via Clinical Management System (CMS). The nurses’ understanding and satisfaction level are measured after the organization of training workshop by using questionnaires (Appendix 6) at 1 week. The intermediate term of measurements is set at 6 months to evaluate the survival and neurological function of target patients. Face-to-face interview is needed to measure these outcomes.

For the long term, it is set to be 1 year for frontline nurses to do a questionnaire about
their satisfaction on inducing therapeutic hypothermia and workload.

4.3.3 Nature of clients to be involved

The eligibility criteria is defined as same as the developed clinical guideline (Appendix 10) and pilot study. The main characteristics are ageing from 18-75, comatose survivors with VF/pulseless VT as initial cardiac rhythm, presumed cardiac origin, interval from patient collapse to start CPR by medical personnel within 15 minutes and interval of <=60 minutes from collapse to ROSC, and hemodynamically stable. Patients should be excluded if pregnancy, known coagulopathy, history of terminal illness and active internal bleeding exist.

4.3.4 Determining the number of clients

The primary outcome is the survival of patients at 6 months. It is used to determine the number of patients involved. The desired sample size can be estimated by using the Computer software of Java Applets for Power and Sample Size (Lenth, 2006-9), confidence interval (CI) for one proportion is chosen to estimate the number of patients involved. Assuming the infinite population, confidence as 0.95, worst case as pi 0.5 and margin of error as 0.15, the estimated sample size is 43.

4.3.5 Data analysis

SPSS software, version 17.1 is used for statistical analyses. Primary outcome and secondary outcome which are survival and good neurological outcome respectively are binary and chi-square test is used to compare the outcomes. Descriptive statistics is used to summarize the baseline characteristics e.g. age, sex, medical history. Baseline data are compared by t-tests for continuous variables and by chi-square test or Fisher's exact test for categorical variables.
For evaluation of nurses' satisfaction, an evaluation form (Appendix 13) which is similar to the questionnaire for the training workshop, is distributed to evaluate the satisfaction and compliance on inducing therapeutic hypothermia. A t-test is used to evaluate the job satisfaction and compliance after each time of performing the innovation. A p-value of 0.05 or less is considered as statistically significant.

4.3.6 Basis for an effective change of practice

The proposed new practice targets at improving the survival and neurological outcome of comatose post cardiac arrest patients with VF/pulseless VT as initial cardiac rhythm in Emergency Department. The intervention is considered as effective if the primary outcome - survival can be achieved. As the survival to hospital discharge rate is very low, inducing therapeutic hypothermia may significantly influence survival and neurological outcome. According to the literature reviews, HACA (2002) and Bernard et al. (2002) showed favorable neurological outcome and reduced mortality. In addition, a systematic review of Maria et al. (2015) showed that "in patients with VF/VT rhythm low temperature reduced short and long-term mortality when compared with no targeted temperature". Therefore, the survival rate is expected to increase by at least 14% so the practice is considered as effective. The guideline will be regarded as effective if 80% of frontline staffs are satisfied with the implementation of the new guideline.

For the cost-effective ratio, it only uses low cost but has better patients' outcome in ED, i.e. purchasing the disposable ice packs.
Chapter 5: Conclusion

In Emergency Department, inducing therapeutic hypothermia as soon as possible for post cardiac arrest patients with ventricular fibrillation / pulseless ventricular tachycardia after return of spontaneous circulation is beneficial. This can improve their survival and neurological outcome. Implementing this evidence-based guideline can help those patients and their relatives to improve quality of life as the mortality of cardiac arrest is very high. The early induction of therapeutic hypothermia can be used by simply applying ice packs to patients' head, sides of neck, axillae and groins to provide cooling effect. The therapeutic hypothermia will be continued in Intensive Care Unit once the patients are transferred from Emergency Department.

In this study, the evidence-based guideline is designed to improve the neurological function and survival of the post cardiac arrest patient with initial rhythms of ventricular fibrillation or pulseless ventricular tachycardia. Establishing it in all Emergency Departments as usual practice is recommended in order to yield more benefits to those target patients.
References


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Cardiology, 102, 607-614.

Polderman, K. H. (2009). Mechanisms of action, physiological effects, and

Philadelphia: Lippincott Williams & Wilkins.


### Appendix 1: Search History

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<td>4 and 6</td>
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<td>9</td>
<td>4 and 5 and 6</td>
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## Appendix 2a: Data Extraction

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<th>Resuscitation via ScienceDirect</th>
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<td>Remove duplicates</td>
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<td>3</td>
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<tr>
<td><strong>Total number of articles reviewed without duplication</strong></td>
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<td></td>
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</table>
Appendix 2b: PRISMA 2009 Flow Diagram

Records identified through database searching (n = 1351)

Additional records identified through other sources (n = 87)

Records after duplicates removed (n = 763)

Records screened (n = 456)

Records excluded (n = 307)

Full-text articles assessed for eligibility (n = 189)

Full-text articles excluded, with reasons (n = 267)

Studies included in qualitative synthesis (n = 0)

Studies included in quantitative synthesis (meta-analysis) (n = 8)
## Appendix 3: Table of Evidence

