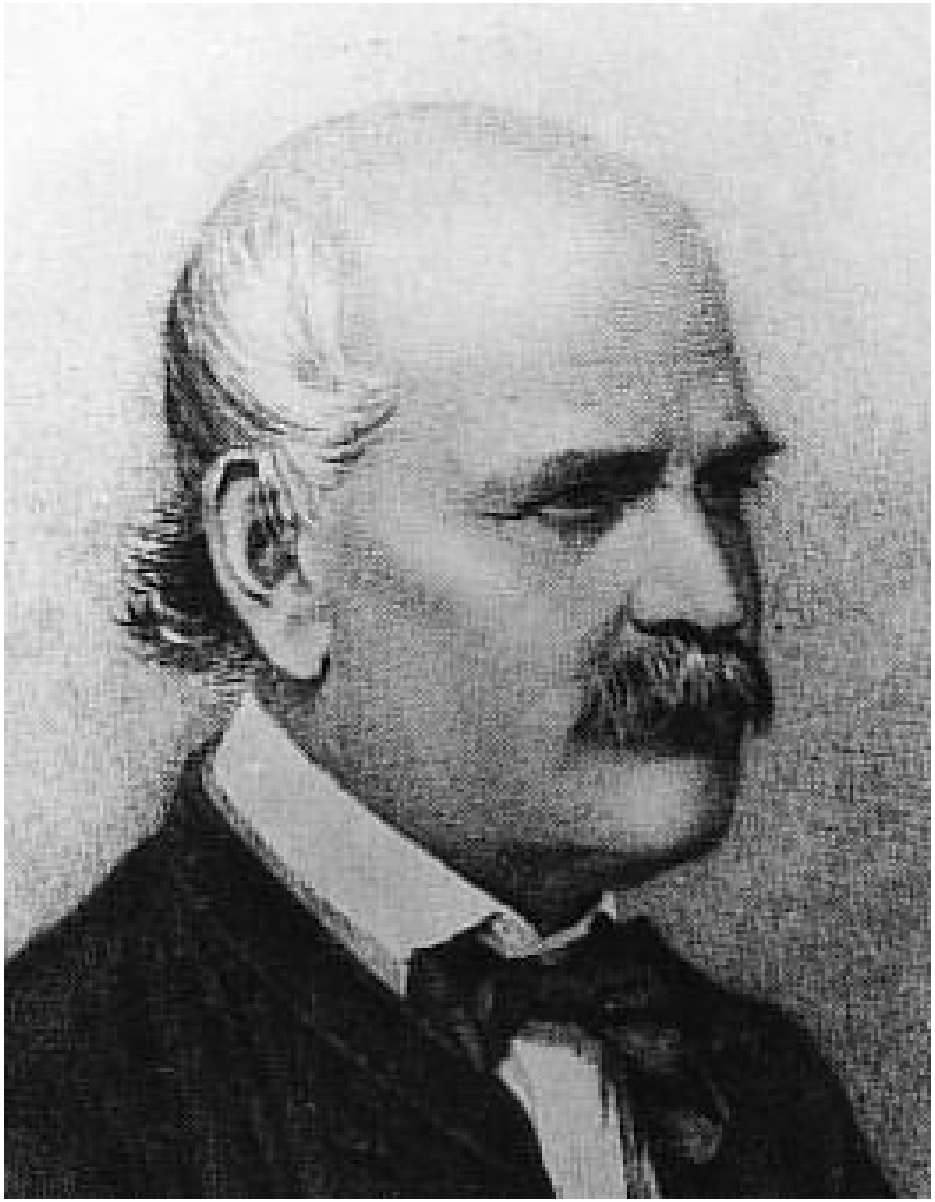
Centre for Perioperative Medicine and Critical Care Research

