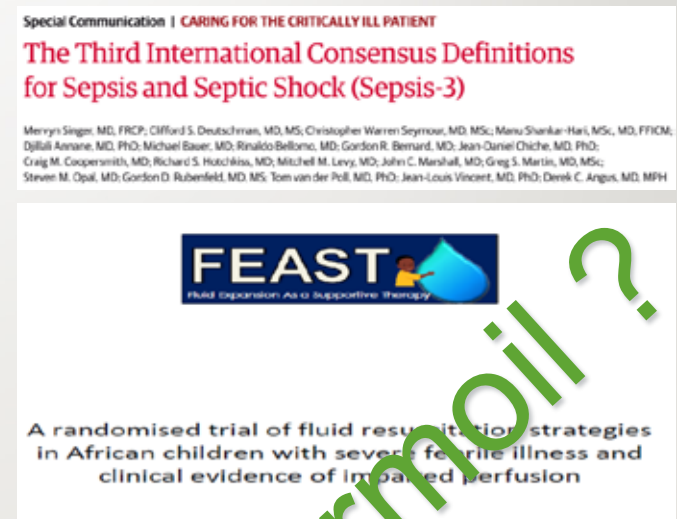


Sepsis in the tropics

– a constantly changing and challenging topic –



UNIVERSITY OF MALAWI
Department of Anaesthesiology and Intensive Care

Humanitarian Symposium on Development Cooperation and Humanitarian Aid Munich 2018

Gregor Pollach (Assoc. Prof. M.A.,M.A.,FCAI hon.)

turnmoil?

Importance:

- In Germany 56.000 deaths/year (36 %), almost as MI (sepnet).
- In Europe 146.000 deaths/year (sepnet-?).

- Worldwide 500.000 deaths/year (sepnet -??).
- 75% of sepsis deaths in low-income countries (Cheng 2008)
- 90% of trauma deaths in low-income countries (Mock 2005)
- Published data suggest, sepsis causes 10% of maternal / 26% of neonatal deaths – underestimated due to methodological limitations.”(Seale 2009)

Definitions (Adult)

Sepsis

- Documented or Suspected Infection
- 2 or more of
Fever/ hypothermia, HR>90, RR>20, WBC >12 or <4

Severe Sepsis

- New Organ Dysfunction
- Hypoperfusion (lactate >2.1, decreased capillary refill)

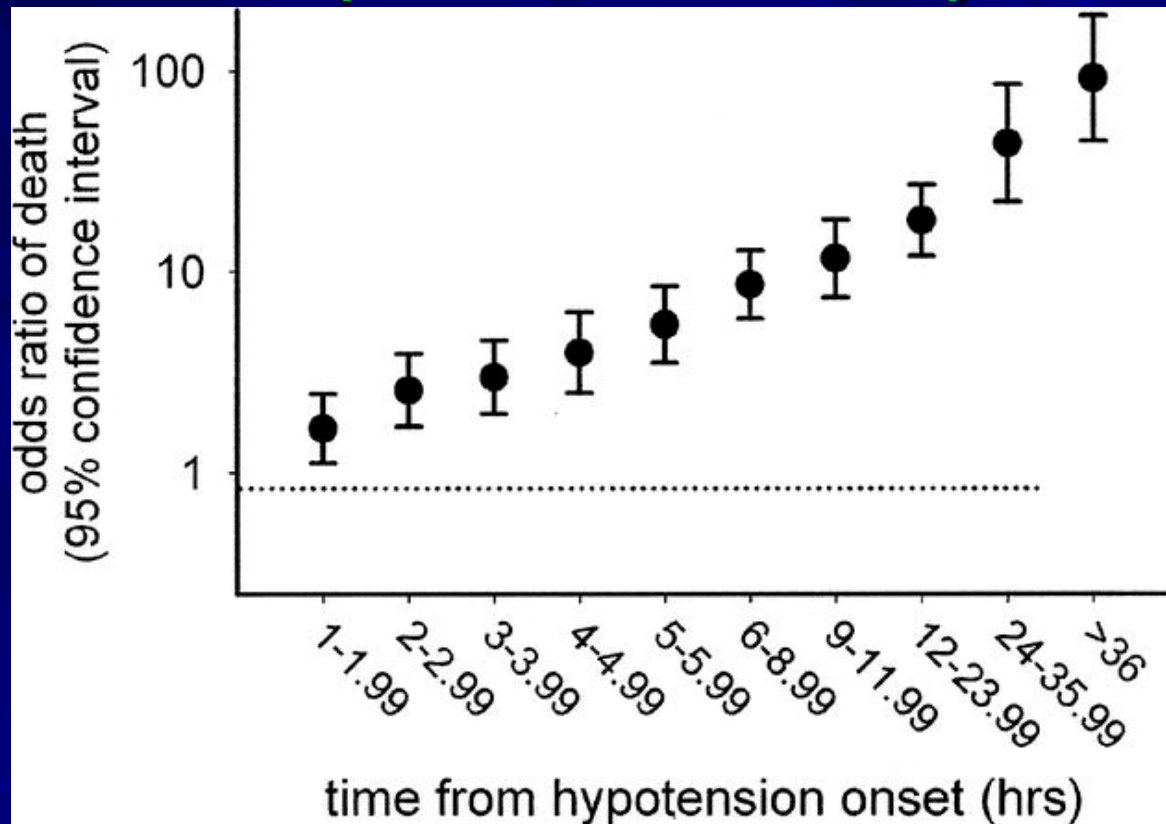
Septic Shock

- Arterial hypotension (SBP<90, MAP<70) **DESPITE** adequate resuscitation (CVP>12)

BONE Clinics in Chest Medicine, Volume 17, Issue 2, Pages 175-181 R.

Two important papers:

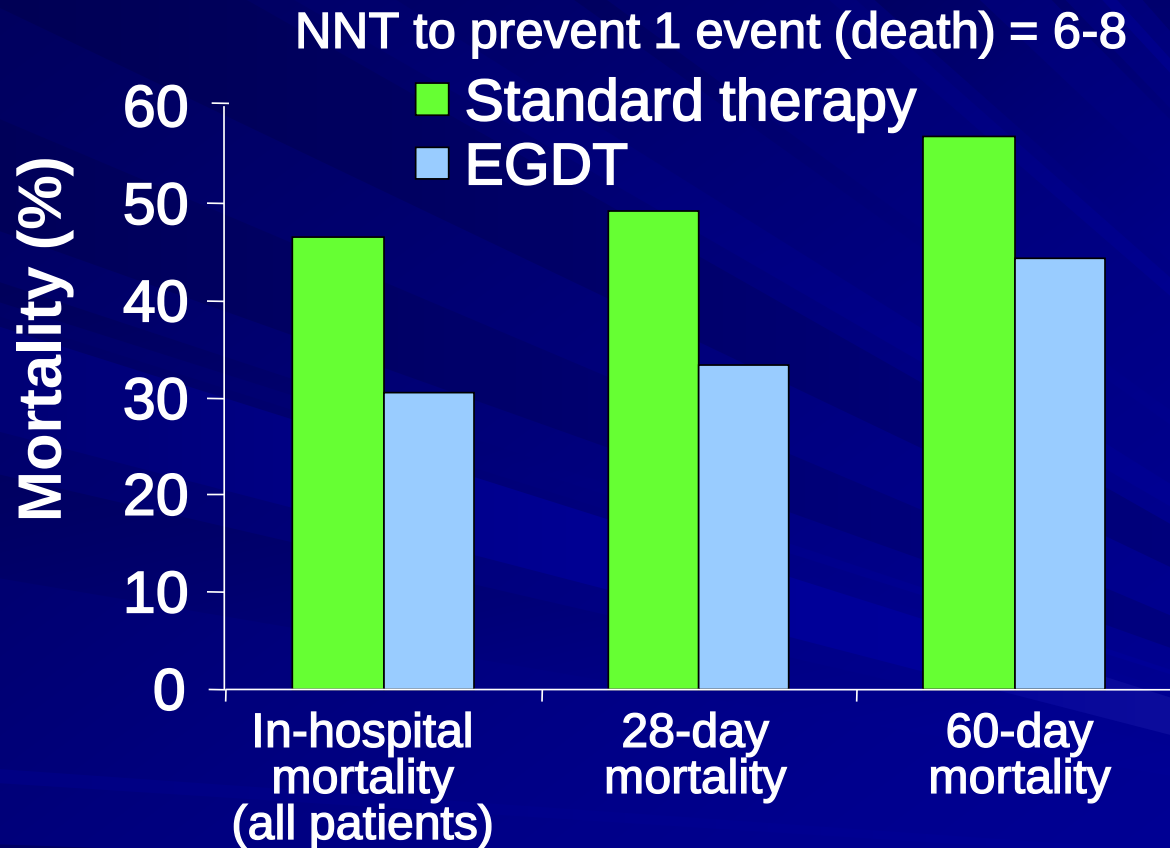
1. Start of antimicrobial therapy in sepsis (infection control)



