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Targeted Temperature Management Following Cardiac Arrest

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Executive Summary

Cardiac arrest is often associated with the death of brain tissue resulting from the lack of oxygen supply caused by the interruption of blood circulation. For this reason, good neurological outcome following cardiac arrest is difficult to achieve. Targeted temperature management, formerly known as therapeutic hypothermia, is the maintenance of specific body temperature parameters after the return of spontaneous circulation (ROSC) following cardiac arrest (Donnino et al., 2015). The goal of therapy is to improve neurological status and facilitate healing by reducing the metabolic requirement of the brain. (Saigal et al., 2015). Therefore, the question arose, in adult patients who remain comatose following a non-traumatic cardiac arrest (P), how does implementation of targeted temperature management (I) compared to normal core temperature (C) affect neurologically intact discharge rates (O) during a three-month period (T)? A benchmark project was completed to address this topic.

Rationale for the Project

In the United States, greater than 350,000 people experience an out-of-hospital cardiac arrest (OHCA) each year in addition to more than 200,000 in-hospital patient cardiac arrests (IHCA) (Meaney et al., 2013). Cardiac arrest claims many of these lives, but its survival is often associated with additional injury to the brain and other organs related to anoxia, affecting quality of life. The rate of survival to hospital discharge for patients who suffer an arrest is only 17% for IHCA and an even more discouraging 11% for OHCA (Meaney et al., 2013) The neurologically intact discharge rates are even lower. Some of the consequences for a brain that has survived cardiac arrest include memory impairments, movement disorders, and impaired attention, processing speed, and/or executive function (Elmer & Callaway, 2017). These impairments can prevent many from returning to work and normal daily activities, placing economic burden on

the survivor, their families, and society due to loss of productivity and contribution to the work force (Sawyer et al., 2020).

Literature Synthesis

A review of the literature was conducted with systematic searches of The Cumulative Index to Nursing and Allied Health Literature (CINAHL) Complete, Cochrane Library, and PubMed databases. Evaluation and synthesis of data from the intervention studies selected were performed to compare the efficacy of targeted temperature management on improving neurological outcomes of adult patients who remain comatose following a non-traumatic cardiac arrest. (See Appendix A: Evaluation Table) The independent variables across the studies compared a control group of normothermia with induced hypothermia at temperatures ranging from 32°C-36°C. Each of the studies utilized Cerebral Performance Categories as standardized measurement tools to evaluate the incidence of the desired outcome of neurologically intact discharge. A CPC score of 1 or 2 is associated with good neurological recovery while a score of 3, 4, or 5, is associated with an unfavorable recovery (Arrich at al., 2016; Donnino et al., 2015; Lascarrou et al., 2019; Schenone et al, 2016).

Statistical analysis for each of the studies showed an increase in favorable neurological outcome for the intervention group. One study showed an improvement in desired outcomes when targeted temperature management was initiated at 33°C when compared with the same intervention at 36°C (Bray et al., 2017; Johnson et al., 2020). There was no significant difference in results when the length of the intervention was extended beyond 24 hours to a 48-hour duration (Kirkegaard et al., 2017). However, a slower rate of rewarming following the cooling phase is associated with more favorable neurological outcomes (Hifumi et al., 2020). Based on the best available evidence, it is recommended that targeted temperature management be

implemented using conventional cooling methods, including cooling pads, ice packs, and cold intravenous fluids, to induce a patient body temperature of 32-34°C for a period of 24 hours in an effort to improve patient rates of neurologically intact discharge (Arrich at al., 2016; Donnino et al., 2015; Lascarrou et al., 2019; Schenone et al, 2016). This intervention is recommended regardless of initial cardiac arrest rhythm, unwitnessed arrest status, or persistent shock of the patient (Rout et al., 2020; Schenone et al., 2016). This should be initiated when the patient is in the hospital emergency department, where the patient's core temperature can be accurately monitored. Prehospital cooling with large amounts of cold IV fluid is not recommended (Donnino et al, 2015).

