

Last frontier of infection in critically ill patients

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Many Frontiers – and not the last...

- Sepsis
 - Recognition
 - Management
- Multidrug resistance
- System approaches

Not included

- Point of care tests
- Laboratory markers of infection eg Procalcitonin
- Selective decontamination
- Line management
- Ventilator associated pneumonia
- Other bundles of care
- Specific multiresistant organisms

Importance of Sepsis

- Increasing incidence
- 2% of hospital patients and 75% of ICU patients
- Overall mortality ~35%
- Leading cause of morbidity and mortality in ICU
 - Bacteraemia 10-15%
 - Severe sepsis 20-40%
 - Septic shock 40-60%
 - Sepsis and MOF >70%

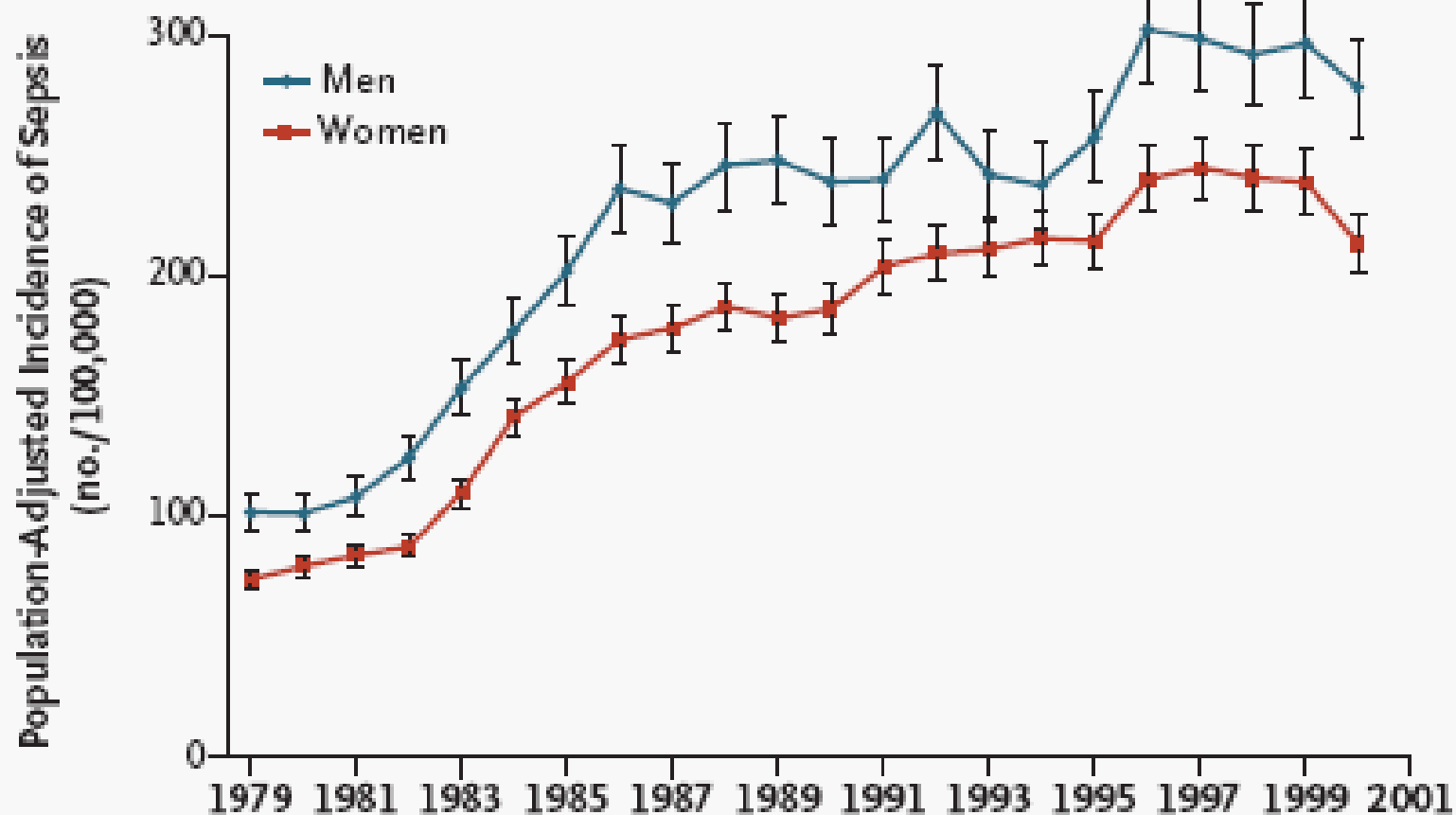
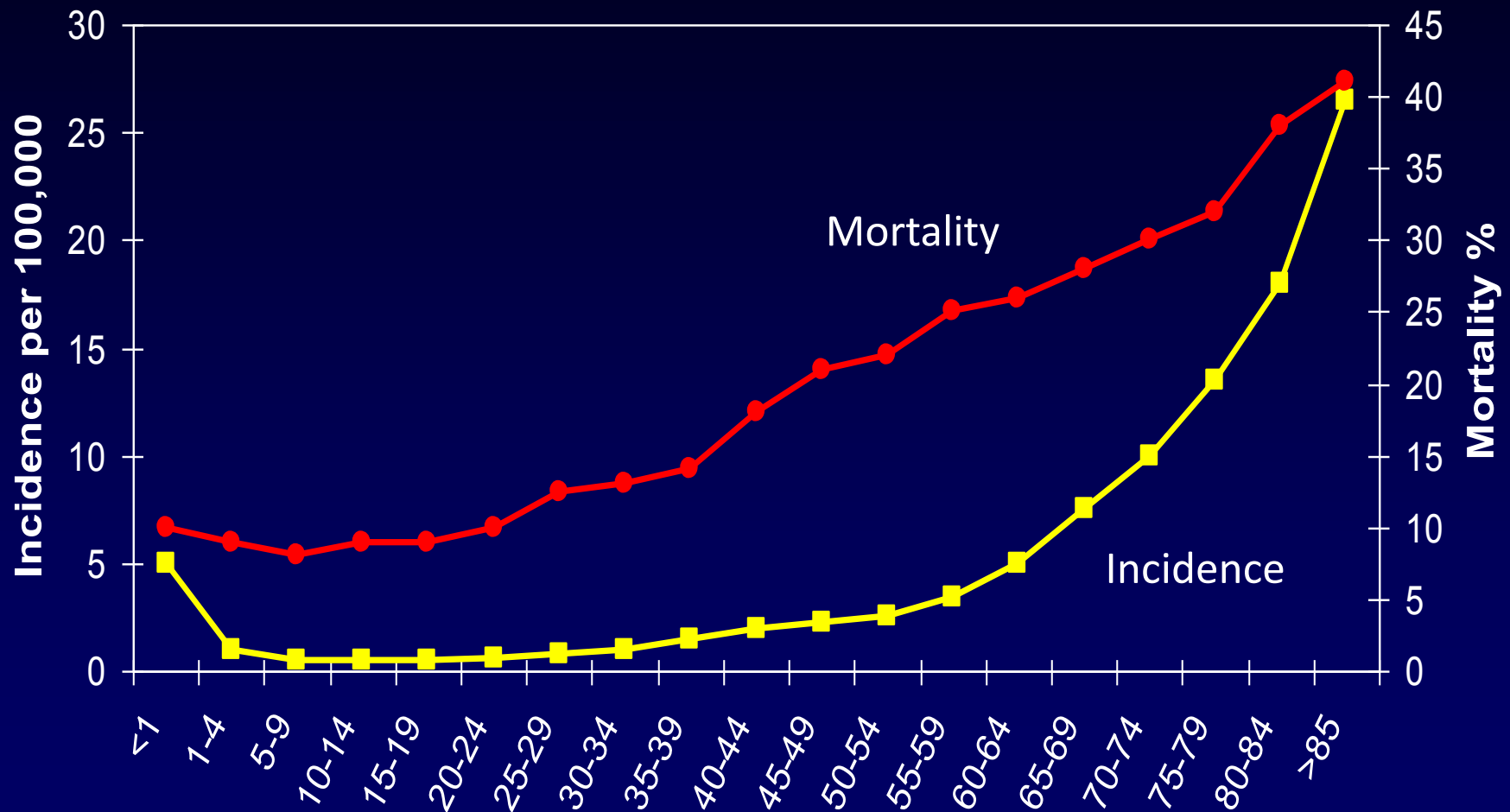