Mortality risk (expressed as adjusted odds ratio of death) with increasing delays in initiation of effective antimicrobial therapy. Bars represent 95% confidence interval. An increased risk of death is already present by the second hour after hypotension onset (compared with the first hour after hypotension). The risk of death continues to climb, though, to >36 hrs after hypotension onset.

From: Kumar: Crit Care Med, Volume 34(6).June 2006.1589-1596

2. Recommendations for initial resuscitation through EGDT



Rivers E, Nguyen B, Havstad S, et al. : Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368-1377

Initial recommendations - EGDT

Goals during first 3 - 6 hours:

A) Infection control:

Source control / Bloodculture

Broad spectrum antibiotics



B) Resuscitation:

1. CVP of < 8 : Fluid Bolus -12 /often 50ml/1.h/kg)

2. MAP still < 65 : Vasopressor (NA)

**3. ScvO₂ still $< 70\%$: Hct < 30 : Blood transfusion
Hct > 30 : Cardial support (Dob.)**

4. Lactate measurement ($< 1,5\text{mmol/l}$) / Urine $> 0,5\text{ ml/kg/h}$

J.) Scrutinizing is always good - EGDT nowadays:

- **ARISE (2014):**
No advantage of EGDT
- **ProCESS (2014):**
No advantage of EGDT

Ø **Cave:**

ScvO₂: 

Volume: 

Management: 

Surviving sepsis in the tropics is a little bit different

1. Different disease patterns

Crocodile bites



Snake bites



“MAI- Syndrome”