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study Type</th>
<th>Patients Characteristics</th>
<th>Intervention (IG)</th>
<th>Comparison (CG)</th>
<th>Length of Follow-up</th>
<th>Outcome Measures</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HACA, 2002 RCT, (multicenter in Europe) 1++</td>
<td>Unconscious, witnessed cardiac arrest of cardiac origin, VF or pulseless VT as initial cardiac rhythm, Age of 18-75 years old, mean - IG: 59 CG: 59 5-15 min from arrest to CPR and &lt; 60 min to ROSC Exclusion criteria: Tympanic temperature &lt;30°C on admission, pregnancy, hypotension, comatose state before cardiac arrest</td>
<td>Use cold blanket, target temperature of 32°C -34°C for 24 hours, followed by passive rewarming over 8 hours If the goal temperature cannot be achieved, ice packs were applied N=137</td>
<td>Standard intensive care treatment No temperature control N=138</td>
<td>6 months</td>
<td>1. Favorable neurologic outcome 2. Mortality 3. Rate of complications</td>
<td>1. Neurological outcome: p=0.009 IG: 75/136 (55%) CG: 54/137 (39%) 2. Mortality: p=0.02 IG: 56/137 (41%) CG: 76/138 (55%) 3. Complication: p=0.70 IG: 98/135(73%) CG: 93/132(70%)</td>
<td></td>
</tr>
<tr>
<td>Citation</td>
<td>Study Type</td>
<td>Patients Characteristics</td>
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<td>Comparison (CG)</td>
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</tbody>
</table>
| Bernard et al., 2002 | RCT (multicenter in Australia) 1+ | - post cardiac arrest  
- VF as initial rhythm  
- Coma after successful ROSC  
- age of >= 18 years old for men  
- age of > 50 years old for women  
- mean age - IG: 69 CG: 63  
- Exclusion criteria: Cardiogenic shock, hypotension, if ICU bed not available | Use ice packs placed around head, neck, torso and limbs, target temperature of 33°C for 12 hours  
Passively rewarm after 12 hours  
Actively rewarmed by using heated air blanket started at 18 hours N= 43 | Standard pre-hospital & intensive care treatment  
No temperature control N=34 | No exact date, assessed when patients ready for discharge from hospital | 1. Survival to hospital discharge with good neurological function  
2. Mortality  
3. Frequency of adverse events | 1. Neurological function: p=0.046  
IG: 21/43 (49%)  
CG: 9/34 (26%)  
2. Mortality: p=0.145  
IG: 22/43 (51%)  
CG: 23/34 (68%)  
3. No significant difference p> 0.05 |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Study Type</th>
<th>Patients Characteristics</th>
<th>Intervention (IG)</th>
<th>Comparison (CG)</th>
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<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Nielsen et al., 2013</td>
<td>RCT (multicentre) 1+</td>
<td>&gt;=18 years old, post cardiac arrest, unconscious (GCS &lt;8), irrespective of the initial rhythm, more than 20 consecutive minutes of ROSC after resuscitation Exclusion criteria: Interval from ROSC to screening of &gt;=240 minutes, unwitnessed arrest with asystole as initial rhythm, suspected stroke, body temperature &lt;= 30°C Mean age - IG: 64 CG: 64</td>
<td>Use of ice-cold fluids, ice packs, &amp; intravascular or surface temperature-management devices, target temperature of 33°C for 28 hours, then gradually rewarm to 37°C at rate of 0.5°C/hour</td>
<td>Use same methods to maintain target temperature of 36°C for 28 hours, then gradually rewarm to 37°C at rate of 0.5°C/hour</td>
<td>1. end of trial 2. 180 days</td>
<td>1. All-cause mortality 2. Poor neurological function 3. Serious adverse event</td>
<td>1. Mortality: p=0.51 IG: 235/473 (50%) CG: 225/466 (48%) 2. Poor neurological function: p=0.78 IG: 251/469 (54%) CG: 242/464 (52%) 3. Hypokalemia: P=0.02 IG: 19% CG: 13% One or more serious adverse events occurred IG: 439/472 (93%) CG: 417/464 (90%) P=0.09</td>
</tr>
<tr>
<td>Citation</td>
<td>Study Type</td>
<td>Patients Characteristics</td>
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</table>
| Hachimi-Idrisi et al., 2001 | RCT (Belgium) 1++ | Remain unconscious after ROSC, cardiac arrest due to asystole or PEA, presumed cardiac origin                 | Cool to target temperature of 34°C within 4 hours using a helmet device, containing a solution of aqueous glycerol, placed around the head and neck Once temperature to 34°C, passively rewarm for 8 hours N=16 | Standard post-resuscitation care protocol to rewarm passively N=14 | 14 days | 1. Median time to target temperature of 34°C  
2. Survival  
3. Complication | 1. Core temperature: 180 min Central temperature: 60 min p<0.05  
2. IG: 3/16  
CG: 1/14 p>0.05  
3. no significance difference p>0.05 |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Study Type</th>