Stakeholders

There are both internal and external stakeholders invested in the project. Internal stakeholders are mainly within the organization or facility and include administration and management team members who provide leadership to facilitate the change as well as the physicians, nurses, and other healthcare professionals who translate the evidence into actual practice. External stakeholders include the patients and their families who are the consumers of healthcare services, suppliers and financial organizations who provide the necessary resources, and finally, society and the economy as a whole (Horev & Babad, 2005).

Implementation

The first objective of the planned implementation is meeting with hospital administration, such as the chief nursing officer, and managers of specific departments including finance, education, risk management, and case management. Managers of units including the emergency department and cardiovascular intensive care units that care for the category of critical patients targeted by this project will also be included. The purpose of this meeting is to engage these

stakeholders by presenting the clinical evidence for the practice change and obtain permission for the project within the facility. Once approval is gained, it is important to begin generating awareness of the project and motivation for change among the staff.

The next phase of the implementation plan consists of obtaining baseline data for the facility. This consists of auditing charts of patients who experienced cardiac arrest to determine an average for CPC scores at disposition prior to implementation of the project. This also includes gathering information about any protocols that may already in place regarding this topic. This is followed by establishment of new written protocols and tools for data documentation. The protocol that was selected for this project is similar to that established by The University of Texas MD Anderson Cancer Center. The protocol follows an algorithm which indicates an initial cooling phase to 33°C with a goal to target temperature of less than 4 hours. After the target temperature is maintained for 24 hours, the rewarming phase begins at a rate of 0.20°C per hour with a normothermia target of 37°C. Once the normal temperature is sustained for 72 hours, the ICU team may begin to assess neurologic prognosis. This protocol also outlines the inclusion and exclusion criteria for TTM eligibility that will be used and provides additional details and supportive care, including shivering management, analgesia, sedation, paralytics, baseline labs, etc., for a more standardized experience (Pravinkumar et al., 2022).

The final task prior to beginning rollout of the project to the ER and ICUs is development and execution of a staff education plan. The nurses and healthcare team members will attend in-service training sessions on proper use of the Arctic Sun equipment. The unit educators will provide instruction for management of this patient population and expectations for temperature charting and nursing assessment scales to be documented in the electronic health record.

Once the project goes live, the intervention will be applied following all new incidences of cardiac arrest that qualify, and the team can begin to collect and analyze data. Weekly meetings with staff will be held to obtain feedback on the change process, determine areas where support is needed, and make adjustments if necessary. The final phase of the project involves presenting and disseminating the results and acknowledging the staff for their role in the process. If successful, the next step would be facilitating a formal policy reform to make the practice standard of care for the hospital.

Timetable/Flowchart

The project is scheduled to be completed over a span of 14 weeks to align with the length of the Capstone course (See Appendix B: Timetable/Flowchart). This is done with the understanding that the relatively short time frame of 10 weeks allotted for data collection may not produce enough instances of cardiac arrest for the effects of the intervention to be proven statistically significant depending on the volume seen by the location. The solution for this is an extension of the length of the intervention phase for a more accurate reflection of outcomes before and after its introduction.

Data Collection Methods

The purpose of this EBP project is to increase the rates of neurologically intact hospital discharge following cardiac arrest with the use of targeted temperature management. Cerebral Performance Categories, or CPC scores, will be utilized as standardized measurement tools to evaluate the incidence of the desired outcome. A CPC score of 1 is associated with good performance (conscious, alert, able to work), 2 with moderate disability (can independently complete activities of daily living), 3 with severe disability (dependent on others for daily support), 4 with coma or vegetative state, and 5 with brain death. Therefore, a CPC score of 1 or

2 is associated with good neurological recovery while a score of 3, 4, or 5, is associated with an unfavorable recovery (Ajam, et al., 2011). CPC scores will be evaluated and documented in the EHR at the time of patient disposition from the hospital, whether that is to their home, a nursing facility, expired, etc. The patient should be rewarmed for a minimum of 72 hours before this determination is made (Dale et al., 2016).