- Malnutrition
- Anemia
- Infection

TB - spine

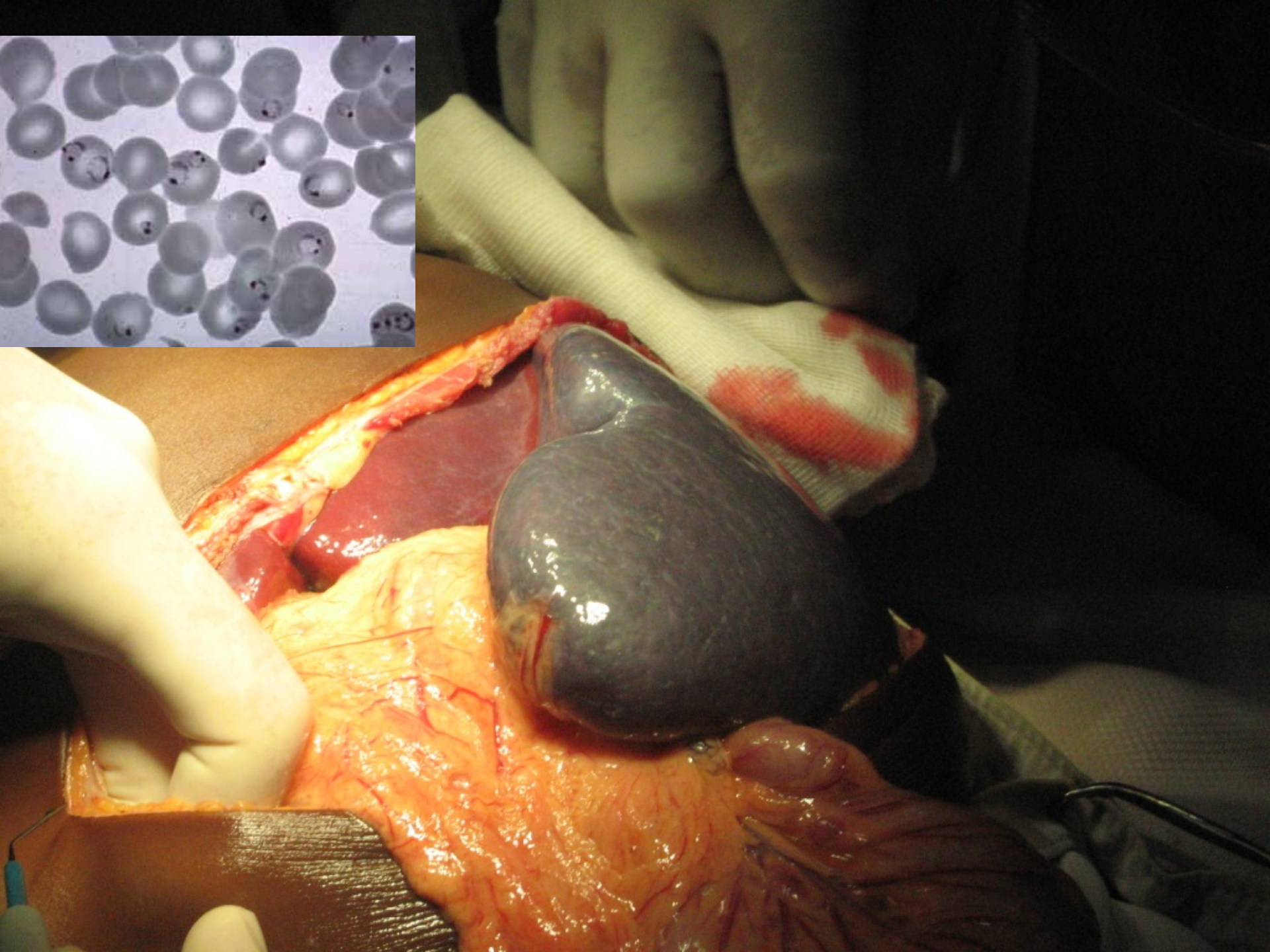


Surviving sepsis in the tropics

2. Different combinations of diseases

Sepsis and -





Schistosomiasis as underlying condition is often neglected



Syndrom of multiple infections



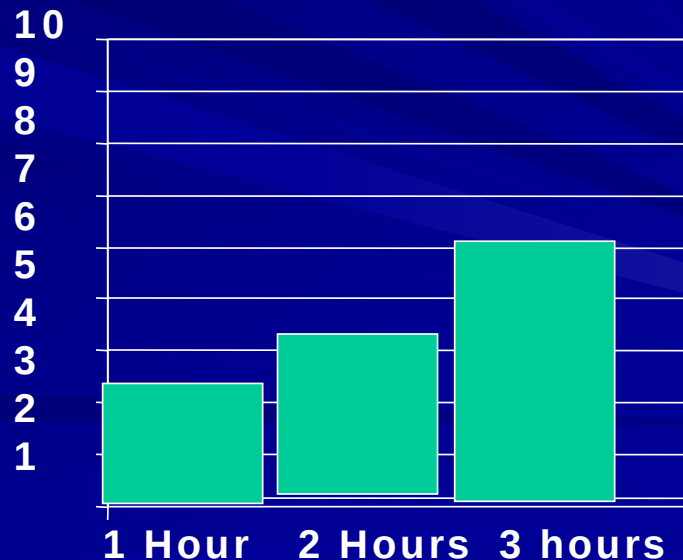
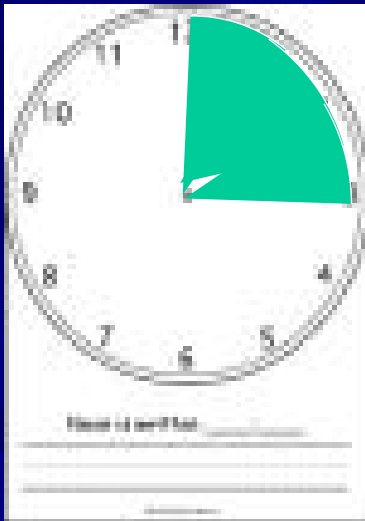
- Tetanus
- Syphilis
- HIV +
- Malaria
- Pneumonia
- >>Sepsis

Surviving sepsis in the tropics

3. Different ages of our patients

Children: Rivers is “called”: Han / Carcillo

After adjustment for Patient Severity:
Every hour without appropriate resuscitation and
restoration of capillary refill < 2 s and normal
blood pressure increases mortality risk by 40%!
(Han et al Pediatrics 2003)





Wonderful – we know what to do !

A randomised trial of fluid resuscitation strategies
in African children with severe febrile illness and
clinical evidence of impaired perfusion

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

JUNE 30, 2011

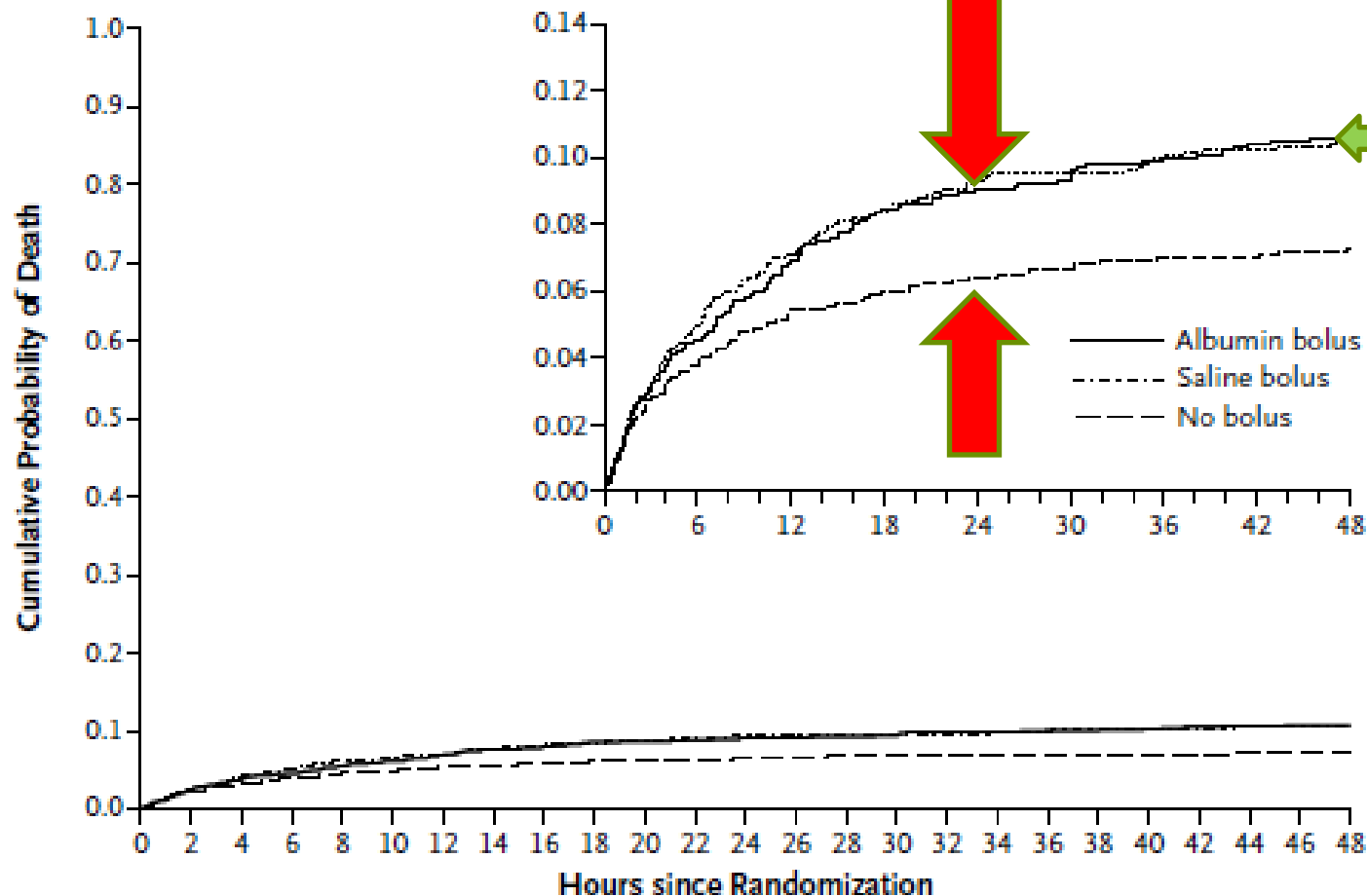
VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

A Mortality at 48 Hours

Primary
End
point:
48 hrs
mortality



	Hr 1			Hr 2			Hr 3			Hr 4			Hr 5-8			Hr 9-24			Hr 24-48		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	1037	1033	1030	1024	1018	1021	1016	1010	1015	1010	1001	1011	992	980	996	954	945	975
Died	13	12	14	13	15	9	8	7	6	6	9	4	17	20	14	38	34	20	16	13	9
%	1.2	1.1	1.3	1.3	1.5	0.9	0.8	0.7	0.6	0.6	0.9	0.4	1.7	2.0	1.4	3.8	3.5	2.0	1.7	1.4	0.9



From the study protocol:

	ALBUMIN-BOLUS			
	all fluids	Bolus	Blood	Maintenance
Total number enrolled.	1050	1050	1050	1050
Total fluid received in first 1 hour				
number of children that received fluid (%)	1045 (99%)	1045 (99%)	26 (2%)	10 (1%)
median amount of fluid (IQR) mls/kg/hr in those that received fluid	20 (20,20)	20 (20,20)	(0.07, 1.5)	0.06 (0.06, 2.2)
mean amount of fluid (sd) mls/kg/hr in those that received fluid	22.2 (6.6)	22.2 (6.5)	1.7 (4.0)	1.0 (1.7)
median amount of fluid (IQR) mls/kg/hr in all children alive	20 (20,20)	20 (20,20)	0 (0, 0)	0 (0, 0)
mean amount of fluid (SD) mls/kg/hr in all children alive	22.1 (6.7)	22.1 (6.7)	0.04 (0.7)	0.01 (0.2)
Total fluid received in second hour				
number alive at beginning of second hour	1032	1032	1032	1032

NO BOLUS CONTROL			
all fluids	Bolus	Blood	Maintenance
1044	1044	1044	1044
640 (61%)	2* (0.2%)	207 (20%)	439 (42%)
2.2 (1.4, 3.2)	28.3 (12.8, 43.7)	1.9 (1.6, 4.4)	1.9 (1.3, 2.7)
2.7 (2.9)	28.3 (21.8)	3.2 (2.2)	2.3 (2.3)
1.2 (0, 2.5)	0 (0,0)	0 (0,0)	0 (0, 1.8)
1.7 (2.6)	0.05 (1.4)	0.6 (1.6)	1.0 (1.9)
1031	1031	1031	1031

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension

A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwangi Bwalya, MBChB; Gordon R. Bernard, MD

Zambia: 1500 bed hospital.