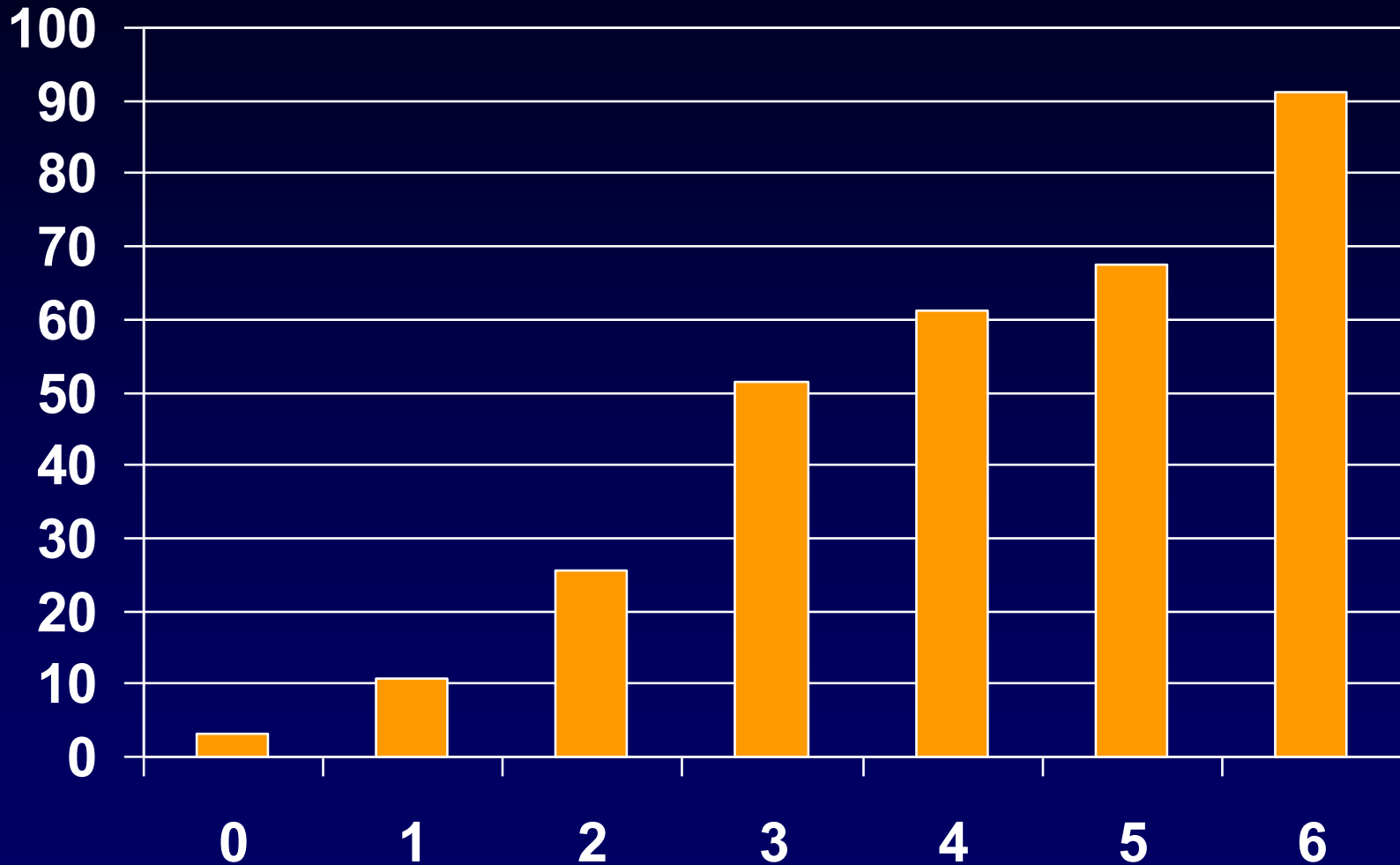
Figure 1. Population-Adjusted Incidence of Sepsis, According to Sex, 1979–2000. Points represent the annual incidence rate, and I bars the standard error.

Severe sepsis incidence and mortality increase with age



Angus et al. Crit Care Med 2001; 29:1301

Relationship between mortality on ICU and the number of failed organs



From Brealey & Singer, 2000

BUT

In the UK only ~20% of cases are recognised and managed correctly in the emergency room



National review of sepsis deaths just starting late 2013

Pathogenesis

Sepsis and septic shock

Bacterial infection



Excessive host response (SIRS)



Host factors lead to cellular damage



Organ damage



Death

Sequelae of Sepsis

- **Balanced response**
 - **Resolution**
- **Host hyper-responsive**
 - **SIRS/sepsis and Multi-Organ Dysfunction**
- **Host hypo-responsiveness**
 - **Overwhelming sepsis and death**

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Severe Sepsis and Septic Shock

Derek C. Angus, M.D., M.P.H., and Tom van der Poll, M.D., Ph.D.

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SEPSIS IS ONE OF THE OLDEST AND MOST ELUSIVE SYNDROMES IN MEDICINE. Hippocrates claimed that sepsis (*σήψις*) was the process by which flesh rots, swamps generate foul airs, and wounds fester.¹ Galen later considered sepsis a laudable event, necessary for wound healing.² With the confirmation of germ theory by Semmelweis, Pasteur, and others, sepsis was recast as a systemic infection, often described as “blood poisoning,” and assumed to be the result of the host’s invasion by pathogenic organisms that then spread in the bloodstream. However, with the advent of modern antibiotics, germ theory did not fully explain the pathogenesis of sepsis: many patients with sepsis died despite successful eradication of the inciting pathogen. Thus, researchers suggested that it was the host, not the germ, that drove the pathogenesis of sepsis.³

Host response

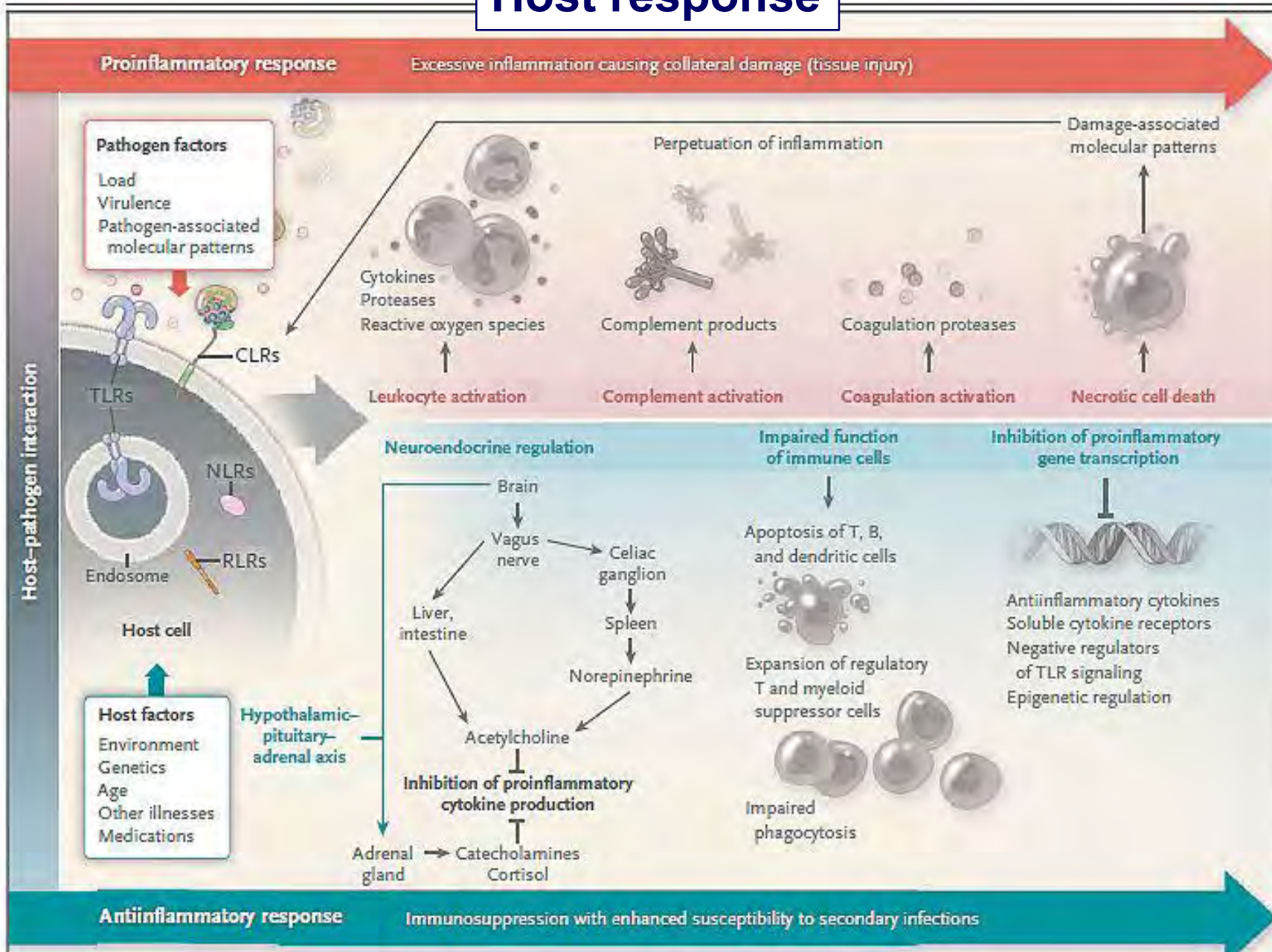
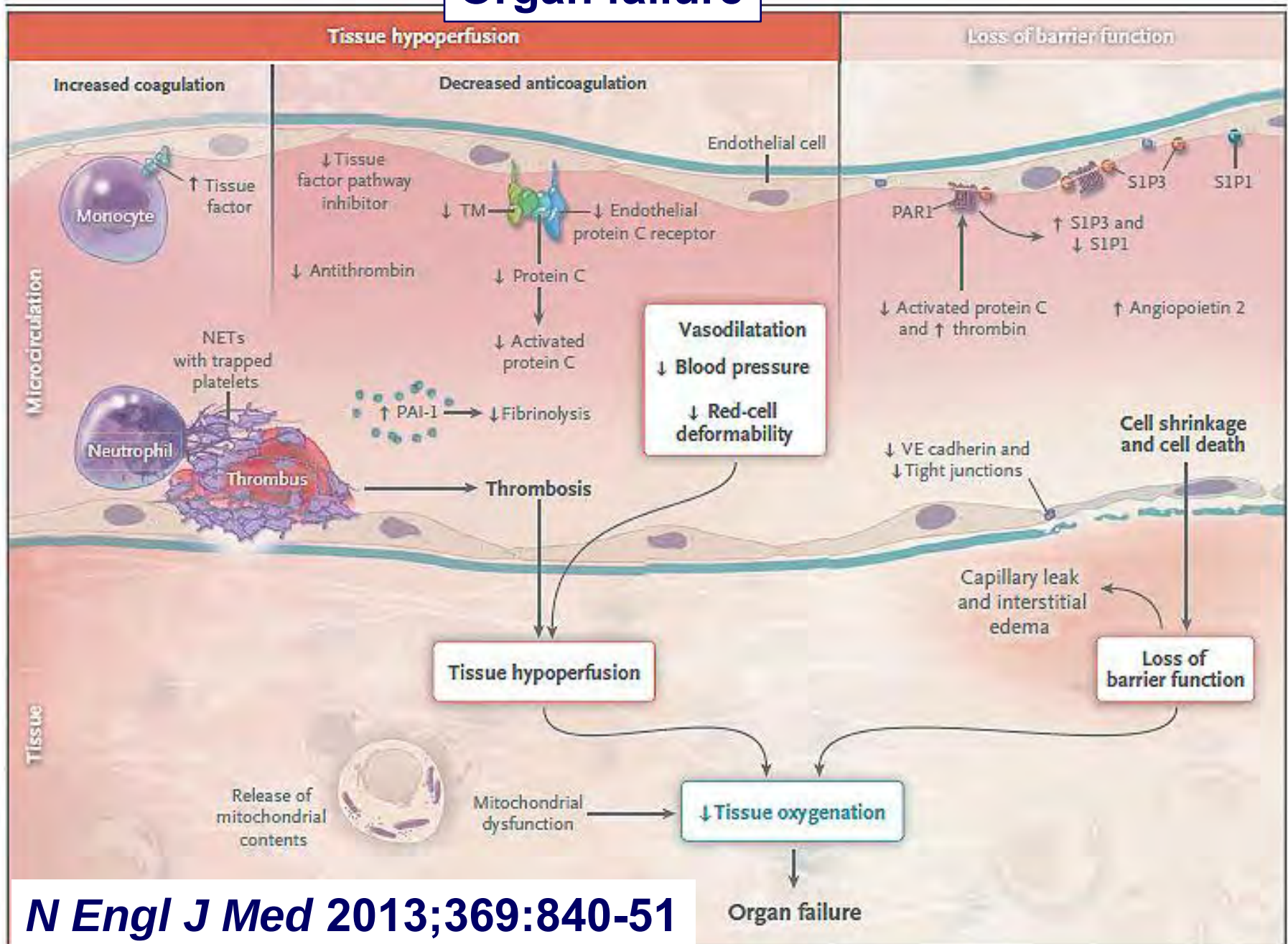