Cost/Benefit Discussion

Much of the cost associated with the project is related to equipment: The price of one Arctic Sun 5000 system is approximately $23,500, the single-use gel pads cost between $650 and $1200 depending on the size of the patient, and machine maintenance is roughly $2,000 yearly (National Institute for Health and Care Excellence, 2017). Although the cost of the intervention slightly exceeds that of traditional treatment, targeted temperature management has shown to be a cost-effective treatment when using the ratio of quality-adjusted life years (QALY) gained to the cost of cooling procedure, hospital stay, etc. (Behringer, 2015).

Overall Discussion/Results

To determine if the intervention is effective, baseline data from the facility prior to introduction of the targeted temperature management protocol must be obtained first. This involves auditing charts of patients who experienced a non-traumatic cardiac arrest and recording their neurological status at discharge. For the next 3 months after the launch of the protocol, the same data will be collected for all new incidences of non-traumatic cardiac arrest with the use of targeted temperature management. The descriptive statistic of interest is a comparison of the mean of the CPC scores of the population groups with and without the intervention. A reduction of mean CPC scores by 0.5 points is considered a success for the project.

Since this project was completed as a benchmark, there was no data collected. However, with the help of my nursing educator, we were able to arrange for the local medical device representative for the Arctic Sun Temperature Management System to set up a station at the Critical Care Skills Fair that is required for all nurses at my current facility to attend. The representative was able to provide a presentation on how to use the equipment and encourage its use since it is already available in the hospital.

Recommendations

In alignment with best evidence and current guidelines, for adult patients who remain comatose following a non-traumatic cardiac arrest, it is recommended that targeted temperature management be implemented to improve rates of neurologically intact discharge. The next step for this project is the advancement from a benchmark to a true change project. The idea is to pilot the project at the main campus of a hospital system with the goal of eventually expanding implementation to additional facilities. To ensure that the intervention is sustained beyond the initial efforts of the project, EBP mentorship for direct care nurses and staff should be provided on the clinical units by the educators. There should be initial training on the intervention for new hires as well as a required attendance of in-service trainings at scheduled intervals throughout the year to ensure competency is maintained by all ED and ICU staff.

References

Arrich, J., Holzer, M., Havel, C., Mullner, M., & Herkner, H. (2016). Hypothermia for neuroprotection in adults after cardiolpulmonary resuscitation (Review). *Cochrane Database of Systematic Reviews, 2*(CD004128). DOI: 10.1002/14651858.CD004128.pub4

Behringer, W. (2015). Targeted temperature management: A health economic perspective. *BMC Emergency Medicine, 15*(1), A5. Doi: 10.1186/1471-227X-15-S1-A5

Bray, J. E., Stub, D., Bloom, J. E., Segan, L., Mitra, B., Smith, K., Finn, J., Bernard, S. (2017). Changing target temperature from 33°C to 36°C in the ICU management of out-of-hospital cardiac arrest: A before and after study. *Resuscitation, 113*(2017), 39-43. DOI: 10.1016/j.resuscitation.2017.01.016

Dale, C. M., Sinuff, T., Morrison, L. J., Golan, E., & Scales, D. C. (2016). Understanding early decisions to withdraw life-sustaining therapy in cardiac arrest survivors. A qualitative investigation. *Annals of the American Thoracic Society, 13*(7), 1115-1122. https://doi.org/10.1513/AnnalsATS.201511-751OC

Dankiewicz, J., Cronberg, T., Lilja, G., Jakobsen, J. C., Levin, H., Ullen, S., Rylander, C., Wise, M. P., Oddo, M., Cariou, A., Belohlavek, J., & Hovdenes, J. (2021). Hypothermia versus normothermia after out-of-hospital cardiac arrest. The *New England Journal of Medicine, 384*(24), 2283-2294. DOI: 10.1056/NEJMoa2100591