<th>Patients Characteristics</th>
<th>Intervention (IG)</th>
<th>Comparison (CG)</th>
<th>Length of Follow Up</th>
<th>Outcome Measures</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Laurent et al., 2005</td>
<td>RCT 1+ (multicenter)</td>
<td>Cardiac arrest of presumed cardiac origin, VF or asystole as first rhythm, unconscious after resuscitation Age 18 - 75, mean age 52 &lt;10min from cardiac arrest to start of CPR &lt;50min from start of CPR to ROSC</td>
<td>(IG1) HF+HT group: Direct external cooling of the blood during high-flow hemofiltration to target temperature of 32-33°C for 8 hours and surface cooling for 16 hours Then passive rewarming N=22 (IG2) HF group: High-flow hemofiltration maintaining 37°C for 8 hours, then no temperature control N=20</td>
<td>Standard supportive care, no temperature control N=19</td>
<td>6 months</td>
<td>1. Survival 2. Rate of death of intractable shock</td>
<td>1. Survival curve (IG1) HF+HT: p=0.018 (IG2) HF: p=0.026 2. Rate of death of intractable shock (IG1) HF+HT: 3/22 (14%) (IG2) HF: 2/20 (10%) CG: 9/19 (42%) p=0.009</td>
</tr>
<tr>
<td>Citation</td>
<td>Study Type</td>
<td>Patients Characteristics</td>
<td>Intervention (IG)</td>
<td>Comparison (CG)</td>
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<tr>
<td>Pittl et al., 2013</td>
<td>RCT (German) 1++</td>
<td>Admitted to ICU with ROSC after cardiac arrest, presumed cause of cardiac origin, remain coma after successful resuscitation, age&gt;18years, mean age: 62</td>
<td>Invasive cooling by endovascular catheter via femoral vein Administration of intravenous ice-cold fluids Target temperature of 33°C for 24 hours followed by active rewarming N=39</td>
<td>Non-invasive temperature controlled circulation of distilled water through hydrogel-coated pads applied to patients' skin Target temperature of 33°C for 24 hours followed by active rewarming N=39</td>
<td>72 hours</td>
<td>1. Neurological outcome 2. Survival 3. Efficacy of invasive &amp; non-invasive cooling 4. Cooling-associated complications</td>
<td>1. IG:14/39 (35.9%) CG: 14/39 (35.9%) p=0.99 2. IG: 24/39 (61.5%) CG: 21/39 (53.8) p=0.65 3. Time to target temperature IG: 180min CG: 240min p=0.29 4. Bleeding complications IG: 17/39 (43.6%) CG: 7/39 (17.9%) p=0.03 Other complications: p&gt;0.05</td>
</tr>
<tr>
<td>Citation</td>
<td>Study Type</td>
<td>Patients Characteristics</td>
<td>Intervention (IG)</td>
<td>Comparison (CG)</td>
<td>Length of Follow Up</td>
<td>Outcome Measures</td>
<td>Effect Size</td>
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<tr>
<td>Heard et al., 2011</td>
<td>RCT (Multicenter) 1++</td>
<td>Unconscious, age 18 years or older, post cardiac arrest with ROSC within 60min of collapse, presumed cardiac cause, with all initial rhythms, temperature of &gt;=35°C, start CPR within 15min</td>
<td>Target temperature to 33.5°C Arctic Sun - temperature management system with energy transfer pads applied to the back, chest &amp; thighs N=34</td>
<td>Target temperature to 33.5°C Standard cooling by using two cooling blankets, one wrapped around upper torso, one wrapped on lower torso/thighs Application of ice bags to axillae &amp; groin, changed every 30-60min N=30</td>
<td>3 months</td>
<td>1. Proportion of subjects who reach target temperature of 34°C with 4 hours of beginning cooling 2. Time interval to achieve target temperature of 34°C 3. Survival rates with good neurological outcome</td>
<td>1. IG: 24/34 (71%) CG:15/30 (50%) p=0.12 2. Median time to target temperature - IG: 190min CG: 244min p&lt;0.01 3. IG: (46%) CG: (38%) p=0.6</td>
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<tr>
<td>Citation</td>
<td>Study Type</td>
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<td>Intervention (IG)</td>
<td>Comparison (CG)</td>
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<tr>
<td>8</td>
<td>RCT (United Kingdom) 1++</td>
<td>Out-of-hospital witnessed cardiac arrest, age 18-75 years, VF or pulseless VT as initial rhythm, unconscious, presumed cardiac origin, interval of 5-15 mins from collapse to first attempt of resuscitation, interval of &lt;60 mins from collapse to ROSC</td>
<td>Actively cooled externally to core temperature 33+/-1°C by cold mattress that delivers cold air over the entire body for 24 hours</td>
<td>Standard post cardiac arrest care Allowed to rewarm passively to normothermia</td>
<td>1. 6 months 2. 24, 36, 48 hours</td>
<td>1. Favorable neurological outcome 2. Decrease in serum neuron-specific enolase (NSE)</td>
<td>1. IG:25/36 (69%) CG: 16/34 (47%) p=0.005 2. p=0.007</td>
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# Appendix 4: Appraisal Checklist for Randomized Controlled Trials (SIGN)

