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Commentary and concepts

The formula for survival in resuscitation☆

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A B S T R A C T

The International Liaison Committee on Resuscitation (ILCOR) Advisory Statement on Education and Resuscitation in 2003 included a hypothetical formula – 'the formula for survival' (FfS) – whereby three interactive factors, guideline quality (science), efficient education of patient caregivers (education) and a well-functioning chain of survival at a local level (local implementation), form multiplicands in determining survival from resuscitation. In May 2006, a symposium was held to discuss the validity of the formula for survival hypothesis and to investigate the influence of each of the multiplicands on survival. This commentary combines the output from this symposium with an updated illustration of the three multiplicands in the FfS using rapid response systems (RRS) for medical science, therapeutic hypothermia (TH) for local implementation, and bystander cardiopulmonary resuscitation (CPR) for educational efficiency. International differences between hospital systems made it difficult to assign a precise value for the multiplicand medical science using RRS as an example. Using bystander CPR as an example for the multiplicand educational efficiency, it was also difficult to provide a precise value, mainly because of differences between compression-only and standard CPR. The local implementation multiplicand (exemplified by therapeutic hypothermia) is probably the easiest to improve, and is likely to have the most immediate improvement in observed survival outcome in most systems of care. Despite the noted weaknesses, we believe that the FfS will be useful as a mental framework when trying to improve resuscitation outcome in communities worldwide.

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1. Introduction

Many factors determine outcome after cardiac arrest and there is a large variation in reported survival rates.[1] Following a consensus meeting at Utstein Abbey, Norway in 1990, the first of a series of Utstein guidelines was published in 1991.[2] This established a set of common definitions for reporting out-of-hospital cardiac arrest (OHCA), enabling comparisons across communities and nations. A revised Utstein reporting format, published in 2004, attempted to clarify and simplify the required data elements for both OHCA and in-hospital cardiac arrest (IHCA).[3] By defining and using an 'Utstein comparator' (witnessed cardiac arrest of presumed cardiac cause with first monitored rhythm of ventricular fibrillation (VF)), large differences between communities in the reported survival after OHCA became apparent.[1,4] Although many key factors associated with survival have been identified,[5] a full explanation for the variability in survival rates has not been found. Differences in the quality of the local 'chain of survival'[6] may be the major factor contributing to the large worldwide survival differences.

In 2003 the International Liaison Committee on Resuscitation (ILCOR) published an Advisory Statement on Education and Resuscitation.[7] This paper described the discussions that took place during a resuscitation education symposium held at the Utstein Abbey in 2001. It included the statement that "survival rates for unexpected cardiac arrest depend not only on the quality of the education given to potential caregivers but also on the validity of treatment guidelines and a well-functioning chain of survival". The authors described a hypothetical formula – 'the formula for survival' – where three interactive factors, guideline quality (science), efficient education of patient caregivers (education) and a well-functioning chain of survival at a local level (local implementation), form multiplicands in determining survival from resuscitation (Table 1).

2. Utstein 2006 formula for survival meeting

In May 2006, a further symposium was held to discuss the validity of the formula for survival hypothesis and to investigate the influence of each of the multiplicands on survival. The symposium was again held at the Utstein Abbey. Thirty-five invited international experts participated in the symposium and a well-described Utstein rotating group format was used.[7] This enabled small group discussion to develop key pathways that were then refined by moving the groups through a series of panel discussions before the refined product was presented to all participants for consideration as a consensus viewpoint. The participants agreed that the proposed Formula for Survival (FfS) in a simpler format (Fig. 1) could constitute a valid concept worth pursuing and decided to divide the following discussion based on the four parts of the theoretical FfS equation starting with the end product-survival.

The 2005 ERC guidelines published just before the Utstein FfS meeting incorporated a new Chain of Survival (Fig. 2) with a greater focus on pre-arrest identification of patients at risk and post cardiac arrest care.[6,8] It was therefore timely to use elements from three of the rings in the Chain of Survival – rapid response systems (RRS),[9] therapeutic hypothermia (TH)[10] and bystander cardiopulmonary resuscitation (CPR),[11] – to illustrate each multiplicand of the FfS.