Donnino, M. W., Anderson, L. W., Berg, K. M., Reynolds, J. C., Nolan, J. P., Morely, P. T., Lang, E., Cocchi, M. N., Xanthos, T., Callaway, C. W., Soar, J., & the ILCOR ALS Task Force. (2015). Temperature management after cardiac arrest. *Circulation, 132*(25), 2448-2456. https://www.ahajournals.org/doi/10.1161/CIR.0000000000000313

Elmer, J. & Callaway, C. W. (2017). The brain after cardiac arrest. *Seminars in Neurology, 37*(1), 19-24. Doi:10.1055/s-0036-1597833.

Hifumi, T., Inoue, A., Kokubu, N., Hase, M., Yonemoto, N., Kuroda, Y., Kawakita, K, Sawano, H., Tahara, Y., Nishioka, K., Shirai. S., Hazui., H., Arimoto, H., Kashiwase, K., Kasaoka, S., Motomura, T., Yasuga, Y., Yokoyama, H., Nagao., K., & Nonogi, H. (2020). Association between rewarming duration and neurological outcome in out-of-hospital cardiac arrest patients receiving therapeutic hypothermia. *Resuscitation, 146*(2020), 170-177. DOI: 10.1016/j.resuscitation.2019.07.029

Horev, T. & Babad, Y. (2005). Healthcare reform implementation: Stakeholders and their roles-The Israeli experience. *Health Policy, 71*(1), 1-29. https://doi.org/10.1016/j.healthpol.2004.05.001

Johnson, N. J., Danielson, K. R., Counts, C. R., Ruark, K., Scruggs, S., Hough, C. L., Maynard, Sayre, M. R., Carlbom, D. J. (2020). Targeted temperature management at 33 versus 36 degrees: A retrospective cohort study. *Critical Care Medicine, 48*(3), 362-369. Doi: 10.1097/CCM.0000000000004159.

Kirkegaard, H., Soreide, E., de Haas, I., Pettila, V., Taccone, F. S., Arus, U., Storm, C., Hassager, C., Nielsen, J. F., Sorenson, C. A., Ilkjaer, S., Jeppesen, A. N., Grejs, A. M., Valdemar-Duez, C. H., Hjort, J., Larsen, A. I., Toome, V., Tiainen, M., Hastbacka, J., … & Skrifvars, M. B. (2017). Targeted temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: A randomized clinical trial. *Journal of the American Medical Association, 318*(4), 341-350. Doi: 10.1001/jama.2017.8978.

Larsson, I., Wallin, E., Rubertsson, S., & Kristoferzon, M. (2012). Relatives' experiences during

the next of kin's hospital stay after surviving cardiac arrest and therapeutic hypothermia. *European Journal of Cardiovascular Nursing, 12,* (4), 353-359. DOI:10.1177/1474515112459618

Lascarrou, J. B., Merdji, H., Gouge, A. L., Colin, G., Grillet, G., Girardie, P., Coupez, E., Dequin, P. F., Cariou, A., Boulain, T., Brule, N., Frat, J. P., Asfar, P., Pichon, N., Landais, M., Plantefeve, G., Quenot, J. P., Chakarian, J. C., Sirodot, M., … Reigner, J. (2019). Targeted temperature management for cardiac arrest with nonshockable rhythm. *New England Journal of Medicine, 381*, 2327-2337. DOI: 10.1056/NEJMoa1906661

Meaney, P. A., Bobrow, B. J., Mancini, M. E., Christenson, J., de Caen, A. R., Bhanji, F., Abella, B. S., Kleinman, M. E., Edelson, D. P., Berg, R. A., Aufderheide, T. P., Menon, V., & Leary, M. (2013). Cardiopulmonary resuscitation quality: Improving cardiac resuscitation outcomes both inside and outside the hospital. *Circulation, 128*, 417-435. https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000747