Critical Appraisal (Scottish intercollegiate Guidelines Network (SIGN) Randomized controlled trials methodology checklist)

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<th>Level of Evidence</th>
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<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
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<tr>
<td>1+</td>
<td>Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias</td>
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<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews, or RCTs with a high risk of bias</td>
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<tr>
<td>2++</td>
<td>High quality systematic reviews of case control or cohort or studies High quality case control or cohort studies with a very low risk of confounding</td>
</tr>
<tr>
<td>2+</td>
<td>Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
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<tr>
<td>2-</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
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<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
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<tr>
<td>4</td>
<td>Expert opinion</td>
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Methodology Checklist 2: Randomised Controlled Trials

Student identification


### Section 1: Internal validity

<table>
<thead>
<tr>
<th></th>
<th>In a well conducted RCT study...</th>
<th>In this study this criterion is:</th>
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</thead>
<tbody>
<tr>
<td>1.1</td>
<td>The study addresses an appropriate and clearly focused question.</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed</td>
</tr>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomised</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed</td>
</tr>
<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed</td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td><strong>Well covered</strong> <strong>Adequately addressed</strong> Poorly addressed</td>
</tr>
<tr>
<td>1.5</td>
<td>The treatment and control groups are similar at the start of the trial</td>
<td><strong>Well covered</strong> <strong>Adequately addressed</strong> Poorly addressed</td>
</tr>
<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed</td>
</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed</td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or</td>
<td>2/275 = 0.7%</td>
</tr>
</tbody>
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63
clusters recruited into each treatment arm of the study dropped out before the study was completed?

<table>
<thead>
<tr>
<th>1.9</th>
<th>All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)</th>
<th>Well covered</th>
<th>Adequately addressed</th>
<th>Poorly addressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
</tr>
</tbody>
</table>

Section 2: Overall assessment of the study

| 2.1 | How well was the study done to minimise bias? Code ++, +, or - | ++ |
| 2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? | yes |
| 2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? | yes |
| 2.4 | Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. | Therapeutic hypothermia increased chance of survival & favorable neurologic outcome. Large sample size gives a great contribution. Not feasible to blind clinicians to the patients' treatment-group assignments |

All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). Where the study is carried out at more than one site, results are comparable for all sites.
Methodology Checklist 2: Randomised Controlled Trials

Student identification


### Section 1: Internal validity

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<th>In this study this criterion is:</th>
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</thead>
<tbody>
<tr>
<td>1.1</td>
<td>The study addresses an appropriate and clearly focused question.</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomised</td>
<td><strong>Well covered</strong> <strong>Adequately addressed</strong> Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed Not addressed Not reported <strong>Not applicable</strong></td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td><strong>Well covered</strong> <strong>Adequately addressed</strong> Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.5</td>
<td>The treatment and control groups are similar at the start of the trial</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
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<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
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<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td><strong>Well covered</strong> Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or 0/77=0%</td>
<td></td>
</tr>
</tbody>
</table>
clusters recruited into each treatment arm of the study dropped out before the study was completed?

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>Well covered</td>
</tr>
<tr>
<td>-</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>

1.10 Where the study is carried out at more than one site, results are comparable for all sites

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>Well covered</td>
</tr>
<tr>
<td>-</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>

Section 2: Overall assessment of the study

2.1 How well was the study done to minimise bias? Code ++, +, or -

2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?

2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?

2.4 Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

- Induced hypothermia improve outcomes of post cardiac arrest patients
- It use the method of odd and even days for randomization
- Not feasible to blind clinicians to the patients' treatment-group assignments
Methodology Checklist 2: Randomised Controlled Trials

Student identification

Section 1: Internal validity

<table>
<thead>
<tr>
<th></th>
<th>In a well conducted RCT study...</th>
<th>In this study this criterion is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>The study addresses an appropriate and clearly focused question.</td>
<td>Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomised</td>
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</tr>
<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
<td>Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td>Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.5</td>
<td>The treatment and control groups are similar at the start of the trial</td>
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</tr>
<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
<td>Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable</td>
</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td><strong>Well covered</strong></td>
</tr>
<tr>
<td></td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
</tr>
<tr>
<td></td>
<td>Not addressed</td>
<td>Not reported</td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?</td>
<td>17/950=1.7%</td>
</tr>
<tr>
<td>1.9</td>
<td>All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)</td>
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</tr>
<tr>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites</td>
<td><strong>Well covered</strong></td>
</tr>
<tr>
<td></td>
<td>Adequately addressed</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

**Section 2: Overall assessment of the study**

| 2.1 | How well was the study done to minimise bias? Code ++, +, or - | + | |
| 2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? | moderate | |
| 2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? | neutral | |
| 2.4 | Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. | Targeted temperature at 33°C & 36°C did not confer benefit to unconscious patient after resuscitation from cardiac arrest |
|     | This study is irrespective of the initial rhythm, including all rhythms like pulseless electrical activities, asystole, ventricular fibrillation, pulseless ventricular tachycardia, unclassified rhythms | |
A big difference in the control group with other earlier trials is that the target body temperature of 36°C was actively controlled, it did not allow the natural trajectory of temperature evolution.

