SAM
The Society for Acute Medicine

Severe Sepsis: international and specialty variations in initial management

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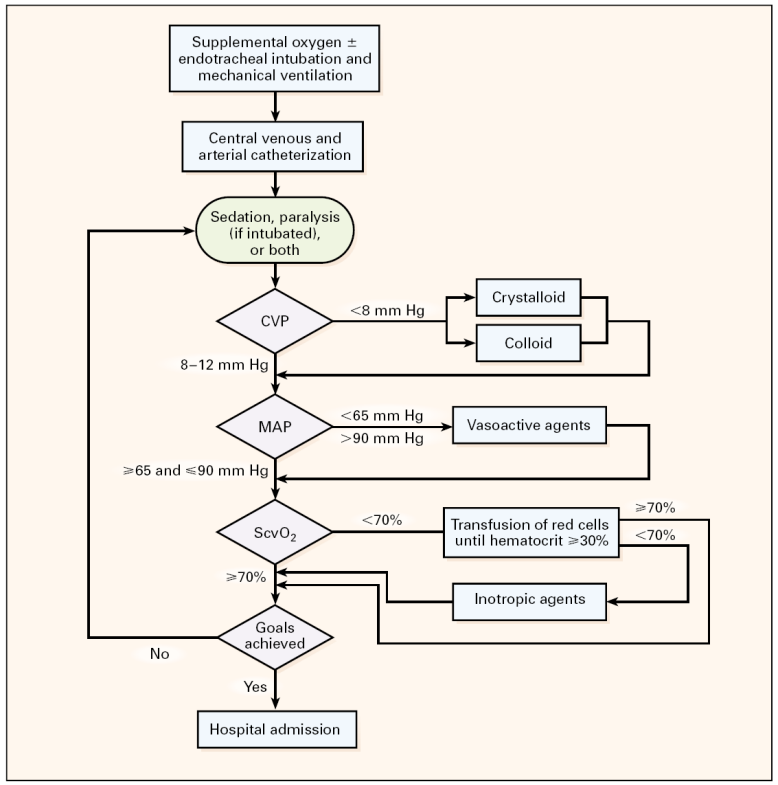
Early Goal Directed Therapy (EGDT)

The NEW ENGLAND JOURNAL of MEDICINE

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

N Engl J Med, Vol. 345, No. 19 · November 8, 2001 · www.nejm.org



VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03

Existing knowledge of EGDT implementation

Critical Care Medicine
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE MEDICINE

Alan E. Jones, MD, Jeffrey A. Kline MD,
Department of Emergency Medicine,
Carolinas Medical Center, Charlotte, NC

Crit Care Med 2005 Vol. 33, No. 8

Use of Goal-Directed Therapy for Severe Sepsis and Septic Shock in Academic Emergency Departments

To the Editor:

Society of Critical Care Medicine (2). The purpose of this study was to quantify the proportion of academic EDs that have implemented early goal-directed therapeutic intervention for sepsis and to identify barriers for adoption.

In July 2004, a survey was sent by electronic mail to an emergency medicine attending physician, all with more than 2 yrs postresidency clinical experience, at 30 academic tertiary care hospitals. All study

The response rate was 100% (n = 30). The results of the survey are shown in Table 1. Key findings include the observation that only 7% of clinicians report the use of goal-directed therapy in their ED. The most commonly cited barriers to the use of goal-directed therapy were lack of specialty monitoring equipment (75%), too many ED resources required for implementation (43%), and that the protocol requires central venous cannulation (36%). Most of the respondents (82%) reported the availability of an arterial blood gas analyzer for routine use by the ED 24 hrs a day, 7 days a week. The majority of responders treated more than ten septic patients per year (77%).

Existing knowledge of EGDT implementation

Critical Care Medicine
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE MEDICINE

Tiffany M. Osborn, MD, Charlottesville, VA; Stephen Trzeciak, MD, R. Phillip Dellinger, MD, Camden, NJ; Mitchell M. Levy, MD, Providence, RI; Herwig Gerlach, MD, Germany; on behalf of the Surviving Sepsis Campaign

The authors reply:

However, the fact that EGDT has not been widely adopted yet is not compelling evidence that it does not qualify as a "best practice."

Sepsis survey: study team

	Michael Reade	Critical Care Medicine
	David Huang	Critical Care Medicine
	Don Yealy	Emergency Medicine
	Derek Angus	Critical Care Medicine
	Derek Bell	Acute General Medicine
	Timothy Coats	Emergency Medicine
	Mervyn Singer	Intensive Care Medicine
	Sandra Peake	Intensive Care Medicine
	Anthony Cross	Emergency Medicine

C·R·I·S·M·A

University of Pittsburgh

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Sepsis survey: aim

To characterise intended management of sepsis 'for a patient presenting to your hospital today'

To measure intended adherence with the EGDT protocol

To compare

- **Emergency physicians, intensivists, and, in the UK, acute general physicians**
- **UK, US, and ANZ**

Method: survey invitation

Attitudes towards the management of severe infection

Dear Colleague,

The University of Pittsburgh is leading a large, NIH-funded, multicentre trial in the US (ProCESS) looking at the early management (1st 6 hrs) of patients presenting with severe infection. ANZICS and the ESICM will be shortly applying for funding to do parallel studies in Australasia and Europe. There's also a great opportunity for the UK to do something similar as the DoH have put out a call for trials in emergency medicine. ICNARC with the ICS will hopefully be collaborating with the College of Emergency Medicine and the Society of Acute Medicine for a multi-disciplinary bid.

As a prelude to this study, we are very interested in knowing how you currently manage these patients. We suspect doctors in different specialties and countries may have different approaches. We have designed a short survey to assess these approaches.

Our survey asks how you would manage two different patients presenting to your Emergency Department with pneumonia. Even if you do not usually see patients in the Emergency Department, we are still interested in your responses.

This invitation is being sent with the help of a number of the professional bodies and societies. If you receive more than one invitation, please accept our apologies, and respond to only one.

We need your responses to provide an accurate comparison between specialties and countries. The survey should take you 10 minutes to complete. We will not collect any information that could identify you personally or the hospital where you work.

Click on the link: http://www.surveymonkey.com/s.asp?u=467543748887 and you will be directed to our automated survey.

Many thanks,

Not another survey!

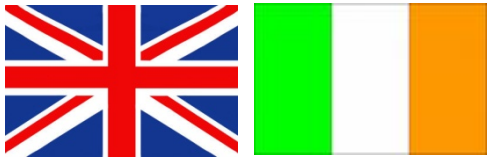
Well .. No:

- Designed to inform trial design
- Supported by 7 national specialty societies
- The largest ever survey of acute care practice

Features:

- Asks about practice intentions, not knowledge
- Forces a decision in each case – just like real life – rather than asking for a 'general feeling'
- Standardised patient to ensure all EGDT points addressed – but did not mention EGDT

Method: survey invitation & responses



Invitation by email
x 2 +/- newsletter
or website
advertisement

The College of Emergency Medicine

The Intensive Care Society

SAM

CEM (UK)
505 invitations

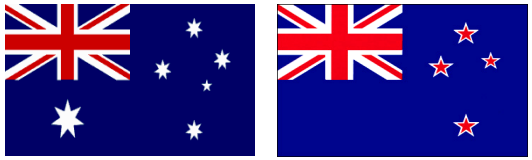
ICS (UK)
2003 invitations

SAM (UK)
525 invitations

707 full or partial responses
23.3%

505 complete* eligible** responses analysed
71.4% of total responses
16.7% of invitations

Method: survey invitation & responses



Invitation by email x 2

ACEM
927 invitations

JFICM (ANZ)
537 invitations

469 full or partial responses
32.0%

408 complete* eligible** responses analysed
87.0% of total responses
27.7% of invitations

Method: survey invitation & responses

Invitation by email x 2

American College of Emergency Physicians®
ADVANCING EMERGENCY CARE

Society of Critical Care Medicine
The Intensive Care Professionals

Penn. ACEP
1182 invitations

SCCM (USA)
6203 invitations

1285 full or partial responses
17.4%

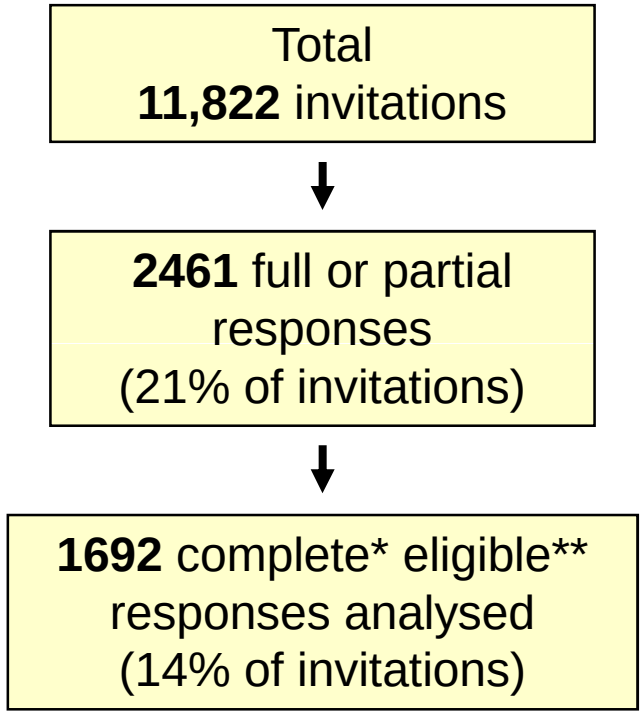
779 complete* eligible** responses analysed
60.6% of total responses
10.5% of invitations

Method: survey invitation & responses

* 356 responses excluded if they were incomplete, as it was impossible to know specialty and country.

