

# ICU

## MANAGEMENT & PRACTICE

THE OFFICIAL MANAGEMENT JOURNAL OF ISICEM

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# Quality

### PLUS

Biomarkers in Heart Failure

Difficult Intubation

Emergency Intraosseous Access

Pain Assessment and Management

Dexmedetomidine, Delirium & Sleep

Early Mobilisation: From Concept to Reality

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# QUALITY

An emphasis on quality of care has always underpinned healthcare, but in recent years quality measurement has come to the fore, as countries around the world seek to provide the best outcomes for patients while facing ever-increasing healthcare costs. In intensive care, despite the heterogeneity of the patient population, great strides have been made in defining and measuring quality in order to improve organisational structures, processes and outcomes. Where perhaps quality has not been so well-defined are the areas of post-intensive care and end-of-life care in the intensive care unit. In intensive care we are well aware of the limitations of randomised controlled trials, and the quote from Richard Payne, professor of medicine and divinity at Duke University, is apposite. Do patients and families' views about quality of care differ from those of clinicians and how can these be reconciled? Are improved survival rates for intensive care patients reflected in long-term consideration of quality outcomes in the healthcare continuum of care?

▲▲ A definition of "high-quality" medical care is too narrow when it relies only on empirical evidence gathered by randomized controlled clinical trials ▲▲  
(Payne 2009)

Our cover story considers aspects of quality in the individual ICU as well as intensive care medicine as a whole. First, Bertrand Guidet explores what quality means in intensive care practice. He argues that intensivists need to change to a patient-centred perspective, which requires a global integrative approach to quality. Next, Hans Flaatten explains the variety of national quality indicators for intensive care, and how they may help improve quality of care. Last, Sten M. Walther explains the role of intensive care registries in quality management and how they can support individual intensive care units in their quality improvement programmes.

Our 2016 Series on biomarkers concludes with an article by Jason M. Duran and colleagues on biomarkers for heart failure. They review two of the most commonly used cardiac biomarkers in the treatment of heart failure:

the natriuretic peptides (NPs) and troponins, and discuss two novel biomarkers, ST2 and procalcitonin.

In the Matrix section, Audrey de Jong and colleagues describe a new tool to better identify patients at high risk for difficult intubation, and outline new strategies for improving preoxygenation before intubation and decreasing difficult intubation incidence. Mats Eriksson and colleagues explore the potential of intraosseous access in diagnostics and therapy using point-of-care technology, drawing on their research in porcine models. Kathleen Puntillo reviews recent advances in pain assessment and management in the ICU, advising that clinicians consider multimodal analgesia techniques. Xian Su and Dong-Xin Wang explore the evidence on sleep disturbances, delirium and the effects of dexmedetomidine in ICU patients. Jean-Michel Constantin considers the barriers and challenges to making early mobilisation of ICU patients a reality. Put simply, when healthcare staff say that it is too difficult, they should consider early mobilisation as a quality-of-care assessment tool, he suggests.

In the Management section we continue our series on ICU team roles with an article by Dorothy Wade and David Howell about psychologists in critical care, who can provide interventions for patients, families and staff to manage intensive care-related stress during the ICU stay as well as in follow up. Next, Clarence Chant and Norman F. Dewhurst explore the advantages of having a clinical pharmacist in the ICU, and provide sound advice on putting the business case forward. Ruth Endacott reflects on the broader view of social media in intensive care, which may be considered a blessing or a curse but should be managed, she argues. Last, a preview of a new course we are running in Brussels in January 2017, on ICU Leadership.

Clinical trials on renal replacement therapy are illuminating further the question of when to initiate therapy, and Eric Hoste provides his take on recent and ongoing trials in this issue's Interview.

Our Country Focus is the UK, and Brexit in particular. Rachel Clarke writes from the heart about how it felt when the news broke the day after the referendum, in a health service where many staff are from outside the UK.

As always, if you would like to get in touch, please email [JLvincent@icu-management.org](mailto:JLvincent@icu-management.org)

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## Reference

Payne R (2009) The quality mantra: proceed carefully. *Hastings Cent Rep*, 39(6): 14-5.



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## PATIENT HANDOFF PROTOCOLS



Joseph Keebler

Whether they are called handoffs or handovers, it is known from the literature that the transfer of patient information between caregivers at shift changes has the potential for error. Although the U.S. Joint Commission requires healthcare providers to implement a standardised approach to handoff communication as a national patient safety goal, clear instructions and evidence on effective protocols are still being worked on. A recently published meta-analysis of studies on handoff protocols set out to evaluate the patient, healthcare provider and organisational outcomes of the various protocols that have been developed and studied, as

well as the content of handoff information. Joseph Keebler, PhD, Assistant Professor of Human Factors, Embry-Riddle Aeronautical University, and colleagues, included in their analysis 36 studies, which met the criteria of implementation in a live setting with comparison of pre- and post-intervention. The study is published in *Human Factors*.

### Results

The researchers found that protocols that include 12 or more pieces of information (e.g., allergies, chief complaint, current medications) resulted in more details being passed to caregivers coming on shift compared to items using 11 or fewer items. In an email to *ICU Management & Practice*, Keebler explained that their moderation analysis of the longer protocols found an effect only with the amount of information passed and these really showed this effect, because some include 50+ items. Their analysis also showed that using handoff protocols had positive effects on patient outcomes (e.g. decreasing number of complications) and on organisational outcomes (e.g. increased pre-planning).

There were 34 negative effects of using protocols. Twelve of the negative effects were errors from lack of information or omission, and nine related to delays or duration of

handovers. The researchers note that introducing a protocol can sometimes lead caregivers to pass on only information in the protocol and miss out other valuable information.

The researchers write that “it appears that using any protocol is better than using nothing at all”, and observe that protocols may serve as a foundation for building shared mental models between providers, and that this structured communication facilitates better outcomes. They provide recommendations to reduce an apparent publication bias in the field, as they found that studies with null findings are not being published. They add that in future studies it is important to include the implementation details of handoff protocol interventions. They recommend that randomised placebo control designs are used where applicable. Keebler explained that while this design is hard to implement it would really improve the ability to say that protocols cause positive changes. ■

### Reference

Keebler JR, Lazzara EH, Patzer BS et al. (2016) Meta-analyses of the effects of standardized handoff protocols on patient, provider, and organizational outcomes. *Human Factors*, 58(8): 1187-1205. Published online before print October 17. <https://iii.hm/6vs>



## NEW RESOURCE FOR CHILDREN

An activity book for children visiting intensive care units (ICUs) has been published by ICUsteps, the UK intensive care patient and relative support charity. The resource comes with an information sheet for parents and carers to help them support the child. Printed copies are available free to UK hospitals, and it can be downloaded from the ICUsteps website (<https://iii.hm/6vr>).

Catherine White, Information Manager, ICUsteps, who developed the resource, said: “My son was three years old when I was critically ill. It is a tribute to my family that in all the uncertainty and distress, they

kept his needs and emotional wellbeing centre stage—to this day, I don’t know how they managed to do that, but I do know how hard it was for them. I wanted to give other families a helping hand—to do the thinking and preparation on their behalf, so when in that situation, there are ready made resources to help them support their children.”

The activity book helps introduce children to ICUs with pictures and explanations. It has activities to help them understand what ICUs do, what they might see when they visit one and space to write about how they feel. ■





## EDITORIAL BOARD WELCOMES NEW MEMBER



Flavia Machado

Prof. Flavia Machado has recently been welcomed to the Editorial Board of *ICU Management & Practice* by Editor-in-Chief, Prof. Jean-Louis Vincent. Dr. Machado is Professor of Intensive Care and head of the Intensive Care Section of the Anesthesiology, Pain and Intensive Care Department at the Federal University of São Paulo in São Paulo, Brazil. She is one of the founders of the Latin America Sepsis Institute (LASI), which is devoted to quality improvement process in Brazilian hospitals as well as to the coordination of multicentre studies in the field of sepsis.

Dr. Machado was president of LASI between 2008-2011 and vice president between 2012-2015. She is currently its CEO. She is on the executive board of the Global Sepsis Alliance and the executive committee for the World Sepsis Day. She served on the 2012 Surviving Sepsis Campaign International Guidelines committee and is in the 2016 committee. She integrates the International Sepsis Forum (ISF) council since 2014. She is also a member of the Executive Committee and the Scientific Committee of the Brazilian Research in Intensive Care Network - BRICNET.

Dr. Machado is well published in the fields of sepsis and haemodynamics. Her research focuses primarily on improving the care and outcomes of critically ill patients with sepsis as well as on the quality improvement process. She has lectured at scientific congresses nationally and internationally and is also an author or co-author of numerous invited book chapters as well as an editor of critical care books. She has received multiple grants from the São Paulo State Research Foundation. She is a member of many medical societies, including the Brazilian Critical Care Society, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine. Dr. Machado is the former editor-in-chief of *Revista Brasileira de Terapia Intensiva*, the official journal of the Brazilian Critical Care Association and the Portuguese Critical Care Association (2010 to 2015). ■

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1. Bouadma L et al. *Lancet* 2010, 375 (9713): 463-474 2. Schuetz P et al. *Expert Rev Anti Infect Ther* 2010, 8 (5): 575-87.  
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# QUALITY IN PRACTICE

## TOWARDS A PATIENT-CENTRED VIEW

Professor Guidet has been a university medical professor since 1997. He is a member of the research unit INSERM U1136 at the National Institute for Health and Medical Research (INSERM), the French public organisation entirely dedicated to biological, medical and public health research.

Guidet is past President (2008 – 2010) of the French Society for Intensive Care and is currently a member of the Health Research and Services outcome section of the European Society of Intensive Care Medicine (ESICM). He has written more than 250 articles published in international journals.

### What does quality of care mean in an intensive care unit?

When we speak of quality it means that we manage the patient as a whole, including not only the technical aspects, but also communication, comfort and so on, working with the intensive care team. We need to change our perspective to a patient-centred perspective, and consider not only the disease of the patient, but also plan a global integrative approach.

### Does this global integrative approach happen enough now?

Intensive care units (ICUs) have been very much oriented on techniques and procedures, but we need to consider other aspects of patient care besides technical skills. We need to work on people management and their importance in the care of the patient. It is a kind of transition from cure to care. We have to take care of the patient as a whole person, including the families and relatives.

### Who should set quality indicators? Is accreditation or standardisation helpful?

The European Society of Intensive Care Medicine (ESICM) has published a paper on quality indicators (Rhodes et al. 2012). We came up with 9 indicators: on structure (e.g., to be recognised as an intensive care unit, you need minimum criteria in terms of number of beds, equipment); on process, for example, if an ICU has a sedation protocol; and outcome indicators. We recommend that ICUs look at mortality and adjusted mortality, taking into account the severity of the patient and co-morbidities. Self-extubation rate is also an indicator, as it suggests that there may be a problem with the sedation or the weaning process. The ESICM Working Group on Quality Improvement also published a paper on minimal requirements for ICUs that sets out minimum criteria, such as the number of nurses needed according to the severity of the patient (Valentin

et al. 2011). In France we require authorisation to run an ICU: we have national criteria and these are much the same, with structure, process and outcomes criteria (Décret n°2002-465).

We published a review paper showing that in most situations in ICUs there is a relationship between volume and outcome: the more you are doing the procedure the better the outcome (Nguyen et al. 2015). This is proven for many patients, such as patients suffering from shock, acute respiratory failure or polytraumatism. If we want to deliver high-quality care, we need to work in an ICU with a high volume of activity. You cannot perform good quality of care, for example with mechanical ventilation, if you treat fewer than 80 patients every year. We realised that we need to rationalise intensive care and to merge some ICUs. On the one hand we don't want to reduce too much the number of ICUs. However, if we want to keep all ICUs open, the quality of care in the small ICUs will be sub-optimal.

### Is it a requirement that ICUs in France follow these standards?

Yes. In France we have the definition of ICUs in terms of the minimum number of beds, i.e. 8 beds (Décret n°2002-465). We are working with the Ministry of Health to maybe increase the minimum number of beds to 10 or even 12. Second we need to have intermediate care units working together with the ICUs with a minimum number of beds, i.e. half the number of ICU beds and with an appropriate nurse-patient ratio. So we have criteria to define an ICU and then the team to work in the ICU. As a consequence some ICUs were transformed into intermediate care units. So in several small hospitals, there is no

ICU but only an intermediate care unit with a network organisation enabling transfer to the referring ICU.

### And that process has gone smoothly?

Yes, because we are facing two problems. First, an ICU physician shortage. In some regions of France, it is very difficult to attract ICU physicians in public hospitals. Second, you need the whole environment around the ICU. In hospitals if you want to have an ICU, you need to have an anaesthesia department, emergency room, radiology department and so on. For some hospitals it is difficult, because if they have to close the ICU, it is a challenge for the whole hospital. We have sometimes to struggle with the mayor of the city, because they don't want to close their hospital, and if the ICU is closed many activities might be jeopardised.

### Patients' and families' views of what constitutes quality care may be quite different from the views of intensivists. How can their views be taken into consideration?

In some countries ICUs have organised long-term multidisciplinary follow up of patients. We are new to this assessment of patients a few months after their discharge from the ICU. The main information emanating from this consultation is that people suffered from pain, discomfort, noise, lights, lack of information and so on. So now we have information on the improvements we can introduce during the ICU stay. For example, we should work on the problem of sleep deprivation, we should try to avoid unnecessary noise, we have to work on the alarms, to try to reduce the

numbers of alarms, to reduce noise generated by all types of alarms (e.g. monitoring system, respiratory system, infusion pump, nutrition equipment, bed). The number of devices that have alarms and so produce noise is enormous. We need to recognise that we are antagonising the patient with a lot of noise. We should try to work together to reduce the noise.

Also we need to work on the way we are explaining to the patient their disease, the procedures we perform, and work on communication with the family. We need to work on communication skills, since we work in different shifts on the ICU. The way people communicate information and handover procedures is very important. Again this is quite new, because we are handling a lot of information and we want to make sure that important information is not lost. In this new paradigm we need to work differently in the ICU and the answer is the team. This is not just the doctor's, the nurse's, the helper's or the physiotherapist's business, this is the business of the whole team (Guidet and González-Romá V 2011).

### How can ICU leaders avoid quality becoming just a tickbox exercise?

I think it is not a tick box; it is not work that you have to do in parallel with your daily work, it is integrated in your work and we need to consider the patient perception of the ICU stay. We need to circulate satisfaction questionnaires and to get feedback from the patients and the family. We can learn a lot from this. Sometimes we don't consider easy things that for us are little things but for patients are very important. My position is that quality is part of our work; quality assessment is not 'another thing'. It is part of our duty on a daily basis. We need to collect indicators that are able to help in the improvement of the whole process.

### Do you have examples from your own ICU of such an improvement that was "little" to the ICU but very important to patients and their families?

An example is the policy for visiting hours in the ICU. It used to be only two hours a day and now it is the whole afternoon and evening. We are thinking of opening visiting hours to all day long. This is already the case in some French ICUs and also around the world. When you ask the patient and the family about satisfaction, they think this is much better.

We are also working with patients and families on the way we handle interviews. The way we

have conversations together with the family is different now. The way I am handling things in conversation is different—we need to sit, we need to have time, shut down the phone and we need to listen to the relatives. The way we are communicating within the ICU team, between the head nurse and the nurses and also between the team and the patient's family members is very important.

### Is it as important to measure processes as outcomes when assessing the quality of intensive care?

The problem with collecting information about processes is to make sure that by improving the process we will ultimately improve the outcome. For example, if you had a procedure to avoid central venous catheter bloodstream-related infections, we have learned from the literature that if you apply some simple rules you will have an impact on those infections. So we need to have a protocol for insertion and catheter use. Another example is that if we don't have a weaning protocol it carries the risk of the patient receiving mechanical ventilation for a long duration, and if we don't have a weaning protocol we probably have no sedation protocol. It means that those protocols are not appropriate, are not used by the nurses and we know that nurses at the bedside are much more optimal than the doctors. So we want to make sure that these protocols are used and run by the nurses. So we start with the weaning protocol and if we use the weaning protocol then we will see what is in the weaning protocol, so the patients that should be weaned are on low sedation. This type of approach is an integrative approach.

### Are there sufficient quality tools for intensive care?

Yes, we have enough tools. The issue is to prioritise our working patterns, because it is difficult to handle everything in the ICU. Again I like to emphasise the importance of the team (Guidet and González-Romá). The different people in the team should be in charge of different aspects of patient care according to their expertise. For example, we have a problem dealing with end-of-life decisions. Everybody needs to play a role in the end-of-life decision making process. We need to make sure that the process is patient-centred, as in most cases the patient is unable to communicate, so we need to work with the family members. We need to work with the whole team and to get the opinion of the nurses, the physicians and the family. I think it is a good

example of how we need to work together, it is not only the physician's or the nurse's business. Many different studies indicate that in more than 50% of deaths occurring in the ICU there were end-of-life discussions prior to death (Joynt et al. 2015). This is good routine and we have tools, we know how to adjust expressions, but we have to do it collectively, as sometimes nurses are not very happy as they are not allowed to do what they are supposed to do.

### It is often said that not enough negative trials are published. Could the same be said about research into improving quality of intensive care?

My point is it that we should work on organisation and make sure that everybody is pushing in the right direction. These studies are pretty difficult to conduct, because of the involvement of families and sometimes the approach to publishing, funding and the design is difficult. Just to give you an example, in a multicentre randomised study looking at ICU admission we cannot randomise at the patient level, we need to randomise at the unit level, using a cluster design (Boumendil et al. 2016). We need to work on this type of study. We will improve the outcome of the patient, if we look at the organisation of the ICU, the admission process, the care of the patient, the discharge decision, location. I think the perspective should not be ICU-centred; the perspective should be at the hospital level, and how the hospital together with the ICU take care of critically ill patients. This will include the triage process (Guidet et al. 2013), decisions during the ICU stay, end-of-life decisions (Joynt et al. 2015), discharge policy (Guidet and Bion 2014), readmission policy, as well as the way we manage information between the ward and the ICU, the medical emergency team and so on. So we need to look at the ICU as part of the hospital, not on its own, we need to look at the pathway in the hospital and the way we work in the emergency department and the ICU. How can this information be used to create better outcomes? If we want to improve the outcome of the patient, we need to work maybe in another way, for example using sepsis care bundles in the emergency department, it's not only ICU business. How to make sure the patient gets the right treatment as soon as possible is certainly relevant. ■

For full references, please email [editorial@icu-management.org](mailto:editorial@icu-management.org), visit [icu-management.org](http://icu-management.org) or use the article QR code.

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# NATIONAL ICU QUALITY INDICATORS REVISITED

The last two decades have seen an accelerated interest in quality management in healthcare in general, and also in intensive care specifically. Often safety has been the main issue, but increasingly a more general approach to quality has emerged, in particular with a focus on quality indicators (QI).

It is now more than 15 years since Pronovost and co-workers approached this area systematically and published a list (Table 1) of what they considered to be core QI for intensive care (Pronovost et al. 2001). Later fundamental work in this area was followed up in the Netherlands, which resulted in the publication of the development of QI for Dutch intensive care units (ICUs) in 2007 (de Vos et al. 2007). Spain (2006) and Sweden (2006) were out early with web publication of their lists of QI for intensive care.

In 2012 the European Society of Intensive Care Medicine (ESICM) published the development of what they considered to be 9 core QI for Intensive care (Rhodes et al. 2012); also shown in Table 1. Apparently the views on what are considered important QI have changed over time, and only two of the total 27 QI are the same: standardised mortality ratio (SMR) and blood-borne infections (BBI). This is an interesting observation, and demonstrates that what was considered important in the first place is not necessarily perceived the same way at a later stage.

## Indicator or Standard?

These terms are often used interchangeably, but do they reflect the same content? In the Quality Assurance “bible” Avedis Donabedian in fact does not discuss the term indicator, and in particular not the Quality Indicator (Donabedian 2003). He defined criteria and standards, the latter defined as “a specified quantitative measure of magnitude or frequency that specifies what is good or less so”. In most ways this is what we today perceive as a QI. On the other hand, the

UK’s National Institute for Health and Care Excellence (NICE) has somewhat different definitions: a quality standard is a statement to help improve quality, and an indicator is a measure of outcomes that reflect the quality of care, or process linked, by evidence, to improved outcome (NICE n.d.).

Today, most countries actively using QI prefer Donabedian’s method to assess clinical performance, and hence use three different classes of QI:

1. Structure
2. Process
3. Outcome

The **structure** QI is very similar to what other organisations may refer to as standards: either you fulfil it or not. An example: An ICU must have a system for reporting adverse events: Yes or No.

The **process** QI includes treatment, diag-

Table 1. QI from Pronovost and ESICM

Quality Indicator	Pronovost (2001)	ESICM (2012)
<b>SMR</b>	<b>X</b>	<b>X</b>
Patient/family satisfaction	X	
Ventilator-associated pneumonia	X	
ICU readmission rate	X	
<b>Central venous line infection</b>	<b>X</b>	<b>X</b>
ICU LOS	X	
Monitoring of sedation	X	
Monitoring of analgesia	X	
Duration of MV	X	
Multiresistant bacteria in the ICU	X	
Occurrence of thromboembolism	X	
Inappropriate RBC transfusion	X	
Ulcer prophylaxis during MV	X	
Delayed ICU discharge	X	
ICU LOS ≥ 7 days	X	
Delayed ICU admissions	X	
ED bypass hours	X	
Cancelled surgery	X	
ICU fulfils national requirements		X
24-h consultant level intensivist		X
Adverse event reporting system		X
Multidisciplinary rounds		X
Standardised handover		X
ICU readmission (< 48h)		X
Rate of unplanned extubations		X

ED emergency department ICU intensive care unit LOS length of stay MV mechanical ventilation RBC red blood cell

noses, prevention etc. and is often given as a percentage. An example: The time for start of antibiotic therapy should be < 1 hour in more than 90% of cases with suspected sepsis.

The **outcome** QI describes real results like various changes in health status. An example: The SMR should be less than 0.8.

### Status in Europe

Use of QI at a national level (NQI) has increased, and in Europe at least 9 countries today have published their list of ICU QI either on web or in a formal publication.

In 2012 the author conducted a search about the current use of NQI in Europe (Flaatten 2012), and the present update was performed in order to reveal further development in the field with the main focus on Europe, and with particular attention to documented results of use of NQI. Two more countries have since the publication established intensive care medicine as a primary speciality: UK and Ireland, and it was of particular interest to see if this major initiative had resulted in new or revised quality indicators.

The updated list is shown in **Table 2**, where the year of last revision is given. Ten countries (7 from Europe) had published their list of QI either as a publication or on the web. Three more have by personal communication given data. The number of outcome QI and if the QI includes patient-reported outcome measures (PROM) and if data on QI are published openly are also given.

Some national health services now require their healthcare providers to report back PROM

**Table 2.** National Quality Indicators Overview

Country	Last update (year)	Number of QI	Outcome QI	PROM	Open access to results
Norway	2013	7	3	0	Yes
Sweden	2013	8	2	0	Yes
Germany	2013	10	1?	0	No
Scotland	2015	17	4	1?	Yes
Netherlands	2007	11	3	1?	Yes
Denmark	2013	8	2	0	Yes
Spain	2011	20 (core)	6	1	No
Austria	2008	14	5	0	No
Canada	2015	22	4	1	No
AUS/NZ <sup>1</sup>	2010	16	NA	NA	No
India	2009	17	2	1	No
Ireland <sup>2</sup>	2011	24	NA	NA	No
UK <sup>3</sup>	2013	57	NA	NA	No

1. Named Intensive care indicators

2. Core standards for ICU

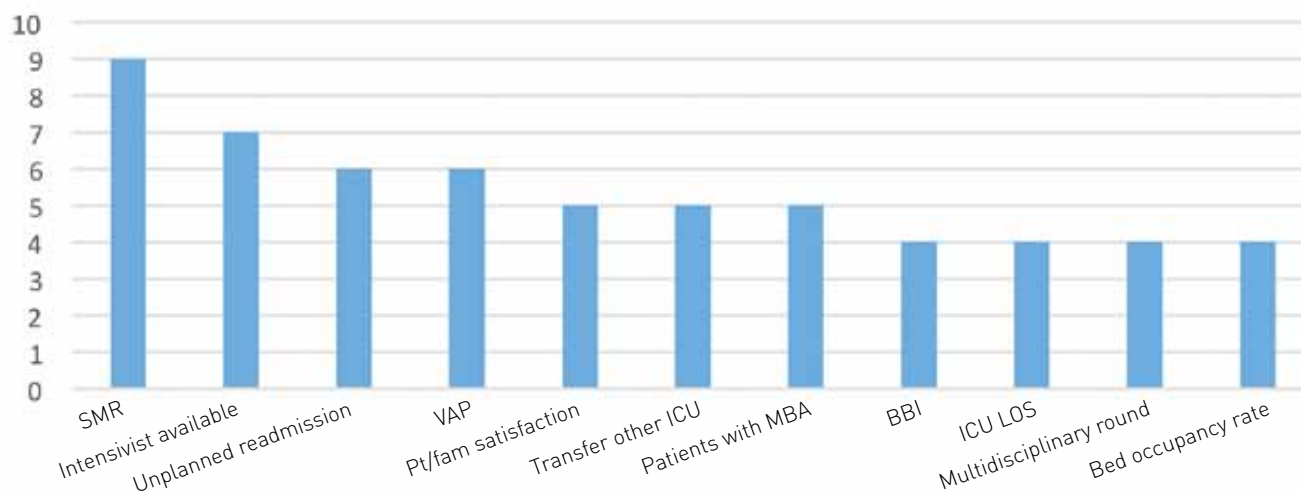
3. National Standards/priority areas for Intensive Care

in various areas of healthcare. This is now mandatory in Norway, and was introduced in the English National Health Service in 2009 with yearly publications of results (National Health Service 2015). Open access to results, also down to the level of individual hospitals, has been a demand in many northern European countries. The argument has been: since healthcare is publicly funded (by tax) the public has a right to know the results.

At present, the UK NICE has no specific standards or indicators published for intensive care, but the Faculty of Intensive Care Medicine

(UK) with a number of other relevant UK societies has published core standards for ICUs, which they all require their ICUs to comply to (Faculty of Intensive Care Medicine 2015). Many of these standards are what are called process or structure quality indicators, so the difference is in reality not large. Ireland has a similar system with its *National Standards for Adult Critical Care*, a less comprehensive list but similar in structure to the UK (Joint Faculty of Intensive Care Medicine of Ireland 2015). At present neither country has introduced formal QI as in other European countries.

### Most frequently used QI (10 countries)



**Figure 1**

These standards are organised differently from ordinary QI and are included in Table 2 for the reason of completeness.

It is interesting to see that there seems to be a great diversity in regards to what QI are chosen by individual countries. None are common for all: the ones used by most are the SMR (9/10) and the availability of an intensivist in the ICU (7/10). Most QI are only used by 1-2 countries. Figure 1 shows the QI used by more than 4/10 countries. The results may indicate that more countries have started to use indicators or standards to measure the quality of their healthcare and also intensive care. However, still many countries in Europe do not have such a system in place. The reasons for this are probably multifactorial. They may in fact have a system, although it was not detected/documentated by this search (if so please contact the author). There may in addition be a language barrier for this; the Norwegian Intensive Care registry only documents on the web in Norwegian, which of course is

a problem to access for non Norwegians. Another reason may be a high fraction of private healthcare in a country, which of course would make introduction of such bench-marking more demanding. The last could be cultural, with laws and regulations making such data difficult to retrieve and probably publish.

## the quality circle: Plan, Do, Evaluate, Change can be put into action

### Conclusion/Future

The use of QI at a national level is a suitable method to focus on quality in healthcare. Independently of public access to the results, a local or national ICU network will have a lot to gain from engaging in the process of first

finding and defining QI and later retrieval of data. This can also be used in a more stringent way by benchmarking, but even without such formal listing, comparable units will immediately spot if they are deviating from the mainstream. Those units with particularly good results can be approached in order that others can learn from their experience. Using national QI in this way, the quality circle: Plan, Do, Evaluate, Change can be put into action, and hopefully contribute to improved healthcare. ■

### Abbreviations

BBi blood-borne infections  
ICU intensive care unit  
LOS length of stay  
QI quality indicators  
SMR standardised mortality ratio  
VAP ventilator-associated pneumonia

For full references, please email [editorial@icu-management.org](mailto:editorial@icu-management.org), visit [icu-management.org](http://icu-management.org) or use the article QR code.

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# QUALITY MANAGEMENT

## THE ROLE OF INTENSIVE CARE REGISTRIES

To initiate, maintain and advance a quality improvement programme in your intensive care unit consumes large amounts of time and energy. There are many advantages for quality management in joining an intensive care registry; the most important is access to precisely defined data for comparative audit.