Obstetrics and sepsis

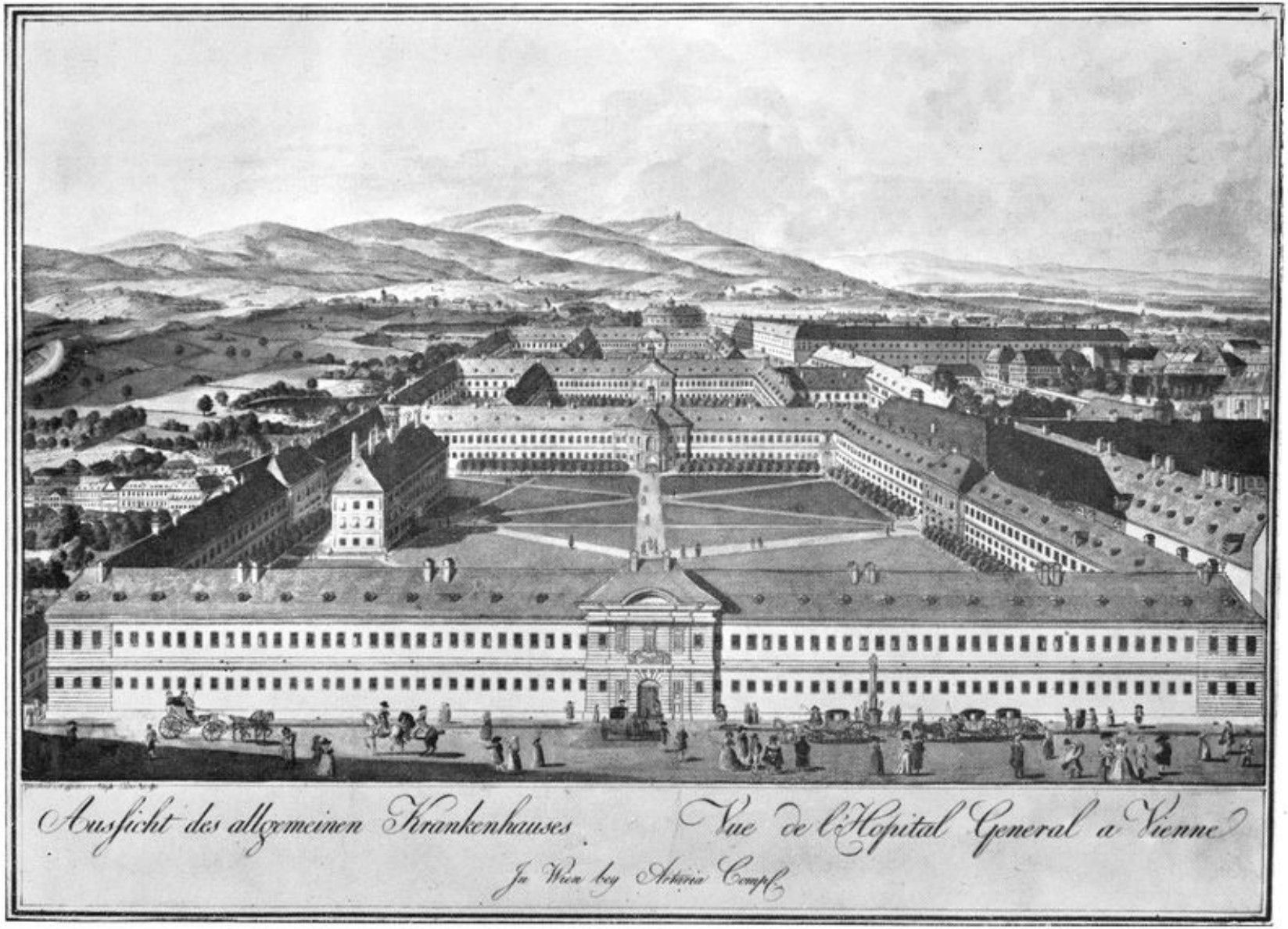
Dr Stephen Brett

Imperial College Healthcare NHS
NHS Trust

Dr Ignaz Philipp Semmelweis, 1818-1865



Vienna General Hospital



Puerperal sepsis

	Didn't die of it	Died of it
First obstetrical clinic	87	13
Second obstetrical clinic	98	2