Figure 1. The Host Response in Severe Sepsis.

The host response to sepsis is characterized by both proinflammatory and antiinflammatory responses.

N Engl J Med 2013;369:840-51

Organ failure



N Engl J Med 2013;369:840-51

Figure 2. Organ Failure in Severe Sepsis and Dysfunction of the Vascular Endothelium and Mitochondria.

Recognition

Frequent failures

- Failure to recognise deteriorating patient
- Failure to recognise sepsis
 - Postural hypotension
 - Raised respiratory rate
 - Hypoxia
 - Acidosis

Scoring systems

- Gradation of specific state eg GCS
- Composite scores
 - Readily available data eg age, pulse etc
 - With/without laboratory variables
- Uses
 - Diagnostic discrimination eg Meningitest
 - Predict death/deterioration eg APACHE
 - Determine management eg CURB 65

“Track and trigger” tools

Modified Early Warning Score

	3	2	1	0	1	2	3
Systolic blood pressure (mmHg)	≤70	71-80	81-100	101-199		≥200	
Heart rate (bpm)		<40	41-50	51-100	101-110	111-129	≥130
Respiratory rate (bpm)		≤ 8		9-14	15-20	21-29	≥30
Temperature (°C)		<35		35-38.4		≥38.5	
AVPU				A	V	P	U

Table 1. Modified Early Warning Score..

- Simple measurements to alert busy ward staff of patient deterioration (MEWS)
- NICE “track& trigger” tool (2007)

Observation Scores and

Date	Time	Obs Frequency/Sig	TEMP	Blood Pressure & Heart Rate	RESP. RATE	SpO ₂	FIO ₂	TARGET SpO ₂	MEWS	RR	SpO ₂	HR	SBP	CNS	Urine Output	Temp	MEWS TOTAL	PAIN SCORE	NAUSEA SCORE	OTHER OBS	ACTION NAME/SIG
2223	2335	2300	38.0	100/50	24	95X	100X	100X	1	0	3	2	0	0	0	2	10	0			
03	04	05	39.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
06	07	08	38.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
09	10	11	37.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
12	13	14	36.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
15	16	17	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
18	19	20	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
21	22	23	39.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
24	25	26	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
27	28	29	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
30	31	32	36.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
33	34	35	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
36	37	38	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
39	40	41	39.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
42	43	44	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
45	46	47	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
48	49	50	36.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
51	52	53	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
54	55	56	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
57	58	59	39.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
60	61	62	38.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
63	64	65	37.0	100/50	24	97X	100X	100X	1	0	3	2	0	0	0	2	10	0			
66	67	68	36.0	100/50	20	95X	100X	100X	1	0	3	2	0	0	0	2	9	0			
69	70	71	37.0	100/50																	

MODIFIED EARLY WARNING SYSTEM (MEWS)

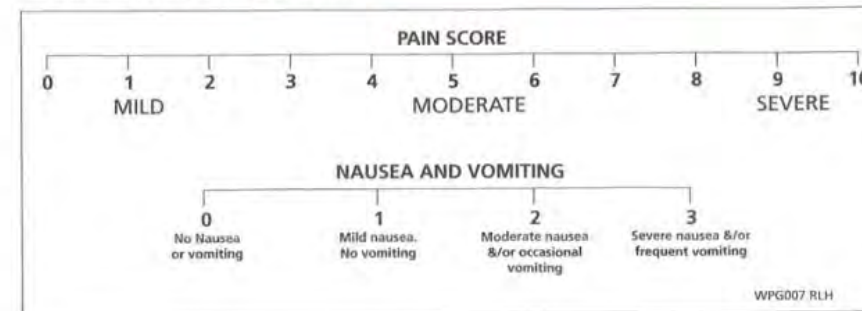
SCORE	3	2	1	0	1	2	3
RR (If patient not on oxygen then record score from this box) OR ✓	<85% *	86-89% or fall in SpO ₂ by 3% *	90-95% or fall in SpO ₂ by 2%	> = 96%	20-24 *	25-29 *	>29 *
SpO ₂ on O ₂ (O ₂ must be prescribed) †	<89% or on CPAP *	89-93% *	94-97% *		FiO ₂ 24-35% Or chronic NIV	FiO ₂ 40-60% *	FiO ₂ >60% Or Acute NIV *
HR		<40	40-50	51-100	101-110 *	111-130 *	>130 *
SBP	<80 *	80-90 *	90-100 *	101-199		>=200	
CNS level			New Agitation or Confusion *	Alert	Voice *	Pain *	Unresponsive *
Urine output ml / hr	<10 or not PU'd in 10 hr *	<30 or not PU'd in 8 hr *		>30 or on Renal Replacement Therapy			
Temp		<35.1 *	35.1-36	36.1-37.9	38 - 38.5 *	>38.5 *	

- * Consider Sepsis: See Surviving Sepsis Campaign overleaf
- † If patient is on O2 therapy then record the highest score
- Not applicable to patients on the Liverpool Care Pathway
- Patients on Beta blockers may not exhibit tachycardia
- If the patient is not catheterized then an average urine output over the previous 4 or 6 hours may have to be used, or scored

MEWS ACTION PLAN

ACTION Please record appropriate letter on obs chart	A	B	C	D	Cardiac Arrest Team Call criteria Ring 2222
MEWS SCORE	0-1	2-3	4-5	>5	
Patient Risk	Stable	Risk of Deteriorating	Deteriorating	Acutely / Critically Ill	
Frequency of observations	Min 12 hourly	Min 4 hourly	Min hourly	Min every 15 mins	
Action	Continue with observations at current frequency	Inform Nurse in Charge. Consider contacting patient's own team (should respond within 30mins). Consider contacting Nurse Practitioner (Hospital at Night/Day Team)	Inform Nurse in charge and Contact patient's own team and The Acute Response Team (ART Bleep 4444)	Inform Nurse in charge, patient's own team and The Acute Response Team (ART Bleep 4444). Consider contacting CCOT / ICU.	

Nb. Note Calling criteria for Cardiac arrest team





National Early Warning Score (NEWS)



Resources

Browse resources by category.

- Choose -
- Clinical resources
 - Clinical audit
 - Audit tool
 - Clinical guidelines
 - Concise guidelines
 - Quality improvement projects
 - Invited service reviews
 - NICE quality standards
 - Partnership projects

Standardising the assessment of acute-illness severity in the NHS

An elearning tool is available to train and support healthcare professionals in the use of the NEWS charts and scoring system. To find out more and access the tool, click the 'Full details' heading below.

Full details

ISBN: 978-1-86016-4

EISBN: 978-1-86016

Type: Clinical resour

Download

Size



National early warning score (NEWS) Standardising the assessment of acute illness severity in the NHS

693.84 KB



NEWS observation chart (with explanatory text)

1.52 MB

<http://www.rcplondon.ac.uk>



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Setting higher standards

National Early Warning Score (NEWS)

Standardising the assessment of
acute-illness severity in the NHS

Primary aim

- To identify sick patients early
- To detect and document changes in status
- To dictate changes in management
- In a standard manner across the NHS

Fig 1: Six physiological parameters included in the NEWS

Respiratory rate

Oxygen saturations

Temperature

Systolic blood pressure

Pulse rate

Level of consciousness

Measure and record the score for each of the 6 physiological parameters.