3. Survival

Survival after cardiac arrest can be defined in several ways. The demonstration that an intervention improves disease-specific short-term outcomes such as return of spontaneous circulation (ROSC) provides insight into the physiology of cardiac arrest and successful resuscitation and may have implications for the further evaluation of the interventions. However, most resuscitation experts place higher value on evidence of sustained improvements, and neurological outcome at 90 days has most recently been proposed as a reasonable outcome parameter for many clinical trials.[12] Good neurological outcome is generally defined as a Cerebral Performance Category (CPC) ≤ 2 or a modified Rankin scale (mRS) score of ≤ 3; both broadly representing the ability to live independently.[12]

4. Medical science

Although science is one of the three multiplicands in the FfS, it is recognised as an integral part of the other two factors: education and implementation. For many years, ILCOR has coordinated the review of science and the development of evidence-based resuscitation practice.[13] Given the nature of resuscitation, high-quality scientific evidence from randomised controlled trials (RCTs) is often difficult to obtain and in many cases generation of clinical guidelines requires extrapolation from observational studies or from animal experiments. Furthermore, science cannot be regarded as

Table 1
Components of the formula for survival.

	1. Guideline quality	2. Efficient education of patient caregivers	3. A well-functioning local chain of survival	Patient survival relative to theoretical potential (factors multiplied)
Utopia	1	1	1	=1.00
Ideal	0.9	0.9	0.9	=0.72
Attainable	0.8	0.9	0.5	=0.36
Actual	0.8	0.5	0.5	=0.20

Adapted from Chamberlain DA, et al. Resuscitation 2003; 59:11-43 with permission.

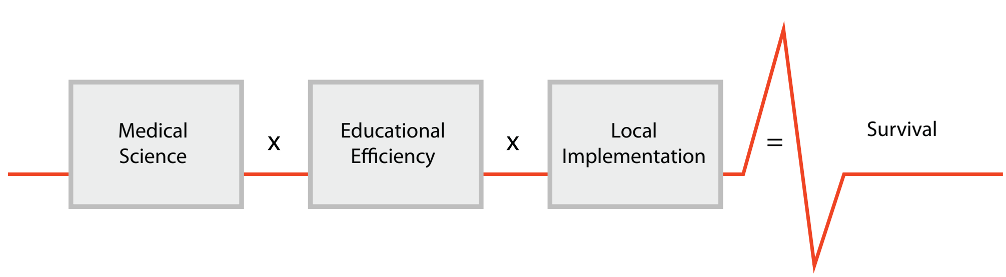

Fig. 1. The Utstein formula for survival.