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### Intensive Care Registries

Joint collection of information about intensive care patients, their treatment and outcomes began in the 1950s with the aim of communicating and exchanging experiences (Norlander et al. 1961). From these early attempts several initiatives to collect and analyse comprehensive sets of information from a large number of intensive care units (ICUs) emerged, with a focus initially to document and learn from daily practice. Registries then developed from collecting data from discharged patients' charts to collect more reliable data that were defined in advance. The relevance of registries grew by moving from information that was accumulated at the ICU level to individual patient-level data. While sketchy data that characterised ICUs by describing levels of activity (i.e. number of admissions, length of stay, workload etc.) were useful at the start, registries holding detailed individualised information on consecutive patients (i.e. characteristics, diseases, interventions, outcomes) for long periods of time became powerful tools, which generated important observations from the 'real world' (Goldfrad and Rowan 2000). Over the years the scope of registries has expanded and the current agenda of many include issues of performance and accountability, often in partnerships with national intensive care societies or similar professional bodies with the general purpose to improve intensive care quality (for a collection of registries see [icuregsw.org/registries](http://icuregsw.org/registries)).

### Intensive Care Quality

A commonly applied framework to define intensive care quality uses five domains ([www.qualitymeasures.ahrq.gov](http://www.qualitymeasures.ahrq.gov)). These are the classical three domains of the Donabedian model (structure, process and outcome) (Donabedian

1978) and two additional domains: access to intensive care and patient experience. Structure indicators represent organisation, resources and equipment; process indicators are about the process of care between caregiver and patient, what we do or fail to do for patients and their families; and outcome indicators represents the results that we achieve at the patient level. Access to intensive care is the ability to provide

■ ■ **The most important undertaking of a registry is to support collection of precisely defined data from a group of ICUs** ■ ■

timely and appropriate care. Patient experience in the context of intensive care may not only include patients' experiences but also include family members' observations. The structure, process, access and experience domains must be linked to a clinically relevant set of outcomes. Collectively they determine the value of intensive care, since value may be defined as a given outcome divided by the cost associated with the particular outcome. This relationship provides a link between quality and value of care (Murphy et al. 2015).

### Management of Intensive Care Quality

Goodwill and enthusiasm of bedside physicians and nurses are important but not sufficient for improvement of intensive care quality. ICU directors and leaders who foster and enhance professional collaboration, authentic communication and transparent governance are instrumental for effective teamwork and delivery of high

quality care. Numerous practices and tools that improve intensive care have been described, some operational in the ICU microsystem (close to the patient) others at the organisational level (Guidet et al. 2016). *The critical first step to most approaches is measurement.* However, as Deming pointed out, collecting a profusion of figures and turning out volumes of records is not quality management (Deming 1972). Measurements, commonly used to construct quality indicators, must fit into an ICU quality improvement programme with the purpose of helping us understand, control and improve the processes and systems within which we work. A good quality measure must be important, valid, reliable, responsive, interpretable and feasible (Curtis et al. 2006). The relative emphasis of these properties may vary across cultural and medical contexts, as suggested by the differing choices and priorities of quality indicators among countries and between individuals (Flaatten 2012; Rhodes et al. 2012).

### How Can Registries Support Quality Management?

Initiating, maintaining or advancing a local improvement programme consumes large amounts of time and energy. Joining an intensive care registry reduces the burden for an ICU and is associated with a number of important advantages. The efforts that are needed to educate staff, identify targets for improvement, select appropriate metrics, acquire necessary data, and analyse the data may be shared with other ICUs within the registry. This can be done without abandoning local priorities; it may instead stimulate local quality improvement work.

A few areas wherein participation in a registry may be particularly helpful are discussed briefly below and outlined in **Table 1**.



### Data for Comparison

The need for quality improvement in your ICU is best understood if there are data available about comparative performance (Figure 1). Hence the most important undertaking of a registry is to support collection of precisely defined data from a group of ICUs. The hard work that is needed to establish routines and methods in an ICU for timely and sustainable data collection is often underestimated. Many registries offer a kick start by giving help to create an infrastructure for viable data collection for newcomers; this is useful to increase the chances of success.

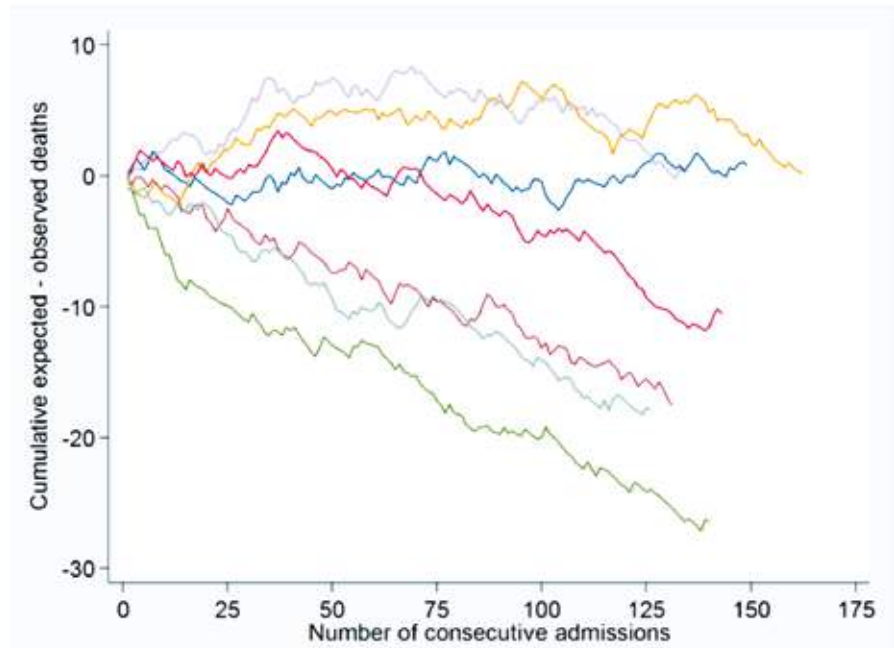
### Data Selection and Definitions

Intensive care is at an advantage in that it is an environment rich in data and has a quite common and clearly defined principal outcome measure (death). An important role of registries is to harmonise selection of variables. However, data collection, whether for use locally or within a registry, must be selected to fit into a carefully considered plan for quality improvement. The recording of information without a specific purpose may otherwise lead to poor data quality and registration fatigue. If there is a need for more extensive recording, the basic dataset may be accompanied by time-limited collection of more extended datasets focusing on specific areas, e.g. treatment and outcomes of a carefully characterised elderly population. Variables should preferably be oriented toward a set of outcomes that matters to patients and families. However, collection of such information, which may include health-related quality of life and long-term survival, requires that we expand our ability to capture data in patients' disease trajectories in other parts of the care delivery system than the ICU. For management of intensive care quality the duration of follow-up must balance between what is most affected by care in the ICU, least affected by varying administrative policies (i.e. discharge to terminal care facilities), practically feasible for caregivers and most relevant for patients.

An important and helpful function that is provided by registries is to develop dictionaries and guidelines for data collection. These contain explicit and detailed definitions of variables as well as explicit rules for deciding how variables must be recorded, and they are regularly updated to fit changing circumstances.

### Data Accuracy and Coverage

To be able to provide meaningful analyses registries must have mechanisms in place that



**Figure 1.** Variable life adjusted display of mortality 30 days after ICU admission due to out of hospital cardiac arrest (OHCA).

The seven lines represent different ICUs with about similar number of OHCA admissions during the study period (2011-2015). Outcomes were risk-adjusted with a freshly calibrated SAPS3 based model (Engerström et al. 2016). Note the comparatively higher mortality in some ICUs; this must be analysed further to separate common cause variation [random noise] from special cause variation (i.e. differences in definitions, therapies, case mix not accounted for by the risk adjustment model and quality of care).

aid and confirm that imported data are valid, accurate and that coverage is complete. Ensuring complete coverage, i.e. that every patient that meets registry entry criteria is recorded, is particularly important to reduce the risk of selection bias. Validation of individual records includes looking for missing, unusual and invalid data, while validation at the ICU level means checking for unusual patterns, duplication and inconsistencies. The methods used by intensive care registries are usually also designed to help participating ICUs to identify and correct errors in their system for local data collection. Besides, registries may coordinate schemes for monitoring of accuracy and coverage by verification of patient records with source data. This is usually done after selecting a random number of records to be analysed with use of specific protocols, either internally by ICU staff or externally by an assessor visiting from the registry or another ICU.

### Case-Mix Adjustment

A challenge for comparative audit of intensive care is that patients of all ages receive intensive care for a variety of disorders and symptoms; any effect of variation in intensive care quality

on outcomes may be hidden by differences in patient demographics, underlying health status, acute conditions and severity of illness (collectively referred to as 'case mix'). Comparing outcomes must take case mix into account and stratify or adjust for factors and circumstances that relate to the patient, comorbidities, acute disease and treatment before admission to ICU. Fortunately, intensive care has a history of using case mix adjusted models (usually risk adjustment models of in-hospital death) for benchmarking and audit of performance. An important mission for a registry is to maintain a validated, customised and updated risk adjustment model (Harrison et al. 2015; Engerström et al. 2016). Adjusting for risk is not only necessary for measuring outcomes accurately, but also for improving them. Understanding the link between risk factors and outcomes of critical illness is important for advancing intensive care.

### Data Feedback and Access

Intensive care registries facilitate discussion and learning by producing reports that display relevant comparisons between member ICUs. If this is done with short report cycles, data

**Table 1.** Possible Roles for Intensive Care Registries in Quality Management

1.	Collect data for comparative audit
2.	Select data, provide definitions and data collection guidelines
3.	Provide mechanisms for accurate and complete data capture
4.	Maintain a customised risk adjustment model
5.	Produce timely reports and provide easy access to data
6.	Support advanced analysis of data
7.	Organise audits and coach improvement programmes locally
8.	Arrange meetings for participants to discuss and develop intensive care quality

quality will most likely benefit from the frequent input of data from participating ICUs. Access to data must allow identification of participants to be useful for comparative audit. Transparent control of registries helps to build trust between participants leading to an environment where openness and sharing of information become powerful factors for delivery of high quality care. Ideally, information for comparative audit should be open and identifiable per ICU to facilitate comparisons. This has been the case in Sweden for more than a decade, where the open web portal of the Swedish Intensive Care Registry allows detailed analysis of frequently updated information ([portal.icuregsw.org](http://portal.icuregsw.org)). The willingness to measure and share results, also when suboptimal, must be tied together with a communication strategy that includes readiness to educate media and the lay public.

### Data Analysis

Best use of the registry is to allow data to be analysed locally by the ICU, in addition to centralised regular production of reports. An added advantage of local analysis is that data

■ Ideally, information for comparative audit should be open and identifiable per ICU ■

are often of better quality if those collecting them are involved in using and analysing them. Registries usually have skills and the infrastructure to perform complex and expanded analyses when asked for by member ICUs. Such analyses may include checking performance of the risk adjustment model and analysing associations between patient and care characteristics, and outcomes.

### Local Audit and Improvement Programmes

Many registries arrange and support clinical audit with the overall aim to establish and improve intensive care quality. Organisation of site visits by peers or regular audits involving similar sized neighbouring ICUs may be an

initial step in an improvement process (Martin and Braun 2014). The science of improving healthcare involves a systems approach, as well as applying specific knowledge in areas such as workplace psychology, practice-based learning and sources of variation. Numerous specific methods and tools are available (i.e. Breakthrough methodology, Clinical microsystem, Plan-Do-Study-Act [PDSA] cycle). Registries with expert knowledge in improvement science should be given the lead to avoid wasting of resources, energy and enthusiasm locally.

### Conclusion

To develop, implement, evaluate and sustain a quality improvement programme in the ICU is an important and demanding undertaking. The work can be made easier by joining an intensive care registry. Mature registries have resources and knowledge that go beyond collection of well-defined data for comparative audit; they provide analyses, feedback reports, and a structure in which ICUs discover and discuss the findings in order to improve treatment and organisation. While improving clinical outcomes may be considered a competitive advantage in some healthcare models, sharing results and best practices is in the interest of the critically ill patients that we all serve.

### Conflict of Interest

Sten Walther is co-founder of the Swedish Intensive Care Registry and has served as board member and chairman of the registry. ■

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# CURRENT STATE OF GLYCAEMIC CONTROL PRACTICE



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Elevated blood glucose is a widely recognised response to critical illness, with most non-diabetic patients exhibiting concentrations outside the normoglycaemic range and a substantial proportion having significantly or hugely elevated blood levels (Farrokhi et al. 2011). It has been 15 years since the publication of the Leuven study abruptly changed the landscape of glycaemic control, highlighting the tolerated wide range of blood glucose levels and the potential benefits of tight glycaemic control in cardiac surgery patients (Van den Berghe et al. 2001).

Since these highly encouraging results, a plethora of studies have been carried out to replicate these outcomes in other patient groups and to better understand the underlying mechanisms of the benefits of insulin infusion therapy (IIT). The latter have identified that hyperglycaemia is associated with morbidity, particularly to the kidney and liver, and that insulin itself does not offer any particular effect beyond control of glucose levels (Ellahham 2010).

However, attempts to apply tight glycaemic control across different groups of critically ill patients have met with mixed success due to the difficulties of maintaining control. Studies encountered increased rates of hypoglycaemic injury when trying to implement tight glycaemic control, and were terminated where the harm was deemed to be greater than any benefit (NICE-SUGAR Study Investigators 2009; Brunkhorst et al. 2008). Furthermore, variability in glucose levels was found to be a strong independent predictor of mortality (Krinsley 2008) and diabetic patients' requirements are distinctly different from non-diabetics (Krinsley et al. 2013).

As noted by Krinsley (2013), this has left clinical staff with the advice that they should "(a) target a discrete blood glucose range by using insulin, (b) avoid hypoglycemia, and (c) minimize glucose variability."

In order to better understand how the current state of knowledge is being applied and where the challenges are, a survey of ninety adult

intensive care units (ICUs), thirty in each of the United Kingdom, Germany and the Benelux countries in a range of teaching and general hospitals was carried out on behalf of Sphere Medical.

## Protocols for Starting and Stopping Insulin Infusion

The survey identified three trigger strategies for starting IIT in the protocols used. These ranged from routine insulin infusion for all patients admitted to the unit, initiation on a single elevated glucose reading through to persistent elevated glucose levels over time or multiple readings.

Overall an estimated 65% of patients admitted to intensive care were treated with IIT. However, strong geographic differences in clinical practice were observed (Figure 1). Fifty percent of centres in the Netherlands routinely implement IIT on all patients, while no units in the UK reported this practice, and the highest proportion of units waited for prolonged elevated glucose levels before initiating control. As a result, IIT is delivered to 50% of patients in the UK but 85% in the Netherlands compared to around 65% in both Germany and Belgium/Luxembourg.

## ▲▲Frequent blood glucose monitoring is essential for optimally managing insulin infusion therapy▶▶

The decision to stop IIT was driven by stability of glucose levels and the establishment of enteral nutrition in the majority of units. In the remainder, and particularly in the Netherlands, it was a part of discharge of the patient from the intensive care unit.

## Tight Glycaemic Control?

None of the centres questioned were trying to maintain control to normoglycaemia in their patients. Around half of centres have a relatively liberal upper threshold of 10 mmol/l (180 mg/dl). Most of the rest of the centres were maintaining a moderate level of control keeping below 8 mmol/l (~140 mg/dl) with a minority below 7 mmol/l (~130 mg/dl). Again, there is a distinct difference between the countries in the survey, with ICUs in Benelux most likely to control more tightly than those in other countries (Figure 2).

### Keeping in Control

Survey participants estimated the frequency of testing as every three to four hours. All except one centre used a blood gas analyser (BGA) to measure arterial samples for glucose. However, many units used multiple measurement approaches and just under 70% of samples are arterial blood measured on the BGA. Around 20% of measurements made are capillary samples measured on a glucose test strip meter (Figure 3).

### Barriers to Implementing Protocols

As shown in Figure 4 (p. 210), there are a number of difficulties with implementing an effective glycaemic control protocol.

### Discussion

The benefits of avoiding mortality and morbidity associated with hyperglycaemia in critically ill patients have been demonstrated and are understood. This has resulted in a widespread change in clinical practice to control excessively high glucose levels. However, the difficulty with safely and consistently maintaining blood glucose concentrations has hampered the ability to determine optimal target blood glucose concentrations. Closer control tends to lead to an increase in hypoglycaemic events, themselves associated with increased mortality. As a result, even after fifteen years of investigation, IIT protocols remain highly heterogeneous across northwest European ICUs and 80% of units cite problems with implementing their adopted protocols.

Frequent blood glucose monitoring is essential for optimally managing IIT. However, this can be a significant burden and was the most common problem cited by the clinical staff surveyed. Typical protocols require hourly measurement of blood glucose and, if necessary, adjustments in insulin infusion rates until glucose levels are stable and in the target range, at which time measurements can be taken every two to four hours. Any changes that could affect glucose levels, such as insulin or feed changes require reverting to hourly measurement until stability is evident.

In addition to the increased workload caused by glycaemic control, risks of hypoglycaemia and the widespread use of capillary samples are major concerns. Capillary test strip measurements offer workflow advantages, however, and the use of capillary test strips is associated with a range of limitations and potential sources of harm (Corl et al. 2015) and can lead to significantly biased results (Petersen et al. 2008).

Despite the move away from tight glycaemic control, hypoglycaemia remains a challenge for routine clinical practice, either due to the incidence of hypoglycaemic episodes or the relaxation of target ranges to lower the risk of such incidents.

The ability to better control glucose levels is important both for safer clinical practice and as a necessary condition for any further work to optimise glycaemic control as a therapy in critical care. This requires:

- An accurate measurement method with reduced nursing dependency over BGA readings
- A protocol that can deliver control within the desired limits
- Processes that ensure compliance to the protocol

A number of continuous and intermittent systems for glucose monitoring are now commercially available for use in critical care. Subcutaneous sensors do not appear to be able to provide the level of accuracy required for the management of critical care patients (Wollersheim et al. 2016). Continuous monitoring catheters have been developed, but their adoption has been very limited so far, possibly because of their

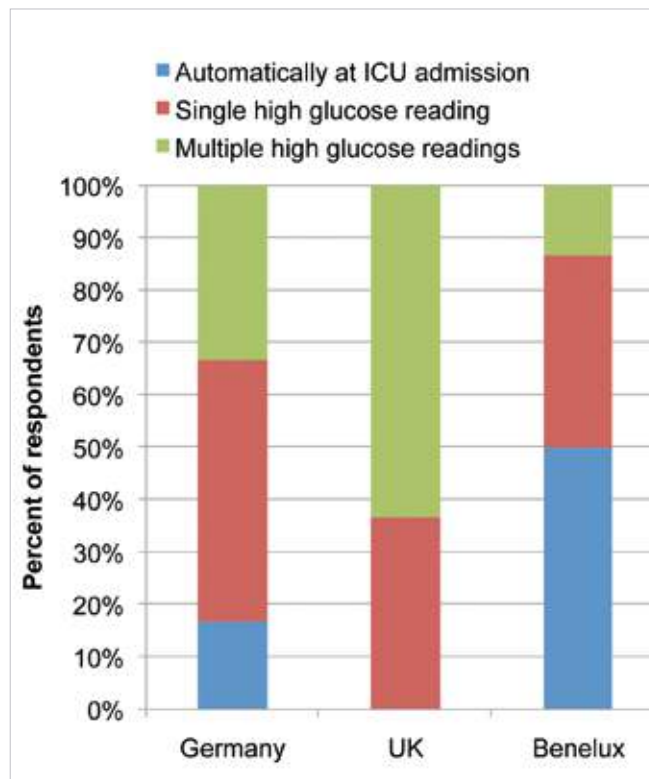


Figure 1. Triggers for Starting Intravenous Insulin Infusion, by Country

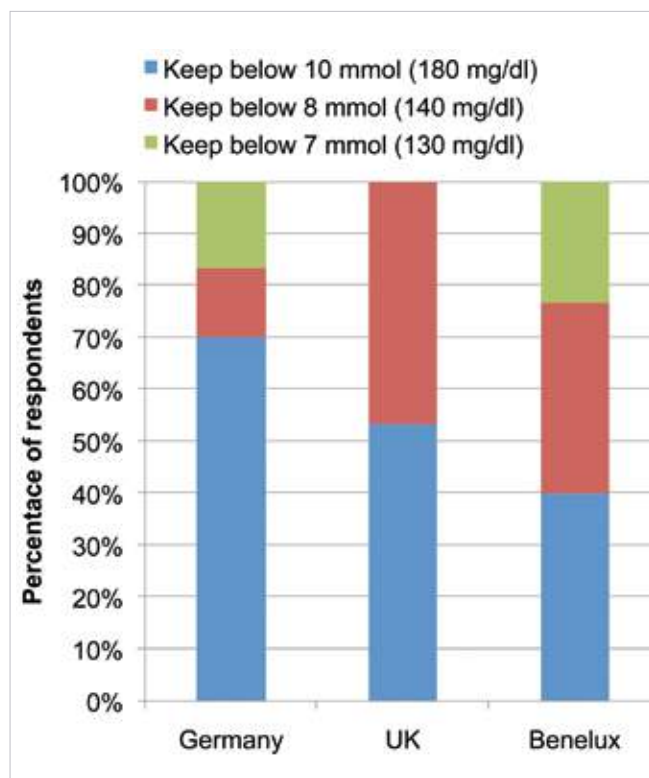
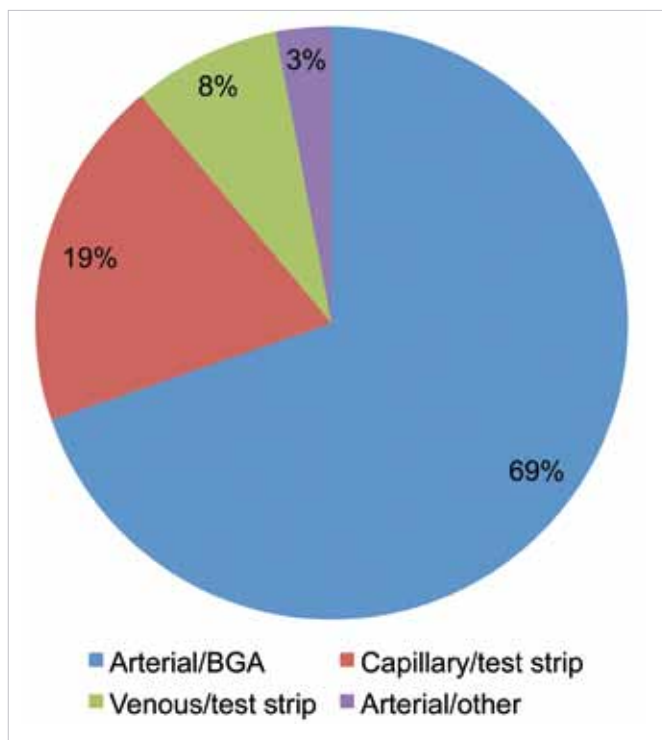


Figure 2. Target Upper Limits for Glycaemic Control Protocols, by Country



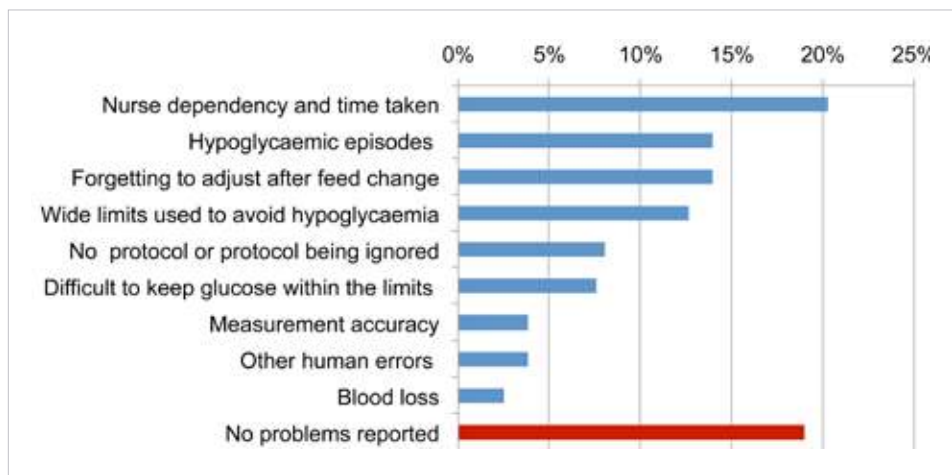
**Figure 3.** Estimated Proportion of Samples Measured, by Sample Type and Measurement Technique

invasiveness (a central venous catheter or dedicated cannula is required) and the costs involved for monitoring a single parameter. Ex-vivo blood gas analysers are now available ([www.spheremedical.com](http://www.spheremedical.com)), which allow intermittent measurement of a fuller panel of analytes with an improved workflow over traditional blood gas analysis.

### Ex-vivo blood gas analysers allow intermittent measurement of a fuller panel of analytes with an improved workflow over traditional BGA

Computer-assisted control systems have demonstrated the ability to provide an acceptable level of glucose control using intermittent measurement (Juneja et al. 2009). These incorporate algorithms that determine the required insulin infusion rate to maintain glucose within the target range as well as the necessary measurement frequency.

In combination, these technologies meet all of the three requirements identified above. At the very least they offer the ability to provide safer, more consistent implementation of existing targets. On the upside, they offer further opportunity to investigate and optimise glycaemic control in critically ill patients. ■



**Figure 4.** Proportion of Respondents Citing Challenges to Implementing their Glycaemic Control Protocol

#### Abbreviations

BGA blood gas analyser  
ICU intensive care unit  
IIT insulin infusion therapy

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# BIOMARKERS IN HEART FAILURE

Cardiac biomarkers, including natriuretic peptides and troponins, have become widely used in the treatment of heart failure and acute coronary syndrome. As we learn more about the function of these markers, their use has begun to expand. We can now track and utilise natriuretic peptides throughout hospital admission to monitor progress of heart failure therapy. Troponins and natriuretic peptides can provide useful prognostic data and help stratify more high-risk patients. Novel biomarkers, such as ST2, can also aid in prognostication, and may be beneficial in guiding initiation of therapies that reduce cardiac remodeling, including beta-adrenergic receptor and mineralocorticoid receptor antagonists. Finally, procalcitonin can help distinguish dyspnoea secondary to heart failure from pulmonary infection and can help guide use of antibiotics in patients with heart failure who present with shortness of breath.

**H**eat failure (HF) is the leading cause of mortality in the United States (Lloyd-Jones et al. 2009). Advances in medical therapies have improved outcomes for patients with heart failure with reduced ejection fraction (HFrEF), but these patients still account for over 1 million hospitalisations annually and generate billions of dollars in healthcare costs (Mozaffarian et al. 2015; Go et al. 2014; Ambrosy et al. 2014). Cardiac biomarkers are noninvasive and inexpensive to measure, and they allow for more accurate and rapid diagnosis of acute heart failure exacerbation in the emergency department (ED), which can reduce rates of hospitalisation and health care costs. Cardiac biomarkers can also improve prognostication and help guide medical therapy for heart failure and this therapeutic guidance may improve patient morbidity and mortality. In this review, we will examine two of the most commonly used cardiac biomarkers in the treatment of heart failure: the natriuretic peptides (NPs) and troponins. We will also discuss two novel cardiac biomarkers: ST2, a marker of cardiac remodelling and fibrosis with

prognostic value, and procalcitonin, a marker of inflammation that can help guide treatment of bacterial infections.

## Natriuretic Peptides

Brain or B-type natriuretic peptides (BNPs) are proteins synthesised by cardiac ventricular myocytes in response to mechanical stretch (Yasue et al. 1994; Yoshimura et al. 1993). At the cellular level in the setting of volume overload, mechanical stretch on cardiomyocyte membranes activates downstream transcription and translation of a 134 amino acid precursor peptide pre-proBNP (Sudoh et al. 1989). This biologically inactive protein undergoes enzymatic cleavage twice: first producing proBNP<sub>1-108</sub>, and with a second cleavage producing BNP<sub>1-32</sub> (the biologically active carboxy-terminal peptide) and the inactive amino terminal fragment NTproBNP (Figure 1, Left Panel). Both peptides are secreted in equimolar amounts into circulation (Daniels and Maisel 2007; Nakagawa et al. 2009; Kojima et al. 1989). Unlike the other natriuretic peptides (Atrial and C-type natriuretic peptides), BNP is minimally stored. It is

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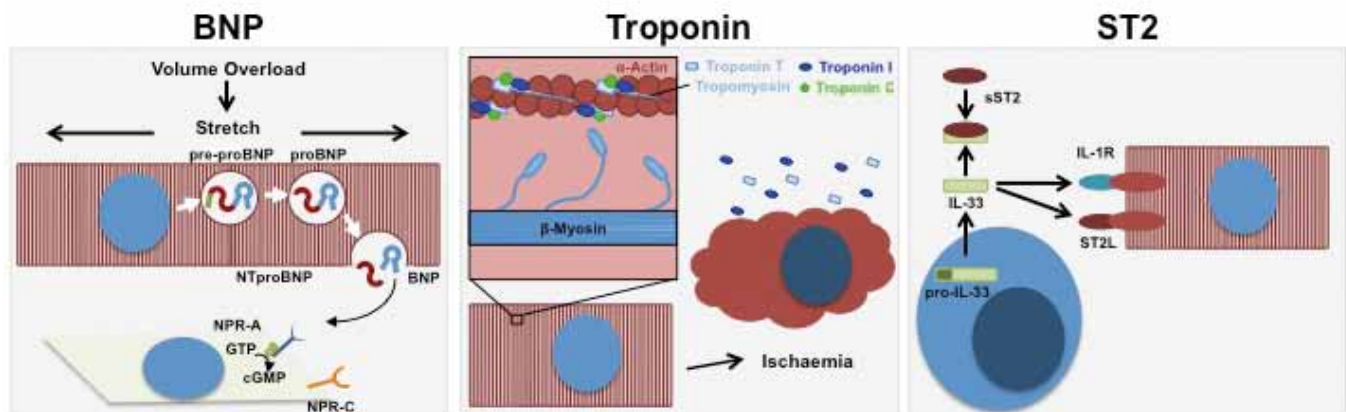
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synthesised and directly secreted in large bursts from the ventricular myocardium (Maisel et al. 2002). NPs act on membrane-bound natriuretic peptide receptors (NPRs) in target tissues to induce vasodilation, diuresis, natriuresis and inhibition of the renin-angiotensin-aldosterone system (RAAS) system. These actions act to reduce cardiac preload and afterload (Daniels and Maisel 2007). BNP is cleared from circulation by binding to NPRs, by degradation by circulating neutral endopeptidases, and to a lesser degree through renal excretion (Daniels and Maisel 2007).