P=0.005

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

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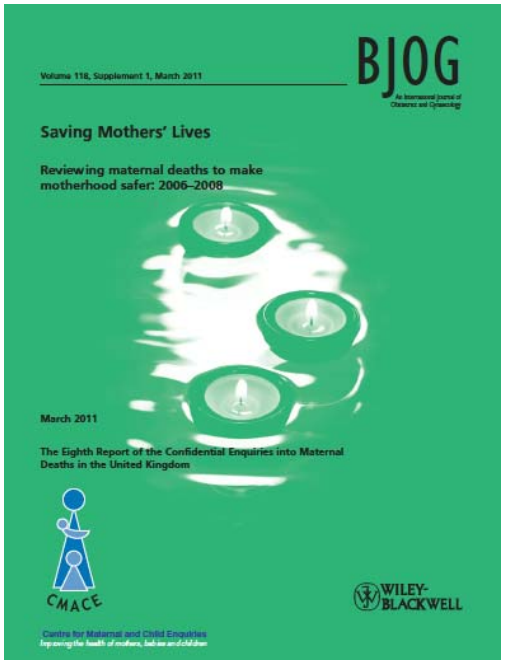
Puerperal sepsis

N. Arulkumaran, MRCP *, M. Singer, MD

Bloomsbury Institute of Intensive Care Medicine, University College London, Cruciform Building, Gower Street, London WC1E 6BT, UK

- 5 million cases per year
- 62,000 maternal deaths
- 0.6-1 per thousand deliveries
- 2.1% maternal deaths globally
- 11.6% maternal deaths in low income countries
- 10% mortality rate for maternal sepsis in developed countries
- 33% mortality rate for puerperal sepsis in developing countries

In the UK……



- 0.85 deaths per 100,000 deliveries in 2003-2005
- 1.13 deaths per 100,000 deliveries in 2006-2008
- Commonest cause of direct maternal deaths

- ?…….

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Maternal Sepsis – an update

Marian Knight
NIHR Research Professor in Public Health
National Perinatal Epidemiology Unit, University of Oxford

University of Oxford · University of Leicester · TIMMS · University of Birmingham · Sands Stillbirth & neonatal death charity · UCL · University of Liverpool · npeu National Perinatal Epidemiology Unit

Sepsis Confidential Enquiry progress

- Topic Expert Group convened:
- Key standards identified
- All maternal deaths included
- 34 morbidity cases selected
  - Stratified sample of women with septic shock
- Case notes obtained and local clinician reports requested

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Key standards for assessors - sepsis

1. **Recognition**
   - RCOG Green-top Guideline 64a: Bacterial sepsis in pregnancy: Sections 5 and 6
   - RCOG Green-top Guidelines 64b: Bacterial sepsis following pregnancy: Section 7
2. **Response and management**
   - Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012: Tables 5,6 and 8, Figure 1.
   - The Sepsis Six (http://survivesepsis.org/the-sepsis-six/):
   - RCOG Green-top Guideline 64a: Bacterial sepsis in pregnancy
   - RCOG Green-top Guidelines 64b: Bacterial sepsis following pregnancy
3. **Investigations**
   - Surviving Sepsis Campaign Bundles: (http://www.survivingsepsis.org/bundles/Pages/default.aspx)
4. **Condition-specific guidance**
   - British Thoracic Society guidelines for the management of community acquired pneumonia in adults: update 2009: Figure 8
   - Critical care management of adults with influenza with particular reference to H1N1 (2009)
   - Surgical site infection – NICE Guideline CG74 Prevention and treatment of surgical site infection

Sepsis morbidity - epidemiology

Two UK national studies:

- UKOSS study of severe sepsis in pregnancy: June 2011-May 2012
- ICNARC data on all admissions to critical care of pregnant or recently pregnant women with a diagnosis of sepsis within the first 24 hours of admission

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Deaths from genital tract sepsis UK 1985-2008

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Source: Saving Mothers' Lives 2006-8

Key message 1

- Genital tract infection forms only a small proportion of maternal morbidity and mortality from infectious disease
- Consideration of the source is important when planning management

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Key messages 2

- Antibiotics should cover the appropriate spectrum, dependent on suspected source and mode of delivery
- If there appears to be no response, rethink
  - Antibiotic spectrum
  - Collection
  - Other infection source

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Key messages 3

- Use of a sepsis bundle
  - International Surviving Sepsis Campaign
  - "Sepsis six" (within the first hour):
    - Administer high flow oxygen
    - Take blood cultures
    - Give broad spectrum antibiotics
    - Give intravenous fluid challenges
    - Measure serum lactate and haemoglobin
    - Measure accurate hourly urine output