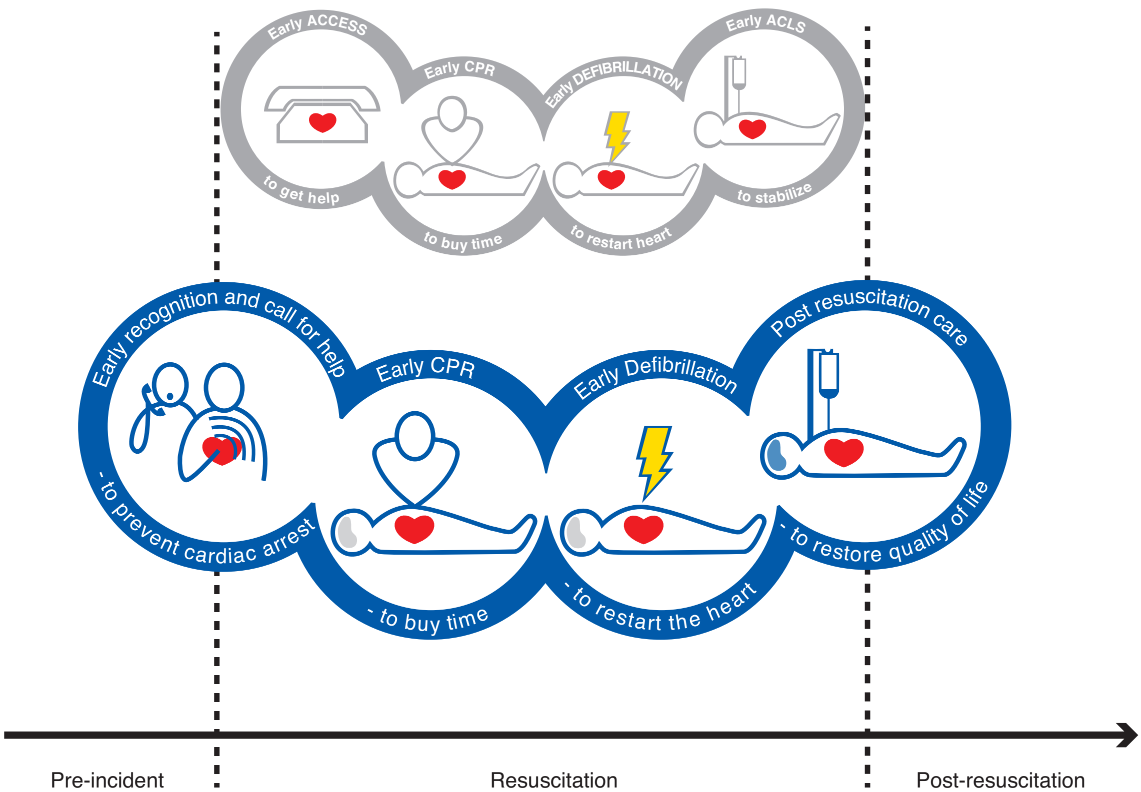

Fig. 2. The ERC chain of survival 2005 (lower illustration) compared to the 2000 version above.

evidence in isolation but should be reviewed in relation to current practice and the benefit that change would bring about. There must be a threshold ('tipping point') for a change in practice and it is recognised that this may be variable and difficult to set in some circumstances. To assist in this process it is necessary to review all evidence-based science using the following:

- Level of evidence
- Quality of evidence
- Magnitude of effect and its clinical significance
- Necessity for change – relevance to current practice
- 'Ease' (including costs) of training/implementation.

5. Educational science and efficiency

Chamberlain and Hazinski identified several critical areas for improvement in resuscitation education.[7] Just as there is a hierarchy of outcomes in resuscitation research and practice, there is a similar set of outcomes in resuscitation education (Table 2).

The expert panel recognised the difficulty in applying the same standards of evidence to educational recommendations as to treatment recommendations. However, resuscitation education designers can draw appropriate extrapolations from the vast body of adult learner literature, including psychology, human factors, engineering and other relevant fields to create learning experiences highly likely to result in acquisition and retention of skills, knowledge and attitudes needed for good performance.

Table 2
Comparison of the hierarchy of clinical versus education outcomes.

Clinical practice	Learning
Conversion of rhythm	Will they train?
ROSC	Do they learn skills?
Survival to admission	Do they retain skills?
Survival to discharge	Do they act in a real emergency?
Neurologically intact	Do they act well?
Functional status	Will they train again?

6. Local implementation

Implementation is the third multiplicand in the FfS. It was clear from the outset of the discussions that implementation based on scientific evidence was the strategy for success. The panel based the discussion on the innovation principles by Rogers.[14] In 2003, Don M. Berwick published an excellent review of Rogers classical work and described how it may help to disseminate innovations in health care.[15] The panel set out to define components that would optimise local implementation.