## Clinical Use of Natriuretic Peptides

It is now a Class I indication in the American Heart Association / American College of Cardiology (AHA/ACC) guidelines for management of HF that BNP should be measured on hospital admission for all suspected cases of acute HF exacerbation (Yancy et al. 2013). ED providers should utilise BNP levels for risk stratification, with BNP < 400 pg/mL indicating a lower-risk patient that could be safely discharged from the ED with close outpatient follow-up (Maisel et al.



**Figure 1.** Cardiac Biomarker Production and Signalling

**Left Panel:** Brain or B-Type natriuretic peptide (BNP) is produced by cardiac myocytes in response to mechanical stretch during volume overload. The peptide is first translated as the precursor peptide pre-proBNP, which is cleaved to proBNP, and a final enzymatic cleavage produces two excreted products: NTproBNP and BNP. **Middle Panel:** Cardiac troponins are calcium-handling proteins associated with the thin filaments (alpha sarcomeric actin) of the myocyte contractile apparatus. During prolonged ischaemia, such as myocardial infarction, myocytes undergo widespread necrosis and release their intracellular proteins (troponin I and T) into circulation. **Right Panel:** ST2 is produced by myocytes and fibroblasts in response to mechanical stress. IL-33 is a cardioprotective cytokine that binds IL-1 receptors on the cardiac myocyte and fibroblasts and has antihypertrophic and antifibrotic effects. Soluble ST2 [sST2], which is overexpressed during heart failure, acts as a decoy receptor for IL-33, blocking its cardioprotective effects.

2015; Maisel et al. 2008). Several clinical trials have demonstrated the utility of BNP measurement in the ED (Table 1). In the 2002 Breathing Not Properly multinational study of 1586 patients presenting to the ED with dyspnoea, measurement of serum BNP had higher accuracy in diagnosing heart failure than the ED physicians (Maisel et al. 2002). Using a cutoff of 100 pg/mL, serum BNP was 90% sensitive and 76% specific for heart failure in this trial. The 2005 PRIDE study similarly demonstrated that NT-proBNP was highly sensitive and specific at diagnosing heart failure among 600 ED patients presenting with dyspnoea (Januzzi et al. 2005). This study suggested a cutoff NT-proBNP level of 300 pg/mL to rule out heart failure in these patients. Other studies have demonstrated how measurement of BNP (Mueller et al. 2004) and NT-proBNP (Moe et al. 2007) in the ED can reduce hospitalisation rates, median length of stay, and thus reduce overall healthcare costs.

BNP has demonstrated prognostic value in both acute (Doust et al. 2005; Maisel et al. 2004) and chronic HF (Berger et al. 2002; Anand et al. 2003), with elevated BNP levels associated with worse outcomes, greater morbidity and higher mortality (Table 1). In both the acute and chronic setting, for every 100 pg/mL increase in BNP, there is a 35% increase in risk of death (Doust et al. 2005). Elevated BNP levels in the ED patient should be considered relative to their last baseline outpatient BNP or from prior to discharge from a previous hospitalisation (Maisel

et al. 2015). It may not be necessary to trend NPs daily during the hospitalisation, but serial measurements should be considered in patients who are not clinically improving. BNP values should decrease with diuresis, as studies have demonstrated that in acute decompensated heart failure (ADHF), treatment-related decreases in pulmonary capillary wedge pressure (PCWP) are correlated with a drop in NP levels (Kazanegra et al. 2001). Additionally, failure of NP levels to decrease during a hospitalisation is associated with worse prognosis (Bettencourt et al. 2002; Cheng et al. 2016).

In severely volume-overloaded patients, BNP may not immediately decrease, because fluid volume is initially diuresed primarily from interstitial tissues. So in a severely volume overloaded person, they may diurese several litres initially from their lower extremity or pulmonary interstitium without producing any change in intravascular volume or preload (Wettersten and Maisel 2016). As such, their BNP may not begin to decrease until several days into the hospitalisation when diuresis has begun to affect intravascular volume and cardiac preload. Once intravascular volume and preload begin to decrease, ventricular stretch lessens and BNP production by strained cardiac myocytes begins to decline. With continued diuresis, serum BNP levels will decline towards their baseline/outpatient values. BNP levels should be measured in all patients prior to discharge, as elevated serum BNP at discharge is associ-

ated with worse outcomes, including increased readmission rates and mortality, regardless of presenting BNP levels (Dokainish et al. 2005; Logeart et al. 2004). This pre-discharge BNP level may also be used to monitor patients at subsequent outpatient follow up visits (Maisel et al. 2015; Wettersten and Maisel 2016; Maisel 2006).

#### Caveats of BNP Interpretation

Several factors can cause elevated baseline BNP and NT-proBNP levels, including age (Redfield et al. 2002; Wang et al. 2002; Costello-Boerrigter et al. 2006), female gender (Redfield et al. 2002; Wang et al. 2002; Costello-Boerrigter et al. 2006), and renal dysfunction (Tsutamoto et al. 2006). The higher levels of circulating NPs at baseline with advanced age are independent of age-related diastolic dysfunction (Redfield et al. 2002), and may be due to age-related reduction of NPRs, which results in decreased clearance of circulating NPs (Daniels and Maisel 2007). In these studies, age-matched cohorts demonstrated that BNP and NT-proBNP levels are higher in women than men at any age (Redfield et al. 2002; Wang et al. 2002). Several researchers have proposed that oestrogen levels may be involved, as women on hormone replacement therapy (HRT) had higher BNP levels than women not on therapy (Redfield et al. 2002), although oestrogen replacement had only minimal effects on NT-proBNP levels in this same study (Costello-Boerrigter et al. 2006).

**Table 1.** Clinical Evidence for Use of Biomarkers in Heart Failure

	Trial Name	Methods/Results
BNP	Breathing Not Properly (BNP) (Maisel et al. 2002)	BNP levels improved accuracy in diagnosing HF exacerbation in ED patients presenting with acute shortness of breath (n=1586).
	B-type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) (Mueller et al. 2004)	Single BNP measurement by ED physicians was associated with 10% decrease in hospital admission and decreased median length of stay.
	Pro-BNP Investigation of Dyspnea in the Emergency department (PRIDE) (Januzzi et al. 2005)	NT-proBNP levels were sensitive and specific for diagnosing HF exacerbation in 600 ED patients with dyspnoea using a cutoff of 300 pg/mL.
	Improved Management of Patients With Congestive Heart Failure (IMPROVE-CHF) (Moe et al. 2007)	NT-proBNP had similar improvements in diagnosis and cost savings to BNP.
	Berger et al. (2002)	BNP > 130 pg/mL in patients with chronic HF had higher rates of sudden cardiac death.
	Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT) (Maisel et al. 2004)	Elevated BNP level was strong predictor of 90-day outcome (CHF visits, admissions and mortality) in ED patients with dyspnoea.
ST2	Valsartan Heart Failure Trial (Val-HeFT) (Latini et al. 2007)	4053 patients with stable/chronic HF underwent serum analysis for cTnT (10.4% positive) or hsTnT (92.0% positive). Elevated troponins were associated with increased risk of death with both assays, and with hsTnT proving more sensitive and retaining prognostic value.
	Acute Decompensated Heart Failure National Registry (ADHERE) (Peacock et al. 2008)	Troponins were measured in 84,872 patients hospitalised for acute decompensated HF; 4,240 had positive troponins on admission, and this group had lower blood pressure on admission, lower EF and higher in-hospital mortality.
	Xue et al. (2011)	144 patients admitted for acute HF were followed from admission until 90 days post-discharge and had serial troponins and BNP's monitored. Elevated troponin was associated with increased mortality and risk of readmission, even if BNP was low at discharge.
	Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) (Felker et al. 2012)	Troponin I measured in 808 patients hospitalised for ADHF. Elevated troponins were associated with increased length of stay and worsening HF during index hospitalisation, but did not predict worse long-term outcomes (at 30 or 180 days post-discharge).
	Pascual-Figal et al. (2012)	Compared hsTnT to standard cTnT and found similar nearly all patients (98%) had +hsTnT (only 56% had +cTnT), n=202. Elevation of either troponin predicted risk of death.
	Atherosclerosis Risk in Communities (ARIC) (Hoogeveen et al. 2011)	9698 patients age 54-74 in general population who had no known underlying CHD, stroke or HF had hsTnT, BNP and CRP measured. hsTnT was associated with increased risk of CHD, fatal CHD and HF. hsTnT was equally predictive of HF as NT-proBNP.
	Atherosclerosis Risk in Communities (ARIC) (Nambi et al. 2013)	Both hsTnT and NT-proBNP had significant value in predicting HF risk in general population over 10 year follow-up, and combining the two markers had the highest sensitivity at predicting development of HF.
Procalcitonin	Daniels and Bayes-Genisal (2014)	Patients admitted for ADHF with ST>35 ng/mL should receive closer monitoring. ST2 has less variation over time and varies less than BNP relative to age, gender, BMI and renal function.
	Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department (PRIDE) (Januzzi et al. 2007)	ST2 levels were elevated in hospitalised HF patients, and ST2 levels correlate with mortality.
	Gaggin et al. (2013)	Patients with elevated ST2 should have beta blockers maximised to reduce cardiac remodelling.
	Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) (Maisel et al. 2014)	Patients with elevated ST2 should have MRAs maximised to reduce cardiac remodelling.
Troponin	Assicot et al. (1993)	In 79 children (newborn-12 years), elevated PCT was associated with severe bacterial infections, and serum PCT decreased rapidly with antibiotic therapy. PCT was normal or only mildly elevated in patients with viral infections or with peripheral bacterial colonisation.
	Gendrel et al. (1998)	CSF was analysed from 23 children hospitalised for bacterial meningitis and 51 patients hospitalised for viral meningitis, and PCT was elevated in bacterial but not viral infections. PCT dropped to undetectable levels with antibiotic treatment in the bacterial meningitis group.
	Moosig et al. (1998)	Study of 26 patients with granulomatosis with polyangiitis, who had serum taken during active vs inactive disease states. Slight PCT elevations were detected during active disease state. In patients with inactive disease, PCT levels correlated with other inflammatory markers (ESR, CRP, sIL-2, ANCA) suggesting that in inactive disease, PCT correlates with bacterial infections.
	Muller et al. (2000)	Procalcitonin was most reliable marker of infection in 101 ICU patients compared to CRP, IL-6 and lactate. PCT was 89% sensitive and 94% specific for diagnosing sepsis, and PCT elevation was associated with poor prognosis.
	Schwarz et al. (2000)	Procalcitonin was elevated in patients with bacterial meningitis and not in patients with abacterial (viral or aseptic) meningitis. PCT sensitivity of 69% at identifying bacterial meningitis.
	Wang et al. 2014	HF patients have a higher serum PCT than healthy controls. Patients with HF and bacterial infections had the highest serum PCT levels in this study, but the high baseline PCT observed in HF patients complicates the use of PCT as an infectious biomarker in the HF population

ADHF acute decompensated heart failure ANCA antineutrophil cytoplasmic antibodies BNP Brain or B-Type natriuretic peptide CHD coronary heart disease CHF congestive heart failure CRP C-reactive protein cTnT cardiac troponin T ESR erythrocyte sedimentation rate HF heart failure hsTnT high sensitivity troponin T MRA magnetic resonance angiogram PCT Procalcitonin



The relationship of BNP to renal function is more complex and likely multifactorial, as BNP is mostly taken up by NPRs or enzymatically degraded in serum rather than cleared renally (McCullough et al. 2003). Older patients with renal dysfunction may have chronically higher intravascular volume, increased ventricular strain and reduced glomerular filtration, which could all contribute to the elevated BNP levels observed in patients with chronic kidney disease.

Low BNP levels may result in obese patients and during early flash pulmonary oedema. The negative correlation between obesity and baseline serum BNP levels is well documented (Wang et al. 2002; Wang et al. 2004; Mehra et al. 2004; Daniels et al. 2006), but the exact mechanism remains unclear. Some have hypothesised that adipocytes have increased concentration of NPRs, which could increase BNP clearance (Sarvani et al. 1996), but others have demonstrated a positive correlation between BNP levels and lean mass rather than fat mass (Das et al. 2005). There is conflicting evidence as to whether NT-proBNP levels are similarly low in obese patients, which could be explained by the fact that NT-proBNP is not cleared through NPRs. Although BNP levels are low in obese patients, they still retain their diagnostic and prognostic values if measured relative to a known baseline (Daniels and Maisel 2004). BNP levels may similarly be low early in flash pulmonary oedema. This is due to the insufficient time for BNP gene expression and translation in the setting of rapid interstitial fluid accumulation (Yoshimura et al. 1993).

### Troponins

Troponins are calcium-handling proteins integral to excitation-contraction coupling in the cardiac myocyte (Figure 1, Middle Panel) (Sharma et al. 2004; Parmacek and Solaro 2004). Cardiac troponins and other intracellular myocyte proteins are released into circulation after myocardial infarction, in which prolonged ischaemia resulting from coronary artery occlusion causes myocyte necrosis. Detection of cardiac troponins in the blood (Troponin T or I) is useful for diagnosis of acute coronary syndrome (ACS), as troponin I has not been identified in tissues outside the myocardium (Bodor et al. 1995), and troponin T is only minimally expressed in skeletal muscle tissues (Ricchiuti et al. 1998). As these serum markers are specific for myocardial damage (Collinson et al. 2001), they are now considered the gold standard for diagnosis of ACS (Braunwald et al. 2000; Bertrand et al. 2000).

### Clinical Scenario

A 79-year-old male with history of heart failure presents to the ED with shortness of breath. The man has known ischaemic cardiomyopathy secondary to coronary artery disease and prior non-ST segment elevation myocardial infarction (NSTEMI), with last known left ventricle ejection fraction (LVEF) of 40% (measured on echocardiography in the last year). His heart failure has been medically managed with a beta-blocker and angiotensin converting enzyme (ACE)-inhibitor for the last 2 years. He says his symptoms began 2 days ago and have become progressively worse. He is unable to lie flat to sleep at night and he is exhausted. He also reports subjective fevers, non-productive cough and swelling around his ankles. He denies chest pain at rest or on exertion. On physical exam, the patient appears uncomfortable, he is tachycardic to the high 90s and afebrile, blood pressures are normotensive and he also appears to have increased work of breathing. His oxygen saturation is 95% on 4L O<sub>2</sub> via nasal cannula. He has bibasilar lung crackles, JVP to 10 cm, and 3 mm of lower extremity pitting oedema below the knees bilaterally. Initial CXR shows cephalisation and bibasilar opacifications consistent with pleural effusions, but a consolidative infectious process cannot be ruled out. ECG demonstrates sinus tachycardia with heart rate of 95 bpm, evidence of old inferior wall ischaemia (pathologic Q waves in leads II, III, and aVF that are unchanged from prior ECGs) and no new signs of cardiac ischaemia.

The patient is admitted to the inpatient cardiology service, and initial cardiac biomarker labs are drawn. The patient's BNP is 849 pg/mL in the emergency room, and it was 350 pg/mL at clinic visit 6 months prior. With the elevated BNP and signs of volume overload on exam, diuresis was initiated using intravenous furosemide. Initial hsTnT is also slightly positive at 0.10 mg/dL. Initial ST<sub>2</sub> came back at 40 ng/mL. Because initial troponin and ST<sub>2</sub> were elevated, the patient is admitted to the Cardiac Critical Care Unit for closer observation, as elevation of BNP, hsTnT and ST<sub>2</sub> are associated with worse prognosis. Serum procalcitonin drawn in the ED also came back elevated at 1.8 ug/L, suggesting underlying bacterial infection. Given his clinical history of productive cough, community-acquired pneumonia is strongly suspected even though the patient was initially afebrile and did not have clearly visible consolidations on chest x-ray, and the patient was started on intravenous ceftriaxone.

Serial troponin measurements at 12 and 24 hours after initial presentation are subsequently negative, and it was determined that the patient did not have acute coronary syndrome. As the patient is not at risk of ACS and troponins have normalised, he was downgraded to an intermediate care unit on the cardiology service. After diuresing 2 L of fluid in the first 24 hours, BNP measurement was repeated, and was still elevated at 810 pg/mL. Although the patient had diuresed well, the BNP is likely still elevated because the 2 L lost represents interstitial fluid volume, and the patient is still likely intravascularly volume-overloaded (and thus BNP is still being actively produced in response to ventricular volume overload and myocyte stretch at the cellular level).

Over the next 4 days, the patient diuresed a total of 8.5L in the hospital, he now has only trace pedal oedema, he is breathing comfortably on room air and he is feeling much better. Sputum cultures from admission grew *Strep. pneumoniae*. Cardiac biomarkers are repeated prior to discharge. BNP has dropped to 450 pg/mL, PCT is now undetectable on day 5 of IV ceftriaxone, and ST<sub>2</sub> remains elevated at 38 ng/mL. A repeat echocardiogram done during this hospitalisation demonstrated an LVEF of 32% without new regional wall motion abnormalities. The decision was made to discharge the patient with antibiotics, and spironolactone 25 mg daily was added to his current heart failure regimen given his low EF. He was scheduled for follow-up in cardiology clinic in 2 weeks where his primary cardiologist will continue to monitor his BNP and ST<sub>2</sub> levels for further optimisation of antihypertrophic medications (beta blockers and MRAs).

### Clinical Utility of Troponins in Heart Failure

The AHA/ACC guidelines recommend checking cardiac troponins in patients presenting with acute heart failure, both for ACS rule out and risk stratification (Yancy et al. 2013). In patients presenting with exertional chest pain and dyspnoea, cardiac troponins must be trended

over the first 24 hours of hospitalisation to rule out ACS. In patients with acute decompensated HF without ACS (diagnosed by symptoms, ECG changes, and trending cardiac markers), elevated troponins were highly prognostic in several studies (Table 1). Patients admitted for ADHF who had troponin elevation on admis-

sion had higher in-hospital mortality in the Acute Decompensated Heart Failure National Registry (ADHERE) trial (Peacock et al. 2008), with increased length of stay and worsening HF during admission in the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial (Felker et al. 2012). Both the older cardiac troponin T detection assay (cTnT) and the newer high-sensitivity troponin T assay (hsTnT) have been shown to be useful for prognostication in patients admitted for ADHF. Troponin elevation is detected only in a minority of heart failure patients using the cTnT assay, but hsTnT can detect low concentrations of troponins in the majority of HF patients, and HF patients with elevations of either cTnT or hsTnT demonstrated increased risk of death (Pascual-Figal et al. 2012; Latini et al. 2007). Another study demonstrated that serial troponin measurement, in addition to serial BNP, can add prognostic value. Patients in this study with the highest serum troponins at discharge had increased mortality and higher risk of readmission (Xue et al. 2011). The Atherosclerosis Risk in Communities (ARIC) study evaluated the use of cardiac biomarkers at predicting risk of developing coronary heart disease and heart failure in a pool of 9698 patients without known CHD, stroke or HF. Patients in the general population with elevated hsTnT had significantly increased risk of developing CHD, fatal CHD and HF over 10 year follow-up, and hsTnT had equivalent predictive value as NT-proBNP for detecting development of HF (Saunders et al. 2011). In a follow-up study, the ARIC study authors demonstrated that in this same general population elevation of both hsTnT and NT-proBNP was even more prognostic for prediction of developing HF at 10 year follow-up than either marker individually (Nambi et al. 2013).

### ST2

Growth Stimulated expressed gene 2 (ST2) is a receptor for interleukin-33 (IL-33) that is expressed by myocytes and fibroblasts in response to mechanical stress. IL-33 is protective against myocardial hypertrophy and fibrosis in animal models of pressure overload (Schmitz et al. 2005; Kuball et al. 2005). ST2, expressed as membrane-bound (ST2L) or soluble (sST2) isoforms through alternative splicing (Kieser et al. 1995; Yanagisawa et al. 1992; Tominaga 1989), is overexpressed in HF, and sST2 acts as a decoy receptor that binds IL-33 and prevents its cardioprotective actions (Sanada et al. 2007;

Weir et al. 2010). There are no prospective clinical trials that have examined the utility of ST2 as a clinical biomarker, but many retrospective and observational studies suggest its function as a prognostic indicator and for driving medical therapy.

### Clinical Utility of ST2 in Heart Failure

Patients admitted to the hospital with ADHF should have an sST2 level drawn on admission, and patients with serum levels >35 ng/mL should receive closer monitoring, especially if other clinical biomarkers are elevated (i.e. BNP and troponins) (Daniels and Bayes-Genis 2014). In the Pro-BNP Investigation of Dyspnea in the Emergency department (PRIDE) study, ST2 levels were increased in patients hospitalised for HF, and higher ST2 values were correlated with increased risk of death (Januzzi et al. 2007). Similarly to BNP and troponins, serial ST2 measurements during HF hospitalisation were predictive of mortality (Boisot et al. 2008; Anand and Rector 2014). In several studies (Table 1), ST2 has demonstrated some advantages over BNP. There is less variation in sST2 levels relative to age, gender, BMI and renal function, and there is less intra-individual variation in ST2 levels over time (Daniels and Bayes-Genis 2014). Additionally, ST2 is the strongest predictor of mortality both in acute and chronic HF compared to all other biomarkers (Gaggin et al. 2014; Bayes-Genis et al. 2014). Because ST2 is an indicator of cardiac remodelling and fibrosis, antihypertrophic therapies with beta-blockers (Gaggin et al. 2013) and mineralocorticoid receptor antagonists (COACH Trial) (Maisel et al. 2014) should be initiated and maximised in HF patients with elevated ST2 levels.

### Procalcitonin

In the critically ill patient, it is often difficult to determine if symptoms of the systemic inflammatory response are due to underlying infection or other aetiologies, and few early markers of infection have proved reliable. Procalcitonin (PCT) may be a useful marker of bacterial infection. Although the exact mechanism of PCT production is unknown, serum levels of the 116 amino acid peptide are increased in the setting of bacterial infection and sepsis (Schwarz et al. 2000; Assicot et al. 1993; Muller et al. 2000). Increased PCT levels can help differentiate between bacterial and viral infections (Gendrel et al. 1998) or between bacterial infection and disease flare of autoimmune disorders (Moosig et al. 1998). Additionally, procalcitonin levels

were shown to be normalised in patients with bacterial infection as they were treated with antibiotics (Assicot et al. 1993).

### Clinical Use of Procalcitonin in Heart Failure

In patients with a history of CHF presenting with dyspnoea, it is often initially unclear if respiratory symptoms are due to pulmonary oedema or underlying infection. Although many studies suggest PCT can be useful at distinguishing bacterial infection from heart failure exacerbation (Table 1), one study, however, did demonstrate that CHF alone could increase PCT levels independently from infection. It was thought to be due to increased endotoxin resorption in the small bowel in volume-overloaded patients, which can cause falsely elevated PCT in the serum, although patients with HF and underlying bacterial infections were found to have the highest PCT levels (Wang et al. 2014). Despite this study's results, there remains compelling evidence that in patients with acute heart failure exacerbation and elevated PCT levels, treatment with antibiotics results in better outcomes. ■

### Abbreviations

ACS	acute coronary syndrome
ADHF	acute decompensated heart failure
BNP	Brain or B-Type natriuretic peptide
cTnT	cardiac troponin T
ED	emergency department
HF	heart failure
hsTnT	high-sensitivity troponin T
NP	natriuretic peptides
NPR	natriuretic peptide receptors
NT-proBNP	N-terminal pro b-type natriuretic peptide

For full references, please email [editorial@icu-management.org](mailto:editorial@icu-management.org), visit [icu-management.org](http://icu-management.org) or use the article QR code.

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# DIFFICULT INTUBATION IN INTENSIVE CARE UNITS

## WHY AND HOW TO PREVENT AND MANAGE DIFFICULT INTUBATION?

Severe hypoxaemia and cardiovascular collapse, leading to cardiac arrest, cerebral anoxia and death, are the most frequent complications related to intubation in intensive care units (ICU), associated with difficulty of intubation. To prevent and limit the incidence of difficult intubation, specific risk factors for difficult intubation in the ICU have been identified and pre-oxygenation techniques and intubation algorithms have been developed. The objectives of this review are to describe new tools (i.e. MACOCHA Score) to better identify patients at high risk for difficult intubation and new strategies for improving preoxygenation before intubation and decreasing difficult intubation incidence, using specific algorithms.

### Patients At Risk of Difficult Intubation

We assessed for the first time in a large prospective cohort the risk factors of difficult intubation in the ICU (De Jong et al. 2013b). A predictive score of difficult intubation, the MACOCHA score, was developed and then externally validated. The main predictors of difficult intubation were related to the patient (Mallampati score III or IV, obstructive apnoea syndrome, reduced mobility of cervical spine, limited mouth opening), the pathology (coma, severe hypoxia) and the operator (non-anaesthesiologist) (Table 1) (De Jong et al. 2013b; De Jong et al. 2014a). In order to reject difficult intubation with certainty, a cutoff of 3 or greater was appropriate, allowing optimal negative predictive value (respectively 97% and 98% in the original and validation cohorts) and sensitivity (respectively 76% and 73% in the original and validation cohorts). The MACOCHA score allows identification of patients at risk of difficult intubation.

All ICU patients could be considered at risk of complications of intubation, and particularly those with difficult intubation. Anticipating difficult intubation is a challenging issue: the complications of intubation are higher in cases of difficult intubation when compared to non-difficult intubation (65% vs. 41% overall for both moderate and severe complications, 51%

vs. 36% for severe life-threatening complications) (De Jong et al. 2013b).

### Intubation Recommendations Bundle to Limit Complications Related to Intubation Procedure (The Montpellier-ICU Intubation Algorithm)

In order to reduce the complications associated with all intubation in the ICU and in particular difficult intubation, a bundle of techniques has been developed for ICUs and is presented in Table 2 (Jaber et al. 2010; De Jong et al. 2014a; Jaber et al. 2016).

Preoxygenation and recruitment manoeuvres (RM) are one of the procedures that may improve airway safety. Figure 1 summarises the minimal SpO<sub>2</sub> values during the intubation procedure in severe hypoxaemic patients throughout both randomised and non-randomised studies according to the method of preoxygenation (Jaber et al. 2016).

Several manoeuvres in spontaneous ventilation (e.g. 3-8 vital capacities vs 3 minutes tidal volume breathing) exist and seem to be almost equally effective (Tanoubi et al 2009). Some technical details, however, can make a significant difference. First, the clinician needs to make sure the facemask properly fits the patient's facial morphology. Second, fresh gas flow needs to

**A**irway management is one of the most commonly performed procedures in the intensive care unit (ICU). Difficult intubation incidence is 10% on average (De Jong et al. 2013b), ranging from 1% to 23% depending on the centre and the definition used (Martin et al. 2011; Heuer et al. 2012; Simpson et al.; 2012; Le Tacon et al. 2000). Hypoxaemia and cardiovascular collapse represent the initial and most serious life-threatening complications associated with difficult airway access in the critically ill (Jaber et al. 2006; De Jong et al. 2014a; 2015). To prevent and limit the incidence of life-threatening complications following difficult intubation, a score that allows accurate prediction of difficult intubation in the ICU has been developed. In addition, several preoxygenation techniques and intubation algorithms are outlined, including new devices for intubation such as videolarinoscopes.

be set at a high range to homogenise ventilation through the lungs and to decrease the impact of leaks. Third, leaks should be avoided and diagnosed either by a flaccid reservoir bag or by the absence of a normal capnography waveform, since leaks impair the efficacy of preoxygenation.

In critically ill patients, the advantage of a prolonged period of preoxygenation has not been clearly demonstrated. Most of them present with acute respiratory failure with a certain amount of shunt, a reduced functional reserve capacity, and do not respond to administration of oxygen as well as patients scheduled for surgery, even after an increase of preoxygenation duration from 4 to 8 minutes (Mort et al. 2009).