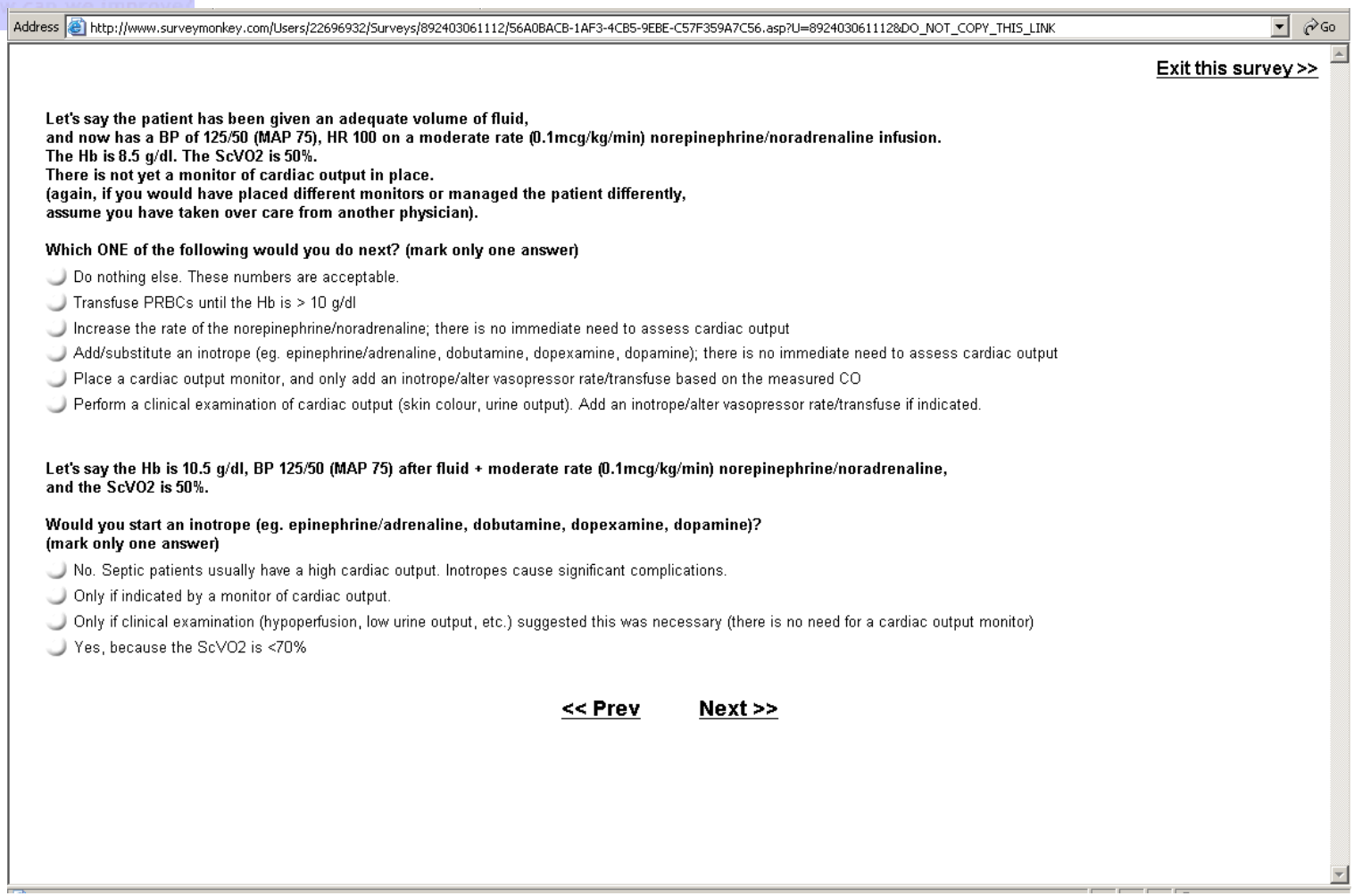
** Respondents were sequentially excluded if they were identified as:

Not in US, UK, Eire or ANZ	24
Not practicing in ED or ICU, or in the UK/Eire, acute general medicine	29
Not board certified or with UK/Eire specialty fellowship	324
Practicing only pediatrics	36



Method: online survey instrument

SurveyMonkey.com
because knowledge is everything


Address http://www.surveymonkey.com/Users/22696932/Surveys/892403061112/56A0BACB-1AF3-4CB5-9EBE-C57F359A7C56.asp?U=892403061112&DO_NOT_COPY_THIS_LINK Go

Exit this survey >>

**Let's say the patient has been given an adequate volume of fluid,
and now has a BP of 125/50 (MAP 75), HR 100 on a moderate rate (0.1mcg/kg/min) norepinephrine/noradrenaline infusion.
The Hb is 8.5 g/dl. The ScVO2 is 50%.
There is not yet a monitor of cardiac output in place.
(again, if you would have placed different monitors or managed the patient differently,
assume you have taken over care from another physician).**

Which ONE of the following would you do next? (mark only one answer)

- Do nothing else. These numbers are acceptable.
- Transfuse PRBCs until the Hb is > 10 g/dl
- Increase the rate of the norepinephrine/noradrenaline; there is no immediate need to assess cardiac output
- Add/substitute an inotrope (eg. epinephrine/adrenaline, dobutamine, dopexamine, dopamine); there is no immediate need to assess cardiac output
- Place a cardiac output monitor, and only add an inotrope/alter vasopressor rate/transfuse based on the measured CO
- Perform a clinical examination of cardiac output (skin colour, urine output). Add an inotrope/alter vasopressor rate/transfuse if indicated.

**Let's say the Hb is 10.5 g/dl, BP 125/50 (MAP 75) after fluid + moderate rate (0.1mcg/kg/min) norepinephrine/noradrenaline,
and the ScVO2 is 50%.**

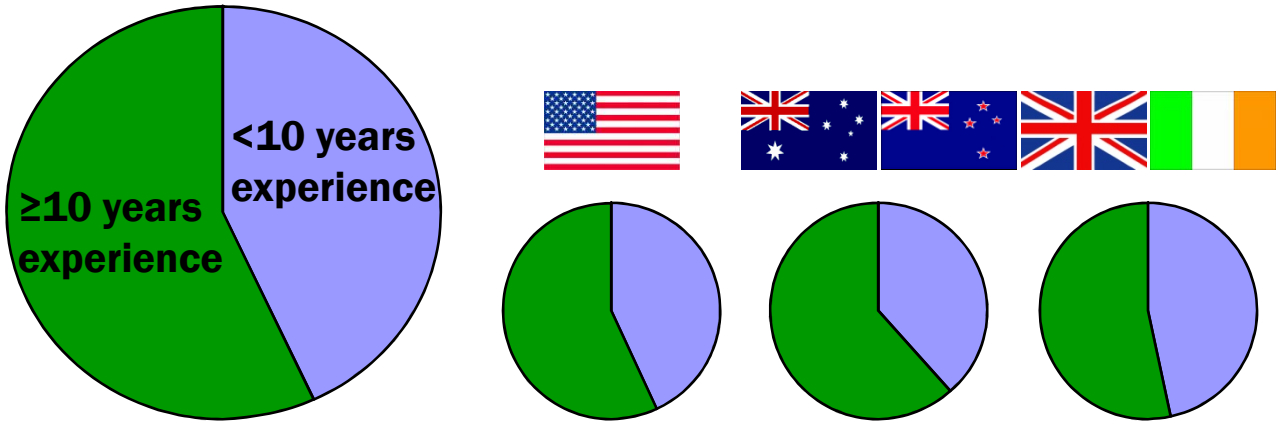
**Would you start an inotrope (eg. epinephrine/adrenaline, dobutamine, dopexamine, dopamine)?
(mark only one answer)**

- No. Septic patients usually have a high cardiac output. Inotropes cause significant complications.
- Only if indicated by a monitor of cardiac output.
- Only if clinical examination (hypoperfusion, low urine output, etc.) suggested this was necessary (there is no need for a cardiac output monitor)
- Yes, because the ScVO2 is <70%

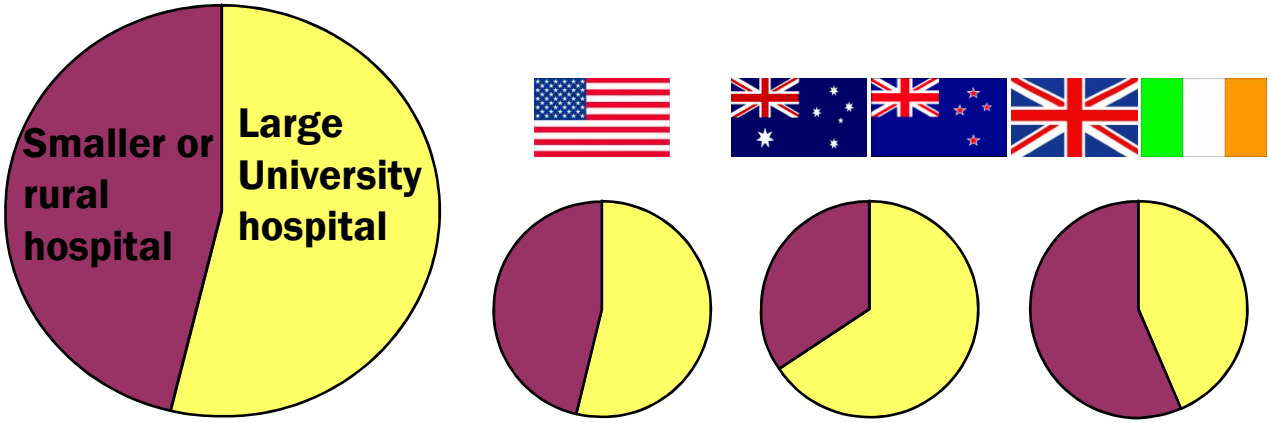
<< Prev Next >>

Respondents

Experience:



Practice location:



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Results: Identifying severity

A 65 year old 80kg previously well male presents with presumed pneumonia:

HR 100,
BP 125/50 (MAP 75),
respiratory rate 22,
SpO_2 95% on room air,
temp 38.7 degrees C

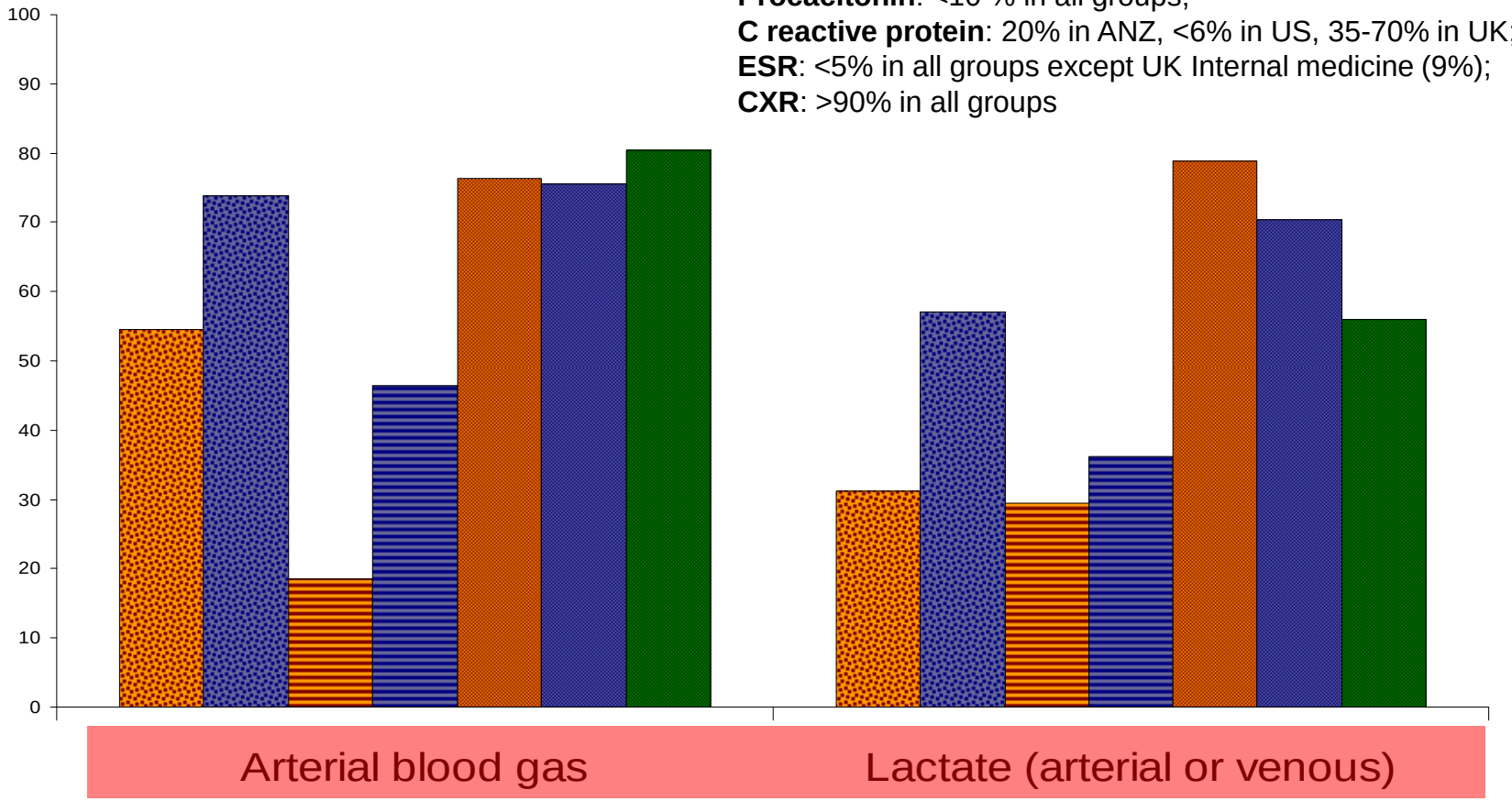
Which tests would you order to help determine illness severity?

- White cell count
- Arterial blood gas
- Lactate (arterial or venous)
- Procalcitonin
- C-reactive protein
- Erythrocyte sedimentation rate
- Chest X ray
- I would not do any of these tests
- Other (please specify)

Results: Identifying severity

Which tests would you order to help determine illness severity?

Other alternatives selected:
White cell count: >80% in all groups;
Procacitonin: <10 % in all groups;
C reactive protein: 20% in ANZ, <6% in US, 35-70% in UK;
ESR: <5% in all groups except UK Internal medicine (9%);
CXR: >90% in all groups



Results: Identifying severity

Let's say the lactate is 4 mmol/L.
(if you would not have ordered lactate, assume another doctor had)

Does the lactate result influence your management plan?

- **No**
- **Perhaps – it would depend on the rest of the history / examination / tests**
- **Yes**

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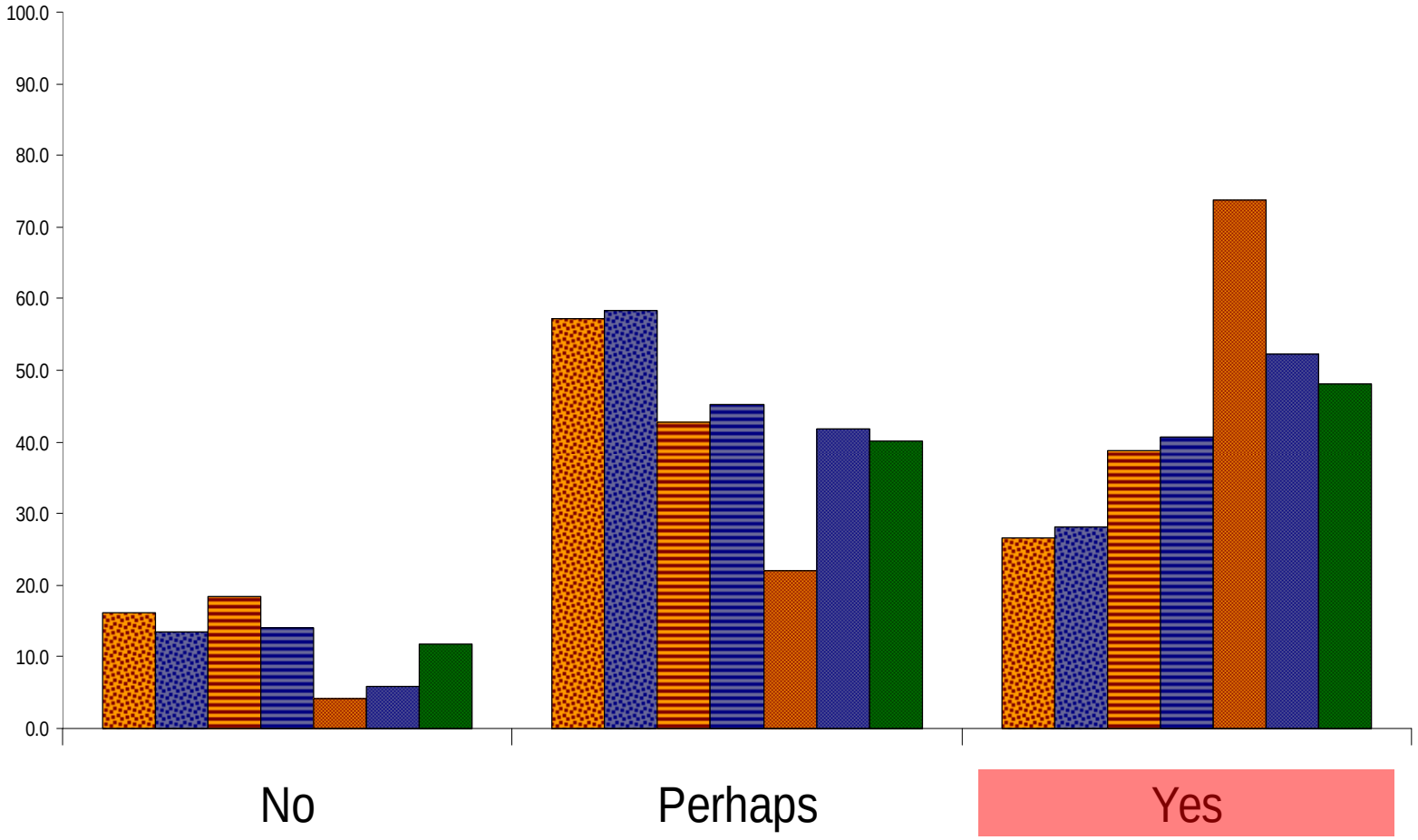
Results: Identifying severity

Does a lactate of 4 mmol/L influence your management plan?



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Results: initial treatment

Now consider a different patient, again a 65 year old 80kg previously healthy male with presumed pneumonia.

This patient is hypotensive.

HR 120
BP 80/35 (MAP 50),
respiratory rate 22,
Sp02 95% on room air,
temp 38.7 degrees C.

How would you first treat the low blood pressure?