Aggregate the scores and add 2 for any use of supplemental oxygen to derive the final NEWS score.

Use the NEWS to define and record:

- whether escalation of clinical care is required and its urgency
- the competencies of the clinical review required
- the frequency of monitoring required
- the most appropriate clinical setting for ongoing clinical care.

Observation chart for the National Early Warning Score (NEWS)

NEWS KEY		NAME:		D.O.B.		ADMISSION DATE:								
0 1 2 3														
DATE						DATE								
TIME						TIME								
RESP. RATE	≥25						3							≥25
	21-24						2						21-24	
	12-20												12-20	
	9-11						1						9-11	
	≤8						3						≤8	
SpO ₂	≥96												≥96	
	94-95						1						94-95	
	92-93						2						92-93	
	≤91						3						≤91	
Inspired O ₂ %	%						2						%	
TEMP	≥39°						2						≥39°	
	38°						1						38°	
	37°												37°	
	36°						1						36°	
	≤35°						3						≤35°	
	230						3						230	
	220												220	
	210												210	
	200												200	
	190												190	

HEART RATE	>140									3									140
	130									2								130	
	120																	120	
	110									1								110	
	100																	100	
	90																	90	
	80																	80	
	70																	70	
	60																	60	
	50									1								50	
	40									3								40	
	30																	30	
Level of Consciousness		Alert																Alert	
		V / P / U								3								V / P / U	
BLOOD SUGAR																		Bl'd Sugar	
TOTAL NEW SCORE																		TOTAL SCORE	
Additional Parameters																			
	Pain Score																	Pain Score	
Urine Output																		Urine Output	
Monitoring Frequency																		Monitor Freq	
Escalation Plan Y/N n/a																		Escal Plan	
Initials																		Initials	

National Early Warning Score: July 2012

Please see next page for explanatory text about this chart.

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Training for Innovation

Chart 1: National Early Warning Score (NEWS)*

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

*The NEWS initiative flowed from the Royal College of Physicians' NEWSDIG, and was jointly developed and funded in collaboration with the Royal College of Physicians, Royal College of Nursing, National Outreach Forum and NHS Training for Innovation.

Chart 2: NEWS thresholds and triggers

NEWS scores	Clinical risk
0	Low
Aggregate 1–4	
RED score* (Individual parameter scoring 3)	Medium
Aggregate 5–6	
Aggregate 7 or more	High

The NEWS trigger system aligned to the scale of clinical risk

Chart 4: Clinical response to NEWS triggers

NEWS SCORE	FREQUENCY OF MONITORING	CLINICAL RESPONSE
0	Minimum 12 hourly	Continue routine NEWS monitoring with every set of observations
Total: 1-4	Minimum 4-6 hourly	- Inform registered nurse who must assess the patient; - Registered nurse to decide if increased frequency of monitoring and / or escalation of clinical care is required;
Total: 5 or more or	Increased frequency to a minimum of 1 hourly	- Registered nurse to urgently inform the medical team caring for the patient; - Urgent assessment by a clinician with core competencies to assess acutely ill patients;

Caveats

- Resources are needed to measure and record data
 - Nurses
 - Charts
 - Information technology
- Need to review and act on changes
- Scores may not reflect illness severity in a minority – review the patient too!
- Only validated in specific settings

The value of the Modified Early Warning Score and biochemical parameters as predictors of patient outcome in acute medical admissions: a prospective study

Acute Med 2011; 10(3): 126-132

YS Perera, P Ranasinghe, AMMC Adikari, WDTs Welivita, WME Perera, WMDR Wijesundara, SAAP Karunanayake & GR Constantine

- 250 patients at National Hospital, Colombo
- Useful to alert staff/prioritise need for ICU
- Modification to include age and laboratory parameters increases predictive values

Early Warning Scores Generated in Developed Healthcare Settings Are Not Sufficient at Predicting Early Mortality in Blantyre, Malawi: A Prospective Cohort Study

India Wheeler^{1*}, Charlotte Price², Alice Sitch², Peter Banda³, John Kellett⁴, Mulinda Nyirenda³, Jamie Rylance⁵

1 College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, **2** Department of Public Health, Epidemiology and Biostatistics, University of Birmingham, Birmingham, United Kingdom, **3** College of Medicine, University of Malawi, Blantyre, Malawi, **4** Department of Medicine, Nenagh Hospital, County Tipperary, Ireland, **5** Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Abstract

Aim: Early warning scores (EWS) are widely used in well-resourced healthcare settings to identify patients at risk of mortality. The Modified Early Warning Score (MEWS) is a well-known EWS used comprehensively in the United Kingdom. The HOTEL score (Hypotension, Oxygen saturation, Temperature, ECG abnormality, Loss of independence) was developed and tested in a European cohort; however, its validity is unknown in resource limited settings. This study compared the performance of both scores and suggested modifications to enhance accuracy.

Methods: A prospective cohort study of adults (≥ 18 yrs) admitted to medical wards at a Malawian hospital. Primary outcome was mortality within three days. Performance of MEWS and HOTEL were assessed using ROC analysis. Logistic regression analysis identified important predictors of mortality and from this a new score was defined.

Frequent failures

- Failure to act on MEWS scores
- Failure to recognise sepsis
 - Postural hypotension
 - Raised respiratory rate
 - Hypoxia
 - Acidosis
- Failure to look for focal signs
 - Source
 - Metastatic spread
- Failure to take blood cultures or do LP

Management

Severe sepsis - management

- Early resuscitation (ABC)
- Adequate fluid replacement
- Control of blood sugar
- Appropriate antibiotics
- Source control
- Role of steroids
- Other ancillary treatments eg GCSF, activated protein C

Surviving sepsis

Special Articles

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

R. Phillip Dellinger, MD; Jean M. Carlet, MD; Henry Masur, MD; Herwig Gerlach, MD, PhD; Thierry Calandra, MD; Jonathan Cohen, MD; Juan Gea-Banacloche, MD, PhD; Didier Keh, MD; John C. Marshall, MD; Margaret M. Parker, MD; Graham Ramsay, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; Mitchell M. Levy, MD; for the Surviving Sepsis Campaign Management Guidelines Committee

Sponsoring Organizations: American Association of Critical-Care Nurses, American College of Chest Physicians, American College of Emergency Physicians, American Thoracic Society, Australian and New Zealand Intensive Care Society, European Society of Clinical Microbiology and Infectious Diseases, European Society of Intensive Care Medicine, European Respiratory Society, International Sepsis Forum, Society of Critical Care Medicine, Surgical Infection Society.

Dellinger et al. Crit Care Med 2004; 32: 858-873

Surviving Sepsis Campaign

sis.org/Pages/default.aspx

Started  <http://www.google.co...>

Campaign

- ABOUT SSC
- GUIDELINES
- BUNDLES
- DATA COLLECTION
- RESOURCES
- IMPROVEMENT
- CONTACT



New Data Collection Tool

Coming Soon! A new data collection tool and resources to implement the Campaign will be added to this site soon. Visit often.



2012 Sepsis Guidelines Published

A revised and updated edition of "Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012" were officially released at the Society of Critical Care Medicine's 42nd Congress.



New York State Adopts Sepsis Rules

In a precedent-setting statement during his State of the State Message, New York's Governor Andrew M. Cuomo announced that every hospital in the state must adopt sepsis screening procedures.



Clinical Conversations

The Campaign's listserv provides an active forum for professionals to share their experiences about sepsis. Visit [Listserv](#)



Patients and Families

The Campaign is unable to respond to individual questions from patients and families. Clinicians may wish to offer information from SCCM's [Patients and Families website](#).



GUIDELINES



BUNDLES

Join The Campaign



www.survivingsepsis.org/Guidelines/Pages/default.aspx

“Resuscitation bundle” <6hrs

- Measure serum lactate (or base excess)
- Blood cultures (x2) before antibiotics
- Broad spectrum antibiotic
 - **Within 3 hours in emergency room**
 - **Within 1 hour in inpatient setting**
- Begin goal directed fluid resuscitation (initial bolus 20ml/kg)
 - **If hypotensive**
 - **If serum lactate >4**
- Infection source identification & “control”
- Goal directed therapy for septic shock – CVP>8, MAP>65 mmHg

Early goal directed therapy

- *Purpose*: to adjust cardiac preload, afterload and contractility to balance oxygen delivery with oxygen demand
- *Entry criteria*: patients in the emergency dept with severe sepsis & shock
- *Plan*: randomise to 6h of EGDT before transfer to ICU

Initial resuscitation of sepsis: therapeutic goals

- Central venous pressure: 8 – 12 mmHg
- Mean arterial pressure: ≥ 65 mmHg
- Urine output: 0.5 mL/kg/h
- Central venous (SVC) or mixed venous oxygen saturation: $\geq 70\%$



Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴; Herwig Gerlach, MD, PhD⁵; Steven M. Opal, MD⁶; Jonathan E. Sevransky, MD⁷; Charles L. Sprung, MD⁸; Ivor S. Douglas, MD⁹; Roman Jaeschke, MD¹⁰; Tiffany M. Osborn, MD, MPH¹¹; Mark E. Nunnally, MD¹²; Sean R. Townsend, MD¹³; Konrad Reinhart, MD¹⁴; Ruth M. Kleinpell, PhD, RN-CS¹⁵; Derek C. Angus, MD, MPH¹⁶; Clifford S. Deutschman, MD, MS¹⁷; Flavia R. Machado, MD, PhD¹⁸; Gordon D. Rubenfeld, MD¹⁹; Steven A. Webb, MB BS, PhD²⁰; Richard J. Beale, MB BS²¹; Jean-Louis Vincent, MD, PhD²²; Rui Moreno, MD, PhD²³; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Objective: To provide an update to the "Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock," last published in 2008.