No specific cooling methods, including invasive and non-invasive.

This study did not standardize the use of interventions in different hospitals.
Methodology Checklist 2: Randomised Controlled Trials

Student identification


### Section 1: Internal validity

<table>
<thead>
<tr>
<th>In a well conducted RCT study...</th>
<th>In this study this criterion is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 The study addresses an appropriate and clearly focused question.</td>
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</tr>
<tr>
<td>1.2 The assignment of subjects to treatment groups is randomised</td>
<td><strong>Well covered</strong>&lt;br&gt;Well covered&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
</tr>
<tr>
<td>1.3 An adequate concealment method is used</td>
<td><strong>Well covered</strong>&lt;br&gt;Well covered&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
</tr>
<tr>
<td>1.4 Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td><strong>Well covered</strong>&lt;br&gt;Well covered&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
</tr>
<tr>
<td>1.5 The treatment and control groups are similar at the start of the trial</td>
<td><strong>Well covered</strong>&lt;br&gt;Well covered&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
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</tr>
<tr>
<td>1.7 All relevant outcomes are measured in a standard, valid and reliable way</td>
<td><strong>Well covered</strong>&lt;br&gt;Well covered&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
</tr>
<tr>
<td>1.8 What percentage of the individuals or clusters recruited into each treatment</td>
<td>0/30=0%</td>
</tr>
</tbody>
</table>
arm of the study dropped out before the study was completed?

| 1.9 | All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis) | **Well covered** | Adequately addressed | Poorly addressed | Not addressed | Not reported | Not applicable |
| 1.10 | Where the study is carried out at more than one site, results are comparable for all sites | Well covered | Adequately addressed | Poorly addressed | Not addressed | Not reported | **Not applicable** |

**Section 2: Overall assessment of the study**

| 2.1 | How well was the study done to minimise bias? Code ++, +, or - | ++ |
| 2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? | yes |
| 2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? | yes |
| 2.4 | Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. | Induced hypothermia by external device was feasible, inexpensive, easy to perform with no increase in complications. This study only included cardiac rhythm of asystole and PEA patients with poor survival prognosis. |
Methodology Checklist 2: Randomised Controlled Trials

Student identification

### Section 1: Internal validity

<table>
<thead>
<tr>
<th>1.1</th>
<th>The study addresses an appropriate and clearly focused question.</th>
<th>Well covered</th>
<th>Not addressed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Adequately addressed</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomised</td>
<td>Well covered</td>
<td>Not addressed</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Poorly addressed</td>
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<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
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</tr>
<tr>
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<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td>Well covered</td>
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</tr>
<tr>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
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<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
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</tr>
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</tr>
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<td></td>
<td></td>
<td>Poorly addressed</td>
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</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td>Well covered</td>
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</tr>
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<td></td>
<td></td>
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<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poorly addressed</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
1.8 | What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? | 0/61=0% |
1.9 | All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis) | **Well covered** | Adequately addressed | Poorly addressed | Not addressed | Not reported | Not applicable |
1.10 | Where the study is carried out at more than one site, results are comparable for all sites | Well covered | Adequately addressed | Poorly addressed | Not addressed | Not reported | Not applicable |

Section 2: Overall assessment of the study

2.1 | How well was the study done to minimise bias? Code ++, +, or - | + |
2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? | moderate |
2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? | neutral |
2.4 | Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. | Early hemofiltration with or without mild hypothermia was associated with better survival. |
## Methodology Checklist 2: Randomised Controlled Trials

### Student identification

### Section 1: Internal validity

<table>
<thead>
<tr>
<th></th>
<th>In a well conducted RCT study...</th>
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</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or</td>
<td>2/80=2.5%</td>
</tr>
</tbody>
</table>
clusters recruited into each treatment arm of the study dropped out before the study was completed?

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)

<table>
<thead>
<tr>
<th></th>
<th>Well covered</th>
<th>Adequately addressed</th>
<th>Poorly addressed</th>
<th>Not addressed</th>
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</tr>
</thead>
</table>

1.10 Where the study is carried out at more than one site, results are comparable for all sites

<table>
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<tr>
<th></th>
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<th>Not addressed</th>
<th>Not reported</th>
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</tr>
</thead>
</table>

Section 2: Overall assessment of the study

2.1 How well was the study done to minimise bias?

|                        | ++           |                      |                  |               |              |                |

2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?

|                        | yes          |                      |                  |               |              |                |

2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?

|                        | yes          |                      |                  |               |              |                |

2.4 Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

Invasive and external mild induced hypothermia had similar efficacy in cooling post cardiac arrest patients and in neurological outcome

Invasive cooling was associated with more bleeding complications

This study was not aimed at measuring their effectiveness
### Methodology Checklist 2: Randomised Controlled Trials