- **No specific treatment** for blood pressure; adequate treatment of the infection is sufficient
- Commence **vasopressor**; do not give fluid
- **Less than / equal to 500ml** fluid bolus (and then reassess)
- **500ml-1L** (7-12ml/kg) fluid bolus (and then reassess)
- **1L-1.5L** (12-20ml/kg) fluid bolus (and then reassess)
- **1.5-2.5L** (20-30ml/kg) fluid bolus (and then reassess)
- **>2.5L** (>30ml/kg) fluid bolus (and then reassess)

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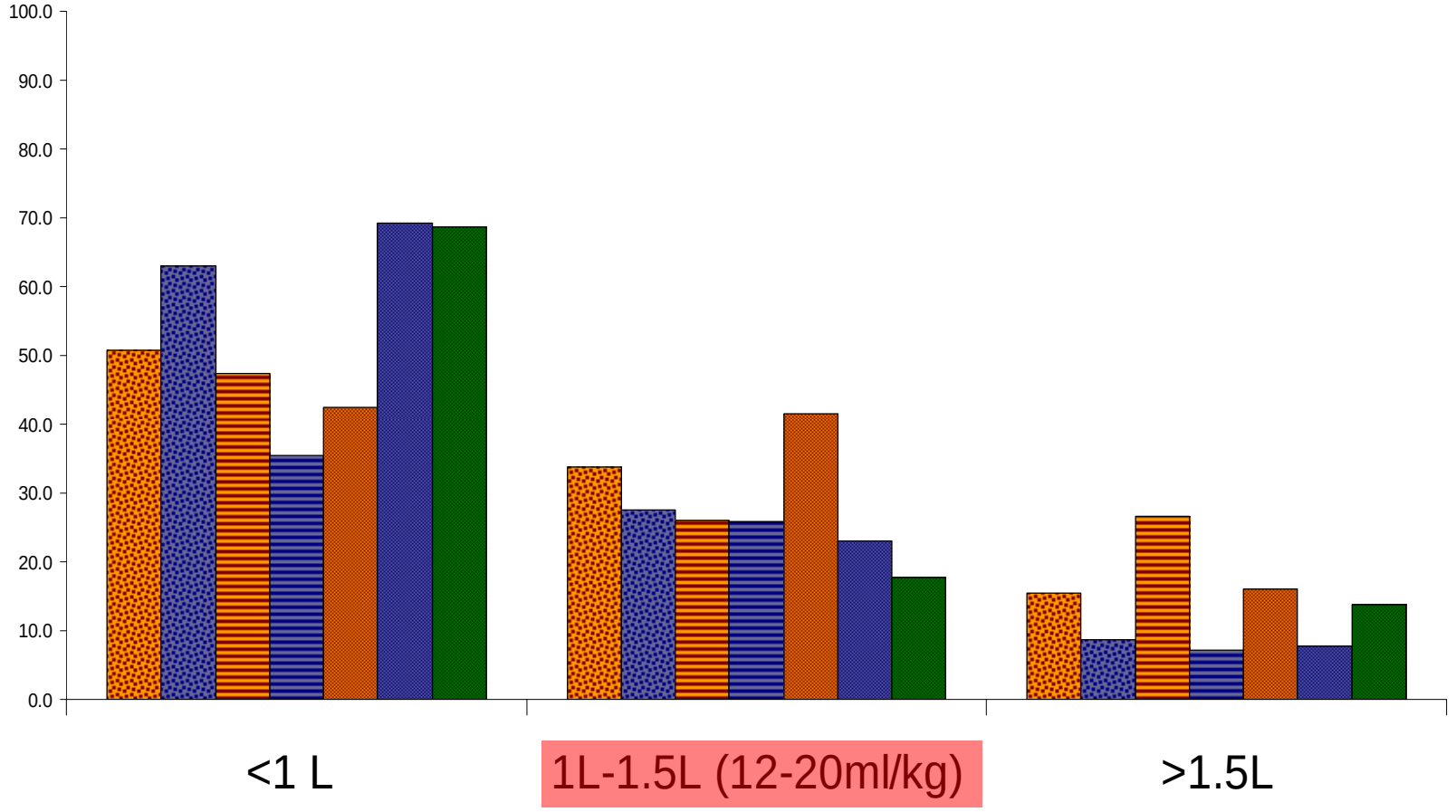
Results: initial treatment

How would you first treat the low blood pressure?



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Results: monitoring

In the same patient, let's assume a 1.5L (=20ml/kg) fluid bolus was given, and no vasopressors have yet been used.
(If you would not have done this, assume another doctor had, and you have now taken over care.)
Vital signs are unchanged.

What monitoring devices would you order?

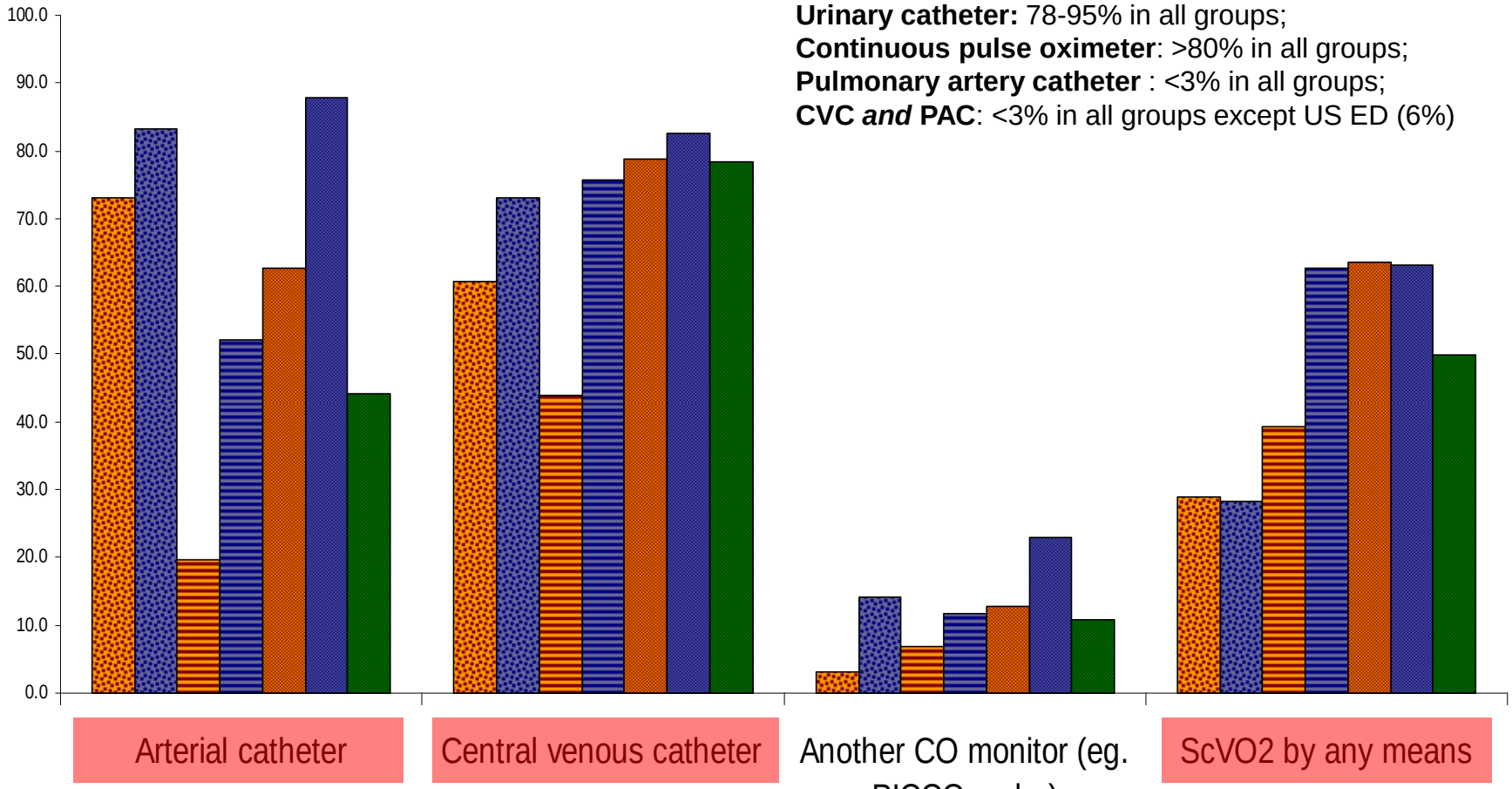
- I would not order any more monitoring (repeating the above vital signs regularly is sufficient)
- Urinary catheter
- Continuous pulse oximeter
- Arterial catheter
- Central venous catheter
- Pulmonary artery catheter
- CVC and PAC
- Another monitor of cardiac output (eg. PICCO, echocardiogram)
- Other (please specify)

(if applicable):
You chose to insert a CVC, PAC or both CVC and PAC.
Would you measure central venous oxygen?

- No
- Yes – via a device which continuously records oxygen saturation
- Yes – via intermittent blood gas analysis from the catheter

Results: monitoring

What monitoring devices would you order?



Other alternatives selected:
Urinary catheter: 78-95% in all groups;
Continuous pulse oximeter: >80% in all groups;
Pulmonary artery catheter : <3% in all groups;
CVC *and* PAC: <3% in all groups except US ED (6%)

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Results: fluid or inotrope?