Methods: The authors were advised to follow the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to guide assessment of quality of evi-

Sepsis Campaign 2012 update

- **Antibiotics** asap **within 1 hour** of septic shock or severe sepsis
- **Fluids 30ml/kg** and use crystalloids in severe sepsis and septic shock
- **Crystalloids** are preferable to colloids
- Use albumin if substantial amounts of crystalloids
- **Target decreasing lactate** with resuscitation
- Conflicting trials however increased need for renal replacement Rx using hydroxyethyl starches
- Use **noradrenaline** not dopamine (meta-analysis)
– risk of tachyarrhythmias
- Tight glucose control is harmful (target 180 mg%)

EDITORIAL



Septic Shock — Evaluating Another Failed Treatment

Richard P. Wenzel, M.D., and Michael B. Edmond, M.D., M.P.H.

Sepsis, severe sepsis, and septic shock are progressively severe stages of the host's systemic inflammatory response to infection.¹ The latter stages carry increasing rates of end-organ failure and death. The spectrum of the sepsis syndrome remains a leading cause of death in the United States, and early intervention with appropriate antibiotics (matching the antibiogram susceptibilities to the drugs administered) saves lives.

Interventions that interfere with these pathways have not shown a benefit. However, in 2001, Bernard and colleagues³ reported a modest improvement in all-cause mortality at 28 days associated with adjunctive therapy with recombinant human activated protein C, or drotrecogin alfa (activated) (DrotAA). The investigators found a death rate of 24.7% in treated patients versus 30.8% in controls, an absolute reduction of 6 percentage points and a relative re-

“Non-antibiotic” therapy for sepsis – evidence base?

- Goal directed therapy
- Low dose steroids (CORTICUS)
- Intensive insulin therapy
 - tight glycaemic control
- Activated protein C (PROWESS etc)

“Non-antibiotic” therapy for sepsis – evidence base?

- Goal directed therapy **Some**
- Low dose steroids (CORTICUS) **No**
- Intensive insulin therapy
 - tight glycaemic control **No**
- Activated protein C (PROWESS etc) **No**

Frequent “medical” failures

- Failure to recognise sepsis
 - Postural hypotension
 - Raised respiratory rate
 - Hypoxia
 - Acidosis
- Failure to look for focal signs
 - Source
 - Metastatic spread
- Failure to take blood cultures or do LP

Antimicrobials

Antibiotics in sepsis

- There is no, single, “best” regimen
- Consider the **site** of the infection
- Consider **which organisms** most often cause infection at that site
- Consider local **resistance patterns**
- Choose antibiotic(s) with appropriate **spectrum**
- After obtaining cultures, give antibiotics **quickly** and **empirically** at **appropriate dose**
- **Revise** the regimen as soon as culture & sensitivity results allow

Rational choice of antibiotics

Efficacy

- Spectrum of activity
- Pharmacokinetics & pharmacodynamics
- Patterns of resistance
- Quality of manufacture (generics, forgery)

Toxicity

Availability

Cost



Initiation of Inappropriate Antimicrobial Therapy Results in a Fivefold Reduction of Survival in Human Septic Shock

*Anand Kumar, MD; Paul Ellis, MD; Yaseen Arabi, MD, FCCP;
Dan Roberts, MD; Bruce Light, MD; Joseph E. Parrillo, MD, FCCP;
Peter Dodek, MD; Gordon Wood, MD; Aseem Kumar, PhD; David Simon, MD;
Cheryl Peters, RN; Muhammad Ahsan, MD; Dan Chateau, PhD; and the
Cooperative Antimicrobial Therapy of Septic Shock Database Research Group**

Objective: Our goal was to determine the impact of the initiation of inappropriate antimicrobial therapy on survival to hospital discharge of patients with septic shock.

Methods: The appropriateness of initial antimicrobial therapy, the clinical infection site, and relevant pathogens were retrospectively determined for 5,715 patients with septic shock in three countries.

Kumar A et al. Chest 2009; 136: 1237-48

Appropriate antibiotics

Study of 5715 patients in 3 countries

- Wide range of infection, in septic shock
- 80% received appropriate antibiotics

Survival appropriate 52%

 inappropriate 10.3%

adj OR 8.99 (95%CI 6.6-12.23) $p < 0.0001$

Kumar A et al. Chest 2009; 136: 1237-48

Timing of antibiotics

Feature Articles **Kumar A et al. Crit Care Med 2006; 34: 1589-96**

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

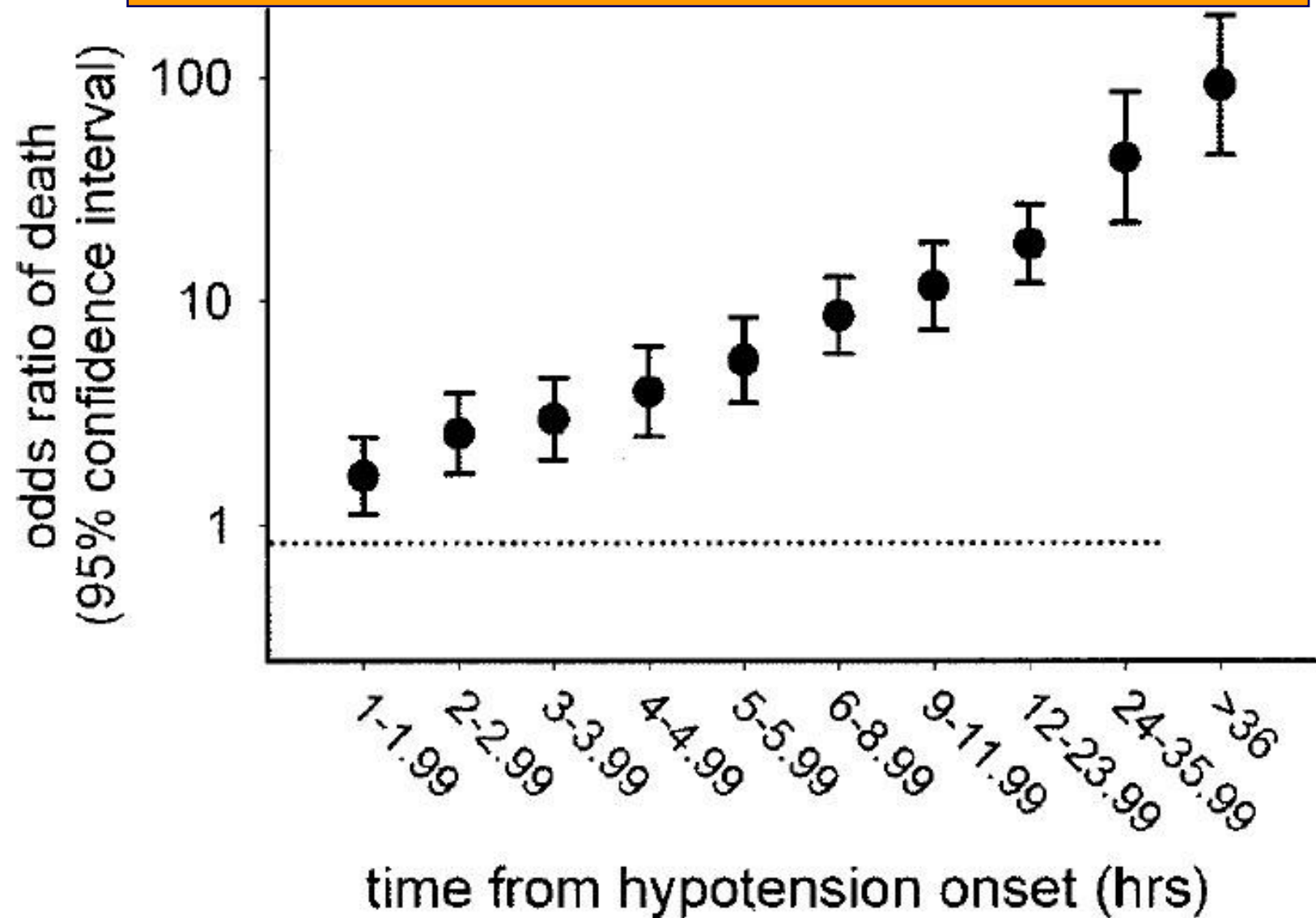
Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

Retrospective cohort 10 ICU N=2731 septic shock

Survival if antibiotics given within 1 hr =79.9%

Each further hour of delay decreases survival by 7.6%

Only 51.4% received antibiotics within 6 hours



Kumar A et al Crit Care Med 2006; 34: 1589-96

Common system failures

- Failure to record MEWS scores
- Failure to act on MEWS scores
 - Nurses calling doctors
 - Doctors responding to call
- Doctors using care bundle early
- Escalating decision to seniors
- Provision of resources including outreach teams and ICU

Common antimicrobial mistakes

- Failure to start early
- Failure to review previous laboratory results
- Failure to take into account previous antibiotic usage
- Failure to target therapy
- Failure to review later

Antibiotic policies

- Limit by consultation
- Limit by paperwork
- Limit by selective lab reporting
- Trust guidelines/formulary
 - Audit & reinforce
- Concept of “antibiotic stewardship”

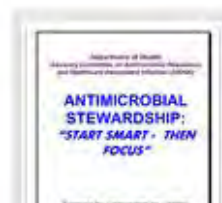
Guidance

Antimicrobial stewardship: Start smart - then focus

Organisation: Department of Health
Page history: Published 17 November 2011
Applies to: England

The aim of this guidance is to provide an outline of evidence-based antimicrobial stewardship in the secondary healthcare setting.