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Key messages 4

- Clinical suspicion of group A strep is a red flag for urgent action
  - Association with spontaneous vaginal delivery
- Positive culture for group A strep should be reported by telephone

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Severity (UKOSS)

	n (%) Total=365
Level 2 or ITU admission	286 (78)
Level 2 admission	171 (47)
ITU admission*	114 (31)
Septic shock	71 (20)
Death	5 (1)

* Irrespective of level 2 admission

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Key messages 5

- Some women may need intensive care on delivery suite
- Some women may need obstetric care in the critical care unit
- Facilities/processes need to be available for both

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Significant medical risk factors (UKOSS)

	Cases n (%)	Controls n (%)	aOR* 95% CI
	n=365	n=757	
Parity			
0	197 (54)	330 (44)	1.6 (1.2-2.2)
≥1	167 (46)	427 (56)	1
Pre-existing medical problems			
Yes	120 (33)	171 (23)	1.4 (1.0-1.9)
No	245 (67)	583 (77)	1
Febrile illness or antibiotics in 2 wks before delivery			
Yes	153 (42)	42 (6)	12.1 (8.1-18.0)
No	212 (58)	715 (94)	1

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*Adjusted for all other factors examined

Significant delivery risk factors (UKOSS)

	Postpartum cases n (%)	Controls n (%)	aOR* 95% CI
	n=302	n=757	
Mode of delivery			
Spontaneous vaginal	57 (21)	443 (59)	1
Operative vaginal	39 (14)	100 (13)	3.4 (1.7-7.0)
Pre-labour caesarean	67 (25)	119 (16)	3.5 (2.0-6.1)
Caesarean after labour onset	108 (40)	92 (12)	6.7 (3.8-12.0)
Complications of delivery			
Yes	103 (34)	279 (37)	1.7 (1.1-2.5)
No	199 (66)	478 (63)	1

*Adjusted for all other factors examined

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Significant factors associated with mortality (UKOSS)

	Survivors n (%)	Deaths n (%)	aOR* 95% CI
	n=610	n=29	
Maternal age			
<25	234 (38)	5 (17)	1
25-34	254 (42)	15 (52)	2.2 (0.7-7.0)
≥ 35	121 (20)	9 (31)	3.3 (0.9-11.0)
BMI			
Unknown	317 (52)	13 (45)	1.2 (0.2-9.1)
<25	126 (21)	3 (10)	1
25-29.9	90 (15)	7 (24)	5.2 (1.4-18.9)
≥ 30	76 (13)	6 (21)	6.3 (1.5-27.0)
IMD Quintiles 4&5	354 (58)	17 (58)	2.6 (1.0-6.7)

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*Adjusted for all other factors examined

Key points 6

- It cannot be assumed that antibiotics will prevent progression to severe sepsis and safety net checks should therefore be in place to make sure a pregnant woman has recovered
- Older and obese women are at particular risk of mortality

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Funders

MBRRACE-UK

- Department of Health, England
- NHSSPS Northern Ireland
- Scottish Government Health Department
- NHS Wales
- Channel Islands and the Isle of Man Government Offices

The contract is managed on behalf of the funding bodies by the Healthcare Quality Improvement Partnership (HQIP)

ICNARC/UKOSS studies

- NIHR

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OPEN ACCESS Freely available online

PLoS one

The Comparative Clinical Course of Pregnant and Non-Pregnant Women Hospitalised with Influenza A(H1N1)pdm09 Infection

Gayle P. Dolan[1*], Puja R. Myles[1], Stephen J. Brett[2], Joanne E. Enstone[1], Robert C. Read[3], Peter J. M. Openshaw[4], Malcolm G. Semple[5], Wei Shen Lim[6], Bruce L. Taylor[7], James McMenamin[8], Karl G. Nicholson[9], Barbara Bannister[10], Jonathan S. Nguyen-Van-Tam[1], the Influenza Clinical Information Network (FLU-CIN)