Noninvasive ventilation (NIV) as a preoxygenation manoeuvre has therefore been evaluated in critically ill patients. The rationale for use of NIV during preoxygenation is to recruit lung tissue available for gas exchange: to “open the lung” with the pressure support and “keep the lung open” with the positive end-expiratory pressure (PEEP), which permits limitation of alveolar derecruitment. Our group reported its benefits compared to administration of oxygen alone (Baillard et al. 2006). Indeed, in a randomised controlled trial including hypoxaemia patients, the incidence of severe hypoxaemia (peripheral saturation in oxygen [SpO<sub>2</sub>] below 80%) within 30 minutes after intubation was 7% in the NIV group, compared to 42% in the oxygen group. To perform NIV for 3 to 5 minutes in critically ill patients, the facial masks available in every ICU room are sufficient. The patient should be in the semi-sitting position, FiO<sub>2</sub> set at 100%, inspiratory pressure set to observe a tidal volume of 6 to 10 ml/kg and respiratory rate of 10 to 25 cycles/minute. However, NIV has to be removed during the tracheal intubation, and no oxygen is administered to the patient during this apnoea period (Mosier et al. 2016; Papazian et al. 2016).

Recently we reported the first trial assessing preoxygenation using a novel strategy of preoxygenation adding apnoeic high-flow nasal cannula oxygen (HFNC) to NIV to perform orotracheal intubation in hypoxaemic ICU patients (Jaber et al. 2016). We found that, despite similar baseline characteristics and oxygenation, this novel strategy of preoxygenation was more effective at reducing oxygen desaturation in comparison to the reference method using NIV alone. This proof-of-concept study suggests that the novel strategy of preoxygenation using the association of NIV and HFNC for apnoeic oxygenation applied together is safe and more effective in preventing oxygen desaturation than the preoxygenation

reference method using NIV alone in critically ill patients with severe hypoxaemic respiratory failure. This novel approach could be used in severe hypoxaemic ICU patients in order to decrease severe hypoxaemia related to intubation procedure, which can result in cardiac arrest, cerebral anoxia and death.

To open the lung after the apnoea period during intubation procedure, an RM, which consists of a transient increase in inspiratory pressure, can be applied after tracheal intubation. Several manoeuvres exist, but the one best described in this situation consists of applying a continuous positive airway pressure (CPAP) of 40cmH<sub>2</sub>O for 30 to 40 seconds (Constantin et al. 2010; Futier et al. 2011; 2010). A randomised controlled trial was conducted by our group in 40 critically ill patients in the ICU who required intubation for acute hypoxaemic respiratory failure (Constantin et al. 2010). Compared to no RM, RM performed immediately after intubation was associated with a higher PaO<sub>2</sub> (under 100% FiO<sub>2</sub>) both 5 minutes after intubation (93 ± 36 vs 236 ± 117 mmHg) and 30 minutes after intubation (110 ± 39 and 180 ± 79 mmHg).

**Table 1.** MACOCHA Score Calculation Worksheet

	Points
<b>- Factors related to patient</b>	
Mallampati Score III or IV	5
Obstructive Sleep Apnoea Syndrome	2
Reduced Mobility of Cervical Spine	1
Limited Mouth Opening <3cm	1
<b>- Factors related to pathology</b>	
Coma	1
Severe Hypoxaemia (<80%)	1
<b>- Factor related to operator</b>	
Non Anaesthesiologist	1
<b>Total</b>	<b>12</b>

Sources: De Jong et al. 2014a; 2013b

M. Mallampati score III or IV

A. Apnoea Syndrome [obstructive]

C. Cervical spine limitation

O. Opening mouth <3cm

C. Coma

H. Hypoxia

A. Anaesthesiologist Non trained

Coded from 0 to 12

0 = easy

12 = very difficult

**Table 2.** Intubation Bundle Care Management, “The Montpellier-ICU Intubation Algorithm”

PRE-INTUBATION
1. Presence of two operators
2. Fluid loading (isotonic saline 500ml or starch 250ml) in absence of cardiogenic oedema
3. Preparation of long-term sedation
4. Preoxygenate for 3 min with NIV in case of acute respiratory failure (FiO <sub>2</sub> 100%, pressure support ventilation level between 5 and 10 cmH <sub>2</sub> O and PEEP of 5 cmH <sub>2</sub> O) combined with high-flow nasal cannula oxygen for apnoeic oxygenation in case of acute respiratory failure
PER-INTUBATION
5. Rapid sequence induction: <ul style="list-style-type: none"> <li>- Etomidate: 0.2-0.3 mg/kg or ketamine 1.5-3mg/kg</li> <li>- Succinylcholine: 1-1.5 mg/kg (in absence of allergy, hyperkalaemia, severe acidosis, acute or chronic neuromuscular disease, burn patient for more than 48h and medullar trauma)</li> <li>- Rocuronium: 0.6 mg/kg IVD in case of contraindication to succinylcholine or prolonged stay in the ICU or risk factor for neuromyopathy</li> </ul>
6. Sellick manoeuvre
POST-INTUBATION
7. Immediate confirmation of tube placement by capnography
8. Norepinephrine if diastolic blood pressure remains < 35mmHg
9. Initiate long-term sedation
10. Initial protective ventilation: tidal volume 6-8 ml/kg, PEEP < 5 cmH <sub>2</sub> O and respiratory rate between 10 and 20 cycles/min, FiO <sub>2</sub> 100% for a plateau pressure < 30 cm H <sub>2</sub> O
11. Recruitment manoeuvre: CPAP 40 cmH <sub>2</sub> O during 40s, FiO <sub>2</sub> 100% (if no cardiovascular collapse)
12. Maintain intubation cuff pressure from 25-30 cmH <sub>2</sub> O

Adapted from De Jong et al. 2014a; Jaber et al. 2010; 2016

Preoxygenation and RM are only one of the procedures that may improve airway safety. Managing the airway of at-risk patients presents some unique challenges for the anaesthesiologist or intensivist. The combination of a limited physiologic reserve in these patients and the potential for difficult mask ventilation and intubation mandates careful planning with a good working knowledge of alternative tools and strategies, should conventional attempts at securing the airway fail. To limit the incidence of severe complications occurring after this potentially hazardous procedure, the whole process (pre-, per- and post-intubation) should be guided by protocols geared towards patients' safety. In the ICU we designed a multicentre study and described how implementation of such bundle protocols improves the safety of airway management (Jaber et al. 2010). This bundle, the Montpellier ICU intubation algorithm, is summarised in Table 2 (De Jong et al. 2014a; Jaber et al. 2010; 2016).

Briefly, pre-intubation period interventions consist of fluid loading in the absence of cardiogenic oedema, preoxygenation with NIV and HFNC for apnoeic oxygenation in the case of acute respiratory failure, preparation of sedation by the nursing team and the presence of two operators.

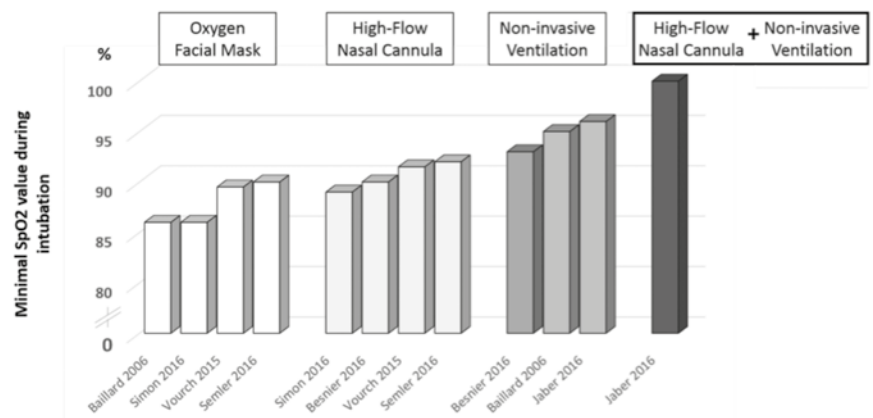
During the intubation period, recommended induction is rapid sequence induction (RSI) using short acting, well-tolerated hypnotics (etomidate or ketamine), and a rapid onset muscle relaxant (succinylcholine), with application of cricoid pressure (Sellick manoeuvre).

Just after the intubation (post-intubation period), we recommend verification of the tube's position by capnography (a technique which allows confirmation of the endotracheal position of the tube and verification of the absence of oesophageal placement), initiation of long-term sedation as soon as possible (to avoid agitation) and use of protective mechanical ventilation settings, with a RM following intubation after haemodynamic stabilisation. At any time, vaso-pressors are mandatory in the event of severe haemodynamic collapse.

### Airway Management Algorithm for Difficult Intubation in the ICU

As previously recommended in the operating theatre (Amathieu et al. 2011), an airway management algorithm is advised in the ICU, as proposed in Figure 2 (De Jong et al. 2014a).

First, the difficulty of intubation is evaluated using the MACOCHA score (De Jong et al. 2013b). The availability of equipment for management of a difficult airway is checked.

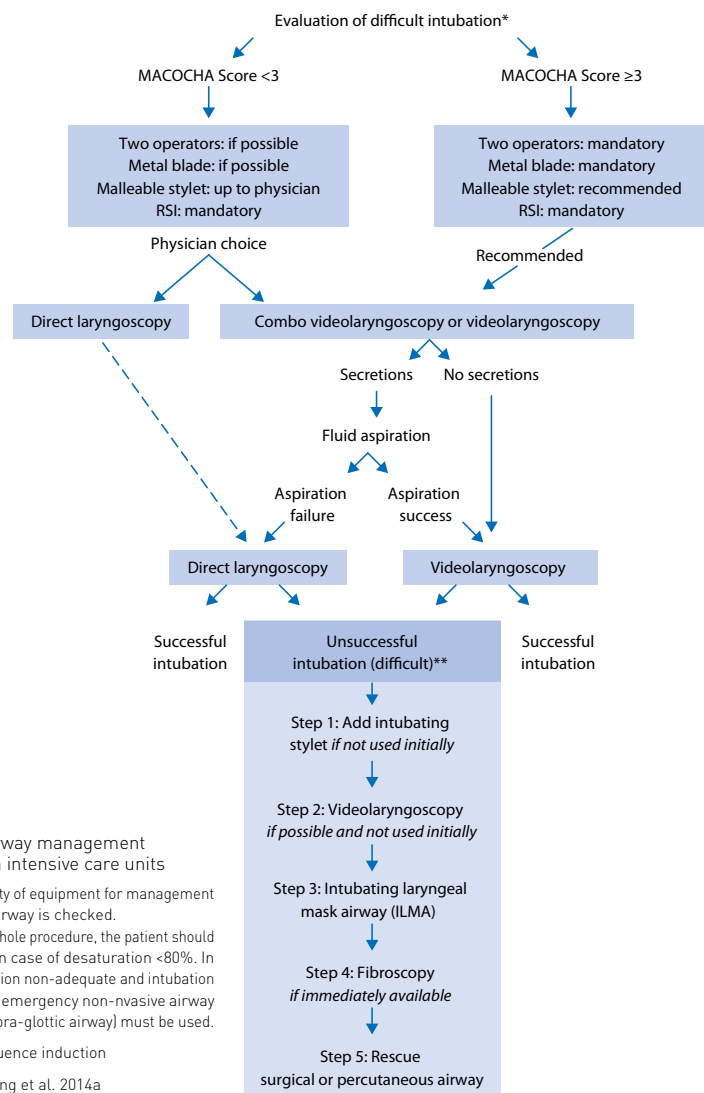


**Figure 1.** Minimal SpO<sub>2</sub> values during the intubation procedure in severe hypoxaemic patients throughout both randomised and non-randomised studies according to the method of preoxygenation

SpO<sub>2</sub> peripheral capillary oxygen saturation

The minimal SpO<sub>2</sub> values increase with the development of the methods of preoxygenation throughout studies and time. Use of high-flow nasal cannula oxygen slightly improved the minimal SpO<sub>2</sub> values compared to traditional preoxygenation using an oxygen facial mask. This improvement was higher using noninvasive ventilation, and even more important when combining high-flow nasal cannula with noninvasive ventilation.

Source: Jaber et al. 2016, with permission of Springer



**Figure 2.** Airway management algorithm in intensive care units

\* The availability of equipment for management of a difficult airway is checked.

\*\* During the whole procedure, the patient should be ventilated in case of desaturation <80%. In case of ventilation non-adequate and intubation unsuccessful, emergency non-nvasive airway ventilation (supra-glottic airway) must be used.

RSI rapid sequence induction

Source: De Jong et al. 2014a

# 22<sup>nd</sup>

INFECTION  
AND  
SEPSIS  
SYMPOSIUM

INTERNATIONAL  
SYMPOSIUM  
ON INFECTIONS  
IN THE CRITICALLY  
ILL PATIENT

The aim of this three days symposium is to review current concepts, technology and present advances in infections in the critically ill patients.

Sepsis, Pulmonary Infections, Basic Research, Pulmonary Infections Treatment and Prophylaxis Therapy of severe infections will be the topics of the main sessions presented by experts who will review and update the new advances on infections in the critically ill patient. At the end of each session a Clinical Controversy, Pannel Discussion or Case Report Discussion will be organized.

## Organized by

Antonio Artigas, MD  
Jean Carlet, MD  
Paulo Mergulhão, MD  
Michael Niederman, MD  
José Arthur Paiva, MD  
Antoni Torres, MD

## Technical Secretariat:

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PORTO  
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ISICIP

During the procedure, the patient should be ventilated in case of desaturation <80%. In case of inadequate ventilation and unsuccessful intubation, emergency noninvasive airway ventilation (supra-glottic airway) must be used.

Then, if difficult intubation is predicted (MACOCHA score  $\geq 3$ ), the presence of two operators and a metal blade is advised, and use of a malleable stylet is recommended. Videolaryngoscopy or combo videolaryngoscopy are also recommended in case of predicted difficult intubation. Otherwise, the choice of the device is at the discretion of the physician. In case of abundant secretions even after aspiration, direct laryngoscopy is preferred rather than videolaryngoscopy. Videolaryngoscopes are indirect rigid fibre optic laryngoscopes with a video camera mounted at the end of an angled blade. Recently, videolaryngoscopes, such as C-Mac® (Karl Storz) (Noppens et al. 2012; Ng et al. 2012) or GlideScope (Verathon) (Kory et al. 2013; Lakticova et al. 2013) have demonstrated their efficiency in the ICU setting. Moreover, a recent study (De Jong et al. 2013a) assessed a new mixed videolaryngoscope that can be used as a direct or indirect view laryngoscope. This before-after prospective study showed that the systematic use of a mixed videolaryngoscope for intubation in a quality improvement process using an airway management algorithm significantly reduces the incidence of difficult laryngoscopy and/or difficult intubation.

These results were confirmed by a systematic review and meta-analysis establishing that use of videolaryngoscopes for intubation in the ICU could reduce the rate of difficult intubation (De Jong et al. 2014b). When used by trained operators, videolaryngoscopes seem efficient to reduce difficult intubation in ICU, but a large multicentre study is needed to assess if the complications of intubation are decreased using videolaryngoscopes.

Finally, in case of intubation failure, an intubating stylet (malleable stylet or long flexible angulated stylet) is added first, followed successively by the use of videolaryngoscopy if not used first, the use of an intubation laryngeal mask airway, the use of fibroscopy and finally the use of a rescue percutaneous or surgical airway.

Studies are needed to assess if applying this protocol in the ICU leads to a reduction of difficult intubations and complications. In each ICU, this airway management algorithm should be adapted according to the ICU ways of working.

### Conclusion

Predicting risk factors of difficult intubation should be assessed in the ICU, in order to identify the patients at risk of difficult intubation using a simple score applicable at the bedside, the MACOCHA score. Preoxygenation is a standard of care before intubation, with the aim of increasing the lung stores of oxygen.

In critically ill patients, the combination of NIV, HFNC to allow apnoeic oxygenation and post-intubation RM is recommended. Then an intubation bundle should be applied in order to reduce complications of difficult intubation, including verification of the endotracheal position of the tube using capnography. Finally, an airway management algorithm is strongly advised in the ICU, adapted according to the ICU's ways of working and the training of operators for new intubation devices such as videolaryngoscopes. ■

### Abbreviations

CPAP continuous positive airway pressure  
 FIO<sub>2</sub> fraction of inspired oxygen  
 HFNC high-flow nasal cannula oxygen  
 ICU intensive care unit  
 NIV noninvasive ventilation  
 PaO<sub>2</sub> partial oxygen pressure  
 PEEP positive end-expiratory pressure  
 RM recruitment manoeuvres  
 RSI rapid sequence induction  
 SpO<sub>2</sub> peripheral oxygen saturation or peripheral capillary oxygen saturation

### Conflict of Interest

Dr. Jaber reports receiving consulting fees from Dräger, Hamilton, Maquet, and Fisher & Paykel. No potential conflict of interest relevant to this article was reported for the other authors.

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## GE SYMPOSIUM

Tuesday, October 4<sup>th</sup>  
12:30-14:00  
Room Glasgow

# Advanced Tools for Lung Protection and Nutrition More Complexity or Less Complication?



# ADVANCED TOOLS FOR LUNG PROTECTION AND NUTRITION

## MORE COMPLEXITY OR LESS COMPLICATION?



**Massimo Antonelli**

President  
European Society of Intensive Care  
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Chair  
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### Introduction

The intensive care unit (ICU) is a complex environment, due to the surroundings, the heterogeneity of patients, caregiver turnover and the at times lengthy patient stays, which lead to increased complexity. The multiple technologies available add another layer of intricacy. However, with the modern tools available to the intensivist, it is now possible to personalize care to meet the heterogeneous needs of our patients. “One size fits all” is not possible or advisable any more, and the technology is crucial to enable intensivists to personalize therapy, whether that is lung protective ventilation or a nutritional plan.

I am delighted to introduce this supplement, based on presentations at a workshop at the European Society of Intensive Care Medicine LIVES 2016 in Milan.

# PROTECTIVE VENTILATION

## WHEN AND WHY TO INDIVIDUALIZE

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### ARDS is Heterogeneous

Acute respiratory distress syndrome (ARDS) is a heterogeneous entity. Calfee and colleagues’ analysis of the ARMA and ALVEOLI trials (Calfee et al. 2015) differentiated two ARDS subphenotypes, one of which was categorized by more severe inflammation and worse clinical outcomes. Response to positive end-expiratory pressure (PEEP) was different in the two subphenotypes. High PEEP showed more ventilator-free days and organ failure-free days and increased survival only in the subphenotype characterized by a greater inflammation. ARDS severity also affects the response to treatment. In a meta-analysis on studies of high vs. low PEEP in ARDS, Briel and colleagues showed that higher PEEP reduced the risk of death and shortened the time to unassisted breathing only in moderate-to-severe ARDS cases (Briel et al. 2010). In mild ARDS the opposite may be true. So, the same treatment may change the outcome according to the phenotype and to severity. This concept has been incorporated in current

recommendations (Ferguson et al. 2012), stating that higher PEEP should be reserved to moderate-to-severe ARDS cases (Figure 1).

### Why and How to Individualize Ventilation

Individualized treatment has the potential to improve patient outcome and reduce side effects of treatment in patients who do not respond, thus allowing better use of resources. Protective ventilation is currently used in ARDS and it is based on the application of low tidal volume (Vt) and moderate-to-high PEEP with the aim of avoiding overdistension and optimizing recruitment. Individualising protective ventilation in ARDS means selecting the right tidal volume and the right level of PEEP for each individual patient.

ARDS is a restrictive disease and this is well reflected in the concept of the “baby lung” (the size of the aerated lung still accessible to ventilation is reduced to the size of the lung of a baby). The obvious implication is that the size of the “baby” lung should determine the ventilator settings. Decreasing Vt from 12 ml/kg of predicted body weight (PBW) to 6 ml/kg PBW was shown to improve survival, likely because of the decrease in lung overdistension (Acute Respiratory Distress Syndrome Network 2000). A Vt of 6 ml/kg PBW does not assure that lung overdistension is always avoided in every patient. A smaller “baby” lung can in fact be hyperinflated even using a Vt of 6 ml/kg PBW (Terragni et al. 2007), suggesting that Vt should be better tailored on the size of the baby lung than on the body weight (Gattinoni et al. 2016). Modern ventilators have the technology to measure directly the aerated lung volume thus allowing to normalize tidal volume on the size of the baby lung.

Another way to try to normalize the tidal volume to the size of the baby lung is to use the compliance of the respiratory system (Crs). Compliance in ARDS is not low because the lung is stiff, it is low because the aerated lung is small. Thus, compliance is a good index of normally aerated lung tissue and can give an estimation of the baby lung size.

Normalising tidal volume to the compliance of the respiratory system gives the driving pressure (Vt/Crs). The driving pressure (ΔP) can be calculated at the bedside as plateau pressure minus PEEP (Pplat – PEEP), and it can be considered as an estimate of the lung strain. Lung strain is the lung deformation imposed by tidal ventilation, and it is equal to the ratio of tidal volume divided by the functional residual capacity, that is the size of the aerated baby lung at end-expiration.

$$\text{Lung Strain } (\Delta P) = \frac{\text{Tidal volume (Vt)}}{\text{Size of the baby lung (Crs)}}$$

An analysis of data on 3562 ARDS patients examined the relationship between driving pressure and survival (Amato et al. 2015), and found that driving pressure was the ventilation variable most strongly associated with survival. Their analysis demonstrated that the mortality rate paralleled changes in tidal volume only when it is expressed as a function of compliance, which is an estimation of the baby lung, that is the driving pressure (Vt/Crs). On the contrary, mortality rate was not correlated with tidal volume when it is expressed as a function of body weight (Vt/PBW). This shows clearly that the tidal volume should not be sized on patient’ predicted body weight but on the size of the baby lung.

There is a relationship between the size of the baby lung, recruitability, recruitment, tidal volume and PEEP. Richard and colleagues demonstrated that low tidal volume promotes alveolar derecruitment that can be prevented by an increase in PEEP (Richard et al. 2003). This study found that, for a given plateau pressure (i.e., similar end-inspiratory distension), a high

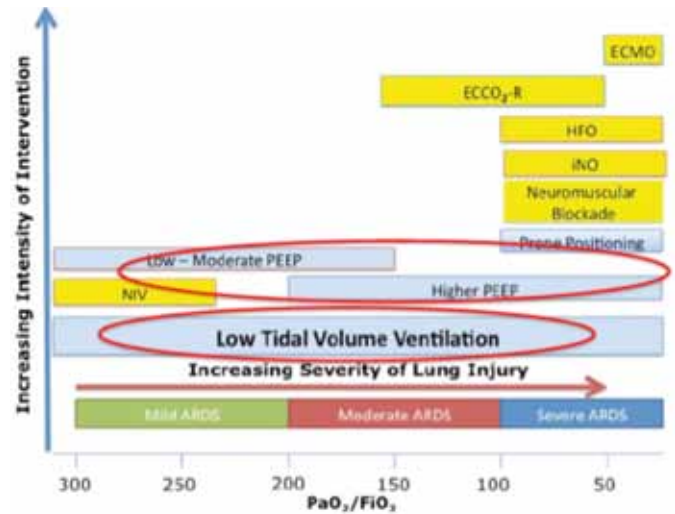


Figure 1. Aligning Therapeutic Options with the Berlin Definition  
Source: Ferguson et al. (2012) With permission of Springer

PEEP-low Vt strategy increased recruitment and PaO<sub>2</sub> as compared to a low PEEP-high Vt strategy, suggesting that the effect of PEEP on recruitment is greater than that of Vt. By promoting alveolar recruitment, PEEP may increase the size of the baby lung, allowing a better accommodation of tidal volume, which is reflected by a decrease in the driving pressure. Thus, PEEP is a measure that can increase the size of the baby lung.

High PEEP is not recommended for all ARDS patients. Two trials comparing high vs. low PEEP failed to show any advantages of an indiscriminate use of high PEEP in all ARDS patients (Brower et al. 2004; Meade et al. 2008). In fact, it is logical to use higher PEEP only in patients who have some parts of the lungs that can be recruited. Recruitability (lung that can be recruited) is clearly correlated with recruitment (lung that is actually recruited) (Gattinoni et al. 2006), suggesting that PEEP should only be applied when there is a potential for recruitment. Gattinoni showed that patients with highly recruitable lung have more severe and more diffuse injury, i.e., they have a smaller baby lung at low PEEP (Gattinoni et al. 2006).

Caironi and colleagues (2015) further elucidated this concept. These authors differentiated patients according to the amount of cyclic lung opening (during inflation) and closing (during deflation), which is a measure of recruitability (the higher the cyclic opening-closing, the higher the recruitability). They demonstrated that increasing PEEP decreases the cyclic opening and closing (i.e., increases lung recruitment) only in patients with higher recruitability. In addition, the increased recruitment obtained with PEEP in these patients was correlated with an increased survival. Thus, using high PEEP increases recruitment when there is a high potential for recruitment and this may improve outcome. Increasing PEEP has no effect and may even be detrimental in patients with a lower potential for recruitment.

### How to Assess Recruitment to Set PEEP at the Bedside

PEEP is used to recruit the lung. Measuring or estimating lung recruitment is therefore important for optimizing the PEEP setting.

A simple way to assess recruitment induced by PEEP is to measure the lung volume. Dellamonica and colleagues (2011) compared a method to estimate alveolar recruitment derived from bedside measurement of end-expiratory lung volume (nitrogen washout/washin technique) with the measurement of recruitment obtained on the pressure volume curves

(standard technique). Estimated recruitment with increasing PEEP was expressed by:  $\Delta\text{PEEP}$  ( $\Delta\text{EELV} \times \text{CrS}$  at low PEEP). They showed that the two methods yielded similar results, thus demonstrating that the nitrogen washout/washin technique can be used for bedside assessment of PEEP-induced recruitment.

Changes in oxygenation can be used to estimate recruitment. Maggiore and coworkers reported that a significant correlation exists between recruitment and oxygenation (Maggiore et al. 2001). This correlation, however, is too weak to allow, in an individual patient, to assess PEEP-induced recruitment by its effect on oxygenation.

Maggiore and colleagues also found a very tight correlation between compliance at zero or low PEEP and recruitment obtained with PEEP 15 cm  $\text{H}_2\text{O}$  (Maggiore 2001). In other words, compliance is an estimate of recruitability—the higher the compliance, the higher the recruitment with PEEP.

It is possible to use compliance to individualize the PEEP setting according to recruitability. Let's imagine to ventilate an ARDS patient with a Vt 6 mL/kg PBW and to keep the plateau pressure at the safe limit of 28-30 cm  $\text{H}_2\text{O}$ . If the compliance at low PEEP (e.g., 5 cm  $\text{H}_2\text{O}$ ) is high, the pressure oscillation due to tidal ventilation (i.e., the driving pressure) will be small. So the maximum PEEP that can be applied to reach a plateau pressure of 28-30 cm  $\text{H}_2\text{O}$  will be high. The opposite will occur if the compliance at low PEEP is low. In this case, tidal volume will produce a higher driving pressure, so that the maximum PEEP that you can use to reach the target plateau pressure is low, because much of the pressure is already taken by the driving pressure. This is a way to individualize the PEEP setting in order to maximize recruitment in a safe way and it was used in the EXPRESS trial.

The EXPRESS trial compared a moderate PEEP strategy (5-9 cm  $\text{H}_2\text{O}$ ), to minimize overdistension, to a PEEP setting to safely maximize recruitment, as described above. In this study, there was no difference in mortality, but there were more patients breathing without ventilator assistance when PEEP was individually set to maximize recruitment. In more severe patients, there was a clear trend to a lower mortality and a significantly higher number of patients breathing without ventilator assistance when PEEP was set to maximize recruitment. On the contrary, higher PEEP had no effect in patients with mild ARDS (Mercat et al. 2008). We also need to consider cases where mechanical ventilation fails, i.e., patients with a too small baby lung to allow for a safe conventional mechanical ventilation. In these patients, Terragni and colleagues (2009) showed that use of extracorporeal carbon dioxide removal (ECCO<sub>2</sub>R) allowed to provide ultraprotective ventilation with a reduction of tidal volume below 6 ml/kg PBW (up to 4 ml/kg).

## Conclusion

The future of mechanical ventilation in ARDS is an individualized approach. First of all, intensivists need to become better at recognising ARDS. As shown by the LUNG-SAFE study (Bellani et al. 2016), ARDS is in fact still under-recognised, undertreated and, probably for these reasons, still associated with high mortality. We should also understand that ARDS is a heterogeneous syndrome, comprised of distinct phenotypes, different severity and different response to treatments. We need to recognise this and to adapt mechanical ventilation to individual patient conditions, particularly when there is a clear failure of the standard lung protective ventilation strategy. This means knowing the size of the lung that should be ventilated, to select the optimal tidal volume, and knowing if the lung is recruitable and how much can be recruited, to optimize the level of PEEP. Modern technology allows us to have this information at the bedside.

As Timothy G. Buchman wrote: "Precision medicine for critical illness and injury is desirable and achievable. Part of precision lies in standardization of practice. Part of the precision lies in individualization of care" (Buchman 2016). These all come together as the right care for the right patient, every time. ■

## Conflict of Interest

Prof. Maggiore is principal investigator of the RINO trial (NCT02107183), sponsored by Fisher & Paykel. He has received research grants from Fisher & Paykel and lecture fees from Draeger and GE Healthcare.