Vital signs after the initial 1-1.5L fluid bolus:

HR 120,
BP 80/35 (MAP 50),
resp rate 22,
Sp02 95%

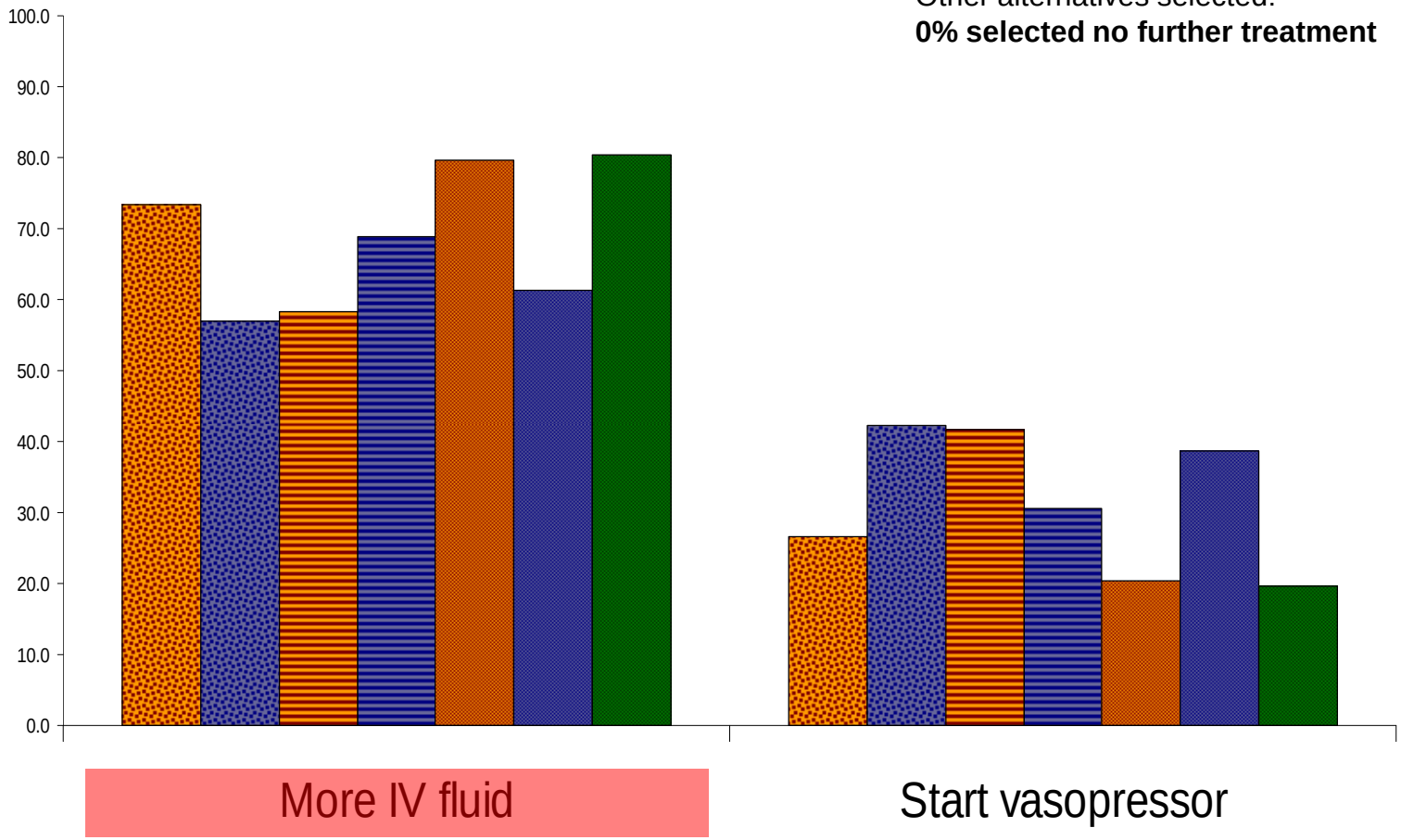
What would you order next to treat the low blood pressure?

(If your answer might depend on the data from a monitoring device, what would you order now, while waiting for the device to be inserted?)

- **Give more IV fluid first. A vasopressor can be considered after more fluid.**
- **Start a vasopressor now (before any more fluid is given)**
- **No further treatment of the BP is required; adequate treatment of infection is sufficient.**

Results: fluid or inotrope?

What would you order next to treat the low blood pressure?



Other alternatives selected:
0% selected no further treatment

ANZ Emergency Medicine | ANZ Intensive Care | US Emergency Medicine | US Intensive Care | UK/Eire Emerg. Medicine | UK/Eire Intensive Care | UK/Eire Acute Internal Medicine

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Results: which vasopressor

Vital signs after the initial 1-1.5L fluid bolus:

HR 120,
BP 80/35 (MAP50),
resp rate 22,
SpO2 95%.

If (despite optimal fluid management if fluid chosen first) you need to use a vasopressor in this patient, which would you choose?

- Dopamine
- Norepinephrine / noradrenaline
- Epinephrine / adrenaline
- Phenylephrine
- Metaraminol
- Vasopressin
- Other (please specify)

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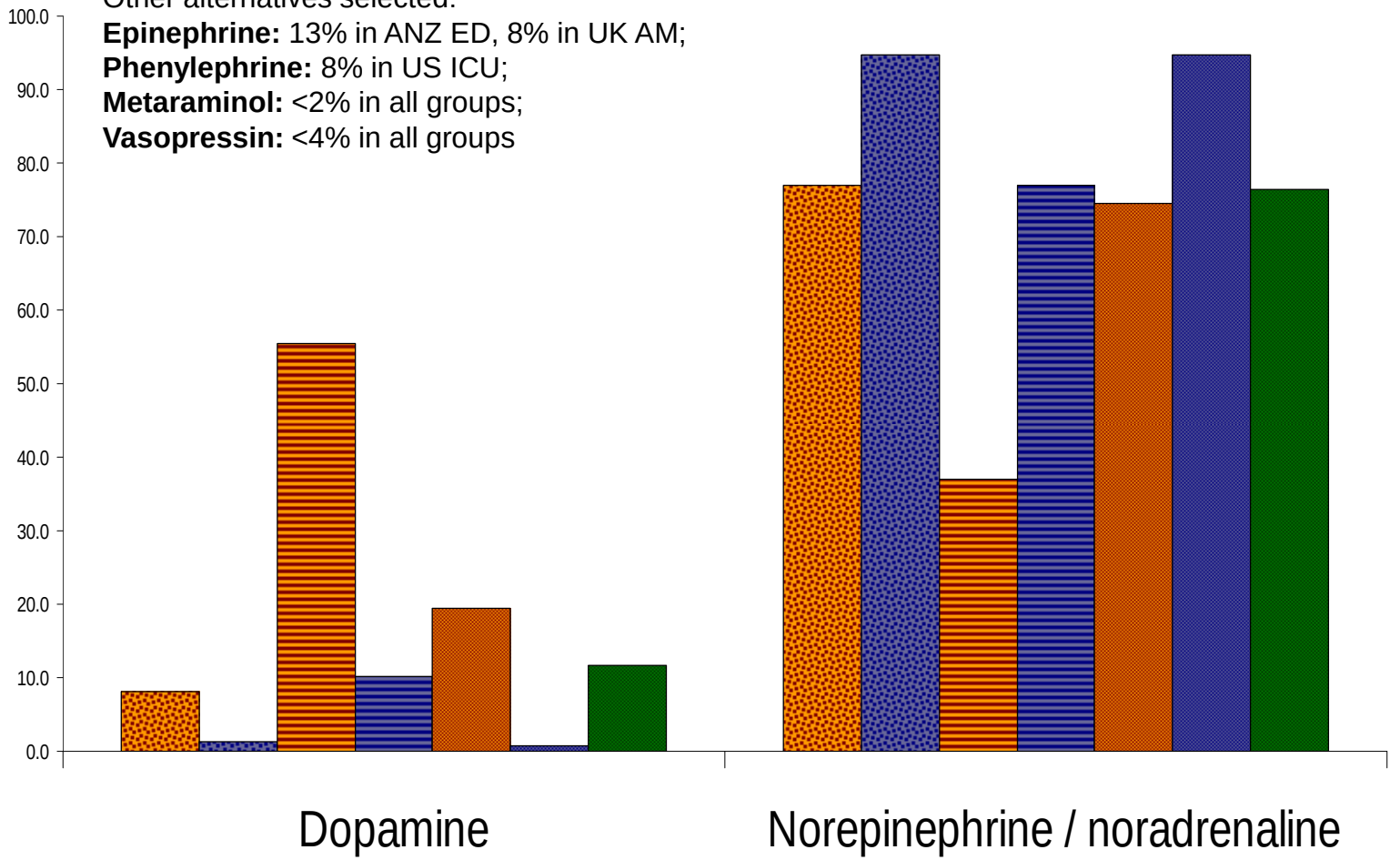
Results: which vasopressor

If you need to use a vasopressor in this patient, which would you choose?