Result:

Mortality high: 48% (4l in 6hrs) / 33 % (only 2l)

But:

More than 98% never saw ICU (!) Only 15% got a vasopressor.

Most patients were malnourished, 89 % HIV reactive.

Conclusion:

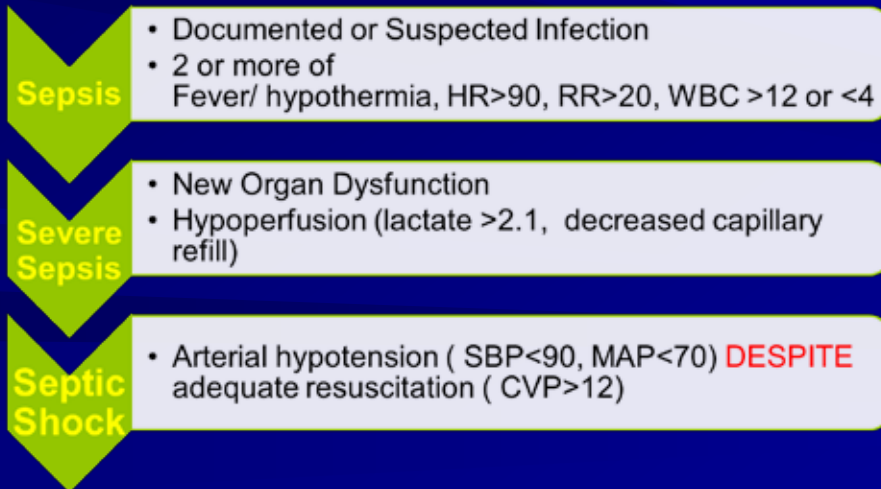
A predictable result: you administer 4 l fluids in malnourished patients with multiple comorbidities and you do not treat them adequately against sideeffects of volume - than they die.

Studies and theories finished ?

No

The 3rd International Consensus Definitions for Sepsis & Septic Shock (Sepsis-3) changed all definitions and abolished severe sepsis.
(Singer , JAMA 2016)

No more :



Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.

Sepsis is represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of ≥ 2 points, which is associated with a mortality $> 10\%$.

Severe Sepsis is not existing any longer and SIRS not either.

Septic shock is defined by a vasopressor requirement for a MAP ≥ 65 mm Hg and a lactate > 2 mmol/L without hypovolemia (mortality $> 40\%$).

Additional: The quick-SOFA (qSOFA) Score.

In emergency departments adult patients with sepsis are rapidly identified for poor outcomes if they have ≥ 2 of the following clinical criteria: RR ≥ 22 /min, GCS < 15 , systolic blood pressure ≤ 100 mm.

Why bother?

Predictive value of the qSOFA score in patients with suspected infection in a resource limited setting in Gabon



Validation Q-Sofa in Gabun: March 12 to July 13: 343 adults q-SOFA ≥ 2

Result:

Good prediction of in-hospital mortality through sepsis.

But:

Strange hospital: It means less than 0.2 patients a day...

Conclusion:

Highly selected population!

In QECH we would probably see several hundreds – **a day !!**

SOFA-Score generates too many patients in the tropics, who do **not** suffer from sepsis.

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score^a

System	Score				
	0	1	2	3	4
Respiration					
Pao ₂ /Fio ₂ , mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, ×10 ³ /μL	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose) ^b	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1 ^b	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 ^b
Central nervous system					
Glasgow Coma Scale score ^c	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio₂, fraction of inspired oxygen; MAP, mean arterial pressure; Pao₂, partial pressure of oxygen.

^a Adapted from Vincent et al.²⁷

^b Catecholamine doses are given as μg/kg/min for at least 1 hour.

^c Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

SOFA-Score generates too much sepsis in one of our most important patient groups:

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score^a

System	Score 0	1	2	3	4
Respiration					
P_{aO_2}/F_{iO_2} , mm Hg (kPa)	≥ 400 (53.3)	< 400 (53.3)	< 300 (40)	< 200 (26.7) with respiratory support	< 100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu\text{L}$	≥ 150	< 150	< 100	< 50	< 20
Liver					
Bilirubin, mg/dL ($\mu\text{mol/L}$)	≤ 1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	≥ 12.0 (204)
Cardiovascular					
MAP ≥ 70 mm Hg		MAP < 70 mm Hg	Dopamine < 5 or dobutamine (any dose) ^b	Dopamine 5.1-15 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1 ^c	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1 ^c
Central nervous system					
Glasgow Coma Scale score ^d	15	13-14	10-12	6-9	< 6
Renal					
Creatinine, mg/dL ($\mu\text{mol/L}$)	≤ 1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	≥ 5.0 (440)
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^a Adapted from Vincent et al.²²

^b Catecholamine doses are given as $\mu\text{g/kg/min}$ for at least 1 hour.

^c Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

Examples:

- Horowitz-Index: Sometimes considered normal with 350
- Blood pressure: BLH-Institute considers 90/60 as normal
- Pregnancy : 10th percentile 97 / 55
- Platelets: Some consider 140000 normal
- For $> 5\%$ of pregnant women normal.
- CNS: GCS 14 vs. Alcohol, neuro-aids, cysticercosis etc.
- Renal: Crea > 1.1 or less than 500ml output

A flu might give a pregnant lady in Africa suffering from hyperemesis gravidarum easily a SOFA –Score > 2 (10% mortality !) without any hint of sepsis.

Surviving sepsis in the tropics

Conclusions

Conclusion: - *Tropical - EGDT*

Goals during first 6 hours:

A) Infection control:

Broad spectrum antibiotics (Ceftriaxon)

Source control (chase the surgeon or diys)

B) Resuscitation:

1. CVP of < 8 : (fill them up clinically often 50ml/first h)

2. MAP still < 65 : (feel the femoral pulse and try to get NA)

3. ScvO₂ still $< 70\%$: Hct < 30 : (very pale – transfuse)
Hct > 30 : (pink – try to org. an inotrop)

Tropical supportive recommendations

C) Steroids : (maybe 3 days 200mg hydrocortison/d)
Insulin : (forget it, but feed orally and try to control it)
Protein C: (forget it)
SDD : (forget it)
Nutrition : (enteral feeding, try to have chiponde for NGT)
Others : (forget it)

D) HIV: (early therapy ?)

E) Renal replacement : (PD?,if possible use in acute renal ins.)

Tropical supportive recommendations

F) General Intensive Care :

Prophylaxis : Prevention of pneumonia, aspiration, dvt, nosocomial infections, pressure sores, contractions and gastric ulcers.

Specific therapy : Coma, myocardial insufficiency (aspiration), myocardial insufficiency, ARDS, DIC etc.