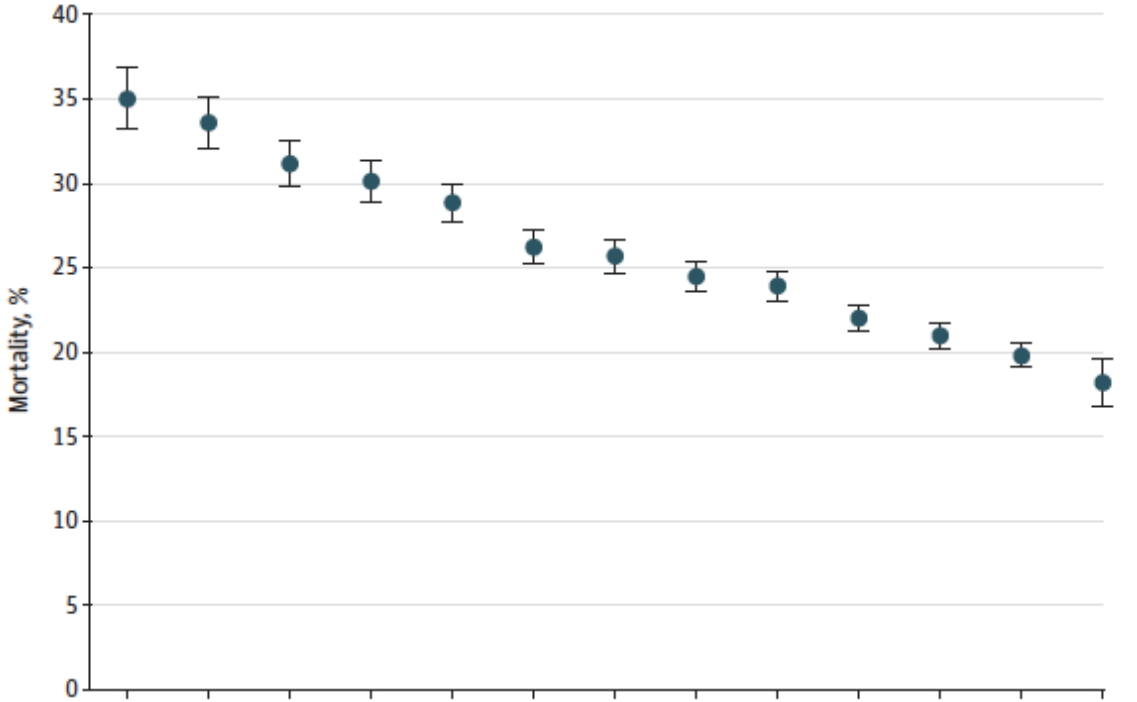
Results: Of the 395 women aged 15–44 years, 82 (21%) were pregnant; 73 (89%) in the second or third trimester. Pregnant women were significantly less likely to exhibit severe respiratory distress at initial assessment (OR = 0.49 (95% CI: 0.30–0.82)), require supplemental oxygen on admission (OR = 0.40 (95% CI: 0.20–0.80)), or have underlying co-morbidities (p-trend <0.001). However, they were equally likely to be admitted to high dependency (Level 2) or intensive care (Level 3) and/or to die, after adjustment for potential confounders (adj. OR = 0.93 (95% CI: 0.46–1.92). Of 11 pregnant women needing Level 2/3 care, 10 required mechanical ventilation and three died.

Conclusions: Since the expected prevalence of pregnancy in the source population was 6%, our data suggest that pregnancy greatly increased the likelihood of hospital admission with A(H1N1)pdm09. Pregnant women were less likely than non-pregnant women to have respiratory distress on admission, but severe outcomes were equally likely in both groups.

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Maija Kaukonen, MD, PhD, EDIC; Michael Bailey, PhD; Satoshi Suzuki, MD; David Pilcher, FCICM; Rinaldo Bellomo, MD, PhD



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
No. of patients	2708	3783	4668	5221	6375	6987	7627	8529	8797	10277	11367	12213	12512

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*

TABLE 3. KAPLAN–MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

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
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (21.0)	12/117 (10.3)	—	0.02
Multiorgan failure	26/119 (21.8)	19/117 (16.2)	—	0.27

*CI denotes confidence interval. Dashes indicate that the relative risk is not applicable.