#### Student identification


#### Section 1: Internal validity

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<thead>
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<th>In this study this criterion is:</th>
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<tr>
<td>1.3 An adequate concealment method is used</td>
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</tr>
<tr>
<td>1.4 Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td><strong>Well covered</strong>&lt;br&gt;Adequately addressed&lt;br&gt;Poorly addressed&lt;br&gt;Not addressed&lt;br&gt;Not reported&lt;br&gt;Not applicable</td>
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<td>1.7 All relevant outcomes are measured in a standard, valid and reliable way</td>
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<td>1.9</td>
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</tr>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites</td>
</tr>
</tbody>
</table>

**Section 2: Overall assessment of the study**

| 2.1 | How well was the study done to minimise bias? Code ++, +, or - | ++ |
| 2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? | **yes** |
| 2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? | **yes** |
| 2.4 | Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. | Both Arctic Sun and cooling blankets were effective in cooling patients after cardiac arrest. The personnel who did the neurological assessment were not blinded. This study did not include the comparison of hypothermia-associated complications. |
Methodology Checklist 2: Randomised Controlled Trials

Student identification

| Section 1: Internal validity | 1.1 The study addresses an appropriate and clearly focused question. | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.2 The assignment of subjects to treatment groups is randomised | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.3 An adequate concealment method is used | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.4 Subjects and investigators are kept ‘blind’ about treatment allocation | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.5 The treatment and control groups are similar at the start of the trial | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.6 The only difference between groups is the treatment under investigation | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.7 All relevant outcomes are measured in a standard, valid and reliable way | Well covered | Not addressed |
|                             | Adequately addressed | Poorly addressed | Not reported |
|                             | 1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? | 0/70=0% |
|                             | 1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis) | Well covered | Not addressed |
Where the study is carried out at more than one site, results are comparable for all sites

| 1.10 | Where the study is carried out at more than one site, results are comparable for all sites | Well covered | Adequately addressed | Poorly addressed | Not addressed | Not applicable |

Section 2: Overall assessment of the study

2.1 How well was the study done to minimise bias? Code ++, +, or -
++

2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?
yes

2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?
yes

2.4 Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.
Therapeutic hypothermia may decrease levels of serum neuron-specific enolase (NSE) so as to improve neurological outcome. The high serum level indicates the severity of ischemic brain injury,
# Appendix 5: Level of Evidence

Level of Evidence (Melnyk & Fineout-Overholt, 2005)

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Evidence from systematic review of meta-analysis of all relevant randomized controlled trials (RCTs), or evidence-based clinical practice guidelines based on systematic reviews of RCTs</td>
</tr>
<tr>
<td>Level II</td>
<td>Evidence from at least one well-designed RCT</td>
</tr>
<tr>
<td>Level III</td>
<td>Evidence from well-designed controlled trials WITHOUT randomization</td>
</tr>
<tr>
<td>Level IV</td>
<td>Evidence from well-designed case-control and cohort studies</td>
</tr>
<tr>
<td>Level V</td>
<td>Evidence from systematic reviews of descriptive and qualitative studies</td>
</tr>
<tr>
<td>Level VI</td>
<td>Evidence from a single descriptive or qualitative study</td>
</tr>
<tr>
<td>Level VII</td>
<td>Evidence from the opinion of authorities and/or reports of expert committees</td>
</tr>
</tbody>
</table>
Appendix 6: Questionnaire on Training Workshop of Therapeutic Hypothermia in Emergency Department

Evaluation of nurses' understanding and satisfaction level on the workshop

Please read carefully on the following instruction:

Please circle the appropriate number to indicate your attitude to each statement.

The rating scale is as follows:


Choose “neutral” if you neither agree nor disagree.

<table>
<thead>
<tr>
<th>Understanding on the therapeutic hypothermia</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I understood the mechanism of post cardiac arrest syndrome</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. I understood the advantages of inducing induction phase of therapeutic hypothermia</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. The selection criteria of targeted patients were understood</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. I understood the necessary nursing skill needed to implement therapeutic hypothermia</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. I was clear about the potential adverse events may occur</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. I was clear about the close monitoring of vital signs and any complications</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. I understood the core temperature needed to be monitored closely</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. I understood the evaluation tool</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Your satisfaction on the course</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>I was clear about the details of the program that expected me to learn</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>The content of the program was well-organized to facilitate implementation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>The duration of the innovation was appropriate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>The teaching materials were properly prepared with clear instructions provided.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>The assessment tools were easy to use and understand</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>The instrument chosen were appropriate in the innovation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>I was able to cope with the program workload and the difficulties encountered during implementation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>I achieved what the programmed expected me to teach</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Overall, I satisfy to the innovation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any comments:

_____________________________________________________________________

Any improvements:

_____________________________________________________________________
## Appendix 7: Cerebral Performance Categories Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPC 1</td>
<td>Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.</td>
</tr>
<tr>
<td>CPC 2</td>
<td>Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.</td>
</tr>
<tr>
<td>CPC 3</td>
<td>Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.</td>
</tr>
<tr>
<td>CPC 4</td>
<td>Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.</td>
</tr>
<tr>
<td>CPC 5</td>
<td>Brain death: apnea, areflexia, EEG silence, etc.</td>
</tr>
</tbody>
</table>