Surviving sepsis in the tropics

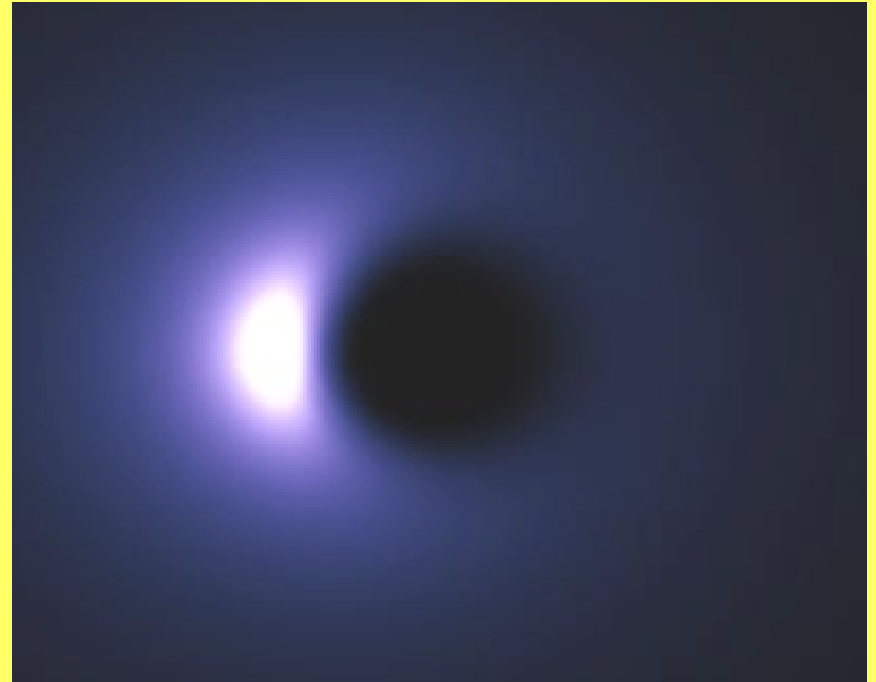
4. More challenges

(why we have to add some conclusions)

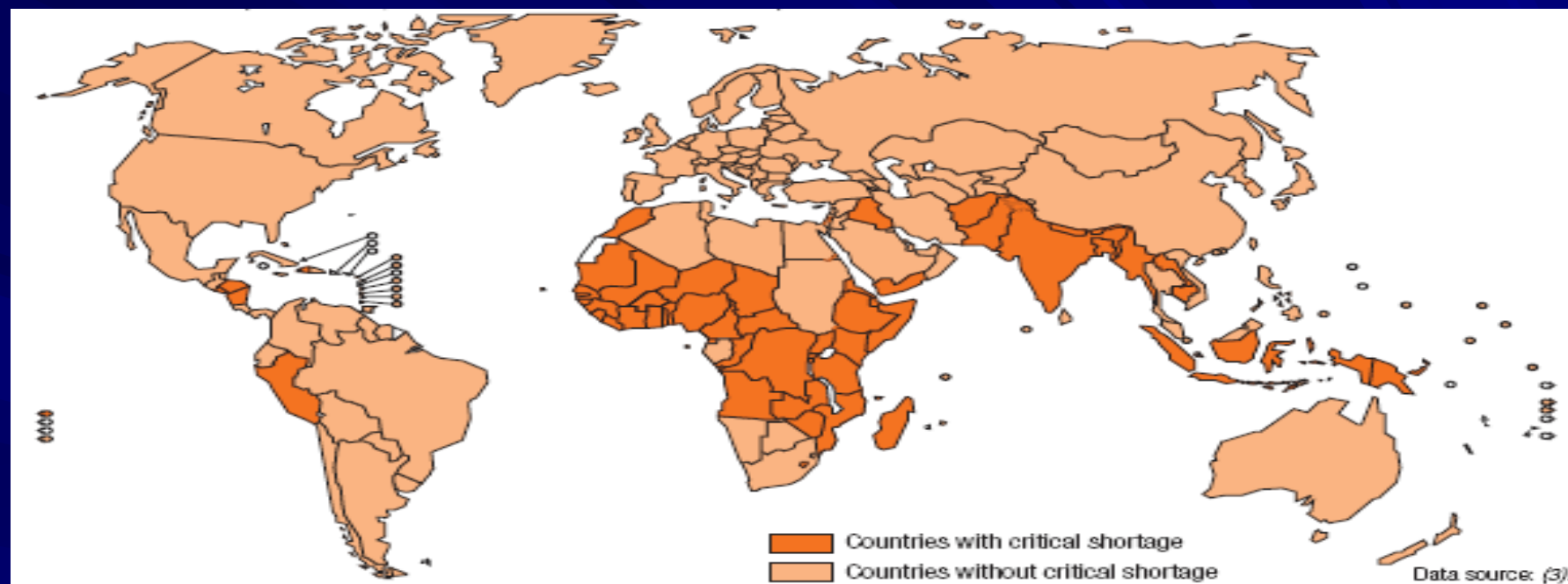
Faked drugs

Corruption

„Central medical stores“
– a black hole.



Global Shortage of Health Workers



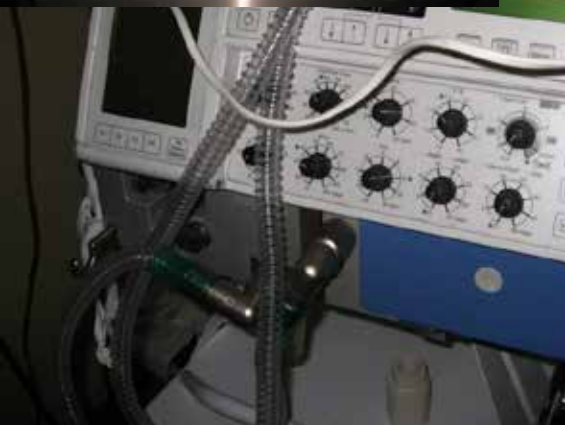
WHO region	Number of countries		In countries with shortages		
	Total	With shortages	Total stock	Estimated shortage	Percentage increase required
Africa	46	36	590 198	817 992	139
Americas	35	5	93 603	37 886	40
South-East Asia	11	6	2 332 054	1 164 001	50
Europe	52	0	NA	NA	NA
Eastern Mediterranean	21	7	312 613	306 031	98
Western Pacific	27	3	27 260	32 560	119
World	192	57	3 355 728	2 358 470	70

Equipment: Let's opt for ICU-Ventilation



2011: 40th birthday!

- ž No spare parts
- ž No maintenance
- ž Need O₂ as driving force
- ž No manual or in chinese
- ž Old and short-lived
- ž How to teach ICU nurses?



or: transport of the septic patient



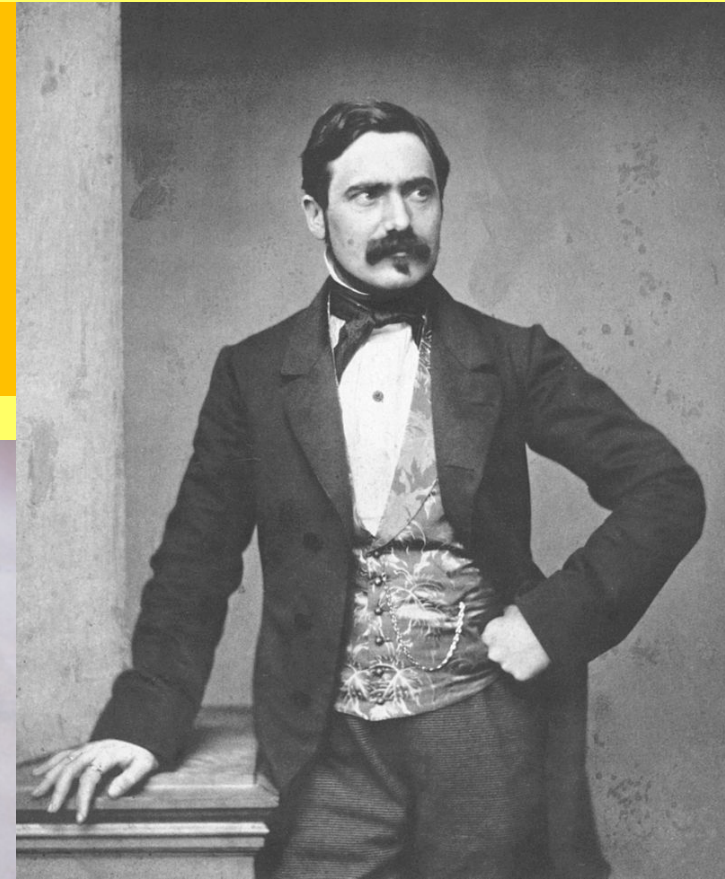
Administration of countries influencing sepsis

Broken old pipes

No rehabilitation of water systems

No clean hands

→ No infection prevention



At all times ...