## Take Home Points

- Individualized ventilation in ARDS can potentially improve outcome, reduce treatment side effects and use resources better
- Recognition and diagnosis of ARDS needs to improve
- Differentiating and recognising the ARDS phenotypes is important for treatment and outcome
- Protective ventilation is mandatory to reduce ventilator-induced lung injury (VILI) and improve survival in ARDS patients
- Individualized ventilation should be based on: 1) recognising ARDS 2) assessing features of lung injury and its severity 3) individually titrating tidal volume and PEEP, according to the lung volume 4) most importantly, understanding the physiology behind mechanical ventilation

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# INDIRECT CALORIMETRY TO MEASURE ENERGY REQUIREMENTS

## FROM CONSENSUS TO DAILY PRACTICE

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### Why Personalize Nutrition Therapy?

The need for personalized nutrition therapy for ICU patients is shown by several observational studies that measured the energy needs of critically ill patients. The 2005 study by Villet and colleagues found that patients with an energy deficit had an increased number of complications, especially infections (Villet et al. 2005). Weijs and colleagues (2014) showed in a cohort of 843 patients that survival varied according to the energy deficit; with no energy deficit there was a high rate of survival, but with a certain energy deficit a low rate of survival. In non-septic critically ill patients, early high protein intake was associated with lower mortality and early energy overfeeding with higher mortality. In septic patients early high protein intake had no beneficial effect on mortality. The study by Krishnan and colleagues showed that a moderate caloric intake of approximately 9 to 18 kcal/kg per day was associated with better outcomes than higher levels of caloric intake, and yet this was below the American College of Chest Physicians' recommendations (Krishnan et al. 2003).

The hypothesis that hypocaloric feeding is beneficial is summarized in a recent review of randomized controlled trials comparing standard amounts of enteral nutrition with lesser amounts (Koretz 2016), with varied outcomes. The study by Petros and colleagues is a small study (n=100) that showed hypocaloric feeding to be associated with more nosocomial infections but with more glucose control and less gastrointestinal intolerance. We are still waiting for conclusive data on hypocaloric feeding, however.

Surveys show that there is a difference between what nutrition is prescribed and what the patient actually receives (for example, Alberda et al. (2009) showed that patients received approximately half of what was prescribed). It seems that we do practise hypocaloric nutrition.

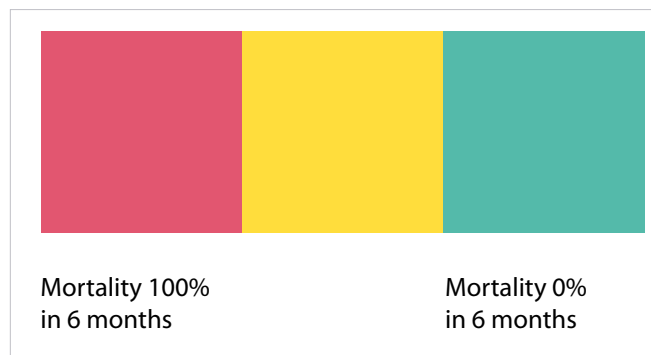
In the ICU there will be a proportion of patients with a high risk of mortality, in whom nutrition is not likely to change the course of the

illness. At the other extreme are the patients who will do well, who have a short stay in the ICU (Figure 1). Then are the others for whom nutrition is very important. But if we included all these groups of patients in a nutrition study, the results would be distorted. That is why many studies are inconclusive, as they do not have clearly defined inclusion criteria.

In ICU patients who receive nutrition there is basal energy expenditure, diet-induced energy expenditure, as we feed the patient, and activity-induced energy expenditure, as we try to mobilise patients. There is exogenous energy intake and the question is if this exogenous energy intake can completely eliminate mobilisation from endogenous stores. Very little is known about this, and there are good examples that it is the case that we cannot completely counteract mobilisation of energy inside the body. It is an important research question, as it relates to whether the energy expenditure we measure is always synonymous with caloric need. We know that we lose muscle regardless of what we do, because of inactivity and allergic reactions. There is much evidence that if you overfeed ICU patients, they are quite capable of having their body fat stores expanded by nutrition. There is a consensus not to overfeed patients, but not on how to define this, and whether energy expenditure is the correct parameter or not.

### Guidelines Recommend Indirect Calorimetry

The European and North American nutrition guidelines both recommend the use of indirect calorimetry to measure energy expenditures (Singer et al. 2009; McClave et al. 2016). The European guidelines state that during acute illness, the aim should be to provide energy as close as possible to the measured energy expenditure in order to decrease



**Figure 1.** A schematic cartoon illustrating the heterogeneity of critically ill patients. Outcome is most often related to acute pathology and co-morbidities not related to nutrition. Therefore it is necessary to define which patients may benefit from the nutrition intervention, which are the patients in the yellow zone. This concern applies both to bedside prescription and to elucidation of the external validity of published evidence.

Source: Wernerman and Rooyackers (2015)

### Arguments for Indirect Calorimetry

- Promotes individualized nutrition
- Prevents overfeeding
- Easy to do
- Puts focus on nutrition
- Best in show

negative energy balance, and there is a recommendation for parenteral nutrition if indirect calorimetry is not used (Singer et al. 2009). The North American guidelines suggest use of indirect calorimetry (IC) to measure energy requirements, in the absence of variables that affect the accuracy of measurement (McClave et al. 2009).

There are arguments heard against indirect calorimetry—that it is expensive, inexact, technically difficult and time-consuming. It is not easy to interpret the data you get in all cases, but measurement is better than guesswork, and nothing is easy in the ICU. To sustain a correct nutrition plan we need the correct data. When continuous indirect calorimetry measurements were compared with formulas used to predict energy expenditure, they were better (Reid et al. 2007). It can be difficult to interpret, depending on the conditions. However, for patients at either extreme of body mass index (BMI), estimation with formulas is very difficult, and indirect calorimetry is the best tool. Indirect calorimetry should be used regularly because there is a learning curve and if it is not used regularly readings may be less reliable (Wernerman and Rooyackers 2015). The greatest difficulty in my view is to have a fair estimate of endogenous energy production that we cannot eliminate by exogenous energy production. And this is not a constant measurement and should therefore be repeated later in the ICU stay.

Indirect calorimetry is not time-consuming. Taking indirect calorimetry measurements for 15 minutes under standardised conditions is usually sufficient to measure energy expenditure. Zijlstra et al. (2007) showed that in their study that took measurements over 24 hours. If the patient has a long stay in the ICU, their energy expenditure will vary a lot, so measurements have to be taken on different days.

Most instruments for indirect calorimetry have sampling close to the patient and they have a flow meter that measures breath by breath. The

International Multicentric Study Group for Indirect Calorimetry explored the issues with measurement for patients on mechanical ventilation; there are some technical difficulties in this as temperature and humidity must be measured (Oshima et al. 2016). Our ICU Metabolism and Nutrition research group at Karolinska Institute has published studies that compared indirect calorimetry instruments, and they compare quite well, with a scatter that, though not ideal, is better than using a formula or some other method of estimating energy expenditure (Sundström et al. 2013; Sundström Rehal et al. 2016).

Indirect calorimetry is integrated on a monitor or on a ventilator, and it does not need to be purchased separately. You should measure the cost of the device against the number of measurements it will take. Indirect calorimetry is not expensive when you consider that most of the ICU costs are staffing costs.

The most compelling argument for indirect calorimetry is that if you want to individualize nutrition for your patients, then you have to measure energy expenditure. Use of indirect calorimetry means there is a large scatter in relation to body size that clinicians need to be aware of. However, indirect calorimetry is an instrument to prevent overfeeding, it is easy to use, and it puts the right focus on nutrition. It is the “best in show”. ■

### Conflict of Interest

Jan Wernerman declares that he is a member of Medical Advisory Boards and also an invited speaker for Baxter, Danone, Fresenius-Kabi, GE Healthcare, Grifols, and Nestlé.

### Take Home Points

- Indirect calorimetry (IC) is the gold standard to assess the energy requirements of patients
- 15 minutes of indirect calorimetry under standardised conditions is sufficient time to measure energy expenditure
- IC is available integrated into monitors or ventilators so technically easy to measure and not an expensive add-on
- The best measurement we have right now
- No more difficult to interpret than many other measures

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# OPTIMIZING NUTRITION WITH AN INTEGRATED NUTRITION MODULE

## MYTH OR REALITY?

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**A**s a neurointensivist with a strong interest in nutritional support, I was delighted to trial a new integrated nutritional module. We know that nutrition really matters to our ICU patients in the context of first indicators. For example, our research group recently published a paper about two patients with viral meningoencephalitis. Invasive neuromonitoring of brain metabolism showed episodes of severe neuroglycopenia (brain glucose  $<0.7$  mM/l) in both patients that were not attributable to decreased cerebral perfusion or hypoglycaemia. CMD-glucose levels changed depending on variations in insulin therapy, nutrition, and systemic glucose administration. The metabolic profile showed a pattern of non-ischaemic metabolic distress suggestive for mitochondrial dysfunction (Kofler et al. 2016).

Our ICU has 10 beds equipped with mechanical ventilation. At the time of the presentation, we had tested this system for 6 weeks.

### IT Solution

The Nutrition Module tested at Innsbruck was created by GE and Nestlé to integrate the hardware (pumps, monitor, ventilator) with the patient data management system software (Centricity). tirolkliniken University Hospital Innsbruck IT supported the installation and implementation. The module is installed on a PC and connected to the nutrition pump and to the monitor (Figure 1).

### Nutritional Needs in a SingleView

After using indirect calorimetry to assess the energy requirements of the patient, the doctor prescribes the nutrition. Using the new Nutrition Module we can also easily input body weight and check the calorie amount the patient needs. The nutrition is delivered through a pump, provided by Nestlé, and at a glance the doctor can see how much has

been administered, compared to the patient's energy needs. The system makes the calculation and shows how many calories and how much protein has been administered. This information can be displayed as a data spreadsheet and we plan to provide this also visually, to show trends. So, in one page view the doctor can see what has been delivered and what the metabolic, caloric and protein needs of the patient are, and can immediately understand and optimize the prescription to achieve those needs and see if this leads to improved patient outcomes.

With the new Nutrition Module our intention was to keep it simple. While the prescription of energy and protein relies on calculations, we are doing it now in a structured way. The module integrates six numbers and we can see the middle or late phase of the treatment period of the patient. The initial system does not have indirect calorimetry attached yet. This will improve it even more. We are also working with our pharmacists to attach other infusion pumps. There are many nutrition products available and we will liaise with our hospital pharmacy so that we can implement the key components of the nutrition formulas so these will be included in the caloric and protein calculations for macro- and micronutrients.

We use blind formulations for ongoing clinical trials on nutrition, and at the moment we cannot account for these in the system. Some medications need to be accommodated in future, for example propofol and those that use glucose as a carrier solution for other medications and contribute non-nutritional calories (Bousie et al. 2016).

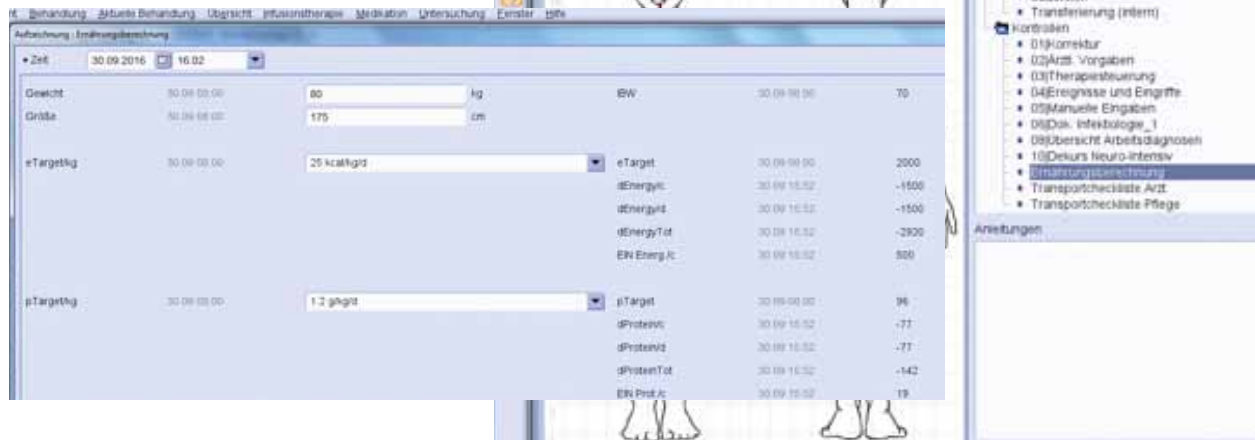


Figure 1. Nutrition Module

## «Critical Care Nutrition Therapy» – Synopsis (My Personal View)

© PDMS Neurological Intensive Care Unit, Innsbruck General Hospital – Medical University of Innsbruck Hospital

→ Using an IT Solution Is Key to Simplify & Improve Nutrition for ICU Patients: Myth or Reality?



- **No more myth (Busted!), it has become real**
- However, there is always **space for improvement** (e. g., **visualization, integration of indirect calorimetry tools, non-nutritional calories** etc.)
- Let's make the next step towards **improving the quality of treatment/care**

### Conclusion

Using the Nutrition Module will enable us to overcome variability in nutritional support, and use the data provided to plan for the future by analysing process and outcome indicators. Using this system is much simpler than our previous method, which involved complex and time-consuming calculations, and switching between screens.

There is room for improvement in this system, including some issues with visualisation, integration of indirect calorimetry tools, non-nutritional calories etc. We have used the system for a few months only and we are working together to improve this tool to provide even better quality of patient care. However, by using an IT solution, we can combine all the different measurements, and optimize and improve the quality of treatment of the patient. ■

### Conflict of Interest

Ronny Beer has received meeting attendance compensation from Baxter, research support and meeting attendance compensation from Bayer Health-Care, speakers' fees from Boehringer Ingelheim and GE, research support and meeting attendance compensation from Pfizer, contract research, speaker's

fees and meeting attendance compensation from Fresenius Kabi, contract research from vasopharm, a research grant from Austrian Science Fund (FWF). He is a member of the European Stroke Organisation's ICH Guidelines Working Group.

### Take Home Points

- A new tool integrates hardware and software to provide doctors with the full picture of the patient's nutritional requirements and intake
- A single view replaces switching between screens
- Data is provided in a spreadsheet and will in future be provided visually, to show trends
- Future development will integrate indirect calorimetry and infusion pumps to account for non-nutritional calories
- We should use these tools to improve further the quality of patient treatment and care

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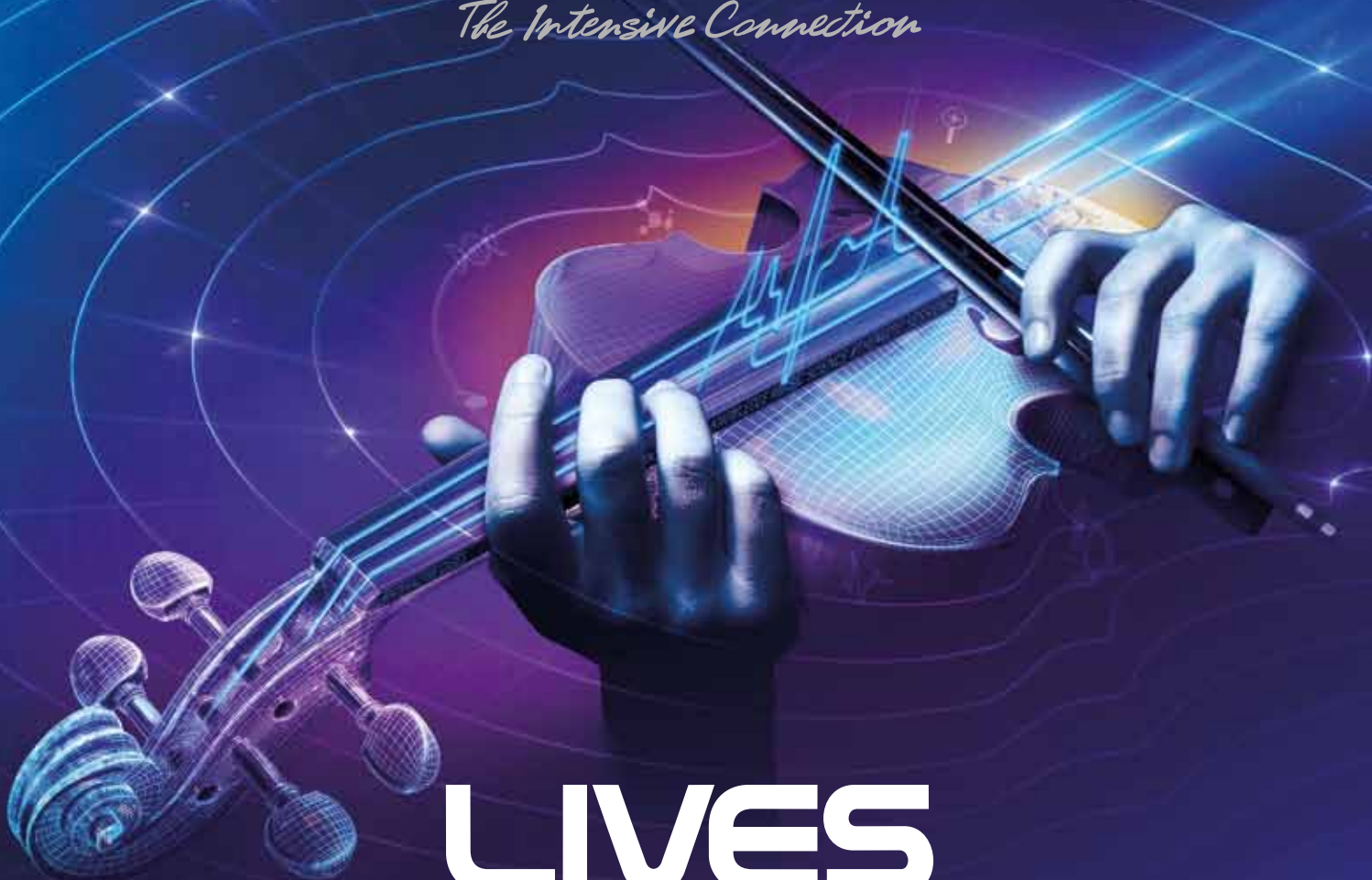
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## Chair's Concluding Remarks

Partnership with companies is essential for technological development in our ICUs. We have to face complexity every day, and if we have the help of an advanced technology in better targeting our therapies, we can better identify the most serious and severe patients. This technology greatly assists intensivists in their everyday clinical practice.



*The Intensive Connection*



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# EMERGENCY INTRASOSSEOUS ACCESS

## NOVEL DIAGNOSTIC AND THERAPEUTIC POSSIBILITIES AND LIMITATIONS

The intraosseous needle is an essential tool in emergency settings when initial vascular access is difficult to achieve. This paper focuses on possible biochemical analyses on blood from emergency intraosseous needles, suggesting principles of use as well as pointing out advantages and shortcomings.

tion n.d.) and Advanced Trauma Life Support (ATLS) (American College of Surgeons n.d.) now recommend placement of an IO line if adequate IV access cannot be established within three attempts or 90 seconds, whichever is sooner. Use of multiple IO needles is also an opportunity, for example in combat injuries (Sarkar and Philbeck 2009). The use of IO access in medical emergencies has recently been reviewed by Weiser et al. (2012).

Given that the indication for intraosseous access is the lack of other access to the circulation, blood from such an access could aid diagnostics in life-threatening conditions. However, potential damage to laboratory equipment, as IO aspirates may contain bone marrow particles, has been suggested (Nicoll and Rochester 2008). When analysing whole blood, bone fragments might lodge in the narrow tubings in modern laboratory analysers. This is feared by laboratory managers, who may be reluctant to analyse IO samples unless appropriately labelled (Salter and Maconochie 2008). Analysing IO samples labelled as venous samples in cell counters may cause delays, as the samples will contain immature cells. When the laboratory finds immature cells they will normally perform manual microscopy of the samples. This will cause delays in the reporting of test results. It is important to respect both the clinician that wants quick test results and the laboratory that does not want to damage their instruments. It is therefore essential to find ways of circumventing this problem and avoid unnecessary conflicts. This scenario has now changed, since point-of-care technology (POCT) with single-use cartridges allows rapid analysis of samples in a separate cassette, where

blood or IO aspirates are never in contact with the analysis device. This further strengthens the choice of POCT as the analysis modality, since POCT, in contrast to conventional laboratory equipment, provides test results within a few minutes. The main difference is the elimination of the transportation time of the samples to the centralised laboratory.

IO access in combination with POCT could allow acute laboratory analyses even in remote conditions or during the ambulance transport of the patient.

### Validation of IO Blood Gases by POCT

It would not be ethically appropriate to compare IO and IV access in critically ill humans without having performed initial animal studies. Utilising a model where healthy anaesthetised pigs were cannulated with a 15 Gauge IO needle, IO aspirates were taken and analysed by POCT hourly during a 6-hour experimental period. This instrument was not only suitable for analysing the samples without technical difficulties, but aspiration of IO samples was usually easily obtained. This was especially the case with the first sample, which probably is of the greatest clinical interest (Strandberg et al. 2012).

In the emergency situation, rough estimates on haemoglobin,  $PCO_2$  and bicarbonate, indicating acidosis/alkalosis of metabolic or respiratory origin, and electrolytes, may guide initial treatment. Arterial oxygen partial pressure and oxygen saturation were poorly reflected in IO samples. Biomarkers that are substantially different in venous and arterial blood are likely to be difficult to analyse adequately in IO samples. Evaluation of oxygenation may be performed utilising other mobile monitoring equipment,

**I**ntraosseous (IO) access has been used since 1922 as a method for delivering fluids and medications when conventional vascular access is difficult to achieve. The method was extensively used during the second world war (Wayne 2006). Today, both the European Resuscitation Council and American Heart Association guidelines state that IO access should be the first alternative when IV access is unsuccessful (European Resuscitation Council 2015; American Heart Association 2015). Pediatric Advanced Life Support (PALS) (American Heart Associa-

i.e. pulse oximeter. In a subsequent study, IO access and evaluation of blood gases, using POCT, was studied in children according to a similar protocol. IO and IV samples of children scheduled for diagnostic bone marrow aspiration were analysed using POCT. Similar to our results, IO samples did not differ considerably from IV, and may be clinically acceptable alternatives in an emergency. POCT analysis of intraosseous aspirates may thus be a useful guide for treatment (Veldhoen et al. 2014).

However, a more clinically relevant question is whether IO aspirates reflect arterial blood gas values during shock. Previous studies have demonstrated acceptable agreement between IO and central venous measurements of pH and  $\text{PCO}_2$  during cardiopulmonary resuscitation (Kissoon et al. 1997). We studied blood gas and acid base parameters in a porcine septic shock model. This experiment, for obvious reasons, could not be performed in humans. Endotoxaemic shock, frequently used to mimic septic shock, was induced by a continuous infusion of *E. coli* endotoxin during the entire 6-hour experimental period.

IO pH levels were approximately 0.1 units lower in IO samples than in arterial ones. Base excess was lower in IO versus arterial blood. The  $\text{PCO}_2$  levels in IO samples were clearly

## epinephrine delivered via the IO route is a clinically relevant alternative to IV administration

higher than those seen in arterial blood, with the venous levels on an intermediate level. IO lactate was also higher in IO samples than in arterial blood. Haemoglobin was somewhat lower and glucose was clearly lower in the IO aspirate than in arterial and venous samples, but still seems close enough to diagnose severe hypoglycaemia. Since there was consistency regarding these differences, the direction of bias can be predicted (Strandberg et al 2014).

There are some limitations that should be borne in mind regarding IO blood gases. Most important is the fact that IO aspirates are a mixture of arterial and venous blood. In the event of a severely compromised circulation, one might assume that IO blood gases more resemble venous ones. Also, a POCT instrument is a prerequisite for such analysis. Arterial oxygenation cannot be evaluated by IO blood gases. Still, especially in an emergency situation, IO blood gases may add useful information to the clinical picture.

## IO Administration of Antibiotics During Shock

It has been demonstrated previously in animal models that IO administration of a number of antibiotics results in plasma concentrations equivalent to those seen after intravenous administration (Jaimovich et al. 1991; Pollack et al. 1991). However, this has not been demonstrated in a setting of circulatory shock.

In the patient with an acute life-threatening infection, timely administration of parenteral antibiotics may increase the probability of survival.

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al (Dellinger et al. 2013), and IO administration may be considered as an alternative when IV access is not available. We therefore studied plasma concentrations of cefotaxime and gentamicin after IO and IV administration in a porcine model, using endotoxin infusion to simulate septic shock. At the onset of clinical shock, or alternatively after 3 hours of endotoxaemia, 75 mg/kg of cefotaxime and 7 mg/kg of gentamicin were randomly administered either IO or IV. Plasma concentrations of both antibiotics were then repeatedly measured in central venous samples. AUC (mg x h L<sup>-1</sup>) for cefotaxime was 108.1 ± 19.5 after intraosseous and 116.5 ± 11.1 after intravenous administration; ratio 0.93, (95% CI 0.71 - 1.19). AUC for gentamicin was 28.1 ± 6.8 for intraosseous and 32.2 ± 3.5 for intravenous administration; ratio 0.87 (95% CI 0.62 - 1.19). The peak value of IO-administered gentamicin was clinically equivalent to that of IV administration, and this value is essential for the action of aminoglycosides. Thus, in an emergency, intraosseous administration of these antibiotics may be considered to reduce the time to initiation of treatment (Strandberg et al. 2015).

### Monitoring Creatinine and Troponin I via IO Access

Early monitoring of renal function is of crucial importance in the critically ill patient. In septic shock, early treatment with antibiotics increases the probability of survival (Kumar et al. 2006). Many broad-spectrum antibiotics are eliminated via the kidneys, and some antibiotics may harm renal function. Furthermore, shock, irrespective of origin, may cause acute kidney injury. In order to evaluate the progress of such deterioration, the Risk-Injury-Failure-Loss-End stage kidney disease (RIFLE criteria), based on creatinine measurements and/or urine output, may be an aid when determining when and how to intervene in order to prevent further renal damage.

The feasibility of creatinine analysis in IO aspirate was previously studied in healthy anaesthetised dogs (Orlowski et al. 1989).

We analysed creatinine in IO, central venous and arterial samples in a porcine model of septic shock, during a 6-hour period. Mean creatinine for all sampling sites increased from 70 micromol/L at 1 h to 104 micromol/L at the end of the experiment. Coefficient of variation for the mean of the sampling sites was 1.4% at 1 hour with a maximum value of 8.5% at 5 hours. The blunting of creatinine in IO samples collect-

ed at 5 hours may possibly be due to reduced bone marrow circulation during shock. Thus, IO creatinine reflects values in blood sufficiently well to be used as a glomerular filtration rate marker in an emergency situation (Strandberg et al. 2014).

Troponin I is a marker of myocardial damage. Elevated levels of this protein can be found in several conditions where cardiac injury occurs, e.g. myocardial infarction, cardiac trauma, sepsis, snake venom and other intoxications. Since the kinetics of troponin I in bone marrow aspirates were unknown, anaesthetised pigs were challenged with a 6-hour continuous infusion of *E. coli* endotoxin. IO and IV samples were taken hourly.

Endotoxaemic shock resulted in a marked decrease in left ventricular stroke work index. Troponin I increased, and at 1 hour the values in IO aspirates and venous samples were nearly identical. Troponin I in IO samples increased somewhat less than in venous samples until 3 hours, when the IO samples did not increase further, which was in contrast to venous samples. All samples were above the normal reference interval. Thus, IO analysis of troponin I reflects the values of troponin I in blood sufficiently well to give valuable information on acute myocardial damage in an emergent situation (Eriksson et al. 2015).

### Use of IO Access in Acute Cardiac Care

Induction of hypothermia after cardiac resuscitation using iced saline infusion in IO vs central venous access was evaluated in a swine model of prolonged ventricular fibrillation. The feasibility of inducing therapeutic hypothermia after resuscitation by giving iced saline IO vs IV was evaluated. There were no significant differences between IO and IV access with regard to decrease in core body temperature. Thus mild therapeutic hypothermia can be effectively induced in swine after successful resuscitation by infusion of iced saline through an IO needle (Mader et al. 2010).

Thrombolytic agents may be administered intraosseously during spontaneous circulation, not only in myocardial infarction, but also in massive pulmonary embolism (Wenzel et al. 2006).

In a recent experimental study, tibial intraosseous access was compared with IV access in adult male swine, who received cardiopulmonary resuscitation (CPR) and defibrillation. The animals were placed in cardiac arrest for 2 minutes before CPR was initiated. After 2 minutes of CPR, epinephrine was delivered and serial

blood samples were collected. There were no significant differences between IV versus IO epinephrine in achieving return of spontaneous circulation. Thus epinephrine delivered via the IO route is a clinically relevant alternative to IV administration. When IV access cannot be immediately obtained in cardiac arrest patients, IO access should be considered (Wong et al. 2016).