Other alternatives selected:
Epinephrine: 13% in ANZ ED, 8% in UK AM;
Phenylephrine: 8% in US ICU;
Metaraminol: <2% in all groups;
Vasopressin: <4% in all groups



ANZ Emergency Medicine | ANZ Intensive Care | US Emergency Medicine | US Intensive Care | UK/Eire Emerg. Medicine | UK/Eire Intensive Care | UK/Eire Acute Internal Medicine

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Results: fluid goal

While using a vasopressor you may wish to give more fluid
OR
You chose to give more IV fluid first

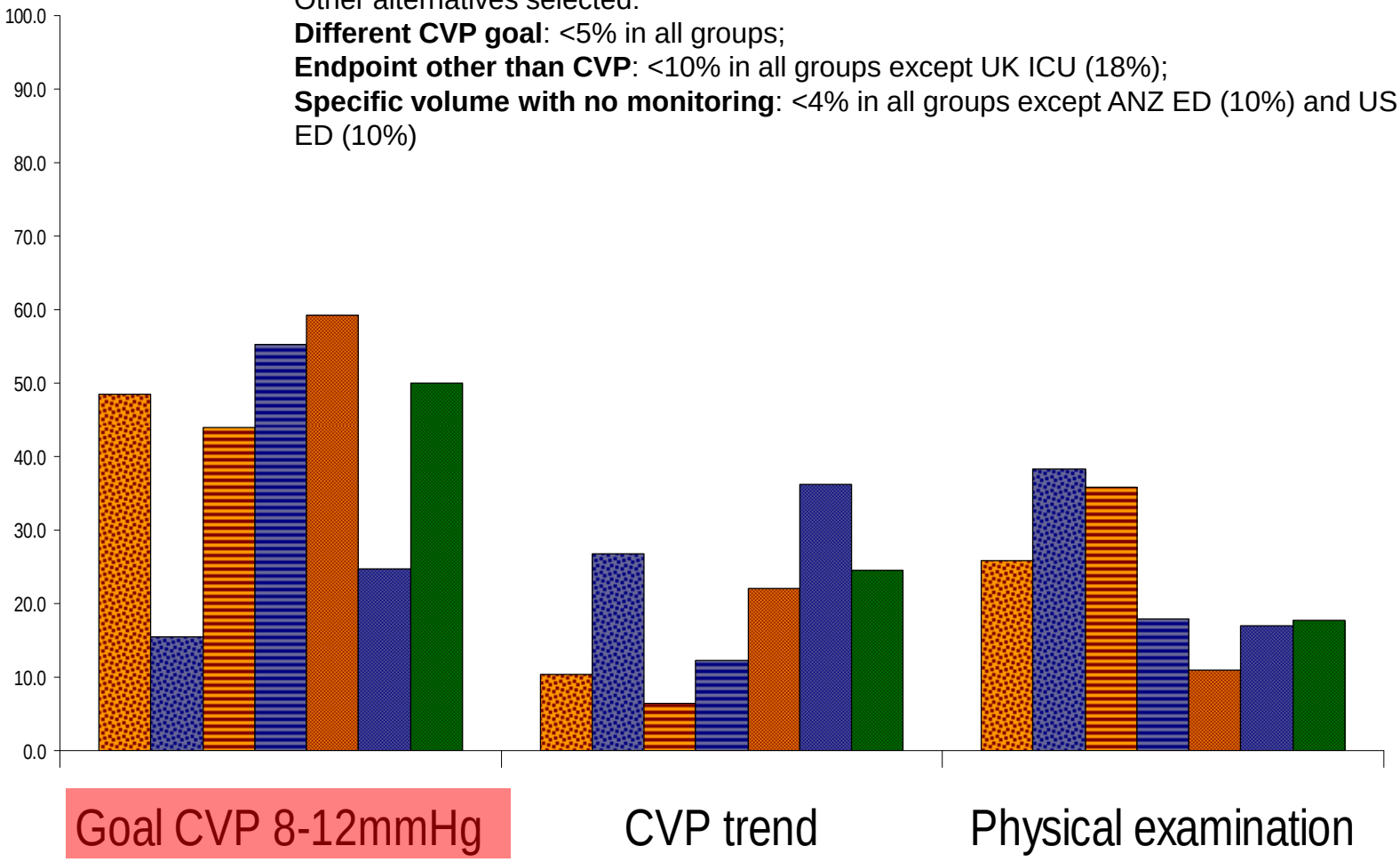
How would you decide how much more fluid to give?

- I would not give any more fluid (only presented to those selecting vasopressor first)
- Titrate fluid to a goal CVP 8-12mmHg
- Titrate fluid to a different goal CVP
- Titrate fluid to a specific change in CVP (ie. CVP trend is more important than the absolute value)
- Titrate fluid to a monitoring endpoint other than CVP (eg. cardiac output)
- Give a SPECIFIC VOLUME of extra fluid (you have a feel for how much is enough)
- Titrate fluid to physical examination / urine output

Results: fluid goal

How would you decide how much more fluid to give?

Other alternatives selected:
Different CVP goal: <5% in all groups;
Endpoint other than CVP: <10% in all groups except UK ICU (18%);
Specific volume with no monitoring: <4% in all groups except ANZ ED (10%) and US ED (10%)



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Results: Rx of low Hb / $ScvO_2$

The patient has received an adequate volume of fluid, and now has:

BP of 125/50 (MAP 75),
HR 100 on a moderate rate (0.1mcg/kg/min) noradrenaline infusion.
The Hb is 8.5 g/dl.
The ScV02 is 50%.

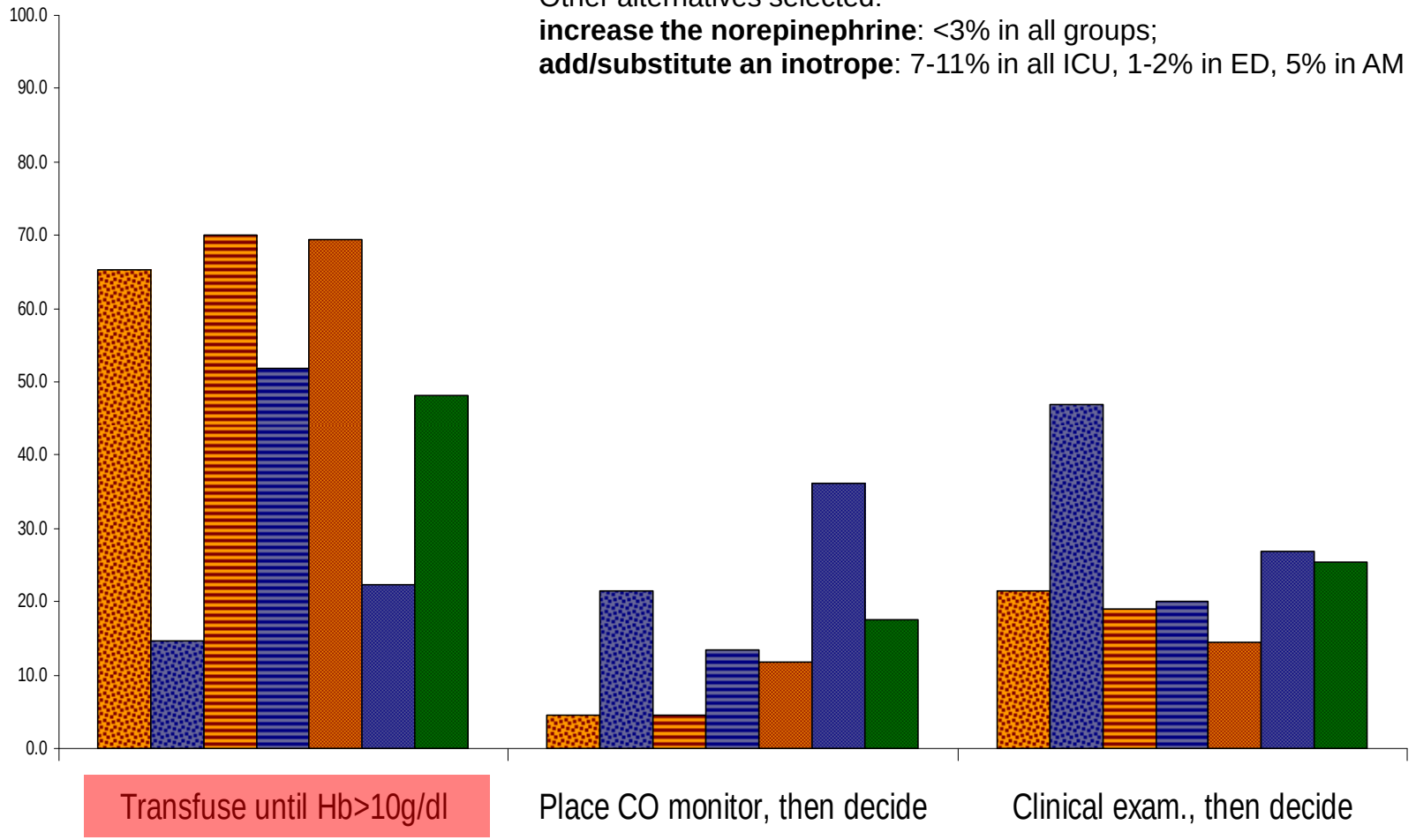
There is not yet a monitor of cardiac output in place.

What would you do next?

- Do nothing else. These numbers are acceptable
- Transfuse PRBCs until the Hb is >10 g/dL
- Increase the rate of the noradrenaline; there is no immediate need to assess cardiac output
- Add / substitute an inotrope (eg. adrenaline, dobutamine, dopexamine, dopamine); there is no immediate need to assess cardiac output.
- Place a cardiac output monitor, and only add an inotrope / alter vasopressor rate / transfuse based on the measured CO
- Perform a clinical examination of cardiac output (skin colour, urine output). Add an inotrope / alter vasopressor rate / transfuse if indicated.

Results: Rx of low Hb / $ScvO_2$

What would you do next?