Hospitals struggle amid water shortage



HEALTH RISK—City residents draw water from unsafe sources

Tropical - EGDT

- G) Transport: Improve before (referral system) and in hospital)
Triage: (later)
- H) Staff: try to educate and find ways to renumerate,
try to steal the good ones (! / ?)
- I) Education: In health centers and district hospitals
Education: Try to establish a preemptive culture in your icu
Talk: to your administration about procurement,
maintenance, repair and replacement until they
can't take it any longer.

J.) Scrutinizing...**ARISE, ProCESS, FEAST...**

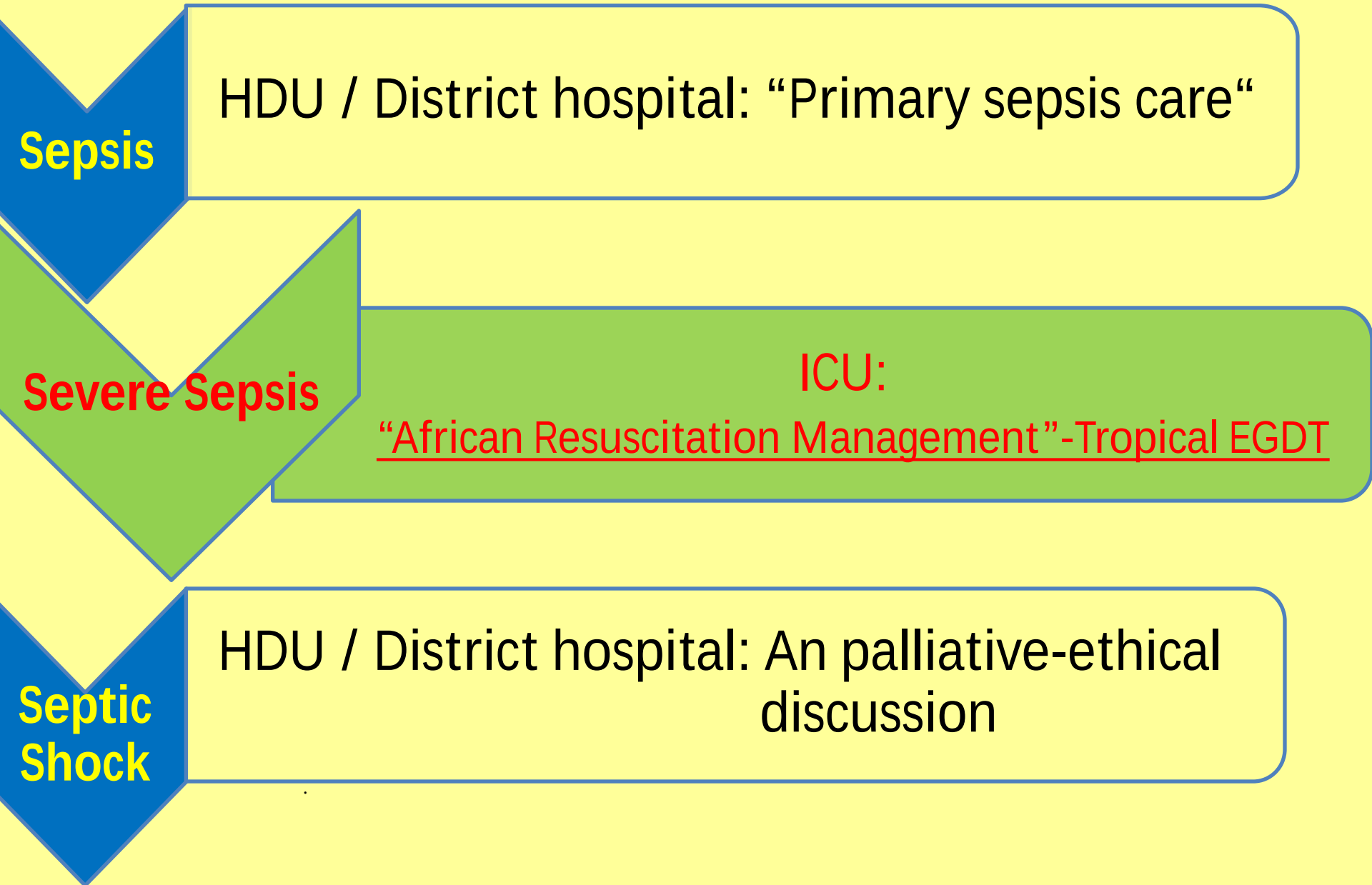
Ø **Haemodynamic monitoring and therapy:**

1. Echo/ sono for heart function and the filling of the heart and the v. cava.
2. CVP is almost out (at least for the preload).
3. More ventilation is needed.
4. Blood is volume for low HB.

Ø **Better ICU management and training:**

1. FEAST showed only (!) 10 % mortality

K.): Triage - ethics & and our precious ressources



Tokosa !



Zikomo Kwambiri !



- Sofa zu viel bei Malaria ?



Sepsis Resuscitation Bundle

The Sepsis Resuscitation Bundle describes seven tasks that should begin immediately, but must be accomplished within the first 6 hours of presentation for patients with severe sepsis or septic shock..

Bundle Element 1

Measure serum lactate

Bundle Element 2

Obtain blood cultures prior to antibiotic administration

Bundle Element 3

Administer broad-spectrum antibiotic within 3 hours of ED admission and within 1 hour of non-ED admission

Bundle Element 4

Treat hypotension and/or elevated lactate with fluids

In the event of hypotension and/or serum lactate >4 mmol/L:

Deliver an initial minimum of 20 mL/kg of crystalloid or an equivalent

Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) >65 mm Hg

Apply vasopressors for ongoing hypotension

Bundle Element 5

Maintain adequate central venous pressure

Maintain adequate central venous oxygen saturation

In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate >4 mmol/L:

Achieve a central venous pressure (CVP) of >8 mm Hg

Achieve a central venous oxygen saturation (ScvO₂) $>70\%$ or mixed venous oxygen saturation (SvO₂) $>65\%$

African Sepsis Resuscitation Bundle

The Sepsis Resuscitation Bundle should begin immediately - The African Resuscitation bundle tries to do the same

Bundle Element 1

Measure serum lactat (not available): Replace by an “Organizing bundle”:

a) Improve: communication before admission, triage (HDU,ICU,non), referral,

transport conditions and staffing levels.

b) Concentrate on the continuous availability of FBC, E'lytes, BS, US, x-ray, HIV, Tb,

malaria testing, pulse oxymeters and - PEP (!)