Documents



Download Antimicrobial Stewardship 'Start Smart, - Then Focus'

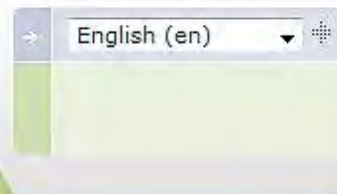
PDF, 667KB, 27 pages

www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131062

EUROPEAN ANTIBIOTIC AWARENESS DAY



A European Health Initiative



Home

About the day

Campaign materials

National campaigns

Contact

News release

European Antibiotic Awareness Day is marked annually on 18 November.

A number of initiatives are taking place across Europe to spread the messages on the risks associated with inappropriate use of antibiotics and how to take antibiotics responsibly.



National campaigns



News release



Toolkit for engaging in social media to promote prudent antibiotic use



Patient stories



Campaign materials



National campaigns



Data and reports

<http://ecdc.europa.eu/en/EAAD/Pages/Home.aspx>

**EUROPEAN
ANTIBIOTIC
AWARENESS DAY**



ANTIBIOTICS

Start Smart - Then Focus

A European Health Initiative



www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

Anne Neary
Kate Vaudrey

Antimicrobial Pharmacists RLBUHT
European Antibiotic Awareness Day (EAAD) 2013

Start SMART then FOCUS

- DoH guidance on prudent antimicrobial prescribing and antimicrobial stewardship
- Antimicrobial stewardship
 - Optimising antimicrobial prescribing
 - Minimising antimicrobial resistance
 - Those who need antibiotics:
 - Right antibiotic, right dose, right time
 - Avoiding side effects in those who don't need antibiotics
 - *Clostridium difficile*

Start SMART

- Do NOT start antibiotics in the absence of clinical evidence of bacterial infection
- Take relevant microbiological specimens
- Take history of relevant allergies
- Use our Antibiotic formulary to guide choice
- Document clinical indication and duration on the drug chart/EPMA and in the case notes

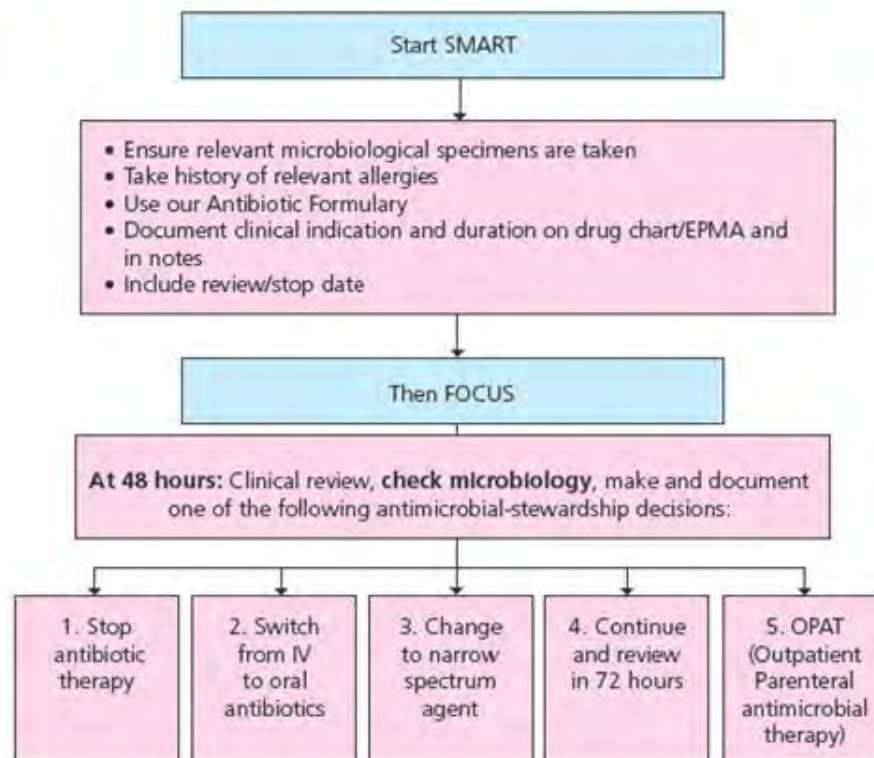
Then FOCUS

- Review at 48 hours
 - Clinical
 - Microbiology
- Make and document one of 5 antimicrobial stewardship decisions
 1. STOP antibiotic therapy
 2. SWITCH – from IV to PO
 3. CHANGE to a narrow spectrum agent
 4. CONTINUE current therapy and review again at 72 hours
 5. OPAT – Outpatient Parenteral Antimicrobial Therapy

****Review and decision making should be clearly documented in the case notes****

The Royal Liverpool and
Broadgreen University Hospitals
NHS Trust

Antimicrobial Prescribing Start SMART then FOCUS



Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

Author: Kate Vaudrey, Antimicrobial Pharmacist
Publish date: September 2012
Review date: September 2015

Better
Together



Annual Report of the Chief Medical Officer

Volume Two, 2011

**Infections and the rise of antimicrobial
resistance**

G8 UK
UNITED KINGDOM 2013

G8 Science Ministers Statement London UK, 12 June 2013



Department
of Health



Department
for Environment
Food & Rural Affairs

UK Five Year Antimicrobial Resistance Strategy 2013 to 2018



The evolving threat of antimicrobial resistance

Options for action



ANTIBIOTIC RESISTANCE THREATS

in the United States, 2013



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention



Transatlantic Taskforce on Antimicrobial Resistance

Recommendations for future collaboration
between the U.S. and EU

2011

ANTIBIOTIC ACTION

Global Antibiotic Resistance Partnership

RS TEAM PUBLICATIONS CONTACT US



- WHO (2009) and G8 (2013) Statements
 - Antibiotic resistance one of the 3 greatest threats to health
- IDSA 10x20 initiative 2009
- BSAC "Antibiotic Action" 2009
- ReAct 2010 (Action on Antibiotic Resistance)
- Transatlantic Task Force on Antimicrobial Resistance (TATFAR)
- European Commission Action Plan 2011
- UK 5 year Antimicrobial Resistance Strategy 2013-18
- Innovative Medicines Initiative (IMI)

Antibiotic resistance: indirect consequences

disease and infections that, previously easy to control, will become much more significant threats to health. Standard surgical procedures, such as hip replacements, could become riskier with widespread antimicrobial resistance, as would treatments that result in immunosuppression, such as chemotherapy or organ transplant, which rely on the ability

UK Chief Medical Officer's report, 2013



Indirect consequences for medical care

- cancer chemotherapy
- complex surgery, implant surgery
- haemodialysis
- Rheumatoid arthritis
- organ transplantation

Consequences beyond human health

- financial cost up to \$36bn p.a. in US (\$70bn including "societal costs")

Integration of AS and IPC



The evolving threat of
antimicrobial resistance
Options for action



Chapter 5.

Infection prevention and control
in health-care facilities

Point Prevalence of Antimicrobial Prescribing in European Hospitals 2009 ESAC-3

30% of inpatients were treated with antibiotics

The proportion for treating HAI was 35%

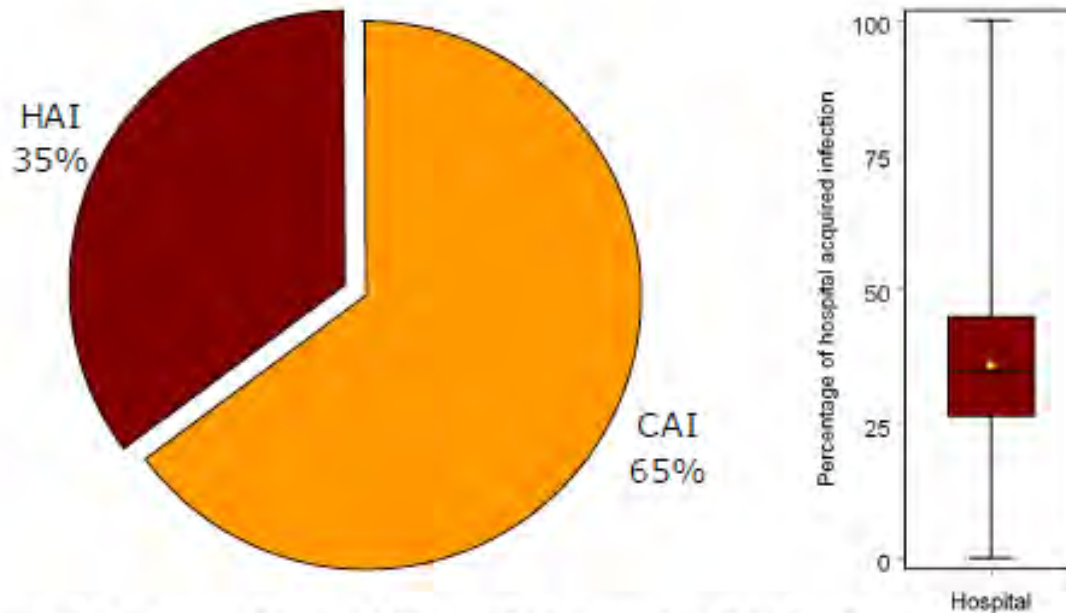
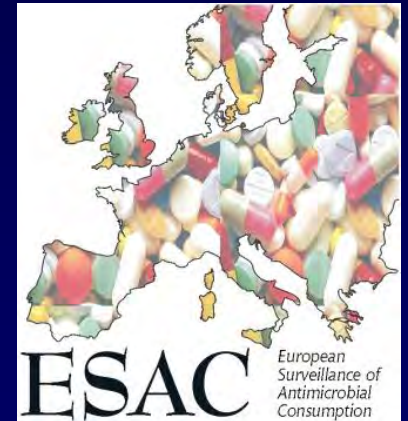


Figure 17 Proportion of Hospital acquired infections



UK CMO Report 2013

The new UK antimicrobial resistance strategy and action plan

A major societal, political, clinical, and research challenge

Seven key areas of focus

Stakeholders

Promote responsible evidence based prescribing

Individual prescribers, NHS providers, national and local commissioning boards, ARHAI, PHE, Department of Health, professional bodies

Improve infection prevention and control

Individual clinical staff, NHS providers, national and local commissioning boards, ARHAI, Department of Health, PHE, professional bodies

Raise public and professional awareness of antimicrobial resistance threat and promote behaviour change

Professional bodies, Department of Health, ARHAI, patient groups

Research programme into new diagnostics, alternatives to antibiotics (such as antiseptics), pathogenesis, effective behavioural change to improve infection prevention and control and prescribing practice

NIHR, universities, Department of Health, ARHAI

Facilitate development of new antimicrobials, vaccines, and immunomodulators

Department of Health, drug industry, European Union

Improve surveillance and data linkage

PHE, ARHAI, Department of Health

Encourage international collaboration and data sharing and learning from best practice internationally

Department of Health, PHE

ARHAI=Department of Health Expert Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection; PHE=Public Health England.