### Conclusion

Although analysis of IO samples can provide valuable information, these answers must be interpreted with care. It should be remembered that the bone marrow not only is the site of platelet generation, but is also rich in leucocytes and contains mature as well as immature blood cells. Peripheral blood leucocyte count should not be determined from IO samples, as the immature cells most likely will lead to manual microscopy, causing delayed test results and may cause damage to automated cell counters. However, if haemoglobin is determined with a POCT instrument blood transfusions can be initiated and the determination of other peripheral blood counts can wait until an intravenous or intra-arterial route has been established. Taking this into consideration, IO samples may be a useful tool, helping us to guide initial therapy. The focus on IO testing should probably be on assays where the test result can be readily available with POCT. It should also be remembered that IO cannulation is not a long-time conventional vascular access, but may buy valuable time in an emergency. ■

### Conflict of Interest

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### Abbreviations

CPR cardiopulmonary resuscitation  
IO intraosseous  
IV intravenous  
POCT point-of-care technology

For full references, please email [editorial@icu-management.org](mailto:editorial@icu-management.org), visit [icu-management.org](http://icu-management.org) or use the article QR code.



# PAIN ASSESSMENT AND MANAGEMENT FOR INTENSIVE CARE UNIT PATIENTS

## SEEKING BEST PRACTICES

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This review article focuses on research-based advances in pain assessment practices in intensive care units (ICUs), and stresses clinician consideration of multimodal analgesic techniques for pain management in ICUs.

Over the past 30 years, attention devoted to pain experienced by intensive care unit (ICU) patients has evolved from recognising pain as co-existing with ICU illness and treatment (Puntillo 1990) to development of research-based guidelines to support assessment and treatment of pain (DAS-Taskforce 2015; Barr et al. 2013; Celis-Rodriguez et al. 2013). Guidelines recommend that monitoring pain in all ICU patients be a routine part of practice through use of subjective (self-report) or objective (behaviour observation) pain assessment scales validated for ICU use. Furthermore, guidelines promote the use of analgesic interventions customised to the individual patient (DAS-Taskforce 2015). While opioids are identified in the guidelines as being the preferential analgesic (Barr et al. 2013), there is an ever-growing emphasis on use of multimodal analgesia. The purpose of this review is to address recent advances in ICU pain assessment and to discuss ICU pain management that emphasises analgesation and multimodal analgesia, while identifying areas needing further attention.

### ICU Pain Assessment

Evaluating pain intensity and pain behaviours prepares ICU practitioners to intervene and relieve patient suffering. A visually enlarged 0–10 linear numeric rating scale (NRS) has been determined to be the most valid and reliable self-report pain intensity scale for use with ICU patients (Chanques et al. 2010). Two pain behaviour scales were identified (Barr et al. 2013) to be the most valid and reliable for monitoring pain in medical, surgical, and

non-brain injured trauma patients unable to self-report: the Behavioral Pain Scale (BPS) (Payen et al. 2001) and the Critical Care Pain Observation Tool (CPOT) (Gélinas et al. 2006). When compared recently in a mixed adult ICU, the CPOT had greater discriminant validation than the BPS (Rijkenberg et al. 2015). However, Chanques and colleagues (Chanques et al. 2014) compared these scales as well as a third behaviour scale, the Non-Verbal Pain Scale (NVPS). They found the psychometric properties to be similar between the BPS and CPOT and better than the NVPS, and the BPS was rated as easiest to use. Until further research determines otherwise, clinicians can be comfortable using either the CPOT or BPS for many types of patients in their ICU.

**Applying the principle of ‘analgesia first’ helps to assure that pain is treated before sedatives and hypnotics are introduced**

However, there are a few patient group exceptions. Until recently, there was little guidance on the use of the CPOT or BPS in ICU patients with delirium. Kanji and colleagues (2016) tested the psychometric properties of the CPOT on 40 delirious positive [i.e., Confusion Assessment Method-ICU (CAM-

ICU)] (Ely et al. 2001) patients. Patients had multiple types of diagnoses and were non-comatose; 90% were mechanically ventilated. The patients were CPOT-tested during both painful and non-painful procedures, and the CPOT showed excellent validity and reliability. A modified version of the BPS was tested in 30 non-intubated, mostly delirious patients, who were unable to self-report their pain but could vocalise sounds, during both painful and non-painful procedures (Chanques et al. 2009). A “vocalisation” section was substituted for the “ventilator” section of the original BPS. The BPS-Non-Intubated (BPS-NI) showed excellent psychometric properties as well. Thus, clinicians now have a choice of two pain behaviour scales for assessing pain in their delirious patients.

Until recently there was also little guidance on the use of pain behaviour scales for brain-injured ICU patients. There is incipient evidence that traumatic brain-injured patients’ pain behaviours differ from other ICU patients, especially in relation to facial expressions (Gélinas and Arbour 2009) and level of consciousness (Arbour et al. 2014). While this research shows promise, as well as research of pain behaviours in non-trauma-related brain injury (Echegaray-Benites et al. 2014; Wibbenmeyer et al. 2011), a pain behaviour scale for brain-injured patients is not developed enough for adoption by ICUs. Research is also limited on pain behaviour scales for several other patient populations, since they were excluded from research studies: those with motor response limitations such as patients with quadriplegia or other spinal cord injuries, patients with burn injuries, especially to the face, patients with a

history of chronic pain or chronic substance abuse, those receiving neuromuscular blocking agents, and patients with dementia or other cognitive deficits (Chanques et al. 2009; Gélinas and Arbour 2009; Payen et al. 2001; Puntillo et al. 2014b; Helfand and Freeman 2009). Regarding ICU patients with cognitive deficits, until further research is conducted on pain assessment methods for them, clinicians can use research findings from non-ICU settings. For example, patients with cognitive impairment may be able to accurately report pain. Those who are markedly cognitively impaired report less intense pain and have a smaller number of pain complaints than those mildly impaired. However, cognitively impaired patients will report pain, if present, when specifically asked, and many can understand some self-assessment scale such as the NRS or a verbal rating scale. Unfortunately, cognitively impaired patients are less likely to ask for and receive analgesics, and providers underestimate their pain (Helfand and Freeman 2009; Buffum et al. 2007).

Important to ICU clinicians is that use of pain behaviour tools in patients unable to self-report has been shown to improve the processes of pain assessment as well as patient outcomes. Table 1 presents the effects of CPOT or BPS use as a result of unit-based pain education programmes. However, in spite of this work, some challenges remain to be addressed in order for patients to reap the benefits of pain assessment practices in ICUs. Rose and colleagues (Rose et al. 2012) found, from 802 ICU nurse surveys, that only 33% of the nurses used a pain assessment tool if patients were unable to communicate. In only 74% of the surveys was the use of behavioural assessment tools noted to be moderately to extremely important. Having pain assessment tools available for clinicians and having a pain assessment protocol in place have been associated with greater odds of tools being used in practice. (Rose et al. 2012) Table 2 offers suggestions for improvement of pain assessment practices in an ICU.

### ICU Pain Management

Management of pain is not only a humane approach to the care of ICU patients; adequate pain management helps prevent both short-term and long-term morbidities from increased physiological and psychological stress (Sigakis and Bittner 2015). Currently, there is increased support for two approaches to pain management in ICU patients: analgosedation and multimodal analgesia.

**Table 1.** Processes and Outcomes of Implementing Use of Pain Behaviour Scales\* in ICUs

Use of Pain Scale	Process Measures	Outcome Measures
CPOT	<p>More frequently documented pain assessments (Gélinas et al. 2011; Rose et al. 2013)</p> <p>More frequently documented pain reassessments after therapy (Gélinas et al. 2011)</p>	<p>Decreased use of sedatives (Gélinas et al. 2011)</p> <p>Decreased use of analgesics and sedatives in cardiac ICU (Rose et al. 2013)</p>
BPS	<p>Increased analgesic titration episodes (Chanques et al. 2006)</p> <p>Administration of analgesic (de Jong et al. 2013)</p> <p>More frequent documentation of pain assessments (Chanques et al. 2006; Williams et al. 2008; Radtke et al. 2012)</p> <p>Increased notification of physician about patient pain (Chanques et al. 2006)</p>	<p>Decreased incidence of pain (Chanques et al. 2006)</p> <p>Decreased duration of mechanical ventilation (Chanques et al. 2006)</p> <p>No impact on duration of mechanical ventilation (Radtke et al. 2012)</p> <p>Decreased duration of nosocomial infections (Chanques et al. 2006)</p> <p>Decreased use of sedatives (Williams et al. 2008)</p> <p>No impact on duration of ICU stay (Chanques et al. 2006; Radtke et al. 2012)</p> <p>Decrease in mortality – yes (Radtke et al. 2012)</p> <p>Decrease in mortality – no (Chanques et al. 2006; Williams et al. 2008)</p> <p>Decreased incidence of severe pain during turning (de Jong et al. 2013)</p> <p>Decreased incidence of at least one severe adverse event (de Jong et al. 2013)**</p>

BPS Behaviour Pain Scale CPOT Critical Care Pain Observation Tool

\* Some studies also used NRS scales in patients who could self-report

\*\* Severe events: tachycardia, bradycardia, hypertension, hypotension, desaturation, bradypnoea, ventilator distress, arrhythmias, cardiac arrest

**Table 2.** Suggestions for Improvement of Pain Assessment Practices in an ICU

Standardise the methods of pain assessment to be used by all ICU clinicians on patients who can communicate and those with communication difficulties.

Provide a section for documentation of pain assessment that is easily accessible in the patient's flow sheet and record.

Offer annual reviews of pain assessment tools to enhance the correct and standardised use of the tools.

Offer support tools such as pocket cards and posters about pain assessment in patients' rooms to remind and encourage clinicians to perform assessments.

Institutionalise the reporting of pain status during clinician handovers and rounds to increase the visibility of patients' pain.

Consider engaging family members in assessing the patient's pain. They may identify the presence of patient's pain more consistently than the ICU clinicians.

Conduct an interprofessional quality improvement project to evaluate the effectiveness of pain assessment interventions in the ICU.

Sources of some material: (Chanques et al. 2006; Puntillo et al. 2012; Puntillo et al. 2014a).

#### Analgosedation

Analgosedation refers to the use of analgesics before sedatives in order to focus first on pain relief. An "analgesia first" approach to pain management is recommended for patients who may be demonstrating agitation and restlessness

as well as pain behaviours and/or for patients that have identifiable, potential causes of pain (Barr et al. 2013; Devabhakthuni et al. 2012). Using analgesics first may also lead to the use of lighter sedation resulting in more awake, responsive patients and better clinical outcomes

**Table 3.** Adjuvant Analgesic Therapy: Classification and Mechanism of Action

Medication Classification	Target	Mechanism of Action
Antidepressants (tricyclics, SSRIs, SNRIs)	Serotonin and norepinephrine synaptic reuptake in CNS	Enhance descending inhibition in CNS
Local anaesthetics, some anticonvulsants and tricyclics	Na <sup>+</sup> channel	Blockade of frequency dependent depolarisation of nociceptive neurons
Anticonvulsants (gabapentin, pregabalin)	N-type Ca <sup>2+</sup> channels	Suppress ectopic discharges in the dorsal horn
Baclofen	Presynaptic GABA-B receptors	Inhibition of synaptic reflexes primarily in spinal cord
Clonidine, tizanidine	α <sub>2</sub> -Adrenergic receptors	Inhibition of neuropeptide release reduction in pain signal transmission
Dexmedetomidine	Selective α <sub>2</sub> -agonist	
Dextromethorphan, ketamine, (and methadone)	NMDA receptors	Inhibit glutamate-mediated nociception Prevent central sensitisation
Corticosteroids	Glucocorticoid receptors	Inhibition of immune mediators and inflammatory cell recruitment
NSAIDs	Prostaglandins	
Acetaminophen	Prostaglandins	Central prostaglandin antagonism

GABA-B γ-aminobutyric acid type B NMDA N-methyl-D-aspartate NSAIDs nonsteroidal anti-inflammatory drugs SNRI serotonin-norepinephrine reuptake inhibitor SSRI selective serotonin reuptake inhibitor

Source: Erstad BL, Puntillo K, Gilbert HC et al. [2009] Pain management principles in the critically ill. *Chest*, 135(4): 1075-86 © 2009, with permission from American College of Chest Physicians.

cessation of opioids (Liatsi et al. 2009, Korak-Leiter et al. 2005). Another current concern is the ongoing opioid epidemic, especially in the United States (Rudd et al. 2016). However, while research-based data are limited on patient progression from acute-to-chronic opioid use after hospitalisation, this progression was not found in a recent study of post-ICU patients (Yaffe et al. 2015). Yet, this topic is in need of further study. In the meantime, patients' pain relief should remain a high priority, with use of opioids continuing for patients in need.

A multimodal analgesia approach to pain management, through the use of opioids and non-opioid analgesics as combination therapy, provides a balanced approach to analgesia (White and Kehlet 2010; Erstad et al. 2009). Advantages of multimodal therapy are that it is an opioid-sparing technique, which helps to avoid the adverse effects of, and possible negative sequelae from, opioid use. It promotes the use of smaller doses of each drug being used, and complements the drugs' effects because of their different pharmacodynamics. **Table 3** presents types of non-opioid agents and their mechanisms of action. Some of these agents, such as antidepressants, baclofen, and corticosteroids are not first-line medications used for pain in ICU due to their side-effect profiles, methods of administration, and/or long onset to effectiveness. However, they could be considered for an individual patient under special circumstances.

Some of the other agents on **Table 3**, along with opioids, could more likely be part of a multimodal analgesia approach. Anaesthetic agents, alone or with opioids, are used in regional analgesia techniques (epidural, intrathecal, intercostal, femoral nerve) (De Pinto et al. 2015; Lindenbaum and Milia 2012). Nonopioids such as nonsteroidal anti-inflammatory agents, acetaminophen, gabapentin, nefopam, dexmedetomidine, and paracetamol or acetaminophen can be considered for multimodal analgesia, according to the particular type of patient pain, mode of administration availability, and co-existing conditions (Payen et al. 2013; Chanques et al. 2011; Pandey et al. 2002). Finally, ketamine, a phencyclidine derivative, has both anaesthetic and analgesic properties (Lindenbaum and Milia 2012). IV infusions of ketamine used for analgesia may decrease opioid consumption, reduce airway resistance, spare bowel motility, lower opioid tolerance, and prevent opioid hyperalgesia (Patanwala et al. 2015; Joly et al. 2005; Lindenbaum and Milia 2012; Erstad and

such as shorter mechanical ventilation and ICU stay durations (Devabhakthuni et al. 2012). Devabhakthuni and colleagues (2012) present a critical evaluation of analgesia studies. They concluded that, despite limitations of the research to date, analgesia can focus on patient outcomes while providing pain relief. For example, use of an analgesia protocol in a neurointensive care unit demonstrated the protocol to be feasible in this patient population with unique needs such as strict control of mean arterial, cerebral perfusion and intracranial pressures (Egerod et al. 2010).

### Multimodal Analgesia

The second recommended approach to ICU pain management is use of multimodal analgesia, which often includes opioid use. Use of intravenous (IV) opioids as the first-line approach to pain management in the ICU is supported by recent guidelines (Barr et al. 2013). The most commonly used opioids are morphine, hydromorphone, fentanyl, and remifentanyl. Reviews exist that compare opioids' mechanisms of action, side-effect profiles, and recommended dosing regimens (Trescot et al. 2008; Erstad et al. 2009; Lindenbaum and Milia 2012). Comparison of IV remifentanyl to fentanyl in ICU patients found those drugs to

be equianalgesic (Spies et al. 2011). An advantage of remifentanyl is that it has a faster onset, shorter half life, and is not metabolised by the liver or kidneys (Sigakis and Bittner 2015). An IV remifentanyl-based intervention for sedation compared to a midazolam-based intervention tested in a random sample of medical-surgical ICU patients on long-term mechanical ventilation (i.e. longer than 96 hours) showed that the former was associated with better outcomes: shorter mechanical ventilation duration, shorter weaning-to-extubation time, and shorter offset of medication effect when discontinued (Breen et al. 2005). There were similar findings in a sample of ICU neurotrauma or neurosurgery patients when a primarily remifentanyl regimen was compared to a primarily hypnotic (propofol) regimen (Karabinis et al. 2004). However, remifentanyl is more frequently associated with secondary hyperalgesia after its withdrawal as an analgesic agent (Angst et al. 2003; Joly et al. 2005) and is more expensive (Sigakis and Bittner 2015). All opioids should be used cautiously due to their well-known potential adverse effects (Erstad et al. 2009). Of additional concern is the possible development of opioid tolerance (Dumas and Pollack 2008), opioid-induced hyperalgesia (Wachholtz et al. 2015) and opioid withdrawal symptoms upon

Patanwala 2016). As a phencyclidine derivative, ketamine has potential psychotomimetic effects such as dysphoria, hallucinations, disorganised thinking and delirium. Use of lower doses may help to avoid these effects (Erstad and Patanwala 2016).

Nonpharmacologic interventions, such as the use of music, relaxation techniques, and/or providing information about expectations during procedures can be considered part of multimodal analgesia (Erstad et al. 2009; Sigakis and Bittner 2015). While research is limited on the effectiveness of these techniques on pain relief, they are generally low-cost, safe, and relatively easy to implement. Further research is warranted on the role of nonpharmacologic interventions in multimodal analgesia.

## Conclusions

The assessment and treatment of pain continue to be challenges for ICU clinicians. These challenges can be mitigated by adoption of well-validated pain assessment methods and a standardised organisational approach to assessment, documentation, and communication of patient pain among ICU team members. Applying the principle of “analgesia first” helps to assure that pain is treated before sedatives and hypnotics are introduced since analgesia may negate the need for other medications. Multimodal analgesia techniques accentuate the positive effects of a combination of opioids and non-opioids while minimising the adverse effects of both. Further research is necessary to demonstrate the beneficial effects of these approaches to

pain assessment and treatment in heterogeneous groups of ICU patients. ■

## Conflict of Interest

Kathleen Puntillo declares that she has no conflict of interest.

## Abbreviations

BPS Behavioral Pain Scale  
 BPS-NI Behavioral Pain Scale-Non-Intubated  
 CAM-ICU Confusion Assessment Method-ICU  
 CPOT Critical Care Pain Observation Tool  
 ICU intensive care unit  
 IV intravenous  
 NRS numeric rating scale  
 NVPS Non-Verbal Pain Scale

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# DOES DEXMEDETOMIDINE REDUCE DELIRIUM BY IMPROVING SLEEP?

Delirium is a common complication in intensive care unit (ICU) patients and its occurrence is associated with worse outcome (Inouye et al. 2014; Abelha et al. 2013). Sleep disturbances are considered one of the important risk factors of delirium development (Flink et al. 2012). Recent evidence shows that dexmedetomidine, either at sedative or non-sedative doses, can improve sleep quality and reduce delirium. Here we review evidence regarding sleep disturbances, delirium, and the effects of dexmedetomidine in ICU patients.

## Normal Sleep and its Importance

Sleep is a naturally recurring state of mind and body, characterised by lowered consciousness, relatively inhibited sensory activity, inhibition of nearly all voluntary muscles and reduced interactions with surroundings. According to polysomnographic study results, sleep is divided into non-rapid eye movement (REM) sleep and REM sleep. Non-REM sleep is further divided into stage 1 (N1, also called light sleep, accounting for 5-10% of total sleep in adults), stage 2 (N2, accounting for 45-55% of total sleep in adults), and stage 3 (N3, also called deep sleep or slow wave sleep [SWS], accounting for 15-25% of total sleep in adults). REM sleep accounts for 20-25% of total sleep in adults.

Normal sleep has a significant circadian rhythm and cycles in the order of N1 → N2 → N3 → N2 → REM. In healthy adults, the duration of each cycle lasts approximately 90 minutes. N3 sleep is a deep stage and is considered the most restful form of sleep. The sleeper is less responsive to the environment and restores the body; night terrors, nocturnal enuresis, sleepwalking and somnolence often occur in this stage. During the REM sleep stage, high-frequency electroencephalogram (EEG) waves, which are similar to a waking state, appear, but the sleeper is harder to arouse than other stages. Vivid dreams may occur during this stage (McNamara et al. 2010). Lack of REM sleep impairs the ability to learn complex tasks, and

deprivation of REM sleep often results in REM rebound, i.e., more REM sleep than usual. Compared with the young, sleep in the elderly tends to show frequent waking, fragmented sleep, decreased N3 sleep and early waking (Elliott et al. 2011).

## Sleep in ICU Patients

Sleep is severely disturbed in mechanically ventilated ICU patients (Delisle et al. 2011). Polysomnographic studies performed in mechanically ventilated ICU patients have demonstrated a severe increase in sleep fragmentation, prolonged N1 and N2 sleep, reduced N3 and REM sleep, and an abnormal distribution of sleep, because almost half of the total sleep time occurred during the daytime (Delisle et al. 2011; Cabello et al. 2008). Patients reported little or no sleep, poor sleep quality, frequent awakening, and daytime sleep. They attributed sleep disruption to environmental noise, intrusive treatment, and thirst etc. (Elliott et al. 2011).

Patients also develop significant sleep disturbances immediately after major surgery. Polysomnographic manifestation usually includes severe sleep deprivation, sleep fragmentation, decrease or loss of SWS and REM sleep during the early period after surgery (Aurell and Elmqvist 1985; Knill et al. 1990). Patients may report decreased sleep time, increased arousals or awakening, lowered sleep quality and increased nightmares (Rosenberg-Adamsen

et al. 1996). During the subsequent postoperative phase, sleep structure gradually returns to normal with a REM sleep rebound within one week (Knill et al. 1990).

## Causes of Sleep Disturbance in ICU Patients

Many factors are responsible for sleep disturbance in ICU patients. These include the ICU environment, the severity of illness, mechanical ventilation, pain, sedatives and analgesics, and various other therapies (Hofhuis et al. 2012; Friese 2008). For postoperative patients, pain, needing to use toilet facilities, disturbances from healthcare staff and other patients, environmental noise as well as many other discomforts constitute the major causes (Dolan et al. 2012). In addition, the severities of preoperative comorbidity (Yilmaz et al. 2016) and surgery (Knill et al. 1990; Rosenberg-Adamsen et al. 1996) may also contribute to sleep abnormalities. A study by Yilmaz et al. (2016) showed that the severity of preoperative angina pectoris is independently associated with worse sleep quality after coronary artery bypass graft surgery. And sleep disturbance is more severe after major surgery (Rosenberg-Adamsen et al. 1996).

## Sleep Disturbances and Delirium

Sleep disturbances are considered important causes of delirium. In a pilot study of adults over 40 years of age, sleep disruption was more severe before surgery in the patients who expe-

rienced postoperative delirium (Leung et al. 2015). Poor sleep quality was also proved to be associated with an increased risk of developing delirium among patients enrolled in a hospice (Slatore et al. 2012) and patients after elective knee replacement (Flink et al. 2012). In recent systematic reviews, use of earplugs and/or eye masks in ICU patients significantly improved subjective sleep quality and reduced the risk of delirium (Litton et al. 2016; Hu et al. 2015).

Similar to delirium, the occurrence of sleep disturbances also produces significant adverse consequences in ICU patients; these include immune system compromise, delayed weaning from mechanical ventilation, cardiovascular events, and post-ICU physical and mental health decline (Kamdar et al. 2012; BaHammam 2006; Salas and Gemaldo 2008; Weinhouse et al. 2009; Roche Campo et al. 2010; Ackermann et al. 2012). Sleep disturbances after surgery are associated with worse outcomes, including prolonged hospital stay and increased long-term cardiac events (Kjohede et al. 2012; Fernandes et al. 2014).

### Effects of Dexmedetomidine on Sleep

Given the importance of good sleep on patients' recovery from critical illness and major surgery, multiple nonpharmacologic interventions have been implemented to improve patients' sleep quality in the ICU, such as elimination of unnecessary noise and light, consolidation of patient care interactions, use of earplugs and eye masks, relaxation techniques, and addition of white noise (Hu et al. 2015; Xie et al. 2009; Li et al. 2011). Unfortunately, traditionally used sedatives and analgesics (such as propofol, benzodiazepines and opioids) deteriorate, rather than ameliorate, sleep architecture disruption in ICU patients, which potentially contributes to the occurrence of delirium (Delaney et al. 2015).

Dexmedetomidine is a selective  $\alpha_2$  adreno-

ceptor agonist with both sedative and analgesic properties (Reardon et al. 2013). Unlike other sedative agents, dexmedetomidine exerts its sedative effects through an endogenous sleep-promoting pathway, preserves sleep architecture to some degree in preclinical settings and produces a N2 sleep-like state (Nelson et al. 2003). In mechanically ventilated ICU patients, nighttime infusion of a sedative dose of dexmedetomidine preserved the day-night cycle of sleep and improved the sleep architecture by increasing sleep efficiency and stage N2 sleep (Oto et al. 2012; Alexopoulou et al. 2014). In a recent study, 76 elderly patients who were admitted to the ICU after surgery and did not require mechanical ventilation randomly received low-dose dexmedetomidine (0.1  $\mu\text{g}/\text{kg}/\text{h}$ ) or normal saline during the first night after surgery. The results showed that dexmedetomidine infusion prolonged total sleep time, increased sleep efficiency and stage N2 (and decreased stage N1) sleep, and improved subjective sleep quality (Wu et al. 2016).

### Dexmedetomidine and Delirium Prevention

Dexmedetomidine is increasingly used for sedation in mechanically ventilated ICU patients (Wunsch et al. 2010), where its use is associated with a decreased prevalence of delirium when compared with other sedatives (Pandharipande et al. 2007; Xia et al. 2013; Riker et al. 2009; Djaiani et al. 2016). Sleep promotion is one of the possible mechanisms of its delirium-sparing effects (Oto et al. 2012; Alexopoulou et al. 2014). However, in these studies, dexmedetomidine was compared with an active sedative drug that modulates the GABA-A receptors, which could aggravate sleep disturbances and increase delirium risk (Fraser et al. 2013).

In a recent large sample size study, 700 elderly patients ( $\geq 65$  yrs), who were admitted to ICU after surgery randomly received either

low-dose dexmedetomidine (0.1  $\mu\text{g}/\text{kg}/\text{h}$ ) or normal saline infusion from ICU admission until 8 am the next day after surgery. The results showed that dexmedetomidine infusion significantly decreased the prevalence of delirium on postoperative days 1 to 3 (OR 0.28, 95% CI 0.16 to 0.50,  $p < 0.0001$ ; OR 0.43, 95% CI 0.24 to 0.77,  $p = 0.005$ ; and OR 0.26, 95% CI 0.13 to 0.53,  $p < 0.0001$ , respectively). This was in accordance with significantly improved subjective sleep quality during the three nights of the same period (all  $p < 0.0001$ ) (Su et al. 2016). Therefore, low-dose dexmedetomidine infusion reduces delirium in this patient population, possibly by improving postoperative sleep.

### Conclusions

Sleep disturbances are common in ICU patients and can produce harmful effects including delirium. Both sedative-dose and low-dose dexmedetomidine can be used to improve sleep quality and decrease delirium occurrence in ICU patients. Future studies are required to verify the casual relationship between sleep promotion and delirium-sparing effects as well as the long-term outcomes of dexmedetomidine administration. ■

### Conflict of Interest

Xian Su declares that she has no conflict of interest. Dong-Xin Wang has received lecture fees and/or travel expenses for lectures given at domestic and international academic meetings from Jiangsu Hengrui Medicine Co., Ltd., China, Yichang Humanwell Pharmaceutical Co. Ltd., China, and Baxter Healthcare Trading (Shanghai) Co., Ltd.

### Abbreviations

ICU intensive care unit  
REM rapid eye movement  
SWS slow wave sleep

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# EARLY MOBILISATION IN ICU - FROM CONCEPT TO REALITY

## FOUR STEPS TO CHANGE PATIENT OUTCOMES

For years, 28-day survival was the holy grail of ICU physicians. As ICU survival continues to improve, a high proportion of these ICU survivors experience significant cognitive, psychological, and physically disabling side effects of their ICU stay. These consequences of critical illness, regardless of their admitting diagnosis, have a dramatic impact on quality of life. Nearly half of these individuals are unable to return to their previous work more than one year after hospital discharge (Pandharipande et al. 2013).

A change in ICU paradigm, sedation-ventilation-organs support, occurred in the last 15 years. Accumulating evidence suggests that the management of sedation can have an important effect on the outcomes of patients who are treated in ICUs. Nevertheless, a systematic review found that reduction of sedation levels decreased ICU

length of stay and ICU-related complications, but failed to improve long term outcomes (Minhas et al. 2015). If avoiding deep sedation is not efficient, by itself, to improve long-term outcomes, it allows early mobilisation in the ICU setting; **this is the first step**. Early rehabilitation in ICU was initially a concept, but several studies were published to highlight the feasibility (Schweickert et al. 2009). The benefits of early mobilisation include reduction in length of stay both in the ICU and hospital as well as improvements in strength and functional status. Such benefits can be accomplished with a remarkably acceptable patient safety profile.

All these studies include recommendations for implementing treatment programmes to improve ICU patients' physical, cognitive and mental health impairments, with structured reha-

bilitative patient physical activity timed closer to ICU admission rather than ICU discharge. This point is crucial. ICU mobilisation should not be reserved for difficult to wean patients, or at the time of discharge. ICU mobilisation must be implemented in the early phase of ICU stay.

Even if feasibility, safety and efficacy have been confirmed by several studies, implementation of early mobilisation in ICU remains anecdotal in daily practice, all over the world (Hodgson et al. 2015). The real question is how to move on from the *New York Times* article about early mobilisation as a "tactic" (Kolata 2009) to making it an integral part of standard care in ICU, as with glycaemic control or basic nursing. In our experience, early mobilisation is an integral part of standard care because it has been protocolised. Implementing an early rehabilitation programme in the ICU is teamwork, that must be built according to published data and adapted to the local environment. **This is the second step** (Hickmann et al. 2016; Morris et al. 2008; Laurent et al. 2016).