c) FOCUS!!! - Focus eradication, Focus on implementation of resources



you have, Focus on control of wrong foci

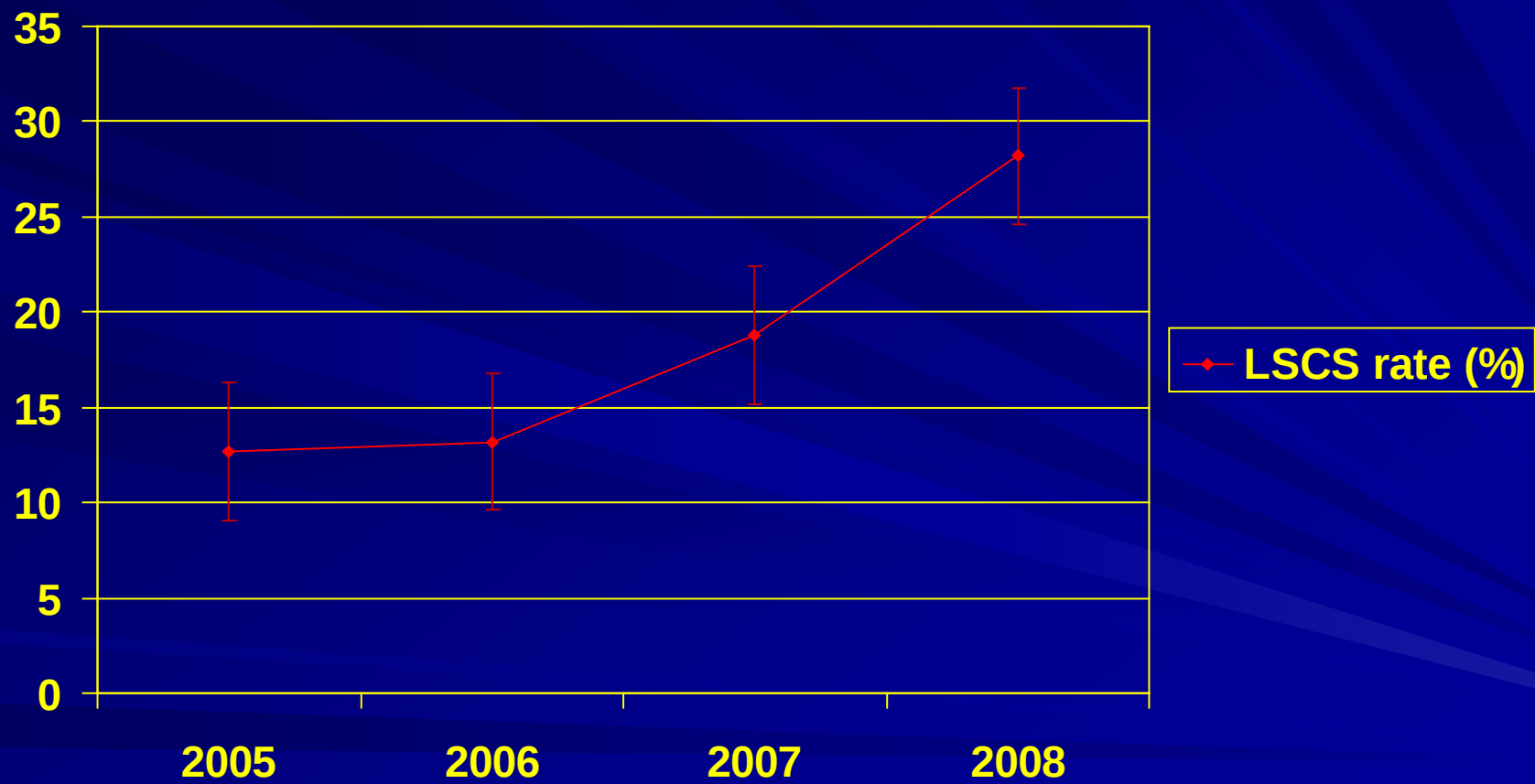
Bundle Element 2

Obtain blood cultures prior to antibiotic administration

a) Obtain blood cultures when possible and consider additional tests for:

1.: HIV, CD4, 2.: MPS, 3.: TB, 4. Pregnancy

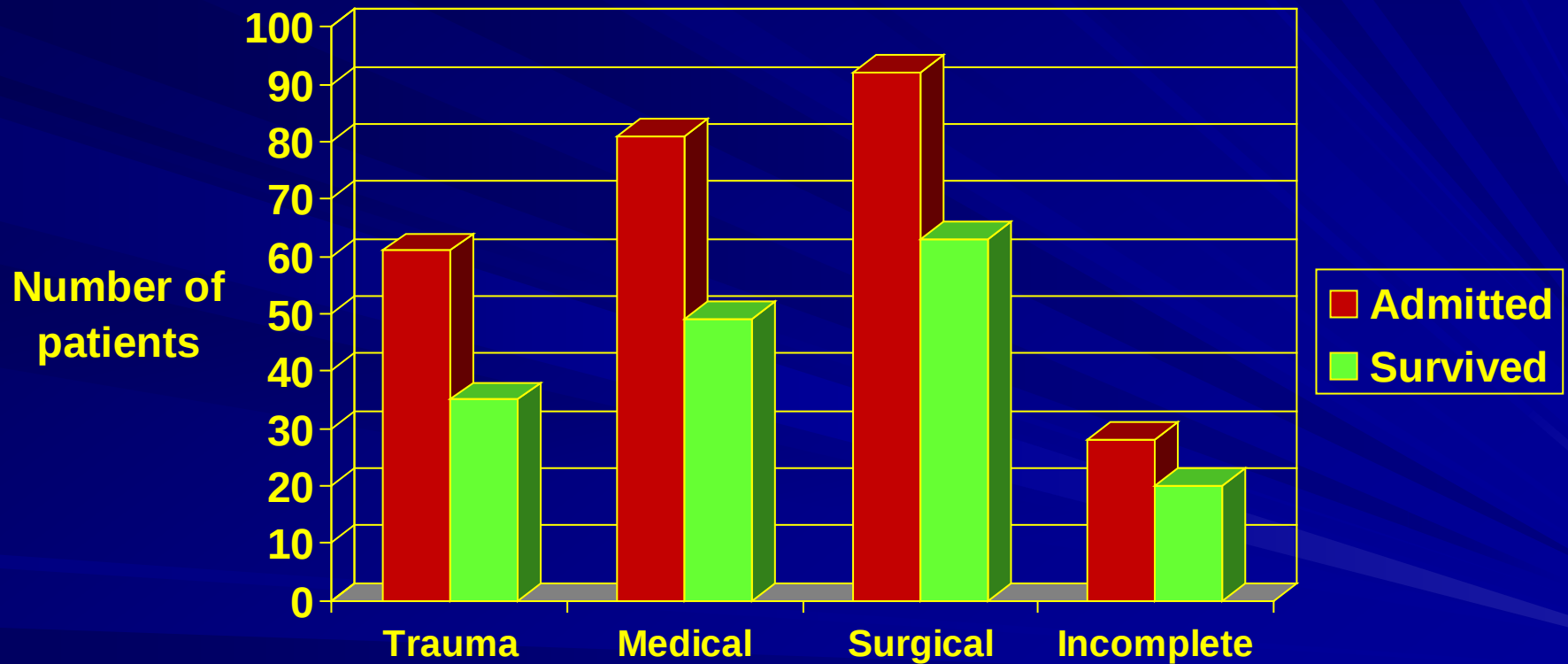
b) Organize focus control:” asap is not tomorrow”, “diys”