National Institute for Health and Care Excellence. (2017). *Arctic sun 5000 for therapeutic hypothermia after cardiac arrest.* https://www.nice.org.uk/advice/mib112/resources/arctic-sun-5000-for-therapeutic-hypothermia-after-cardiac-arrest-pdf-2285963271406789

Pravinkumar, E., Crommett, J., Garcia, W., Hauth, M., Herrington, R., Tucker, A. M., Warren, M. L., & Wilkes, C. (2022). *Post cardiac arrest targeted temperature management (TTM).* https://www.mdanderson.org/content/dam/mdanderson/documents/for-physicians/algorithms/clinical-management/clin-management-targeted-temperature-management-web-algorithm.pdf

Rout, A., Singh, S., Sarkar, S., Munawar, I., Garg, A., D'Adamo, C. R., Tantry, U. S.,

Dharmadhikari, A., & Gurbel, P. A. (2020). Meta-analysis of the usefulness of therapeutic hypothermia after cardiac arrest. *The American Journal of Cardiology, 133*, 48-53. Doi: 10.1016/j.amjcard.2020.07.038.

Saigal, S., Sharma, J. P., Dhurwe, R., Kumar, S., & Gurjar, M. (2015). Targeted temperature management: Current evidence and practices in critical care. *Indian Journal of Critical Care Medicine, 19*(9), 537-546. https://www.ijccm.org/doi/pdf/10.4103/0972-5229.164806

Sawyer, K. N., Camp-Rogers, T. R., Kotini-Shah, P., Del Rios, M., Gossip. M. R., Moitra, V. K., Haywood, K. L., Dougherty, C. M., Lubitz, S. A., Rabinstein, A. A., Rittenberger, J. C., Callaway, C. W., Abella, B. S., Geocadin, R. G., & Kurz, M. C. (2020). Sudden cardiac arrest survivorship: A scientific statement from the American Heart Association. *Circulation, 141*(12), 654-685. https://doi.org/10.1161/CIR.0000000000000747

Schenone, A. L., Cohen, A., Patarroyo, G., Harper, L., Wang, X., Shishehbor, M. H., Menon, V., & Duggal, A. Therapeutic hypothermia after cardiac arrest: A systematic review/meta-analysis exploring the impact of expanded criteria and targeted temperature. (2016). *Resuscitation,* 108, 102-110. DOI: 10.1016/j.resuscitation.2016.07.238

Appendix A: Evaluation Table

Citation: Author, Date of Publ. & Title	Purpose of Study	Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables Studied and Their Definitions	Measurement of Major Variables	Data Analysis	Study Findings	Worth to Practice: LOE Strengths/Weaknesses Feasibility Conclusion RECOMMENDATION
Arrich. (2016). Hypothermia for neuroprotection in adults after cardiolpulmonary resuscitation.	Assess influence of therapeutic hypothermia after cardiac arrest on neurological outcome, survival and adverse events	N/A	SR CENTRAL, MEDLINE, EMBASE, CINAHL, & BIOSIS database searches	6 RCTs (1412 participants overall) Emergency medicine and intensive care, worldwide	IV1- Surface cooling methods requiring cooling pads, ice packs, water immersion IV2- Intravascular cooling with cooling catheters or simply cold fluids DV- Neurological recovery	DV- CPC scale:1 or 2 = good recovery, 3-5 = unfavorable recovery	Relative risk (95% CI)	RR 1.94 (1.18 to 3.21)	3) LOE- 1 2) Strengths: All RCTs, CPC categories well standardized and easy to measure Limitations: Heterogeneity at the study level 3) Recommendations: TTM initiated in ED. Patient body temperature should be lowered to 32-34C using conventional cooling methods including cooling pads, ice packs, and cold IV fluids.
Lascarrou. (2019). Targeted temperature management for cardiac arrest with nonshockable rhythm.	Assess whether moderate therapeutic hypothermia at 33°C compared with normothermia (37°C), would improve	N/A	RCT	584 patients from 25 ICUs underwent randomization Candidates 18 years of age or	IV1- Hypothermia IV2- Normothermia (comparison) DV- Favorable neurological outcome: CPC score 1 or 2	DV-CPC scale	Percents, 95% confidence intervals, and p values	IV1- DV 10.2% had CPC score 1 or 2 IV2- DV 5.7% had CPC score 1 or 2 95% confidence interval [CI], 0.1 to 8.9; P=0.04)	1) LOE- 2 2) Strengths: Blinded-outcome-assessor, pragmatic, multi-center, randomized, controlled trial Limitations: Difference in length of TTM between invention and control groups, Substantial number of patients