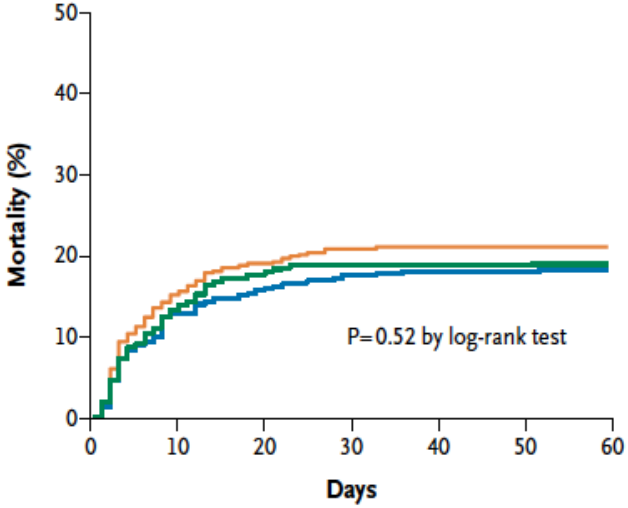
†Percentages were calculated by the Kaplan–Meier product-limit method.

‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

A Randomized Trial of Protocol-Based Care for Early Septic Shock

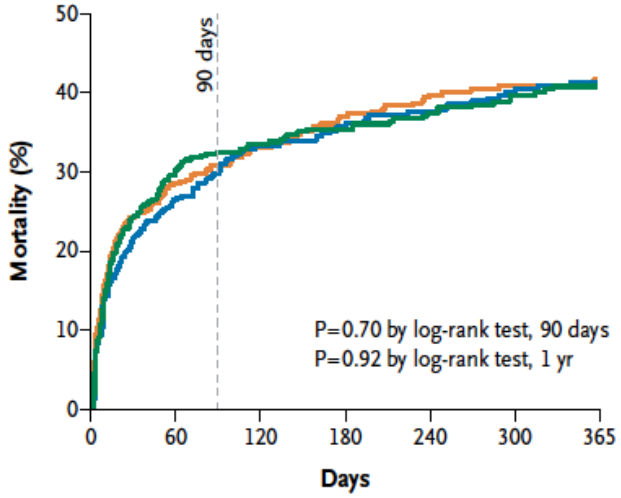
The ProCESS Investigators*

A Cumulative In-Hospital Mortality to 60 Days



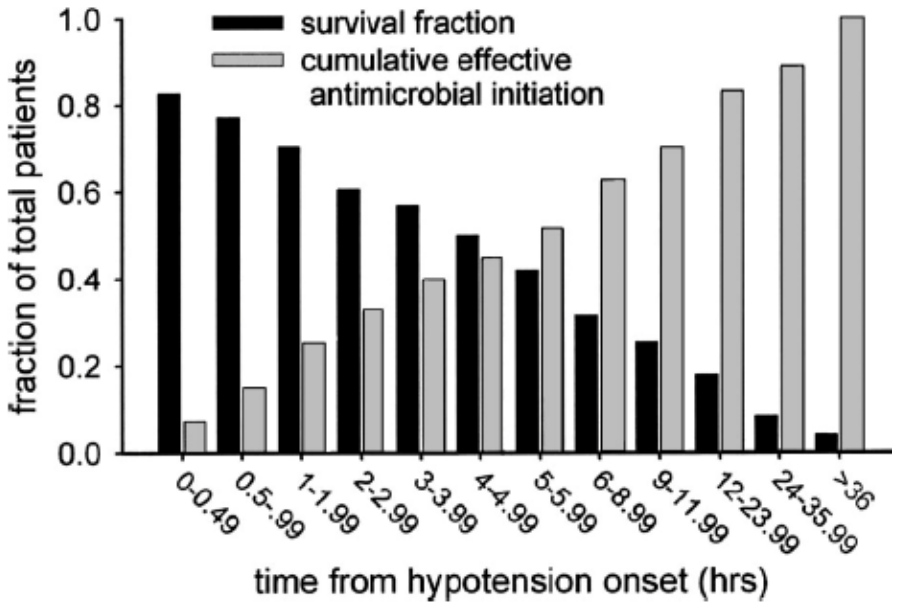
No. at Risk							
Protocol-based EGDT	439	373	356	348	347	347	347
Protocol-based standard therapy	446	389	376	368	366	366	365
Usual care	456	396	376	371	371	371	370