Other alternatives selected:
increase the norepinephrine: <3% in all groups;
add/substitute an inotrope: 7-11% in all ICU, 1-2% in ED, 5% in AM

Results: Rx of low $ScvO_2$

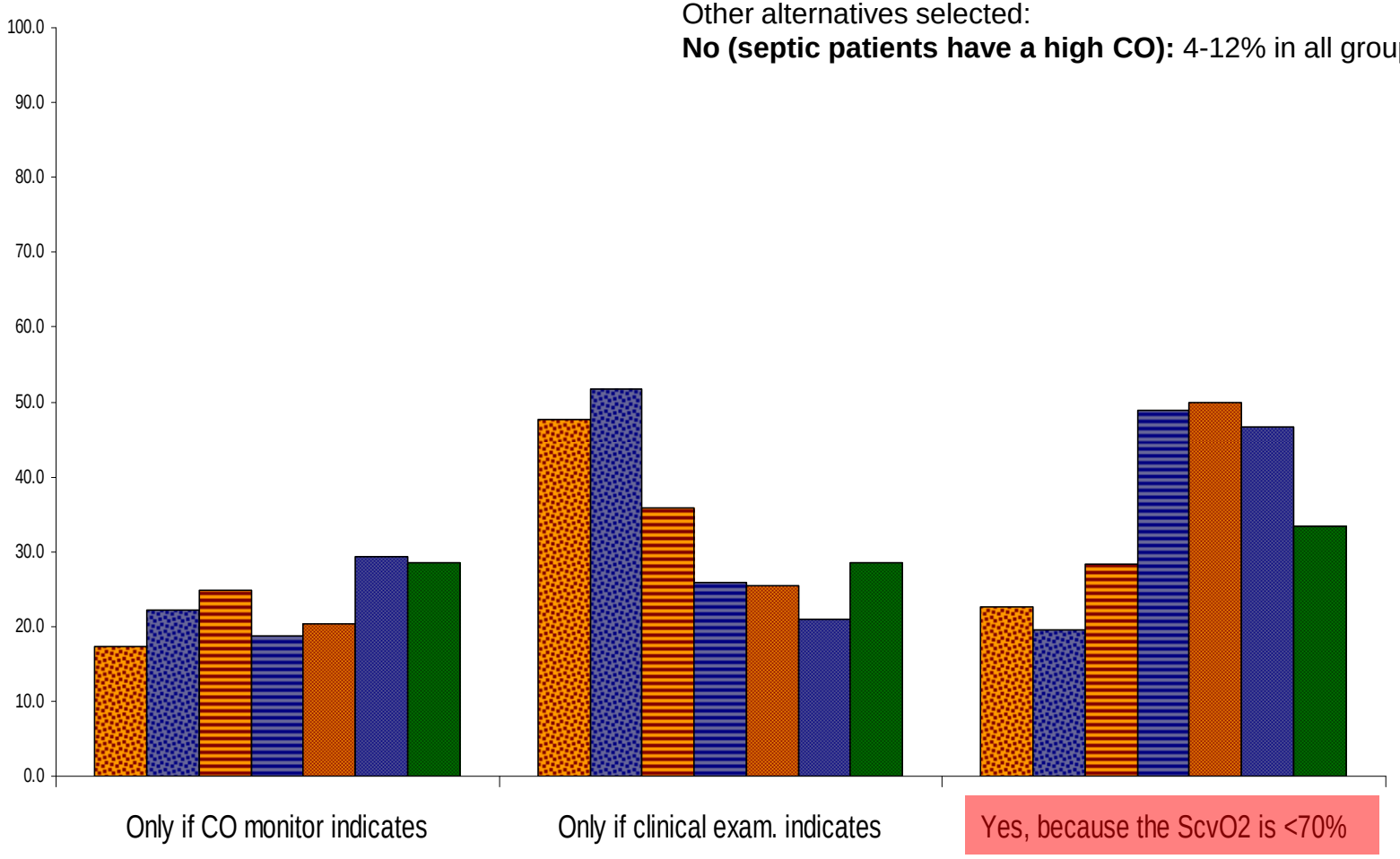
Let's say the
Hb is 10.5 g/dl,
BP 125/50 (MAP 75) after fluid + moderate rate (0.1mcg/kg/min) NAd,
and the ScvO2 is 50%.

Would you start an inotrope (eg. adrenaline, dobutamine, dopexamine, dopamine)?

- No. Septic patients usually have a high cardiac output. Inotropes cause significant complications.
- Only if indicated by a monitor of cardiac output.
- Only if clinical examination (hypoperfusion, low urine output, etc.) suggested this was necessary (there is no need for a cardiac output monitor)
- Yes, because the ScvO2 is <70%

Results: Rx of low $ScvO_2$

Would you start an inotrope (eg. epinephrine, dobutamine, dopexamine, dopamine)?



Other alternatives selected:
No (septic patients have a high CO): 4-12% in all groups

ANZ Emergency Medicine | ANZ Intensive Care | US Emergency Medicine | US Intensive Care | UK/Eire Emerg. Medicine | UK/Eire Intensive Care | UK/Eire Acute Internal Medicine

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Results: Rx of persistently low $ScvO_2$

Let's say that after appropriate fluid, vasopressor, inotropic and blood product support, the patient has improved.

ScvO2 of 60%,
BP 100/40 (MAP 60),
pulse 90,
CVP 11.

The patient is alert, and there are minimal respiratory secretions.
However the respiratory rate is 25, and the SpO2 is 99% on 6L/min oxygen.

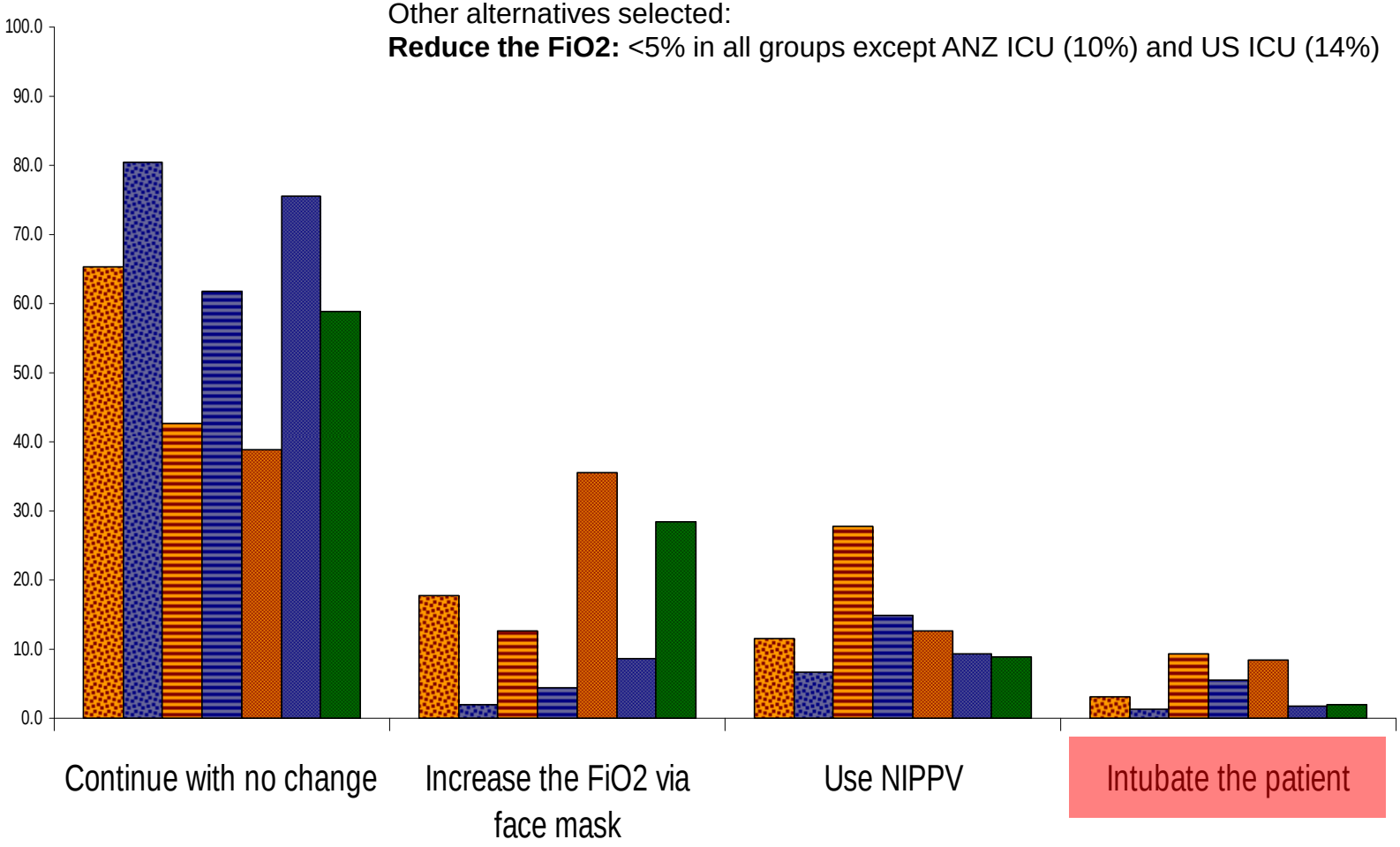
What change in treatment would you order now?

- **Reduce the FiO2 via face mask**
- **Continue treatment as described: these numbers are acceptable**
- **Increase the FiO2 via face mask**
- **Use non-invasive positive pressure ventilation**
- **Intubate the patient**

Results: Rx of persistently low $ScvO_2$

What change in treatment would you order now?

Other alternatives selected:
Reduce the FiO2: <5% in all groups except ANZ ICU (10%) and US ICU (14%)



ANZ Emergency Medicine | ANZ Intensive Care | US Emergency Medicine | US Intensive Care | UK/Eire Emerg. Medicine | UK/Eire Intensive Care | UK/Eire Acute Internal Medicine

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Results: attitudes

Many doctors have not fully adopted all elements of Rivers' Early Goal Directed Therapy the protocol into their practice.

Some see no need for such a protocol.

If you do not currently aim to implement ALL of the Rivers EGDT protocol for ALL patients with sepsis, which of the following best explain why not?