Legend: CI= Confidence interval, CPC= Cerebral Performance Category, GCS= Glasgow Coma Scale, OHCA= Out-of-hospital Cardiac Arrest, RCT= Randomized Control Trial, RR= Relative Risk, TH= Therapeutic Hypothermia, TTM= Targeted Temperature Management

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	neurologic outcome in patients with coma who had been resuscitated after cardiac arrest			older and had been resuscitated cardiac arrest Eligible patients had coma: (GCS score ≤8)					had body temperatures above 38C (100.4F) following period of TTM, Patients with missing data assumed to have died 3) Recommendations: TTM ED. Patient body temperature should be lowered to 33C using conventional cooling methods including cooling pads, ice packs, and cold IV fluids
Dale. (2016). Understanding early decisions to withdraw life-sustaining therapy in cardiac arrest survivors. A qualitative investigation.	Explore clinicians' experiences and perceptions of early withdrawal of life support decisions in comatose survivors of cardiac arrest treated with TTM	Early withdrawal of life-sustaining therapy contributes to majority of deaths following cardiac arrest	Qualitative evidence	21 ICU clinicians, including 9 physicians (2 ICU directors, 5 intensivists, and 2 fellows) and 12 nurses (1 clinical nurse educator, 2 charge nurses, and 9	IV-Early withdrawal of life support DV-Clinician experiences and perceptions	N/A	Core thematic finding	High emotional burden of ICU family–team communication = early decisions to withdraw life support	1) LOE- 3 2) Strengths: Interviews conducted proximal to withdrawal of life-sustaining therapy to reduce recall bias, inclusion of participants with variable duration of professional experience, multicenter recruitment Limitations: Did not include experiences of patient surrogates, Did not address why withdrawal of life-sustaining therapy is recommended for specific patients 3) Recommendations: Healthcare team must collaborate to improve family-

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				frontline nurses)					team communication. Specialized communication training could be beneficial to the team in helping the family understand goals and timelines and, as a result, improve outcomes related to early withdrawal life support
Donnino. (2015). Temperature management after cardiac arrest.	Provide a consensus on science statement and treatment recommendations" regarding the use of induced hypothermia after cardiac arrest	N/A	SR PubMed, EMBASE, Cochrane Library database searches	Q1- 6 RCTs and 5 observational studies Q2- 7 RCTs Adults in emergency medicine and intensive care units	Q1 IV- Hypothermia Q2 IV- start time for TTM Q3 IV- length of time for TTM DV- Survival with favorable neurological/functional outcome	DV-CPC Scale	Relative risk (95% CI)	Q1- Pooled RR 0.75 (95% CI, 0.61–0.92) for mortality and 0.73 (95% CI, 0.60–0.88) for poor neurological/functional outcome at 6 months or hospital discharge Q2- Initiation of TH in the prehospital environment did not differ from no initiation of prehospital TH for poor neurological outcome (RR,	3) LOE- 1 2) Strengths: Provided search strategies for database searches CPC categories well standardized and easy to measure Limitations: Inability to blind clinicians to treatments Evidence for a specific duration of TTM is lacking 3) Recommendations: Recommend TTM for adults with cardiac arrest at a constant temperature between 32°C and 36°C for at least 24 hours Recommend against prehospital cooling with rapid infusion of large volumes of cold intravenous fluid