Seven key areas of focus

Promote responsible evidence based prescribing

Improve infection prevention and control

Raise public and professional awareness of antimicrobial resistance threat and promote behaviour change

Research programme into new diagnostics, alternatives to antibiotics (such as antiseptics), pathogenesis, effective behavioural change to improve infection prevention and control and prescribing practice

Facilitate development of new antimicrobials, vaccines, and immunomodulators

Improve surveillance and data linkage

Encourage international collaboration and data sharing and learning from best practice internationally

ARHAI=Department of Health Expert Advisory Committee on Antimicrobial Resistance

UK CMO Report 2013

„Acute trusts and their boards will need to learn a new language and consider how to strengthen infection prevention and control practice using new methods of organisational and behavioural change to reinforce policy implementation.“

BMJ

BMJ 2013;346:f1601 doi: 10.1136/bmj.f1601 (Published 11 March 2013)

Page 1 of 3

EDITORIALS

The new UK antimicrobial resistance strategy and action plan

A major societal, political, clinical, and research challenge

Anthony S Kessel *honorary professor*¹, Mike Sharland *professor in paediatric infectious diseases*²

¹Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, UK; ²Paediatric Infectious Diseases Research Group, St George's University London, London SW17 0RE, UK

This week the chief medical officer highlighted in her report how the rise of antimicrobial resistance (AMR) poses a threat to healthcare delivery in the United Kingdom.¹ This will be followed shortly by the Department of Health's new UK Five Year Antimicrobial Resistance Strategy and Action Plan, which will reflect the need for a clear change in the understanding and response to AMR by the public, the NHS, and the government in the UK. The rise of AMR as a serious health threat is due to the international spread of multidrug resistant (MDR) Gram negative bacteria, the global overuse of antibiotics in humans and animals, and the almost complete lack of new antibiotic development.² All of these are now of direct concern to the NHS.

The 85% reduction in rates of methicillin resistant *Staphylococcus aureus* (MRSA) bloodstream infections seen in England between 2003 and 2011 has been remarkable. MRSA is now responsible for less than 2% of all bloodstream infections in England. Less remarked on has been the inexorable rise in the number of bloodstream infections attributable to Gram negative organisms (particularly *Escherichia coli*), which now comprise more than half of the around 100 000 of these infections reported in England annually.³ Most large NHS hospitals now identify 50-100 times more patients with Gram negative bloodstream infections than those with MRSA, with antibiotic resistance rates of 10-20% and mortality rates of 30% reported for MDR forms.⁴ In England the successful introduction of conjugate pneumococcal vaccine means that the number of reported *Klebsiella pneumoniae* bloodstream infections in England is now higher than for *Streptococcus pneumoniae*.

In many European countries AMR rates are much worse. In 2011 the European Centre for Disease Prevention and Control reported a significant increase in multidrug resistant *E coli* and *K pneumoniae* (for example, resistance to third generation cephalosporins, fluoroquinolones, and aminoglycosides) in more than a third of European Union/European Economic Area countries.⁵ *Klebsiella* is an important pathogen in the spread of resistance. Many antibiotic resistance genes group together in plasmids easily transferred between bacteria, with particular

clones carrying multiple resistance genes (for example, OXA-48 and CTX-M15). Many EU countries are now reporting *Klebsiella* MDR rates of 25-40%.

Globally, rates of MDR Gram negative bacterial infection can be even higher.⁶ This has inevitably led to a rapid rise in the use of carbapenem antibiotics (for example, meropenem) as empirical treatment for suspected sepsis. In turn, this has led to a rapid increase in hospital outbreaks of carbapenemase producing organisms, which are usually sensitive to only one or two older less effective antibiotics. In the UK, there has also been a sharp rise in meropenem use and increasing reports of carbapenemase producing organisms, with worryingly both clonal outbreaks and interspecies plasmid spread seen in some NHS hospitals. Only one or two new antibiotics that target Gram negative organisms are likely to be marketed in the next decade (<http://antibiotic-action.com>), which raises the concern that virtually untreatable infections will threaten routine NHS care for vulnerable children and adults. Experts in policy analysis describe this type of problem as a "super wicked challenge."⁷

The new UK strategy is an important step in recognising and responding to these concerns, driven by the emergence of carbapenemase producing organisms in the NHS. At its core the strategy recognises that AMR, infection prevention and control, and antimicrobial stewardship are closely interconnected and all need to be strengthened. The seven aims (table 1) reflect that all individuals and organisations have unique roles and responsibilities. Enhanced infection prevention and control are crucial to limiting the spread of MDR Gram negative bacteria, both into and across the NHS.

New challenges will include screening (by rectal swab) and isolation of any patient admitted to the NHS who has received inpatient care outside the UK, with rigorous control of any outbreaks of multidrug resistant infection inside the NHS. Acute trusts and their boards will need to learn a new language and consider how to strengthen infection prevention and control practice using new methods of organisational and behavioural change to reinforce policy implementation. Although zero tolerance to MRSA and *Clostridium difficile* infection remain

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Policies and guidelines are not enough....

BMJ

BMJ 2011;343:d5283 doi: 10.1136/bmj.d5283

Page 1 of 5

ANALYSIS

Breaking the rules: understanding non-compliance with policies and guidelines

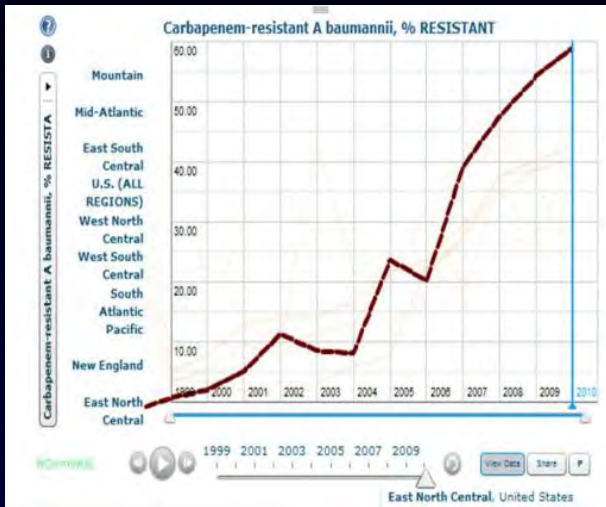
Healthcare organisations use policies and guidelines to standardise and clarify care and improve efficiency, productivity, and safety. But **Jane Carthey and colleagues** are concerned that their burgeoning number makes it impossible to distinguish the essential from the irrelevant and is affecting compliance

Jane Carthey *human factors consultant*¹, Susannah Walker *anaesthetic registrar*², Vashist Deelchand *research associate*², Charles Vincent *professor of clinical safety research*², William Harrop Griffiths *consultant anaesthetist*³

¹Imperial College London, London, UK; ²Department of Biosurgery and Technology, Imperial College London; ³Department of Anaesthesia, Imperial

J Carthey et al BMJ 2011; 343

What could be done differently?



- How can we do better?



- Consider:
- Organisation
- Systems
- Teams



Organisational Approach required

Journal of Hospital Infection (2009) 73, 392–396



Available online at www.sciencedirect.com

ScienceDirect



www.elsevierhealth.com/journals/jhin

REVIEW

Where does infection control fit into a hospital management structure?

E.T. Brannigan^a, E. Murray^{a,b}, A. Holmes^{a,b,*}

^a Imperial College Healthcare NHS Trust, London, UK

^b Imperial College, London, UK

Available online 20 August 2009

KEYWORDS

Hospital-acquired infection;
Organisational change;
Patient safety;
Quality

Summary To be effective, infection prevention and control must be integrated into the complex and multiple interlinking systems within a hospital's management structure. Each of the systems must consider how activity associated with it can be optimised to minimise infection risk to patients. The components of an organisational structure to achieve these quality assurance and patient safety aims are discussed. The use of performance management tools in relation to infection control metrics is reviewed, and the use of hospital-acquired infection as a proxy indicator for deficiencies of system management is considered. Infection prevention and control cannot be the role and responsibility of a single individual or a small dedicated team; rather it should be a priority at all levels and integrated within all management systems, including the research and educational agendas.

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Increasing recognition in last five years that an organisational approach is required, along with appropriate technical expertise

Organisational Approach required

Journal of Hospital Infection (2009) 73, 392–396



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www.elsevierhealth.com/journals/jhin



REVIEW

Where does infection control fit in management structure?