- Local champion and effective team to steer the process.[16,17]
- Simple protocol and an approved order set crossing all departments and disciplines involved in the care process. Make sure it is not only written but also communicated through social interaction.[15]
- Identify and target site-specific barriers to routine implementation (political, legislative, cultural or professional).[18]
- 'Buy-in' through personal, group and organisational ownership and partnership with the required resources to make it happen at the local level.
- Constant feedback based on goal-directed benchmarks, both positive and negative. Not everyone adopts innovation strategies at the same rate – typically individuals are classified into 5 categories; innovators, early adopters, early majority, late majority and laggards.[15] The same is probably true for organisations, institutions and partnerships; they will adopt at different rates. An effective implementation strategy must appeal to the majority of individuals regardless of speed of adoption to optimally effect outcome.

- Constant measuring of quality and outcome: timely summative intra- and inter-institutional benchmarking should be encouraged if it can be done in a meaningful and constructive way. Iterative (formative) evaluations should also be used and the results of these evaluations should guide local changes to improve the benchmarks and ultimately improve care. Analysis of both task and behaviour must be made in a true 'no-blame no-shame' culture if the process is to be seen to be truly iterative and helpful. To complete this process, participants should be engaged in the process and encouraged to perform research and publish their findings both in local publications, media, as well as peer-reviewed journals.

Evaluation should be qualitative and quantitative and the expert panel suggested examples of quantitative evaluation as:

- Number of treated/eligible cases including reporting ineligible patients who are treated in error.
- Number of adverse events/number of eligible cases treated.
- Number of providers using the protocol/number of eligible providers.
- Pivotal steps in the protocol accomplished for the eligible group.

7. Further development of the Utstein formula for survival 2006-2012

The 2006 Utstein FfS consensus meeting did not generate a publication immediately, but it started a process that influenced other publications that have aimed to improve resuscitation outcomes,[19] as well as the 2010 and 2015 ILCOR resuscitation consensus on science with treatment recommendation process.[20]

For the three chosen examples, RRS, TH and bystander CPR, the discussion around the impact of the three multiplicands on survival (Table 1 and Fig. 1) was complicated by several conflicting views. Implementation of RRS is accelerating globally even though the impact on outcome is controversial.[9,21] On the other hand, worldwide implementation of post cardiac arrest TH has been slow despite good supporting evidence in selected circumstances.[22–24] For bystander CPR, the focus is now on whether chest compression-only CPR is better than standard CPR.[25]

In 2012, the original participants decided to produce an updated report on the FfS concept and illustrate the three multiplicands in the FfS (Fig. 1) using RRS for medical science, bystander CPR for educational efficiency, and TH for local implementation. This approach will illustrate how the FfS concept has developed over the last 10 years.

8. Medical science

The RRS concept has now been introduced in the majority of Australasian and North American hospitals as well as in many European hospitals. While most before-after studies have found a significant effect of implementing RRS,[21] the inconclusive results of a large cluster-randomised controlled trial[9] triggered debate about the scientific merit of widespread implementation of such RRS.

The RRS concept involves the *identification* of a seriously ill or deteriorating patient followed by a *rapid response* to those patients and there are many variations on this theme. A meta-analysis of rapid response teams (RRTs) documented a 30% reduction in the rate of cardiac arrests outside the intensive care unit (ICU) among hospitals with such a system but no reduction in hospital mortality rates.[26] In contrast, a recent study from Saudi Arabia has documented a reduction in hospital mortality associated with the introduction of a RRT.[27] Studies involving RRS have led to other important and interesting findings. A seriously ill patient cannot be identified unless their vital signs are monitored, but this is done inconsistently and inaccurately in many hospitals.[9,28,29] Improving communication between the ward nurse and the involved physicians is also of key importance.[30] Use of automated vital signs monitoring should enable early identification of a greater proportion of patients at risk of cardiac arrest.[31,32] Patients not only meet the criteria when they have a potentially reversible cause but also when they are naturally coming to the end of their lives. Studies have now demonstrated that naturally dying patients are not identified by ward staff, leaving the RRT to diagnose these patients and to apply a do-not-attempt resuscitation decision.[33,34] Hence, local implementation of similar RRS based on the same international medical science will have very different impact on survival depending on the local circumstances. The local circumstances, rather than the international consensus on medical science, will also determine whether some form of RRS should be implemented.[21] Consequently, we found it difficult to attach a precise value between 0 and 1.0 for medical science (Table 1) to describe the present status for a RRT.