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								1.00; 95% CI, 0.95–1.06)	
Schenone. (2016). Therapeutic hypothermia after cardiac arrest: A systematic review/meta-analysis exploring the impact of expanded criteria and targeted temperature.	Assess performance of TTM on hospital mortality and good neurological outcome at hospital discharge within and beyond the initial criteria of the landmark trials	.N/A	SR MEDLINE, EMBASE and Cochrane Library databases	Patients 15 years or older 11 studies (3 RCTs and 8 cohort studies)	IV1- Therapuetic hypothermia IV2- normothermia (conrol) DV- survival with good neurological outcome	DV- Cerebral Performance Categories	Odds Ratio (OR) (95% CI)	OR 2.48, 95%CI, 1.91–3.22	3) LOE- 1 2) Strengths: Expanded inclusion criteria for patients included in studies; included studies that compared various target termperatures; more up-to-date clinical practice than landmark trials Limitations: Inclusion of observational cohort studies increases risk of bias 3) Recommendations: TTM implemented to include patients regardless of initial rhythm, unwitnessed arrest status, or persistent shock
Larsson. (2012). Relatives' 16xperience during the next of kin's hospital stay after surviving	Describe relatives' 16xperience during a next of kin's hospital stay after surviving a cardiac	Studies have revealed the importance of hope when a next of kin is critically ill	Qualitative Evidence	20 relatives of survivers of cardiac arrest treated with TH	IV- Cardiac arrest treated with TH DV- relatives' experiences and perceptions	N/A	Core thematic findings	3 themes are described: The first period of chaos, Feeling secure in a difficult situation, and Living in a changed existence.	3) LOE- 3 2) Strengths: Participant selection aimed at variation in demographic characterisitcs; Pilot interview performed to test interview guide and examin researchers

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cardiac arrest and therapeutic hypothermia.	arrest treated with hypothermia			1 university hospital and two general county hospitals in Sweden					Limitations: Only those who could understand and speak Swedish were included as participants; 4 interviews took place over telephone rather than face-to-face 3) Recommendations: More developed/detailed education on the cardiac arrest, the ICU stay, and the continuing care; Education on family-team communication
Johnson. (2020). Targeted temperature management at 33 versus 36 degrees: A retrospective cohort study.	Determine association between TTM goal temp of 33°C versus 36°C and neurologic outcome	N/A	Cohort study	Urban, academic, level 1 trauma center Adults with nontraumatic OHCA who received TTM	IV1- TTM 33°C IV2- TTM 36°C	DV- CPC scores	Odds ratio (OR) (95% CI)	Patients treated during the TTM 33°C period had higher odds of neurologically intact survival to hospital discharge compared with those treated during the 36°C period.	3) LOE- 3 2) Strengths- Research on optimal cooling protocol/ideal target temp Limitations- Inclusion of observational cohort studies increases risk of bias, single medical center 3) Recommendations- TTM should be implemented at 33°C
Kirkegaard. (2017). Targeted	Evaluate the optimal duration of	N/A	RCT	355 adult, unconsci	IV1- TTM 48 hrs	DV- CPC scores	Relative risk (95% CI)	TTM at 33°C for 48 hours did not significantly	3) LOE- 2

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temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: A randomized clinical trial.	TTM for better neurologic outcomes			ous patients with OHCA from 10 ICUs at 10 university hospitals in 6 European countries	IV2- TTM 24 hrs			improve 6-month neurologic outcome compared with TTM at 33°C for 24 hours.	2) Strengths- Previous studies focused on the concept of cooling and which core temperature should be targeted, but not on duration Limitations- not possible to blind the ICU staff to the treatment group; The 5% higher rate of 6-month favorable neurologic outcome in the 24 hr cooling group could represent a clinically meaningful difference. A trial to confirm or reject such a 5% absolute difference would require a much larger study 3) Recommendations- TTM should be implemented for 24-48 hours
Dankiewicz. (2021). Hypothermia versus normothermia after out-of-hospital	Assess the beneficial and harmful effects of hypothermia compared	N/A	Randomized, superiority trial	1900 adults with coma after OHCA at 61	IV1- Targeted hypothermia IV2- Targeted normothermia	DV1- Incidence of death DV2- Functional outcome	Relative risk (95% CI)	No difference in incidence of death or functional outcome at 6 months	3) LOE- 2 2) Strengths- Larger sample size than previous trials Limitations- Rankin scale used to measure outcomes rather than CPC scores used