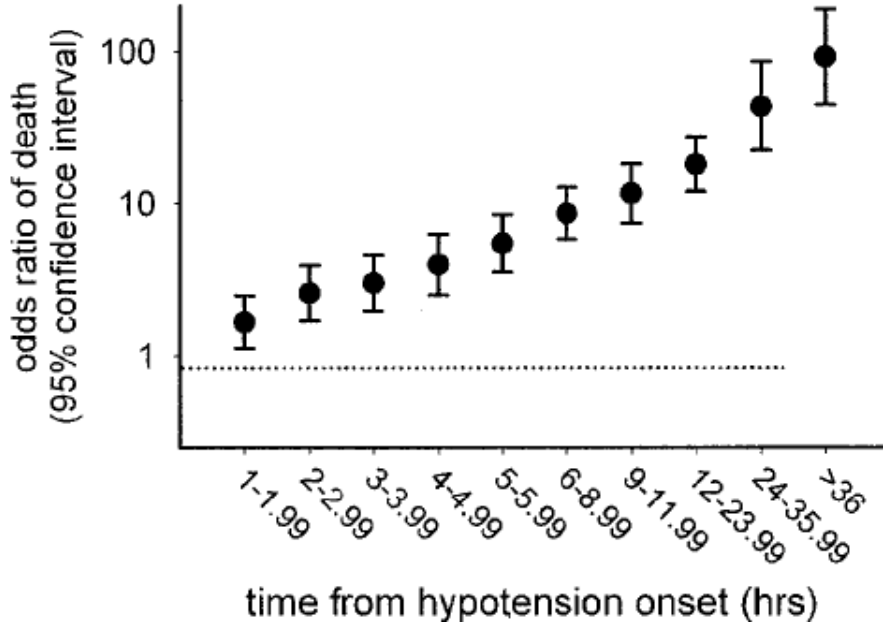
B Cumulative Mortality to 1 Yr



No. at Risk							
Protocol-based EGDT	439	289	217	194	175	156	145
Protocol-based standard therapy	446	308	212	196	179	158	142
Usual care	456	285	211	199	181	164	139

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





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

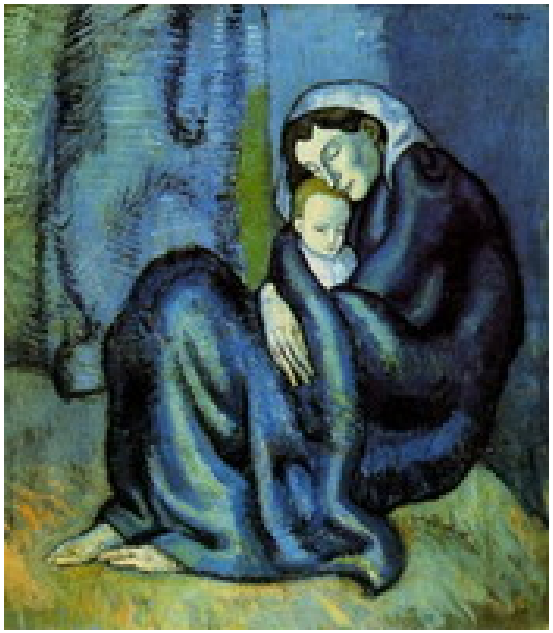
Questions I have
Lessons I have learned

- Have we forgotten this? Forgotten to teach it?
- Have we made silly decisions about staffing and ward care?
- Group A strep is more of an issue than it was
- High index of suspicion
  - Older
  - Socially disadvantaged
  - Unplanned obstetric event
  - Late intra uterine death
  - Obese
  - Diabetic
  - Illness in family- esp. apparent URTI in children
  - Undifferentiated presentation

- Escalation commonly slow

Questions I have
Lessons I have learned

- Presentation seems rarely “typical”
- Delayed re-admission
- Pain, confusion
- Lab tests not specific
  - Low WCC and platelets (watch for TTP)
  - Clotting abnormalities
  - ?? Reluctance to test
  - Results slow or not chased
- “Feel” very important
- “Road trips” for investigations…….!!!!
- Clinical trials virtually impossible
- Role of IVIG



Pablo Picasso 1901 onwards…….