9. Educational efficiency

In 2006, the discussion around bystander CPR and educational efficiency was focused on how to achieve better CPR quality and how to secure higher bystander CPR rates. Recently, teaching chest compression-only CPR (without rescue breaths) has been proposed as the way of improving educational efficiency. It is easier to learn and does not involve mouth-to-mouth contact with the victim, which increases the likelihood that a bystander will attempt CPR and reduces the risk of regurgitation.[35] A manikin study showed that members of the general public were able to deliver high quality chest compressions after only a one-hour instructor-led training.[36] Because instructions to perform compression-only CPR can also be given easily by phone, chest compression-only CPR is now broadly accepted as the preferred method of dispatcher-assisted adult CPR and, based on a meta-analysis of three adult RCTs, has been shown to improve survival in many settings.[37] Chest compression-only CPR may also increase rates of bystander CPR by improving willingness thereby improving educational efficiency.[38] However, with the exception of dispatcher-assisted CPR, implementation of chest compression-only CPR has not been associated consistently with improved survival compared with standard CPR.[39–42] Since treatment of cardiac arrest from non-cardiac causes such as asphyxia, drowning, and most cardiac arrest cases in children does require rescue breaths as well as chest compressions, developing a comprehensive cost-effective CPR training strategy remains a significant challenge. Based on the present controversies we found it difficult to provide a precise value between 0 and 1.0 that represents the educational efficiency of bystander CPR. However, any increase in bystander CPR rate is directly linked to improved survival.[43–45] On this background, it is a major concern that the reported bystander CPR rates, as well as survival rates, remain low in most systems.[46]

10. Implementation

Implementation is the crucial part of changing attitudes and behaviour to ensure local processes of care changes that are maintained with high quality. Publishing clinical practice guidelines is insufficient. Changing clinical practice and maintaining high quality resuscitation practice is often as demanding as the work required to generate the medical science behind the suggested change.[47] Therefore, ensuring that the guidelines are translated into high quality clinical practice is essential if clinical outcomes are to be improved to the extent implied by the clinical trials (e.g. translation

Table 3
A worked example of the formula for survival: therapeutic hypothermia in witnessed ventricular fibrillation out-of-hospital cardiac arrest patients who remain unconscious and are admitted to the intensive care unit.

	Medical science	Educational efficiency	Local implementation rate (fraction of patients)	Number of EXTRA survivors per 100 treated
Best case	Constant A	Constant B	1.0	15
Real world	Constant A	Constant B	0.8	12
Beginners	Constant A	Constant B	0.4	6
Worst case	Constant A	Constant B	0.0	0

In this theoretical example the medical science (and thereby treatment recommendations) and educational efficiency are kept constant. The survival with no implementation of therapeutic hypothermia is set at 30% and with 100% implementation at 45%.[23,52]

of potential efficacy of an intervention in clinical trials to effective and efficient clinical care in common practice).

Change in clinical practice can be slow; for example, it took more than one year for 99% of the more than 200 EMS systems in the dedicated and funded North American Resuscitation Outcomes Consortium to implement the 2005 guidelines.[48] Delays in implementation were attributed to training (instructors and materials), defibrillator technology (software and devices) and slow uncoordinated decision-making. A report from the Netherlands indicates even longer transition time in less resourced, community settings.[49]

Therapeutic hypothermia is relatively simple to deliver, inexpensive and life-saving. Worldwide implementation has been slow despite the strength of the supporting medical science.[23,24] Even five years after the publication of the two randomised, controlled trials in 2002, only a few centres and countries had adopted this therapy.[22,50] A Canadian survey of emergency and critical care physicians reported a lack of awareness of recommended practice, a perception of poor prognosis combined with high workload and shortage of staff were the impediments to changing practice.[48] When this same target group was questioned directly they reported a lack of co-operation between physician and nurses, and between departments; disagreement with the guidelines continued to contribute to the poor universal adoption of TH in Canadian hospitals.[51]