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cardiac arrest.	with normothermia and early treatment of fever in patients after cardiac arrest			institutions in 14 countries		(modified Rankin scale)			by many studies; Inability to blind clinicians to treatments; No control group without temperature management; Concomittent care not part of protocol and left to discretion of participating hospitals 3) Recommendations- Fever is associated with worse outcomes, therefore targeted normothermia is still recommended over no temp management at all
Bray. (2017). Changing target temperature from 33°C to 36°C in the ICU management of out-of-hospital cardiac arrest: A before and after study.	Examine impact of changing target temp from 33°C to 36°C on patient outcomes	N/A	Cohort Study	OHCA patients admitted to a hospital in Melbourne, Australia Jan 2013- Aug 2015	IV1- TTM 33°C IV2- TTM 36°C	DV1- CPC Scores	Percentages, means and standard deviation p-Values	After change from TTM target of 33°C to 36°C, reported low compliance with target temperature, higher rates of fever, and a trend towards clinical worsening in patient outcomes.	3) LOE- 3 2) Strengths- consensus for each recommendation was established to ensure that care would be delivered as per guideline Limitations- single center setting, retrospective collection of data, relatively small sample size; Before & after study: post-arrest care not standardized before guideline introduced in 2012 3) Recommendations- ICUs considering changing their

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									target temp to 36◦C need to be aware that this target may be more difficult to achieve and may require more sedation and muscle-relaxant to avoid fever
Hifumi. (2020). Association between rewarming duration and neurological outcome in out-of-hospital cardiac arrest patients receiving therapeutic hypothermia.	Examine association between rewarming duration and neurological outcomes in OHCA patients who received TH	N/A	Cohort Study	OHCA patients who received TH after ROSC from 2005-2011 in 14 hospitals throughout Japan	IV- Rewarming duration after TH	DV1- CPC scores DV2- Survival proportion DV3- incidence of complications related to TH	Odds ratio (OR) (95% CI)	A longer rewarming duration was significantly associated with and was an independent predictor of favorable neurological outcomes	3) LOE- 3 2) Strengths- Few studies have evaluated rewarming reate; study included relatively large number of patients and adjusted for 12 kinds of factors Limitations- Retrospective collection of data, Each hospital had differing TTM protocols, did not examine the cooling methods 3) Recommendations- Slow rate of rewarming after TTM
Rout. (2020). Meta-analysis of the usefulness of therapeutic	Conduct an updated meta-analysis to evaluate the effect of TH in post	N/A	SR/ Meta-Analysis MEDLINE, EMBASE, &	8 RCTs with a total of 2026 patients (1025 TH &	IV- TH (32-34 °C) Control- Normothermia or temp ≥36°C	DV1- Mortality DV2- Neurological outcomes (CPC scores)	Risk ratio (RR) with 95% confidence interval (CI)	TH was associated with improved neurological outcomes in all patients sustaining cardiac arrest	3) LOE- 1 2) Strengths- Evaluates both shockable and nonshockable CA Limitations- studies differed in terms of target

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hypothermia after cardiac arrest.	cardiac arrest patients		Cochrane databases	1001 Control)				and with decreased mortality in patients with initial shockable rhythm	temperature used in the control, cooling techniques, duration of cooling and difference in time from resuscitation to initiation TH 3) Recommendations- TH (32˚C to 34˚C) after cardiac arrest

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Appendix B: Timetable/Flowchart