## Appendix 8: Material Cost of Implementation of the Proposed Innovation

### Short Term Cost

<table>
<thead>
<tr>
<th>Items</th>
<th>Price ($) x (+/-pages) x Quantity</th>
<th>Amount (HKD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posters on 4 resuscitation room</td>
<td>$2 x 4</td>
<td>$8</td>
</tr>
<tr>
<td>Training for trainers of 1 APN and 2 RNs</td>
<td>Attending course for therapeutic hypothermia</td>
<td>$1000 x 3</td>
</tr>
<tr>
<td>One-hour training workshop for other nursing staff (2 timeslots)</td>
<td>1. Handouts (4 pages)</td>
<td>$0.5 x 4 x 50</td>
</tr>
<tr>
<td></td>
<td>2. Junior RN Pay (for learning)</td>
<td>$ 160 x 20</td>
</tr>
<tr>
<td></td>
<td>3. Senior RN Pay (for learning &amp; 2 for teaching)</td>
<td>$ 250 x 20</td>
</tr>
<tr>
<td></td>
<td>4. APNs Pay (for learning &amp; 1 for teaching)</td>
<td>$ 300 x 10</td>
</tr>
<tr>
<td></td>
<td>5. Medical Staff Pay (for teaching)</td>
<td>$ 500 x 1</td>
</tr>
<tr>
<td>Evaluation</td>
<td>Evaluation audit form for staff</td>
<td>$0.5 x 50</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>$14833</td>
</tr>
</tbody>
</table>
### Long Term Cost (annually)

<table>
<thead>
<tr>
<th>Items</th>
<th>Price ($) x (+/-pages) x Quantity</th>
<th>Amount (HKD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Necessary material</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disposable ice packs</td>
<td>$10 x 200</td>
<td>$2000</td>
</tr>
<tr>
<td><strong>Protocol and checklist</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol for therapeutic hypothermia</td>
<td>$0.5 x 4 x 80</td>
<td>$160</td>
</tr>
<tr>
<td><strong>One-hour refreshment training workshop for new nursing staff +/- current staff</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Handouts (4 pages)</td>
<td>$0.5 x 4 x 10</td>
<td>$20</td>
</tr>
<tr>
<td>2. Junior RN Pay (for learning)</td>
<td>$160 x 10</td>
<td>$1600</td>
</tr>
<tr>
<td>3. Senior RN Pay (for teaching)</td>
<td>$250 x 2</td>
<td>$500</td>
</tr>
<tr>
<td>4. APN Pay (for teaching)</td>
<td>$300 x 1</td>
<td>$300</td>
</tr>
<tr>
<td>5. Medical Staff Pay (for teaching)</td>
<td>$500 x 1</td>
<td>$500</td>
</tr>
<tr>
<td><strong>Evaluation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation audit form for staff</td>
<td>$0.5 x 10</td>
<td>$40</td>
</tr>
<tr>
<td>Evaluation from for patients</td>
<td>$0.5 x 80</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>$5120</td>
</tr>
</tbody>
</table>
## Appendix 9: Grades of Recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
</tr>
<tr>
<td>Good practice points</td>
<td>Recommended best practice based on the clinical experience of the guideline development group</td>
</tr>
</tbody>
</table>
Appendix 10: Evidence-Based Practice Protocol

Title

An Evidence-based Guideline in Inducing Therapeutic Hypothermia to Improve Neurological Outcome of Post Cardiac Arrest Patients in Emergency Department

Objectives

The objectives of this protocol are to:

1. Summarize the clinical evidence for inducing therapeutic hypothermia to post cardiac arrest adults
2. Facilitate the safe and smooth practice of therapeutic hypothermia in indicated patients
3. Standardize the external cooling process to post cardiac arrest patients in ED
4. Promote the use of an evidence-based guideline in the target setting

Intended user

This protocol is to support decision-making in emergency nurses who directly take decisions on initiating the induction phase of therapeutic hypothermia for arrest patients with return of spontaneous circulation (ROSC) in emergency department.

Target group

Patients who are potential to be admitted to adult ICU, aged 18-75, post cardiac arrest comatose survivors with VF or pulseless VT as initial cardiac rhythm, presumed cardiac origin, interval from patient collapse to start CPR by medical personnel within 15 minutes and interval of <=60 minutes from collapse to ROSC.

Patients are excluded if they are hemodynamically unstable, pregnancy, known coagulopathy, history of terminal illness and active internal bleeding.
Recommendations

Recommendation 1 (Grade A)
Post cardiac arrest patients should be cooled to target temperature of 32°C - 34°C for 24 hours.

Available evidence:
The core temperature reduced to target temperature of 33°C within 2 hours after return of spontaneous circulation. (Bernard et al., 2002[1+])
Those patients assigned to hypothermia group were cooled to a target temperature of 32°C to 34°C for 24 hours. (Arrich et al., 2012 [1++]; HACA, 2002[1++]; Walters, Morley & Nolan, 2011[1++])

Recommendation 2 (Grade A)
Comatose adult patients with return of spontaneous circulation after out-of-hospital VF or pulseless VT should be cooled.