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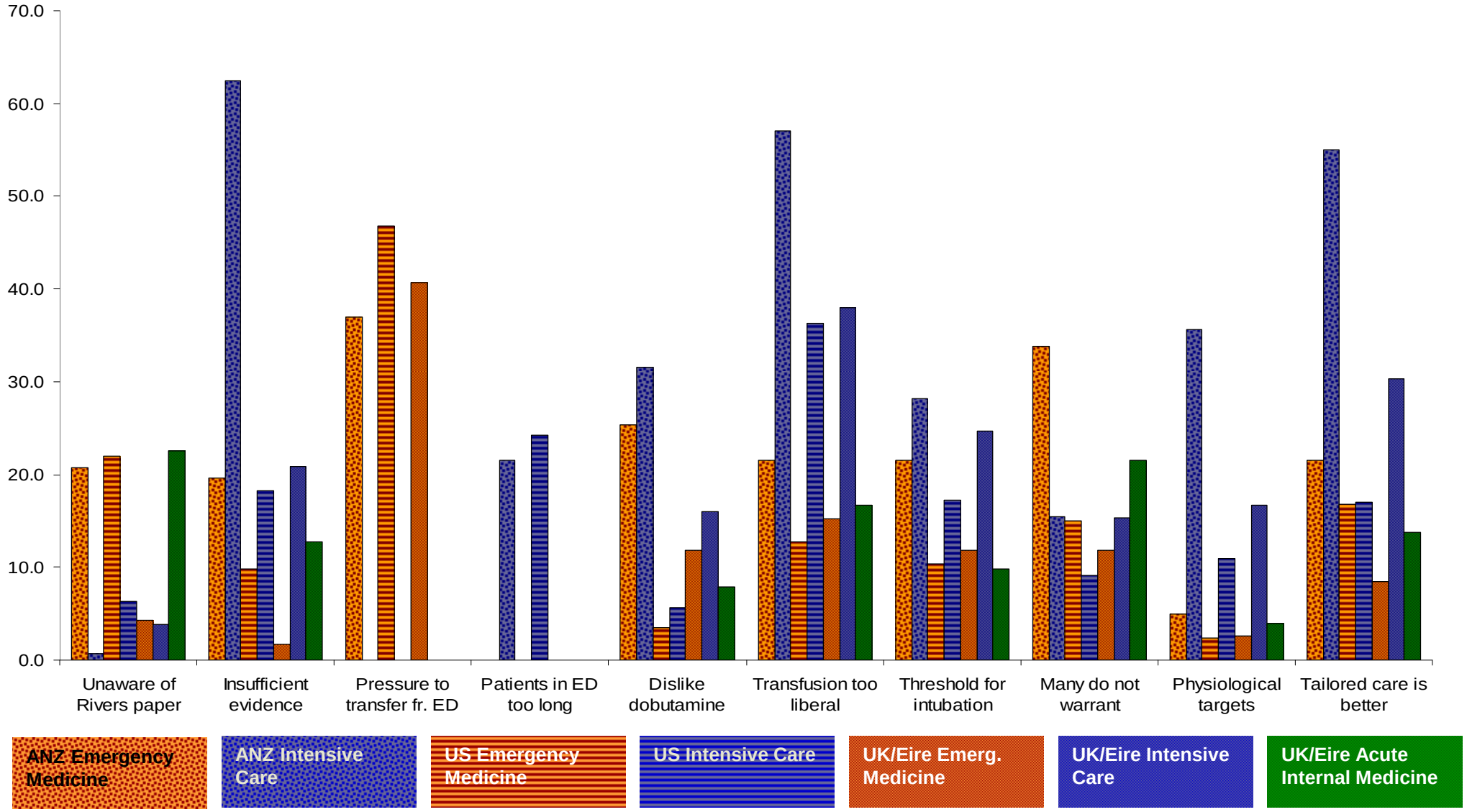
Results: attitudes



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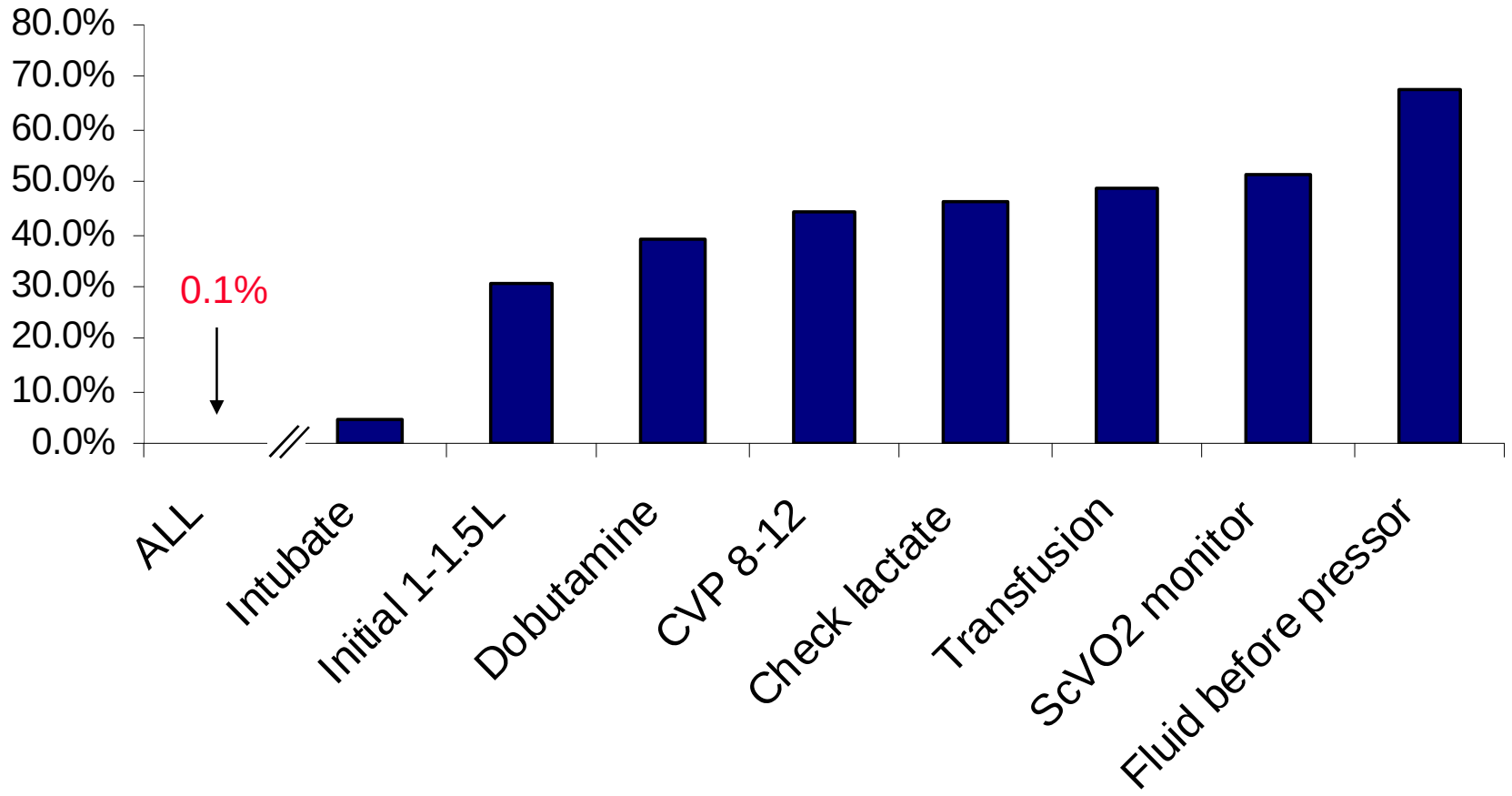
Results: overall EGDT compliance



Compliance with individual components

Results: overall EGDT compliance

Despite 4 years of guideline dissemination, the SSC 6-hour resuscitation bundle is not well supported.

Only TWO survey respondents (one in the UK and one in the USA) (0.1%) would implement all aspects of the guidelines.

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Conclusions

- Sepsis management varies between specialties and countries.
- Barriers to adoption include lack of knowledge, attitudes, and logistic constraints, and differed markedly between groups.
- Trials of sepsis management must understand the variability in the control group
- Comparisons of such trials must account for between-country variations
- As a result, the ANZ trial will be different to that in the US

Characteristics of a good survey

High response rate

Well defined population

- Rarely achieved by surveying all members of a professional organisation
  - Contains retired doctors
  - Excludes most recently qualified
  - Includes doctors other than those in the target group

Respondents verified as representative of the population

- Should ideally quantify characteristics of non-respondents

Should use a validated survey instrument

Email surveys exclude those without email

- And have the lowest response rates of all

Sample vs. population approach:

- Population approach likely to reduce response rate and bias responses

Asks about specific practice intentions rather than an overall 'feeling' about an approach

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Are the results valid?

Anticipated trends are confirmed. eg.:

- **Use of dopamine in the US and by emergency physicians**
- **Use of CRP in the UK and ANZ.**

Large number (if not percentage) of responses

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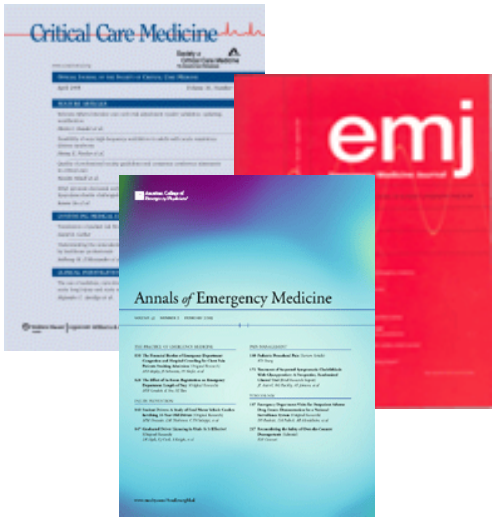
Are the results valid?



or

Maybe not to a statistician

Probably not if you're running the Surviving Sepsis Campaign

To a doctor?

To a patient?

I don't want a doctor who does online surveys –

1,690 (99.9%) of them don't use the 'Right Care, Right Now'

Surviving Sepsis