When the early adopters reported their results, improvement in survival rates matched or were even higher than those achieved in the sentinel studies.[52] By using these data and the recent Cochrane systematic review, which documented a relative risk of 1.55 (95% confidence interval 1.22–1.96) for a good neurological outcome during the hospital stay for those patients treated with TH,[23] we could produce a theoretical FfS example for TH (Table 3). More advanced theoretical calculations have been published to illustrate the large public health problem lack of implementation of TH represents in the US.[53]

The lack of emphasis on implementation science in medicine means we may have to resort to unfamiliar strategies when trying to improve survival in our communities.[47] A focus on implementation science will translate into shortened times to implementation and effective and sustainable change in processes of care and most likely translate into more lives saved.[54]

11. Survival

Most resuscitation research scientists consider that long-term neurological outcome is the best way to describe outcome after resuscitation.[12] In many cardiac arrest survivors neurological status improves in the period between one and six months after the event.[55] Unfortunately, collecting long-term data, such as neurological outcome at 90 days, is expensive and subject to selection bias, thus a balance must be struck between that deemed ideal and that considered feasible. A recent study has shown that the CPC score at hospital discharge can be used as a surrogate measure for long-term survival.[56] Although functional outcomes, health-related quality of life, cognitive and social status among survivors are clearly important, these parameters are harder to assess and fall outside the scope of this review. A systematic review suggests that quality of life among long-term survivors of cardiac arrest is generally good.[57] Thus, survival currently stands as the anchor of the FfS equation without adjustment for functional outcome (Table 1 and Fig. 1).

The FfS is merely a concept developed by consensus and not an explicitly validated tool for explaining community differences in cardiac arrest survival. In general, clinical outcomes are influenced by definitions used, data quality, patient case-mix, clinical quality of care, but also random variation (chance).[58] Before concluding that variation in survival rates reflects a difference in quality of care, all the other factors described previously must first be checked.[59] Not all changes constitute an improvement but every improvement is instigated by a change, hence, we need to document both process and outcome data when changing complex systems like the chain of survival.

12. Conclusion

The FfS concept is an attempt to account for variability in cardiac arrest survival worldwide and provides a conceptual framework for improvement. According to this concept, improvements in one or all three multiplicands, (1) medical science (guidelines), (2) educational efficiency, and (3) local implementation (Fig. 1 and Table 3), will improve cardiac arrest survival. The FfS has been discussed as a template to improve outcomes since 2003, and we have demonstrated its strengths and weaknesses on a theoretical basis using the examples of RRS, bystander CPR and TH. Although defining a precise value for each multiplicand is often difficult, we believe that the FfS is useful as a mental framework. The local implementation multiplicand is probably the easiest to improve, and is likely to have the most immediate improvement in observed survival outcome in most systems of care. It is now time to operationalise, test, critique and further improve the FfS in every community. One way to do this is to focus on communities as a whole system of care, and involve clinicians, stakeholders and the public.[60] We must measure to improve, map to define any weakness and then strengthen any weak part of the system.[61,62] As an example, this has been done nationally by using all present knowledge to estimate the survival benefit by improving logistics of the resuscitation response.[63] The FfS may enable similar estimations of survival benefits linked to improving educational efficiency and local implementation of well-documented therapies. We think resuscitation science researchers should lead in this work by providing persuasive data for the funding agencies and authorities. Only in that way can we improve the survival prospects for future cardiac arrest victims globally.

Conflicts of interest statement

ES has received unrestricted research grant funding from the Laerdal Foundation for Acute Medicine. LJM receives salary support from the National Institute of Health to conduct clinical trials in out-of-hospital cardiac arrest. Dr Morrison has operating

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Appendix A.

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