E.T. Brannigan^a, E. Murray^{a,b}, A. Holmes^{a,b,*}

^a Imperial College Healthcare NHS Trust, London, UK

^b Imperial College, London, UK

Available online 20 August 2009

KEYWORDS

Hospital-acquired infection;
Organisational change;
Patient safety;
Quality

Summary To be effective, infection control must be integrated into the complex and multi-layered management structure of a hospital. Each activity associated with it can be done by different teams. The components of an organisational approach to quality assurance and patient safety management tools in relation to infection control are reviewed, and the use of hospital-acquired infection for deficiencies of system management and control cannot be the role of a small dedicated team; rather it must be integrated within all management and educational agendas.

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J Antimicrob Chemother 2012; **67** Suppl 1: i29–i36
doi:10.1093/jac/dks200

Journal of Antimicrobial Chemotherapy

Addressing healthcare-associated infections and antimicrobial resistance from an organizational perspective: progress and challenges

Eleanor Murray^{1*} and Alison Holmes²

¹Imperial College Centre for Patient Safety and Service Quality, Faculty of Medicine, Imperial College London, 5th floor Medical School Building, St Mary's Campus, Norfolk Place, London W2 1PG, UK; ²National Centre for Infection Prevention and Management, Faculty of Medicine, Imperial College London, Level 2 Infection Control, Hammersmith House, Hammersmith Hospital Campus, Du Cane Road, London W12 0HS, UK

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This paper explores the progress and challenges associated with the application of organizational factors and approaches to infection prevention and control (IPC) and antibiotic stewardship (AS) in England, many of which have been considered and supported by the Advisory Committee on Antimicrobial Resistance and Healthcare-associated Infections (ARHAI). An organizational perspective is described and the wider macro context and socio-political forces that shape an organizational approach are considered. Factors that drive organizational change in IPC and AS are discussed. The tensions, constraints and dilemmas that can occur are identified and outstanding challenges are debated. Some recommendations for the future direction of IPC and AS organizationally focused strategies and research are proposed.

Keywords: organizations, infection control, antibiotic stewardship

Whole Systems Approach

J Antimicrob Chemother 2010; **65**: 2275–2277
doi:10.1093/jac/dkq357 Advance Access publication 16 September 2010

Journal of
Antimicrobial
Chemotherapy

Antibiotic stewardship programmes—what's missing?

Esmita Charani¹*, Jonathan Cooke² and Alison Holmes¹

¹Centre for Infection Prevention and Management, Imperial College, London W12 0HS, UK; ²University Hospital of South Manchester NHS Foundation Trust, Wythenshawe Hospital and Manchester Academic Health Science Centre, Manchester M23 9LT, UK

*Corresponding author. Tel: +44-203-313-1553; Fax: +44-208-383-3235; E-mail: e.charani@imperial.ac.uk

Inappropriate antibiotic use and antibiotic resistance are now major global issues. Antimicrobial stewardship programmes are increasingly being used to optimize antibiotic prescribing in acute care. The central tenet of these programmes tends to be policy and guidelines aimed at prescribers. However, rules and guidelines alone may not be sufficient to bring about effective and sustainable optimization of practice. Best practice needs to be positively reinforced by an environment that facilitates and supports optimal prescribing choices, i.e. a 'choice architecture' that makes prudent antibiotic prescribing the path of least resistance. To make prudent antibiotic management an integral part of the behaviour of all healthcare professionals and to bring about quality improvement it is necessary to adopt a whole-system approach. To do this it is necessary first to understand the factors that influence antibiotic management and prescribing.

Keywords: antibiotics, choice architecture, prescribing

- Necessary to understand the factors that influence prescribing behaviour and decisions
- Address human factors
- Supporting choice architecture
- Making some small changes to existing systems
- Adopt a whole-system approach to support optimal prescribing choices

Charani et al JAC 2010

Greater Understanding of Antimicrobial Prescribing Behaviours

MAJOR ARTICLE

Behavior Change Strategies to Influence Antimicrobial Prescribing in Acute Care: A Systematic Review

Emmit Charani,¹ Rachel Edwards,¹ Nick Sevdalis,² Banos Alexandrou,³ Eleanor Sibley,⁴ David Mullett,⁴ Bryony Dean Franklin,^{3,4} and Alison Holmes¹

¹The National Centre for Infection Prevention and Management, ²Department of Surgery and Cancer and Centre for Patient Safety and Service Quality, Imperial College London, ³Independent Consultant, ⁴Dr Foster Intelligence, ⁵Centre for Medication Safety and Service Quality, Imperial College Healthcare National Health Service Trust, and ⁶The School of Pharmacy, University of London, Pharmacy Department, Charing Cross Hospital, London, United Kingdom

Background. Antimicrobial use in acute care is widely reported to be suboptimal. Inappropriate use of antimicrobials is a major contributing factor to the emergence of multidrug resistance and health care-associated infection. Addressing prescribing behavior is a key component of antimicrobial stewardship.

Methods. We performed a novel systematic review of both qualitative and quantitative literature on antimicrobial prescribing behavior in acute care. We assessed the extent to which behavioral sciences and social marketing were used and whether this could be related to the effectiveness of reported outcomes. MEDLINE, Excerpta Medica Database (EMBASE), Applied Social Sciences Index and Abstracts (ASSIA), Business Source Complete, The Cochrane Library, PsychInfo, Database of Abstracts of Reviews of Effectiveness (DARE) and Health Management Information Consortium (HMIC) were searched for studies undertaken during the period January 1999–April 2011 and published in English.

Results. Five qualitative and 5 quantitative studies met the quality criteria. Qualitative studies highlight the predominant influence of social norms, attitudes, and beliefs on antimicrobial prescribing behavior. Quantitative studies reporting interventions to optimize antimicrobial prescribing behavior do not use theoretical science or primary research to inform the design and choice of the interventions deployed.

Conclusions. Despite qualitative evidence demonstrating the impact of behavioral determinants and social norms on prescribing, these influences are not given due consideration in the design and evaluation of interventions. To ensure a better understanding of prescribing behaviors and to improve the quality of interventions and research in this area, the incorporation and application of behavioral sciences supported by appropriate multidisciplinary collaboration is recommended.

Up to one-third of all hospitalized patients receive antimicrobials [1, 2] and studies show that 25%–68% of hospital antimicrobial prescribing is suboptimal [3, 4]. Unequivocal evidence links inappropriate and excessive use of antimicrobials with an increase in the incidence

of *Clostridium difficile*-associated disease [5] and selection of bacteria exhibiting antimicrobial resistance (AR), such as methicillin-resistant *Staphylococcus aureus* and extended-spectrum β -lactamases [5–7]. The problem of AR is further complicated by multidrug-resistant pathogens against which most antimicrobials are ineffective, with little prospect of new antimicrobials coming into the market [8]. Suboptimal prescribing can also lead to other unintended consequences of ineffective antimicrobial therapy, including delayed administration and subtherapeutic dosing, which can contribute to treatment failure.

In an effort to improve the quality of antimicrobial prescribing in acute care, antimicrobial stewardship (AS) initiatives have been recommended [9, 10]. AS

- Interventions to optimize antimicrobial prescribing behaviour are of poor quality and are not based on robust theoretical science.
- Behaviour and social science research is underutilized in the development of antimicrobial prescribing interventions.
- Qualitative evidence highlights the influence of social norms, attitudes, and beliefs on antimicrobial prescribing behaviour
- When designing and evaluating interventions in antimicrobial prescribing, these influences on prescribing are generally not considered.

Received 2 March 2011; accepted 7 June 2011.
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Clinical Infectious Diseases 2011;53(7):651–662

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1089-4039/2011/070651-12\$14.00
DOI: 10.1093/cid/cir446

Explaining Michigan: Developing an Ex Post Theory of a Quality Improvement Program

MARY DIXON-WOODS, CHARLES L. BOSK, EMMA LOUISE AVELING, CHRISTINE A. GOESCHEL, and PETER J. PRONOVOST

University of Leicester; University of Pennsylvania; Johns Hopkins University

Context: Understanding how and why programs work—not simply whether they work—is crucial. Good theory is indispensable to advancing the science of improvement. We argue for the usefulness of ex post theorization of programs.

Methods: We propose an approach, located within the broad family of theory-oriented methods, for developing ex post theories of interventional programs. We use this approach to develop an ex post theory of the Michigan Intensive Care Unit (ICU) project, which attracted international attention by successfully reducing rates of central venous catheter bloodstream infections (CVC-BSIs). The procedure used to develop the ex post theory was (1) identify program leaders' initial theory of change and learning from running the program; (2) enhance this with new information in the form of theoretical contributions from social scientists; (3) synthesize prior and new information to produce an updated theory.

Findings: The Michigan project achieved its effects by (1) generating isomorphic pressures for ICUs to join the program and conform to its requirements; (2) creating a densely networked community with strong horizontal links that exerted normative pressures on members; (3) reframing CVC-BSIs as a social problem and addressing it through a professional movement combining "grassroots" features with a vertically integrating program structure; (4) using several interventions that functioned in different ways to shape a culture of

Address correspondence to: Mary Dixon-Woods, Department of Health Sciences, Adrian Building, University of Leicester, LE1 7AH, UK (email: md11@le.ac.uk).

Successful interventions based on.....

- Social process
- The sense of community
- Bottom up approach
- Importance of systems with network and teams

The Milbank Quarterly 2011; 89(2): 167–205

Summary

- There are internationally agreed programmes on management of sepsis
- Adherence to these is often poor
- Simple approaches are required at every level of health care
- Sustained behaviour change requires a truly multidisciplinary approach

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Jonathon Folb
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Royal Liverpool University Hospital
- Dr Panduka Karunanayake
Colombo

شكرًا لكم على إهتمامكم

Thank you for your attention