Most times, implementing a protocol is not enough, and reported reasons for not mobilising patients vary widely. They include mechanical ventilation, catecholamine infusion, impaired consciousness, poor functional status, safety considerations, limited staff capacities and so on. To identify local barriers encountered to early mobility is a major issue in this process, and this is the only way to move on. **This is the third step** (Dubb et al. 2016). Barriers and proposals from different hospitals are summarised in Table 1. To summarise barriers and proposals, when we hear: "It is too difficult for us, it's impossible in our ICU", just consider early mobilisation as a quality-of-care assessment tool in ICU. If everything is well done for our patients—light sedation, avoiding fluid overload, providing adequate nutritional support, perfect ventilator support—so early mobilisation will be like the cherry on top of a cake.

**Table 1.** Identified Barriers and Proposals for Early Mobilisation Programme Implementation in ICUs

Barrier	Proposal
My patients are too severe, too sick, unstable ...	Create exclusion guidelines. Consider beginning the protocol progressively, step by step. Promote multidisciplinary discussions.
Fears of patient-ventilator interaction during exercise	Begin slowly, consider ventilator settings in the protocol.
Pain	Pain evaluation before any exercise, with protocolised analgesia before exercise or mobilisation if mandatory.
Denutrition, muscle lost	Consider nutritional support, denutrition evaluation. Begin exercise with movements against gravity.
Obesity	Use specific protocol for obese patients. Enrol more manpower for these patients.
Patients are not conscious enough	Target light sedation for all patients except specified ones. Avoid long-acting drugs.
Delirium	Delirium assessment, treat if productive delirium, avoid benzodiazepines, use specific exercises for delirious patients.
Patient refusal, low motivation	Explain goals of early mobilisation, highlight quality of life.
Tubes, catheters, ...	Secure catheters and tubes before mobilisation, begin slowly.
Continuous renal replacement therapy (CRRT)	Promote jugular access, use long and smooth catheters if femoral, use safety procedures (decrease blood flow, stop ultrafiltration ...) when the patient is mobilised.
Safety doubts	Prospectively set adverse events recorded.



Images credit: JM Constantin, with permission of all pictured.

Providing early mobilisation with a high degree of supportive care requires experienced and coordinated multidisciplinary teams. Nurses in the ICU, especially when they are young professionals, may be frightened to mobilise patients. These fears are justified; this is a mandatory aspect to ensure patients' security during early mobilisation implementation. Formation of professionals involved in mobilisation process is the good answer to fears. Because nurses' turnover in the ICU is sometimes really short, and because ICU staff teams are really large, it is important to identify and promote champions of education in the staff. These champions will be leaders of early mobilisa-

■ ■ If everything is well done for our patients early mobilisation will be like the cherry on top of a cake ■ ■

tion, and they will be able to carry out formation programmes for all the staff. Because the initial and continuing training are key points of success, the formation programme is **the fourth step**.

Team motivation is probably not an issue in the process of early mobilisation; team motivation is just the result of the process. Short-term effects of early mobilisation on delirium and patient feeling, as the hope of long-term quality of life improvement, are sufficient encouragement for ICU staff. But motivation could be in the first plan if fears, doubts and inadequate workload have been removed by a protocol including an algorithm for patient-centred care with an adequate educational programme, which is part of the early Comfort using Analgesia, minimal Sedatives and maximal Humane care or e-CASH concept (Vincent et al. 2016). ■

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# WHAT CAN PSYCHOLOGISTS DO IN INTENSIVE CARE?

As awareness has grown of the great distress intensive care patients may suffer, units have begun recruiting psychologists to their teams. Intensive care unit psychologists aim to assess and reduce distress for patients, families and staff, to improve outcomes. This paper summarises research on the psychological impact of critical illness, highlights the growth of critical care health psychology as a speciality, and discusses potential roles of psychologists and the evidence base for psychological interventions in critical care departments.

It is now widely recognised that the experience of critical illness, with admission to an intensive care unit (ICU), has a powerful psychological impact on people. A body of evidence about the prevalence of acute stress and frightening psychological experiences in the ICU and adverse psychological outcomes post-ICU has grown. Consequently, the necessity of psychological assessment and support of patients has gained acceptance. Since families of critically ill patients and ICU staff can also become stressed or traumatised, they may also require psychological input. With the gradual dissemination of these research findings among clinicians, critical care departments have started to employ psychologists as key colleagues in the multidisciplinary team.

## Psychological Impact of Critical Care

The psychological impact of a critical care admission can be severe. It is known that patients may experience extreme stress (Samuelson 2007; Wade et al. 2012) and altered states of consciousness (Ely et al. 2001). Subsequently there is a high prevalence of psychological morbidity, including post-traumatic stress disorder (PTSD), depression and anxiety among survivors (Wade et al. 2013). Studies have found that more than half of critical care patients suffered symptoms of a psychological disorder after their admission. Cognitive deficits in memory, attention and executive function, affecting activities of daily living, are also common (Pandharipande et al. 2013).

Patients are exposed to multiple stressors in the ICU, including illness, pain, sleep deprivation, thirst, hunger, dyspnoea, unnatural noise and light, nakedness and lack of dignity, inability to communicate, isolation, fear of dying and witnessing other people suffering and dying. They may also have strong emotional or behavioural reactions in response, including anxiety, panic, low mood, anger or agitation. Interventions, such as mechanical ventilation (MV) or invasive monitoring for cardiovascular support, may be difficult for patients to tolerate. Furthermore, the onset of delirium, including frightening symptoms such as hallucinations and paranoid delusions, is common in intensive care.

## Flashbacks, nightmares and traumatic memories of hallucinations and delusions may form part of post-ICU PTSD

Flashbacks, nightmares and traumatic memories of hallucinations and delusions may form part of post-ICU PTSD, while delirium is associated with later cognitive impairment.

There is also evidence that the critical care experience is traumatic for families, with relatives frequently suffering from PTSD (33% in one study) once their family member has left the ICU (Davidson et al. 2012). Critical care staff

have been shown to suffer from high rates of stress, burnout and PTSD in a number of large studies (Moss et al. 2016).

## Need for Psychological Assessment and Support

A landmark document on the organisation of critical care services in the UK (Department of Health 2000) recognised that the ICU environment was “extremely distressing” for relatives and patients, who needed support from staff. However, psychological support was “difficult and time-consuming”, and senior staff and appropriate materials were needed to deliver it. A National Institute for Health and Care Excellence (NICE) guideline (Tan et al. 2009) stated that patients should be assessed during their critical care stay for acute symptoms such as anxiety, depression, panic episodes, nightmares, delusions, hallucinations, intrusive memories, flashback episodes and underlying psychological disorders, to determine their risk of future psychological morbidity. Furthermore, psychological support should be provided to aid rehabilitation and recovery in critical care units, on general wards, and in the community. However, it is not known to what extent psychological assessment and support are really carried out in ICUs.

Research suggests that acute stress in the ICU may be one of the strongest patient risk factors for poor psychological and cognitive outcomes after intensive care (Wade et al. 2012; Davydow et al. 2013). Therefore it is important to detect

and minimise acute stress where possible. It is known that healthcare staff who have not been trained in mental health may find it difficult to recognise that a patient is suffering from acute stress, hallucinations or delusions. However, tools to detect distress in the ICU are now available. The Confusion Assessment Method for the ICU (CAM-ICU) can be used by staff to detect delirium in critical care patients ([icudelirium.org/delirium/monitoring.html](http://icudelirium.org/delirium/monitoring.html)). An intensive care psychological assessment tool (IPAT) has recently been validated and may be used by trained critical care staff to detect acute stress and indicate the risk of future psychological morbidity ([uclh.nhs.uk/OurServices/Consultants/Documents/Dorothy%20Wade%20profile%20documents/IPATTool.pdf](http://uclh.nhs.uk/OurServices/Consultants/Documents/Dorothy%20Wade%20profile%20documents/IPATTool.pdf)).

Families of critical care patients also frequently need support to deal with anxiety and fatigue, to comfort them when they learn that a loved one is dying, or after a death. Conflict may arise between family members who have different views on a patient's care, or between families and staff, particularly around withdrawal of support or non-resuscitation orders.

Staff in critical care have much higher than average rates of stress and burnout than other hospital staff (Moss et al. 2016). This may be related to the responsibility of maintaining lives through sophisticated technological interventions; difficult emotions created by caring for patients who are dying or who die, and a culture in which staff may be perfectionist, driving themselves to provide high standards of care, without utilising appropriate self-care strategies. Conflict between patients' families who are upset, angry or grieving, and staff who are not trained to deal with these emotions, can also escalate. Excessive stress can lead to staff going on long-term sick leave or eventually leaving the service. The United States critical care societies' collaborative has recently issued a call to action on burnout syndrome (Moss et al. 2016).

### Growth of Critical Care Psychology

Acute stress, the effects of delirium, adverse cognitive and psychological outcomes, and family and staff stress are complex matters to manage within a highly complex medical environment. There is evidence that critical care departments are now starting to employ fully-trained, usually senior, psychologists to help manage these issues. A workforce survey of allied health professionals in critical care in England, Wales and Northern Ireland (Critical Care Network National Nurse Leads 2016) found

**Table 1.** Psychological Services Offered in ICUs in England, Wales & Northern Ireland

Intervention	Percentage
Psychological support of patients and families	9%
MDT consultation about patients' psychological welfare	10%
Staff training in providing psychological support	7%
Provide/supervise psychological assessment of patients	3%
Psychological follow-up on general wards	6%
Psychological follow-up post hospital wards	7%
Provide staff support	10%

Source: Reproduced by kind permission of Critical Care National Networks Nurse Leads (CC3N) [cc3n.org.uk](http://cc3n.org.uk)

that 23 of 135 responding units (17%) offered a psychological support service to families and patients. However, the true proportion of ICUs in England, Wales and Northern Ireland offering psychology could be smaller, given that 270 units were sent a survey and 217 were returned. Many units did not complete the psychology spreadsheet, presumably because they have no psychology provision. In 15 units the service was provided by practitioner psychologists (health, counselling or clinical). Of 27 identified psychologists, 15 were senior psychologists in the band 8 range\* (NHS Agenda for Change pay scales range from 1-9, see [healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates](http://healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates)), while 12 were more recently qualified band 7s. The most frequent provision was one psychologist one day a week (range 5-37.5 hours per week). In some units the psychological service was provided by psychotherapists, counsellors, follow-up nurse specialists, bereavement nurses or psychology support workers (band 6s). Table 1 highlights psychological support services offered in a given percentage of the 135 units.

A survey of health psychology in the USA received 175 responses (Stucky et al. 2016). It found that psychologists are involved in critical care settings in various roles. It was not known how frequently psychologists were consulted or what specific services were most effective, valued, or desired.

### Role of Psychologists

Now that psychologists are taking their place in

the critical care team, what should their role be? The role has been recognised and described in a section of the UK *Guidelines for the Provision of Intensive Care Services* (Howell and Wade 2015). Psychologists can play a vital role in the acute critical care setting, and as part of patients' follow-up care, both in- and post-hospital. They are also able to help maintain a healthy working environment and manage workplace stress.

In the acute setting, psychologists should supervise the psychological and cognitive assessment of all patients, both in the critical care unit, and after transfer to other wards, as well as providing or supervising psychological support to patients and relatives who are highly stressed or traumatised. They can also help staff manage communications with distressed families. Psychologists can provide training to increase staff knowledge and understanding of psychological reactions, delirium, stressors in the critical care environment, and psychological and cognitive outcomes of critical illness. They may also deliver training to increase staff competency in providing psychological support to patients who are distressed, agitated, or delirious. Similar types of training have proved successful in cancer services (for example the SAGE & THYME® model (UHSM Academy 2012)).

Psychologists should play a key role in the multidisciplinary team (MDT), attending ward rounds, and being available for consultation on matters such as communication, sleep, effects of sedation, anxiety, stress, mood, delirium, and family issues. They should be involved in developing holistic care plans for long-stay patients.

The psychologist should also play a full role in follow-up care, including assessment and support of patients who suffer traumatic stress reactions such as flashbacks of frightening delusions, or who become depressed in the hospital after discharge from ICU. Their role should also include the psychological (emotional and cognitive) assessment of patients attending critical care follow-up clinics. In a well-resourced follow-up service, a psychologist could ideally offer sessions of CBT (including trauma-focused CBT) and other evidence-based treatments. These sessions would be specifically tailored for critical care patients. If not possible, the critical care psychologist should liaise with GPs and/or community mental health teams regarding appropriate psychological treatment or cognitive rehabilitation in the community.

Finally, psychologists should play a role in addressing stress and burnout among critical care staff. This could include advising senior management at an organisational level on systemic issues influencing patient and staff wellbeing, as well as organising a wellbeing programme for staff (individual and group sessions as well as teaching and proactive work) and coaching or reflective sessions with senior management. (M Smithies & J Highfield, University Hospital Wales, Cardiff, personal communication).

This is a highly complex role in a sensitive, complex, medical environment. To provide a coordinated service across the critical care department, ideally a consultant-level health, clinical or counselling psychologist should be employed to ensure the necessary seniority, experience and expertise. Additional junior

psychology staff could be employed to support the senior psychologist, according to numbers of beds, specialities or units within the department. With such a multi-faceted role, and high-level need, burnout is a risk for the senior psychologist, similarly to other critical care staff, if the psychology service is not properly structured and staffed.

### Evidence Base for Psychological Interventions in Critical Care

There has been little evaluation of psychological interventions for critical care patients to date, but a recent systematic review suggests that a range of non-pharmacological measures, including psychological interventions, could help to reduce both short- and medium-term stress (Wade et al. 2015). For example, an intervention to introduce psychology input to an Italian critical care unit reduced the incidence of post-traumatic stress disorder (PTSD) a year later with a large effect size (using a historical, not randomised control design) (Peris et al. 2011). Small studies point to the value of cognitive rehabilitation, potentially beginning as early as the critical care admission (Jackson et al. 2012).

Editorials have emphasised an increased need for psychological interventions in the critical care setting to be evaluated (Hatch et al. 2011), and such studies are now underway. A cluster randomised controlled trial in 24 hospitals in the UK, aims to evaluate the clinical and cost-effectiveness of a complex, nurse-led, preventative psychological intervention in critical care ([icnarc.org/Our-Research/Studies/Poppi/About](http://icnarc.org/Our-Research/Studies/Poppi/About)). A Danish trial to evaluate a nurse-led

psychological recovery programme beginning 1-10 months post-ICU, found no benefit across a range of outcomes (Jensen et al. 2016). Other post-ICU interventions undergoing evaluation are cognitive rehabilitation (Jackson et al. 2012), coping skills training (Cox et al. 2012) and mindfulness (Cox et al. 2014). The key question is whether psychological interventions can improve patients' clinical outcomes.

Senior psychologists working in intensive care should ideally have the research expertise to contribute to, as well as keep abreast of, the evolving evidence base for this relatively new but rapidly expanding role.

### Conclusion

As recognition of intensive care-related psychological distress grows, senior practitioner psychologists are being recruited to the multidisciplinary team, to assess and manage acute and long-term stress in patients, families and staff. Further evaluation of the effect of specific psychological interventions on critical care outcomes will help to refine the ICU psychologist's role. ■

### Conflict of Interest

Dorothy Wade declares that she has no conflict of interest. David Howell declares that he has no conflict of interest.

### Abbreviations

ICU intensive care unit  
IPAT intensive care psychological assessment tool  
MV mechanical ventilation

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# CLINICAL PHARMACIST ROLE IN THE ICU

We provide an overview of the various facets of pharmacist practice in the intensive care unit (ICU), the current extent to which pharmacists are present in the ICU, along with a discussion on barriers and lessons learned in garnering support for such a role.

## Reduce Medication Errors

A landmark study in 1999 reported that pharmacist attendance in ICU rounds reduced the rate of preventable adverse drug events by 66% (Leape et al. 1999). Using the EU study figures, this would extrapolate to over 1200 lives saved every year. Other publications further support improved clinical outcomes due to pharmacist interventions. In a retrospective review of patients with thromboembolic disease, critical care pharmacists were able to significantly reduce patient mortality, ICU length of stay, bleeding complications, and need for blood product transfusions (MacLaren and Bond 2009). Recently, the PROTECTED-UK study involving 21 ICUs over 2 weeks reported that pharmacists reviewed 20,517 medication orders, 3,294 (16.1%) of which required interventions to optimise medication therapy (Shulman et al. 2015). Of the interventions, the majority (87.7%) were accepted by the prescriber, 6.8% were medication errors and 66% were deemed to be high risk in nature. Other studies have reported estimated cost-savings or avoidance of \$1.7-2.1 million over a 2 year period, making a return on investment of 7 to 1 (Weant et al. 2009).

## Education, Research, Administration

Critical care pharmacists are a valuable resource in providing education to clinical team members in addition to pharmacist trainees. In a neonatal ICU, a pharmacist-led staff education and risk management programme reduced medication errors from 24.1 to 5.1 per 1000 neonatal activity days (Simpson et al. 2004). Similarly, physician orientation and education were shown to reduce prescribing error rates. A panel consisting of a pharmacist and paediatrician, using a standardised predefined criteria, rated the severity of the errors and found a reduction

in severe errors from 29.7% to 7% (Alagha et al. 2011).

Critical care pharmacists can also lead and/or participate in clinical research. In a Canadian survey specifically on this topic involving 215 pharmacists, 41.4% reported being moderately to highly involved in research (Perreault et al. 2012). Finally, pharmacists can also be involved in more administrative/leadership type roles, such as quality improvement. In one pharmacist-driven quality improvement initiative (QI), an interdisciplinary protocol was shown to significantly improve process measure compliance with spontaneous awakening trials from a baseline of 20% to 97-100%, which was sustained 8 months following the programme (Stollings et al. 2015).

It would appear that there is an abundance of literature demonstrating ICU pharmacist ability to improve financial, clinical, and process outcomes. It is therefore disheartening to observe that 17 years after the publication of the landmark study (Leape et al. 1999), adoption is far less than 100%, despite wide support by professional organisations and patient safety experts (MacLaren et al. 2006; Brilli et al. 2001). A few barriers and lessons learned are presented below as a starting point to assist those contemplating such an undertaking.

## Building the Business Case

For most institutions, in order to obtain a new ICU pharmacist, a convincing business case is required. While specific requirements differ depending on local contexts, this usually involves a needs assessment, an environmental scan of comparator institutions, proposed service model, cost of service (e.g. pharmacist yearly salary and benefits), potential cost savings, and risk-benefit assessment of implementation. An environmental scan can be done locally within

Caring for critically ill patients in an intensive care unit (ICU) is considered a standard of care in today's environment. However, the ICU is a rapidly changing, complex, and costly environment where polypharmacy is the norm and medications are frequently used in combinations involving ever-changing doses based on physiologic responses and critical illness-related organ dysfunction. This creates the 'perfect storm' scenario that is ripe for medication errors. A study over a three-week period in two ICUs in the U.S. found an adverse event rate of 80.5/1000 patient-days, with medications being responsible for 78% of the serious events (Rothschild et al. 2005). This error rate is not an isolated phenomenon; a European study conducted across 27 countries and 113 ICUs involving 1,328 patients revealed that during a brief 24-hour observation period 81% of ICUs reported at least one parenteral medication error that involved 37% of patients (Valentin et al. 2009). This translated into an error rate of 74.5 errors per 100 patient days, with 7 patients experiencing permanent harm and 5 patient deaths due to medication errors. From a cost perspective, medications are the fourth largest contributor to total ICU costs, and account for approximately 38% of total drug costs in a hospital (Weber et al. 2003). Fortunately, the role of pharmacists in reducing medication errors and costs is well established.

the city or health region, published literature, or where available, national data such as the Canadian Hospital Pharmacy report (MacLaren et al. 2006; Hospital Pharmacy in Canada Editorial Board 2015). The caveat is that a significant portion of the overall cost savings made by ICU pharmacists is not in direct drug costs, but in prevention of costs due to errors. This is, albeit very unfortunately, viewed differently by administrators and finance personnel as not 'real dollars saved'. Therefore the 'sales pitch' often needs to centre on quality of care and/or meeting of regulatory or accreditation requirements, supported by any local/national quality agenda/initiative, and preferably in alignment with institution-specific objectives. Failing that, another method to demonstrate the worth of an ICU pharmacist has sometimes come from a trial period where another pharmacist with the appropriate knowledge/skills is redeployed to practise in the ICU for a short period while documenting the interventions made. This type of trial period allows for gathering of local data, which may be more convincing, but perhaps more importantly, allows the ICU care team to witness first-hand the benefits of having a pharmacist. Often the clinical team members (e.g. nurses and physicians) will become the best champions and advocates. Relationship building with the ICU team is a key factor in success, and this may be established through other channels such as collaborative work in a project for the ICU (e.g. computer order entry implementation) or through pharmacotherapy guideline development during Pharmacy and Therapeutics committee participation.

### Education and Training

Training for ICU pharmacotherapy is usually not the focus of many undergraduate pharmacy curricula and ICU clinical rotations/clerkships are often viewed by students as 'difficult to pass' rotations. Therefore, students' interest in ICU as a practice area is not widespread, limiting the qualified recruitment pool when a position is secured. While there are specialty residency programmes in critical care, their availability does not match needs, as demonstrated by the recent survey reporting that only 5.9% of critical care pharmacists have completed a critical care specialty residency (MacLaren et al. 2006). Therefore, finding qualified pharmacists to fill ICU positions is challenging and may result in filling them with less trained personnel, often producing less than optimal acceptance. Fortunately, with dedicated courses in ICU pharmacotherapy appearing in the elective portion of some pharmacy curricula, the addition of board certification in Critical Care Pharmacy by the Board of Pharmacy Specialties in the U.S., more and more training programmes and opportunities will be forthcoming to help close the qualified personnel shortage and needs gap.

### ICU Pharmacist Activities

The Society of Critical Care Medicine and the American College of Clinical Pharmacy published a position paper in 2000 on various activities that can/should be performed by an ICU pharmacist, dividing these activities into fundamental, desirable, and optimal levels (Rudis and Brandl 2000). The list is quite all encompassing, and almost daunting for institutions that

currently don't have such a position. Focusing on part of the fundamental activities, along with meticulous documentation of the interventions/outcomes, using either a homegrown or commercially available tool, should be the initial phase before progressing to desirable or optimal activities. This approach is corroborated by the recent U.S. survey where fundamental activities (e.g. providing drug information) are provided by 83.9% of respondents, desirable activities (e.g. therapeutic management advice to physicians) are performed by 63.8% of respondents, and optimal activities (e.g. ICU research) are performed by 19.5% of respondents (MacLaren et al. 2006).

### Conclusion

In conclusion, while it is unsatisfactory to see that ICU pharmacists are not present in all institutions that have an ICU, even in countries such as the U.S. and Canada where this practice is much more developed, ongoing support from professional organisations, such as the Faculty of Intensive Care Medicine and the Intensive Care Society in the UK, will hopefully continue to challenge the status quo. Indeed, even in developing countries such as Jordan, India and Brazil, studies on the impact of ICU pharmacists are being published (Leblanc et al. 2008; Hisham et al. 2016; Fideles et al. 2015; Aljbouri et al. 2013). Hopefully in the near future, critical care pharmacists will indeed be 'critical' in all ICUs. ■

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Clarence Chant declares that he has no conflict of interest. Norman Dewhurst declares that he has no conflict of interest.

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## Social Media in the “Real” World

Social media is all around us, and enables real-time communication with patients, families and with colleagues. There are general social networks (Facebook), professional networks (LinkedIn), blogs (WordPress), microblogs (Tumblr) and media sharing sites for photos, videos and podcasts. The Wall Street fortunes of these companies may wax and wane along with usage, but as health professionals we need to be aware of their benefits, costs and risks.

Do we stop to think how we are using social media? Social media can be cathartic (letting off steam), therapeutic (making sense of experiences), a last resort (e.g. complaints), just routine (Image 1), or “discouragingly daunting” (Widmer and Larsen 2016). Social media can be disinhibiting (think before you post), and true anonymity is virtually impossible to guarantee. Health professionals who might think twice when contacted by a newspaper reporter, for example, may be less inhibited when commenting on social media (media vs social media).

The social media landscape is summarised in Figure 1. It can be a bonus or curse both to patients and to health professionals.

## Social Media Guidance

Many professional organisations have guidelines for their members on social media use. For example, the UK Nursing and Midwifery Council’s social media guidance, a supplement to its professional standards, covers the need to use social media and social networking sites responsibly (Nursing and Midwifery Council 2015). For doctors, the General Medical Council (UK) issued *Doctors’ use of social media* in 2013.

# SOCIAL MEDIA BLESSING OR CURSE?

The UK National Health Service (NHS) Employers organisations advocates a liberal approach:

*The NHS Employers organisation firmly believes in a permissive approach to using social media in the NHS. Individual staff should be permitted and enabled to use social media for work. Only a permissive approach will unlock the innovations within the vibrant creative spaces found on social media sites (NHS Employers 2014)*

Professional guidance is also supplemented by local organisational policies. These can be quite detailed, e.g. Salisbury NHS Foundation Trust’s social media policy and guidance (Salisbury NHS Trust 2015) (sample: “Do not post, upload, forward or post a link to chain mail, junk mail, cartoons, jokes or gossip”). Clinical departmental social media use needs to have full consideration and commitment. For example, East Cheshire NHS Trusts asks that departments wanting to set up a social media site explain how they will manage the risks as well as outline the benefits (East Cheshire NHS Trust 2015).

## ▲▲ A change that has to inform our practice ▼▼

### Patients and Families

Social media use amongst patients and families ranges from routine communication, for example by patients during their ICU stay through to peer-to-peer support. The UK intensive care patient support charity ICUsteps has a peer-to-peer online community with more than 860 members on HealthUnlocked, which is a social network for health (healthunlocked.com/icusteps) (Image 2).

One writer even live-tweeted his mother’s death in an ICU, with his tweets reflecting on the medical care taking place as well as his relationship with his mother (O’Rourke 2015). Social media can also be used for crowdfunding, with many examples on popular websites such as [justgiving.com](http://justgiving.com) and [gofundme.com](http://gofundme.com).

### Education

Social media can be educational, and the Free Open Access Medical (FOAM) education movement ([foameducation.org](http://foameducation.org)) has grown immensely, offering excellent resources for continuing professional development. It includes FOAMcc (FOAM critical care), #FOANed (free open access nursing education) and #FOAMrn (FOAM nursing). For health professionals there are also peer support groups and closed sites that offer crowdsourced answers to clinical problems. Caution must be exercised, however, with the quality of information disseminated. Carroll and colleagues note that ego may outweigh talent: “well-informed participants with important ideas must be strong self-promoters or risk their voices going unheard” (Carroll et al. 2016).

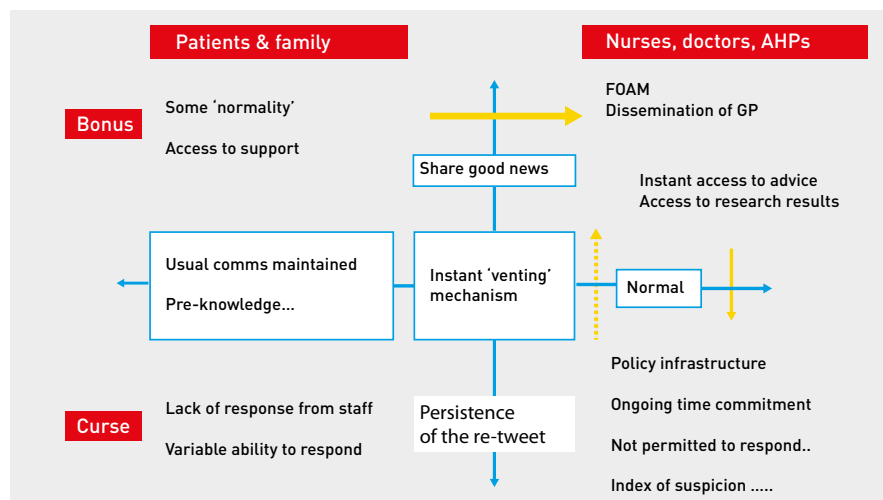
The UK Nursing and Midwifery Council explains the benefits for building professional relationships, accessing support networks and discussing issues with fellow professionals around the world (Nursing and Midwifery Council 2015). The Royal College of Nursing (UK) offers advice on using social media to revalidate, for example by participating in Twitter chats (Royal College of Nursing 2016).