Available evidence:
Among patients in whom spontaneous circulation had been restored after cardiac arrest due to VF or pulseless VT, systemic cooling to a target temperature between 32°C and 34°C for 24 hours increased the chance of survival and of a favourable neurological outcome. (Arrich et al., 2012 [1++], Bernard et al., 2002[1+]; HACA, 2002[1++]; Tiainen et al., 2003[1++]; Walters, Morley & Nolan, 2011[1++])
**Recommendation 3 (Grade A)**

The induction phase of therapeutic hypothermia should be initiated as soon as possible after patients with return of spontaneous circulation.

Available evidence:

The goal was to reach the target temperature within four hours after return of spontaneous circulation. (HACA, 2002 [1++])

Those patients underwent vigorous cooling in the emergency department as soon as possible after the initial assessment, i.e. within 2 hours, to gain maximum benefits in both neurological outcome and survival. (Bernard et al., 2002 [1+])

**Recommendation 4 (Grade A)**

Induction can easily be induced with the use of ice packs, placed in the groins, armpits and around the neck and head.

Available evidence:

Traditional external cooling by using ice packs has proven its feasibility. (Bernard et al., 2002[1+])

Both using simple surface cooling with the cooling blankets or ice packs and the Arctic Sun were able to effectively cool patients after cardiac arrest.(Heard et al., 2011[1+]; Walters, Morley & Nolan, 2011[1++])

Invasive and external mild induced hypothermia showed efficacy in cooling comatose patients after survived out-of-hospital cardiac arrest with respect to neuro-specific enolase levels as a surrogate parameter for brain damage. (Pittl et al., 2013[1++])
Recommendation 5 (Grade A)

Initiation of therapeutic hypothermia is safe, well tolerated and not associated with more complications than in patients not treated with therapeutic hypothermia.

Available evidence:
In these 4 RCTs, there were no statistically significant difference in serious complications between hypothermia group and normothermia group. (Arrich et al., 2012 [1++]; Bernard et al., 2002[1+]; HACA, 2002[1++]; Hachimi-Idrissi et al.[1++], 2001; Nielsen et al., 2013[1+])
Therapeutic hypothermia can be done in conjunction with other interventions such as percutaneous coronary intervention (PCI). (Walters, Morley & Nolan, 2011[1++])
Appendix 11: Induced Therapeutic Hypothermia Checklist in Emergency Department

Please use gum label

Hospital No._____________________
Name___________________________
I.D. No._________________________
Dept.___________________________

<table>
<thead>
<tr>
<th></th>
<th>Inclusion criteria</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Unconscious post cardiac arrest survivors with VF/pulseless VT as initial cardiac rhythm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>Presumed cardiac origin of arrest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td>Interval from collapse to start CPR by medical personnel within 15 mins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>Interval of &lt;= 60 mins from collapse to ROSC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>age between 18-75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Exclusion criteria</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.1</td>
<td>Response to verbal command after ROSC and GCS &gt; 10/15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2</td>
<td>Hypotension &gt; 30mins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3</td>
<td>Hypoxia &gt; 15mins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>Pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>Known coagulopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.6</td>
<td>Active internal bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.7</td>
<td>History of terminal illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Inform ICU for potential case</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Confirm ICU bed is available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Apply ice packs to head, sides of neck, axillae and groins</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 12: Audit Form for Assessing the Use of Evidence-based Guideline of Therapeutic Hypothermia for Comatose Post Cardiac Arrest Patients in Emergency Department

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Ensure post cardiac arrest survivor is comatose, VF/ pulseless VT as initial cardiac rhythm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2  Ensure patient fulfill inclusion criteria and exclusion criteria by using therapeutic hypothermia guideline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3  Ensure patient hemodynamically stable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4  Inform ICU for potential case and confirm ICU bed available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5  Apple ice packs to head, sides of neck, axillae and groins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6  Observe any side-effects, e.g. shivering, cold burn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7  Change ice packs every 20 minutes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Staff name: _______________                     Date of audit: _______________
Appendix 13: Evaluation Form on Therapeutic Hypothermia for Staff

It is used to evaluate the implementation of the evidence-based guideline of inducing therapeutic hypothermia for post cardiac arrest patient in ED, please fill in the following items.

(1=Strongly Disagree, 2=Disagree, 3=Neutral, 4=Agree, 5=Strongly Agree)

<table>
<thead>
<tr>
<th></th>
<th>Implementation of guideline</th>
<th>Disagree ------ Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>It is easy for you to meet the inclusion and exclusion criteria to select suitable patients</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>2</td>
<td>It is easy for you to apply ice packs on patients to induce cooling effect</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>3</td>
<td>The implementation of the therapeutic hypothermia increases your sense of job satisfaction</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>4</td>
<td>The therapeutic hypothermia guideline enhances your sense of achievement</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>5</td>
<td>This guideline is effective and should be continued for favorable patients' outcomes</td>
<td>1 2 3 4 5</td>
</tr>
</tbody>
</table>