### Evidence Dissemination

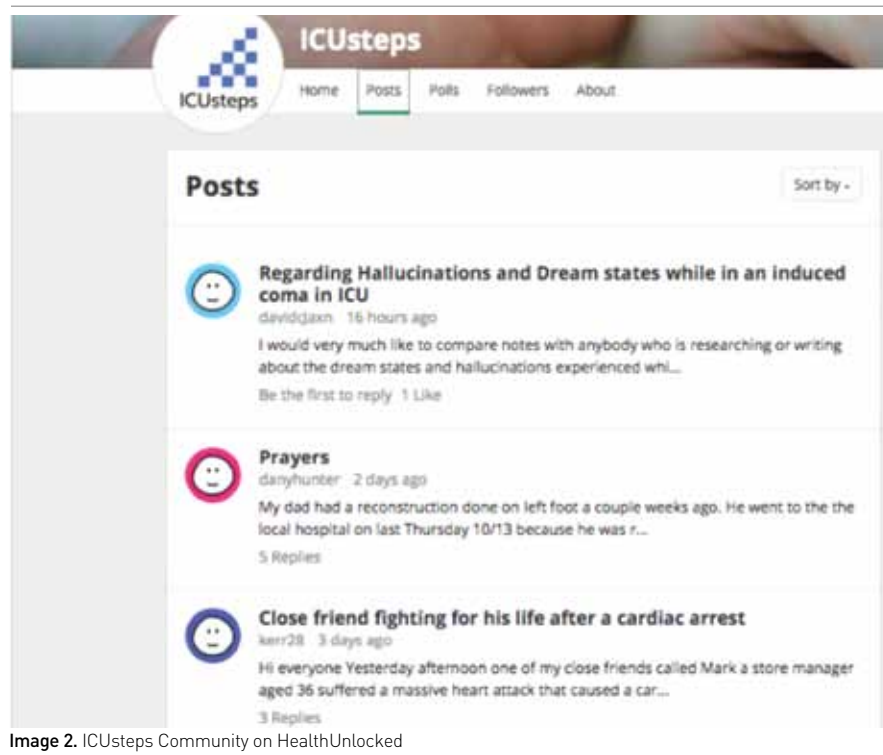
Social media enables rapid dissemination of evidence, both from scientific meetings and from peer-reviewed journals. This rapid dissemination has a different sort of impact to thorough reading of the literature. It allows harder-hitting



Image 1. Royal Devon & Exeter Hospital Tweet to thank fundraisers



**Figure 1.** The Social Media Landscape  
AHP allied health professional FOAM free online access medical education GP good practice



**Image 2.** ICUsteps Community on HealthUnlocked

recommendations (Young et al. 2013), and permits dissemination of the paper plus “the story”, e.g. 10 reasons to... However, there is a danger of premature dissemination without an accompanying ‘cautionary editorial’.

The growth in tweeting at conferences and in educational use has been analysed in the literature (a list is provided on Symplur [symplur.com/healthcare-social-media-research](http://symplur.com/healthcare-social-media-research)). Even if you cannot attend a meeting or sessions are not streamed, it is possible to participate in social media discussions remotely (Widmer and Larson 2016). Attai and colleagues (2016) suggest that “medical conference organizers should encourage Twitter participation and should be educating attendees on the proper use of Twitter.” Many large meetings have large screens showing the congress Twitter feed, as delegates and remote participants use the hashtag to comment, tweet and re-tweet (Stiegler 2016).

## Conclusion

So is social media a blessing or a curse? It is neither. It is a change that has to inform our practice. Healthcare organisations need policies in place so that staff know how to respond, and have the time commitment needed if necessary. Health professionals need to accept and plan for social media usage, collaborate, set boundaries and devise protocols for its use, and above all make it work for them. ■

## Recommended Resources

NHS Employers Social Media resources (includes guide for HR, running social media campaigns, best practice in social media measurement and evaluation, guide for chief executives) [nhsemployers.org/your-workforce/need-to-know/social-media-and-the-nhs/social-media-publications](http://nhsemployers.org/your-workforce/need-to-know/social-media-and-the-nhs/social-media-publications)

## Twitter chats

[wecomunities.org/tweet-chats/chat-guide](http://wecomunities.org/tweet-chats/chat-guide)

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## ICU Leadership

Brussels, January 17-18, 2017

# LEARNING TO LEAD AN ICU

## NEW COURSE

A course for aspiring and practising intensive care unit (ICU) leaders will take place in Brussels in January 2017. *ICU Management & Practice* spoke to some of the faculty, which includes Editor-in-Chief, Prof. Jean-Louis Vincent, to find out more.

### Who is the course for?

This course will attract participants from a variety of backgrounds and experience, including young, motivated doctors who see themselves moving forward in their chosen careers as intensivists into positions of leadership in the near (or more distant) future, through to more experienced physicians, who are perhaps already in leadership roles, but want to enhance their leadership skills and ability to get the most from their ICU teams, and eventually to improve their ICU outcomes. As an interactive course, there will be lots of time for questions, debate and discussion. Small group sessions with members of the experienced faculty will also be employed to enhance the learning experience.

### Why do we need leadership skills?

Good leadership is essential for all aspects of the ICU. Quality of care, safety, research, teaching and work atmosphere are all dependent on leadership. This course aims to provide participants with techniques and strategies to help them become effective, quality leaders, which will have long-reaching impact beyond their personal daily management challenges through to the ICU team as a whole and to patients and their families. Value-based ICU leadership will also help encourage more (young) doctors and other members of the ICU team, for example, nurses, into the profession, which is much needed as the demand for intensive care continues to expand.

### The Faculty

The course chairmen are Prof. Jean-Louis Vincent (Brussels, Belgium) and Prof. Paul Barach (Detroit,

USA). The faculty members are Professors Jacques Creteur (Brussels, Belgium), Bertrand Guidet (Paris, France), Michael Quintel (Göttingen, Germany), Jukka Takala (Bern, Switzerland) and Hans van der Hoeven (Nijmegen, the Netherlands).

**With the benefit of hindsight, what would you tell your younger self, starting out as an ICU leader?**

**PB:** With age and 20 years of clinical, research and administrative experience, comes an understanding that most is not often taught

### Do you wish you had had access to such a course when you were starting out in intensive care?

**Jean-Louis Vincent (JLV):** Yes, as nobody tells us these things when we are starting out, and it is so important.

**Paul Barach (PB):** I believe passionately that this course would have given me the competencies—knowledge, skills and attitudes—needed to manage and lead patients and ICU care towards creating reliable, safe and high quality patient-centred outcomes. I also feel the course would have prepared me to be a better listener to my patients, colleagues and ICU team members.

**Jacques Creteur (JC):** Our medical training doesn't include any teaching of leadership skills or human resource management. Yet good intensive care can only be achieved by good teamwork, and good team leadership will therefore result in better overall patient care.

**Jukka Takala (JT):** When starting my career in the late 1970s and early 1980s, leadership challenges were very different and focused on patient care, teaching, and research. The challenges today are much more complex, covering in addition also management, health economics and societal issues.

in medical schools or postgraduate residency programmes—the true value of building strong and authentic relationships, the real definition of servant leadership, the impact trust can have on your patients/colleagues/managers, and the role of careful and smart risk-taking can play in the trajectory of your careers.

**JC:** The real strength of a department of intensive care lies in its staff. We need to keep all staff members enthusiastic, committed and happy. This is the first challenge for a director and probably the most complex...

## Techniques and strategies to become effective, quality leaders

**BG:** In France we are fortunate to have this specific training. I would tell my younger self that the critical care speciality is the best for three reasons, which we need to keep in mind—diagnostic skills, procedural expertise and ethical issues.

**JT:** Understanding the role of intensive care in the broader picture of acute care specifically and healthcare in general helps to make priorities in patient care, resource allocation and leadership—follow-up of patient oriented outcomes, resource use, and quality are essential components of ICU-leadership. ■

### Further Information & Booking

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Route de Lennik 808 – B-1070 Brussels

veronique.de.vlaeminck@intensive.org

www.intensive.org

## Course Faculty

**Jean-Louis Vincent**, MD, PhD, is Professor of Intensive Care Medicine at the Free University of Brussels and Consultant in Intensive Care Medicine at Erasme University Hospital, Brussels, Belgium. He was Director of the Department of Intensive Care at Erasme until 2014. He founded the International Symposium on Intensive Care and Emergency Medicine in 1980. Prof. Vincent completes his term as President of the World Federation of Societies of Intensive and Critical Care Medicine in 2017. He is Past President of the European Society of Intensive Care Medicine, the Belgian Society of Intensive Care Medicine, the European Shock Society and the International Sepsis Forum. He is Editor-in-Chief of *ICU Management & Practice*, *Critical Care* and *Current Opinion in Critical Care*.

**Paul Barach**, MD, MPH, Maj (ret.), has expertise in ICU safety and quality, clinical strategy, clinical model development & redesign, physician leadership & engagement, performance & quality improvement, perioperative care and anaesthesiology. He is a Clinical Professor at Wayne State University School of Medicine. He was editor of the journal *BMJ Quality and Safety*, a Baldrige and National Quality Forum examiner, member of the National Board of Medical Examiner's Board, and was inducted in 2005 into the honorary society for Anesthesia leaders (AUA). Paul has been visiting professor in Norway, Netherlands, and Ireland and has taught systems improvement, population health, quality improvement, human factors, patient safety and systems re-design for over 15 years. His research examines the changing nature of acute care health systems, sedation management, transitions of care, teamwork, standards and accreditation, leadership and management, and the structure and culture of organisations. He co-developed the award-winning team training program, TeamSTEPPS, designed to create a culture of patient safety and improved communication in acute care areas.

**Jacques Creteur**, MD, PhD, became Professor and Director of the Department of Intensive Care at Erasme University Hospital, Brussels, Belgium in 2014.

**Bertrand Guidet**, MD, is director of the Medical Intensive Care at the Hôpital Saint Antoine in Paris, France, and medical director of the academic hospitals located in East Paris. He has been a university medical professor since 1997. He is a member of the research unit INSERM U1136 at the National Institute for Health and Medical Research (INSERM), the French public organisation dedicated to biological, medical and public health research. Prof. Guidet is past President (2008–2010) of the French Society for Intensive Care and is currently a member of the Health Research and Services outcome section of the European Society of Intensive Care Medicine (ESICM).

**Michael Quintel**, MD, PhD, is Professor and Director of the Department of Anaesthesiology, Emergency and Intensive Care Medicine at the University of Göttingen, Germany. He is a member of the European Society of Intensive Care Medicine (ESICM) group on respiratory failure, a member of the Scientific Committee of International ECMONet, Past President of the German Interdisciplinary Society of Intensive Care Medicine (DIVI) and a past council member of the German Society of Anaesthesia and Intensive Care (DGAI). He is a member of the German Sepsis Society and an Investigator in the SepNet Sepsis Clinical Trial Network in Germany, and he has participated in numerous sepsis and critical care trials.

**Jukka Takala**, MD, PhD, is Professor of Intensive Care Medicine, University of Bern and Director and Chief Physician, Department of Intensive Care Medicine, Inselspital, Bern University Hospital, Switzerland since 1999. In 2004 he became Director of the Division of Intensive Care, Emergency Medicine and Anesthesiology at Inselspital, Bern University Hospital. He has sat on Inselspital's Extended Hospital Management Board since 2006 and is also Chairman of the Medical Information Technology board and a member of the Information Technology Strategy board. Prof. Takala is Past President of the European Society of Intensive Care Medicine. He is a member of the Editorial Board of *ICU Management & Practice*.

**Hans van der Hoeven**, MD, PhD, has been Head of the Department of Intensive Care at Radboud University Medical Center, Nijmegen, the Netherlands since 2003. Previously he was Head of the Department of Intensive Care at Leiden University Medical Centre and also Head of the Department of Intensive Care at the Jeroen Bosch Medical Centre at 's-Hertogenbosch. He is chairman of the congress committee of the Dutch Association for Intensive Care, Course director of Fundamental Critical Care Support and a member of the Joint Intensive Care Committee.



# RENAL REPLACEMENT THERAPY FOR ACUTE KIDNEY INJURY

## QUESTIONS REMAIN

Eric Hoste is Professor in Medicine and Head of Clinic at Ghent University Hospital, Belgium. Prof. Hoste's primary clinical area of interest is clinical critical care nephrology, and he has published more than 190 original papers, review articles and book chapters primarily within this field. He is a Senior Clinical Investigator, Research Foundation-Flanders and a collaborating faculty member of CRISMA (Clinical Research, Investigation, and Systems Modelling of Acute illness). He is Chair of the Acute Kidney Injury Section of the European Society of Intensive Care Medicine (ESICM), and a former president of the Belgian Society of Intensive Care Medicine.



### What should be the definition of "early" renal replacement therapy in your opinion?

There is no agreement currently. The demand for initiation of renal replacement therapy (RRT) is driven by severity of acute kidney injury (AKI), but also by severity of illness, co-morbidity, volume overload and other factors

Two major studies published this year addressed the timing of initiation of renal replacement therapy (RRT). The Early vs Late Initiation of Renal Replacement Therapy in Critically Ill Patients With Acute Kidney Injury (ELAIN) trial (Zarbock et al. 2016) used KDIGO/AKI severity stage 2; the AKIKI trial (Gaudry et al. 2016) used stage 3 AKI. That shows that this is a field that's not so clear. Both trials had divergent outcomes. The ELAIN trial showed benefits for early initiation started at stage 2 AKI, while the AKIKI trial did not show the benefits of starting RRT early. Both trials used increases of serum creatinine and decreases of periods of oliguria and AKI staging as a timing tool. Perhaps that's not really how clinical practice is at present, because when you decide in daily practice to initiate RRT or not of course it is the severity of AKI that's the driver for this decision as well as other factors such as the severity of the patient's illness, volume overload etc. Maybe looking only at kidney variables is a bit too narrow and we need to look at a broader picture of the patient.

There is another trial coming up—the Standard vs. Accelerated Initiation of RRT in Acute Kidney Injury (STARRT-AKI) trial, led by Ron Wald and Sean Bagshaw ([clinicaltrials.gov/ct2/show/NCT02568722](http://clinicaltrials.gov/ct2/show/NCT02568722)). It's an ambitious worldwide trial that aims to enrol 2866 patients, and it is aimed at investigating the timing of RRT. Inclusion of patients in the trial will be when they are at AKI stage 2 or 3, so that is similar to previous trials. However, an important aspect is that patients can only be included when the physician thinks there is a window for waiting or early initiation, delayed or not. If the physician thinks the patient needs an immediate start or thinks this patient needs to wait a little the patient cannot be included and of course the decision of the physician will be triggered by other factors than AKI severity stage.

In addition, an eagerly awaited French trial, the Initiation of Dialysis EARly Versus deLayed in Intensive Care Unit (IDEAL-ICU) ([clinicaltrials.gov/ct2/show/NCT01682590](http://clinicaltrials.gov/ct2/show/NCT01682590)) has started recruiting 800+ patients this year, and it will also address the question of early or delayed RRT initiation.

### What are the most important considerations in deciding which patients should receive RRT?

The first question always is whether there is

consensus amongst the staff and the patient's family to initiate RRT. It is often considered a sign of being very severely ill. Needing RRT is sometimes a step too far for family members or patients themselves. As clinicians you have to inform your patient and make sure that you have a clear mindset to offer this to patients who will receive the benefits or who still have a prognosis. For septic and liver failure patients the consideration is what kind of modality to use. Typically, septic shock and severely haemodynamic unstable patients, or liver failure patients, are initiated on a continuous modality. Because it is better haemodynamically tolerated especially in acute liver failure patients there may be an issue of encephalopathy caused by brain oedema and in these patients you don't want the volume shifts associated with intermittent therapy. We also have volume-overloaded patients, in which we want to remove volume, which is not always well tolerated when you do it on a four-hour basis. These patients are also initially on continuous or sustained low-efficiency dialysis (SLED) therapy, and we review during a 12-hour or 24-hour period.

### What criteria should ICUs use to decide on continuous or intermittent renal replacement therapy?

There is no data to support the superiority of continuous over intermittent or vice versa. How

familiar you are with the technique is important. In expert hands intermittent therapies, using 6-hour duration or 8-hour treatment duration, are also tolerated in haemodynamically unstable patients, but that's in expert hands. The nurses need to be able to do this. It has been demonstrated very elegantly in several studies, especially in France, by Christophe Visonneau and Frédérique Schortgen, that you can also treat severe septic shock patients with intermittent therapies (Visonneau et al. 2006; Schortgen et al. 2000). However, not all units are able to do this. If most of your patients are severe septic shock patients, mechanically ventilated and on vasopressors, then continuous or hybrid blood therapies are preferable. If your patients are less severely ill, intermittent therapies are equally effective and can be used. It's your expertise that really drives the decision.

#### How should the most appropriate anticoagulation strategy be identified?

There are two possibilities—unfractionated heparin and citrate. Unfractionated heparin was the standard up till a few years ago and is now gradually being replaced by citrate in many units. Citrate is associated with longer filter life and less bleeding, so in that respect citrate has replaced unfractionated heparin. There are typical patients who are at risk for systemic bleeding, such as trauma or cirrhosis patients, who probably are better treated with citrate.

Perhaps a third option is also possible and that's something we also tend to do with SLED, which is using heparin-coated membranes and no anti-coagulation at all. That is also an option if the treatment duration is intermittent and not too long.

#### When and how should renal support be stopped?

It is a big question mark. I don't think there is data out to support a clear statement on that, but typically when the patient is passing urine

again continuous RRT is stopped for 12 hours or a day to see how things are going and if the patient tolerates the discontinuation of CRRT. Adequate urine volume is the main driver for stopping renal replacement support as well as adequate clearance, creatinine clearance above 10. Of course you can only measure the clearance when you stop the therapy.

## we should move on and look at specific subgroups

#### Is there good evidence on risk factors for persistent dialysis dependency of AKI patients who receive RRT? Your 2015 study (Oeyen et al. 2015) found that a quarter of long-term AKI-RRT survivors have persistent dialysis dependency. What is needed to improve this?

There is observational data from cohort studies that suggests that continuous RRT patients compared to intermittently treated patients have lower risk for persistent need for RRT (Schneider et al. 2013). But it is still not shown in prospective trials, and it's still an open question. It's strongly suggested, but has yet to be proven. Hybrid therapy with a longer duration of intermittent therapy has probably the same outcomes as continuous RRT so it should be regarded as similar. Other risk factors are the risk factors that can't be altered, such as pre-existing chronic kidney disease. That is one of the most important risk factors and associated with that is hypertension and diabetes, as these patients also tend to have chronic kidney disease. The definitive word on modality is not out but it is suggested and the data have suggested that continuous therapy or hybrid therapies are associated with less persistent need for RT.

#### What should be the priorities for further research into renal replacement therapy for AKI patients?

Timing is the number one priority, and data on this are being generated at the moment. The elements that may decrease persistent AKI or persistent need for chronic renal replacement therapy are also very important, because they have a huge impact on the patient and society, as well as an economic impact. Currently all our studies on AKI patients are as a group. I think we should move on and look at specific subgroups, because it doesn't make sense that patients who develop AKI following cardiac surgery are put in the same basket as septic shock patients. Probably the timing of initiation and choice of modality etc—all these questions have different answers for different subgroups. I see this as an important research question. Hybrid therapies are not well studied yet and should be evaluated in more detail.

#### Should variation in practice at ICU level on initiation of RRT etc. be addressed at a national or European level?

There is already variation in practice within one unit. When I am on call I will have a different opinion on it than my colleague. I think it should be addressed on a global level or even better a European level because there are so many opinions and there is no good data at present. ■

#### Conflict of Interest

Eric Hoste declares a speaker's fee from Alexion and a study grant from Belco for a study on ECCO2R.

#### Abbreviations

AKI acute kidney injury  
CRRT continuous renal replacement therapy  
RRT renal replacement therapy  
SLED sustained low-efficiency dialysis

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# BREXIT'S BRUTAL BLOW TO THE NHS

“I’m sorry. I’m just so sorry.”  
It’s 8am. Two junior doctors, one English, the other Italian, embrace in tears on the steps outside their hospital. We’ve saved lives together, lost patients together, run cardiac arrests, sought to comfort grieving families, seen patients make miraculous recoveries, witnessed death at its most unforgiving and ugly - all of it together. But as of June 23, 2016, while one of us remains fully entitled to be a doctor in England’s National Health Service (NHS), the other may be stripped of her right to live and work here.

Brexit is a brutal blow for one of the most cosmopolitan of UK workforces. The NHS is an extraordinary melting pot of nationalities, and all the richer for it. On my ward alone,

promise to the NHS in the event of Brexit - a pledge that lasted barely an hour beyond the referendum result before pro-Brexit UKIP leader Nigel Farage dismissed it as a ‘mistake’. Worse, our underfunded NHS now faces poten-

tially catastrophic financial consequences of Brexit. But the most immediate threat to the NHS is not financial but human: the risk that members of its most precious, most undervalued asset—its workforce—may now wonder

▲▲ **Stephen Nickell of the Office for Budget Responsibility, has stated that the NHS would be “in dire straits” without migrant workers** ▶▶

the doctors and nurses making up the team are British, Spanish, Nigerian, Portugese, Canadian, Kiwi, French and Filipino. Overall, up to 35 percent of health professionals come from outside the UK, with 55,000 of the NHS England’s 1.2 million staff being citizens of other EU countries. Small wonder one of the UK’s most senior economists, Stephen Nickell of the Office for Budget Responsibility, has stated that the NHS would be “in dire straits” without migrant workers.

Much was made of the ephemerality of the Leave campaign’s 350 million pounds a week

## Statistics

Total population (2015)  
**64,716,000**

Probability of dying between 15 and 60 years m/f (per 1,000 population, 2013)  
**88/55**

Gross national income per capita (PPP international \$, 2013)  
**35,670**

Total expenditure on health per capita (Intl \$, 2014)  
**3,377**

Life expectancy at birth m/f (years, 2015)  
**79/83**

Total expenditure on health as % of GDP (2014)  
**9.1**

Source: World Health Organization. Global Health Observatory [who.int/gho/countries/gbr/en/](http://who.int/gho/countries/gbr/en/)

what on earth they are doing here in the UK.

Already, nursing and medicine in the UK are perilously understaffed. Every day, in every hospital, doctor and nursing rotas are riddled with gaps—unfilled slots—leaving patients exposed to dangerously overstretched staff. If patient safety matters, we simply cannot afford to lose any more doctors and nurses. Yet now vast numbers of them have been made to feel unwelcome and unwanted: first by a campaign based on prejudice, propaganda and xenophobia, second, by the fact that the majority of voters actually embraced this narrative of fear.

We have a long and grubby history of politicians and newspaper editors exploiting Britons' love of the NHS to indulge in immigrant bashing. You know the drill. Why can't you get an appointment at your GP? Because hordes of migrants are clogging up the surgery. Why have you been denied your ground-breaking cancer drug? Because all those brazen 'health tourists' are screwing us out of scarce NHS resources.

The irony is, the NHS's job of caring makes

it in one sense our most egalitarian institution. In death lies the ultimate equality and, when treating sick patients, you are only one step removed from that. Medicine transcends difference. Hearts still pump, blood still flows, whatever skin they're clothed in. My job is to help people, irrespective of race, religion, sexuality, nationality. When you lie before me in a hospital gown—vulnerable, frightened, disorientated, in pain—as your junior doctor I don't care if you are English, Spanish or Outer Mongolian. You could be a communist, a Scientologist, a Prime Minister, an axe murderer. You could even be UK Health Secretary Jeremy Hunt and still I would treat you the same.

Doctors, like nurses, treat one thing alone, the patient, the person in front of them. The values that infuse an NHS ward - kindness, tolerance, decency, humanity - should surely be writ large? I thought my country was inclusive, all-embracing. I've never felt more foreign. To my non-British colleagues, every one of you an asset to the NHS, I'm sorry, so sorry, please stay. ■

### Brexit Fallout Continues

The Leave the EU campaigners claimed "We send the EU 350 million pounds a week. Let's fund our NHS instead." Peer360 surveyed acute hospital managers and health professionals, and the results represent 73% of NHS hospital trusts. Most believed that Brexit would impact on the whole negatively on UK healthcare, not only in terms of funding and staffing, but also potentially on healthcare IT upgrade projects.

Reference: Peer360 (2016) Brexit: where are my NHS funds? [Accessed: 20 October 2016] Available from [peer60.com/report/brexit-impact-on-nhs-healthcare](http://peer60.com/report/brexit-impact-on-nhs-healthcare)

"Currently a quarter of our doctors come from overseas. They do a fantastic job and the NHS would fall over without them. When it comes to those that are EU nationals, we've been clear we want them to be able to stay post-Brexit."

Jeremy Hunt, Secretary of State for Health, speaking to the Conservative Party conference in October 2016, where he announced 1500 more training places for doctors from September 2018. ([gov.uk/government/news/up-to-1500-extra-medical-training-places-announced](http://gov.uk/government/news/up-to-1500-extra-medical-training-places-announced))

## "Brexit means Brexit"

but for the NHS it means possible implications on:

### Budget

The annual funding of the NHS depends on the performance of the economy, with leading economists concerned Brexit could lead to an economic downturn.

The Health Foundation has estimated that the NHS budget could be £2.8bn lower than currently planned by 2019/20.

### Research

UK organisations are the largest beneficiary of EU health research funds, bringing well over €300m into the country since 2014.

EU collaborative research opportunities help the NHS speed up the translation of medical discoveries into healthcare provision.

### Employment

Around 144,000 EU nationals work in health and social care in England.

In the NHS, around 10 per cent of doctors and 5 per cent of nurses are from the EU.

### X-border healthcare

Over 27 million Britons have European Health Insurance Cards (EHIC), facilitating immediate access to healthcare when abroad. Over 1.2 million UK citizens living in the EU, including our pensioners who chose to retire to Europe, are entitled to healthcare abroad.

### Innovation

Having a single EU medical regulation system has enabled new health technologies to be brought to market sooner for the benefit of patients.

The NHS leads 1/4 of the new European Reference Networks, which improve diagnosis and treatment for rare and complex diseases.

### Trials

As clinical trials are regulated by EU rules, uncertainty has emerged on future NHS participation in multi-national trials.

Over 600,000 patients were recruited onto clinical studies by NHS organisations last year.

## NHS European Office



With the NHS experiencing the longest funding squeeze in its history, how can we ensure the NHS budget is not negatively impacted in the event of an economic slowdown?



How can we ensure the NHS continues to take active part in EU collaborative research and that it remains an attractive place for globally renowned researchers?



How can we reduce uncertainty for EU staff currently employed by the NHS and ensure sustainable workforce supply and standards of care are maintained post Brexit?



How can we ensure NHS patients continue to receive safe and seamless healthcare when they travel across borders for holidays, studies or to live abroad?



How can we maintain the UK and NHS as world leaders in medical innovation, allowing patients to benefit from early access to new treatments?



How can we ensure NHS trusts and patients continue to participate in EU clinical trials, allowing them to develop and access innovative, life-saving treatments?



For more information: [www.nhsconfed.org/nhsandbrexit](http://www.nhsconfed.org/nhsandbrexit), @NHSConfed\_UK

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# AGENDA



**29 Nov-1 Dec** 22nd Postgraduate Refresher on Cardiovascular and Respiratory Physiology Applied to ICM, Brussels, Belgium  
<https://iii.hm/5ep>

**30 Nov-2 Dec** DIVI 2016, Hamburg, Germany  
<https://iii.hm/5er>

## DECEMBER

**1-3** 8th International Baltic Congress of Anaesthesiology and Intensive Care Tallinn, Estonia  
<https://iii.hm/5e3>

**1-3** 3rd European Airway Congress, Valencia, Spain  
<https://iii.hm/5e4>

**5-7** Intensive Care Society State-of-the-Art Meeting, London, UK  
<https://iii.hm/5e5>

**6-8** Sepsis 2016, Paris, France  
<https://iii.hm/5ey>

**11-14** Update on Acute Respiratory Failure, Rome, Italy  
<https://iii.hm/5e6>

## JANUARY 2017

**13-14** Deutsches SMART meeting, Frankfurt, Germany  
<https://iii.hm/6vm>

**17-18** ICU Leadership, Brussels, Belgium  
<https://iii.hm/6yl>

**21-25** 46th Annual Meeting of the Society for Critical Care Medicine, Honolulu, USA  
<https://iii.hm/5e8>

**27** Critical Care Reviews Meeting, Belfast, UK  
<https://iii.hm/5e9>

## FEBRUARY 2017

**8-10** 22nd International Symposium on Infections in the Critically Ill Patient and Sepsis Symposium, Porto, Portugal  
<https://iii.hm/6pc>

## MARCH 2017

**21-24** 37th International Symposium on Intensive Care and Emergency Medicine Brussels, Belgium  
<https://iii.hm/6pd>

## APRIL 2017

**6-8** ESICM Euroasia, Hong Kong, China  
<https://iii.hm/6vn>

**20-24** SG-ANZICS Intensive Care Medicine Forum, Singapore  
<https://iii.hm/6pe>

## MAY 2017

**10-12** Smart Meeting Anesthesia Resuscitation Intensive Care, Milan, Italy  
<https://iii.hm/6vo>

**30-31** Metabolic and Nutritional Issues in the ICU, Brussels, Belgium  
<https://iii.hm/6vp>

## JUNE 2017

**3-5** Euroanaesthesia 2017, Geneva, Switzerland  
<https://iii.hm/6pg>

**8-9** Neurosciences in Intensive Care International Symposium, Paris, France  
<https://iii.hm/6ph>

**13-14** BRACE (Brain Critical Care & Emergencies) Meeting, Brussels, Belgium  
<https://iii.hm/6vq>

**15-17** World Congress of the Abdominal Compartment Society Banff, Canada  
<https://iii.hm/6pf>

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