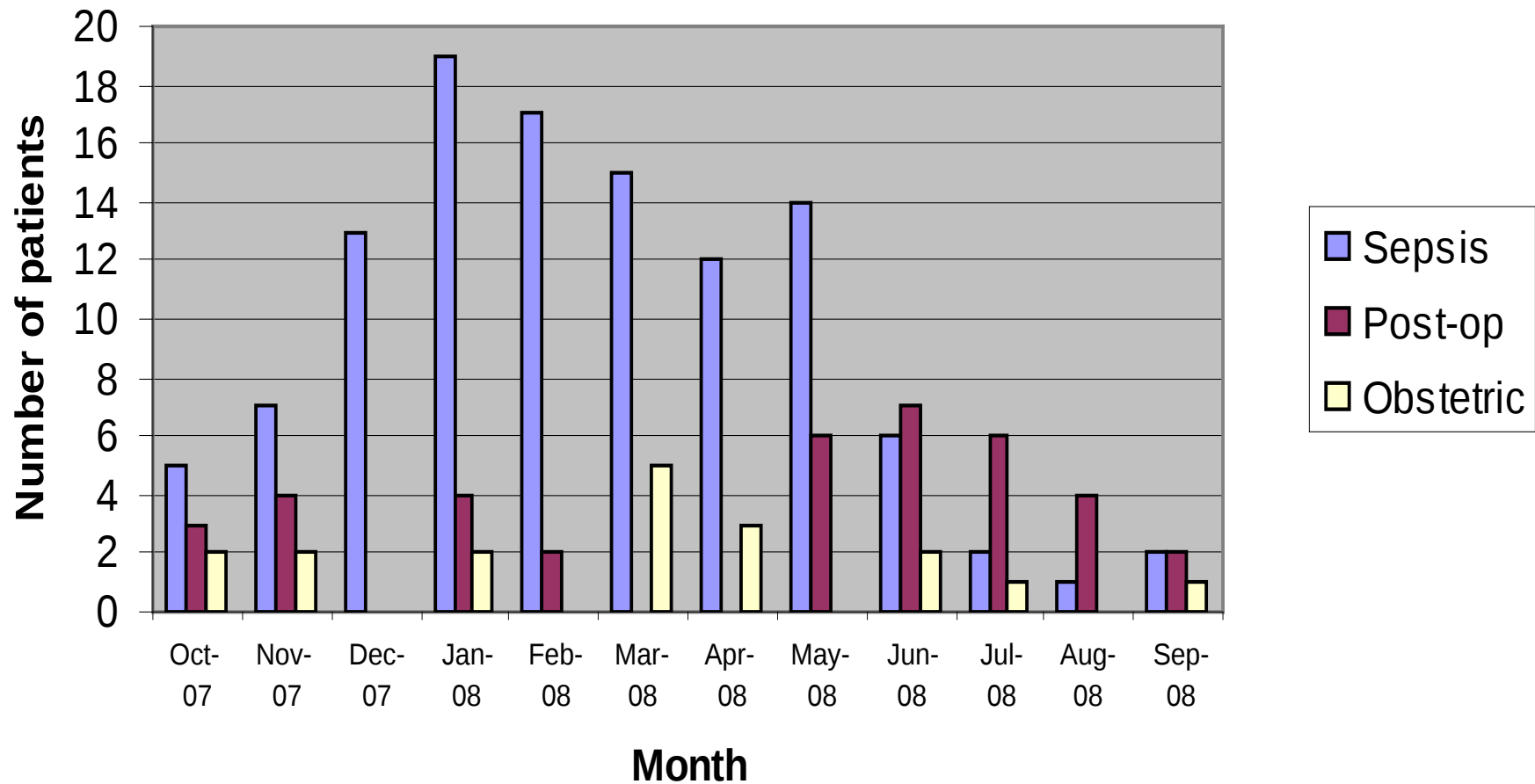
Current supportive recommendations

- C) Steroids : Annane et al. JAMA 02: yes, confirmation ?
(maybe 7 days 200mg hydrocortison/day, reduce)
 - Insulin : van d. Berghe et al. NEJM 01: yes, mortality up?
(feeding, monitoring, <150)
 - Protein C: Bernard NEJM 01: yes, Apache low/surgery30d ?
(for the very sick in first 24 h)
 - Others : AT3, Se, NAC, Pentoxifyllin, ... : no proof !
- D) Renal replacement : Not prophylactic, but in acute insuff.

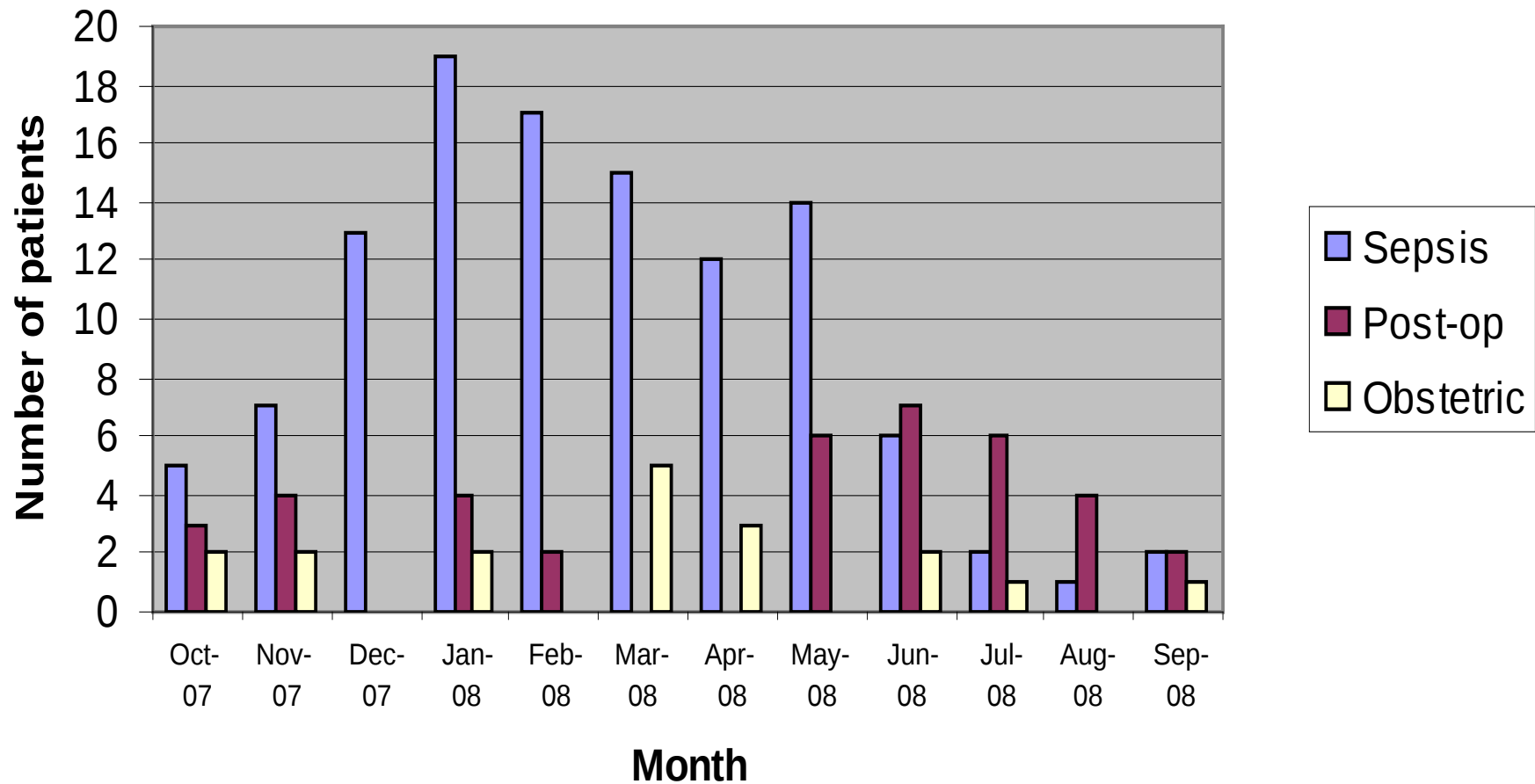
Surviving rates



Reason for admission



Reason for admission



Definitions (Adult)

Sepsis

- Documented or Suspected Infection
- 2 or more of
Fever/ hypothermia, HR>90, RR>20, WBC >12 or <4

Severe Sepsis

- New Organ Dysfunction
- Hypoperfusion (lactate >2.1, decreased capillary refill)

Septic Shock

- Arterial hypotension (SBP<90, MAP<70) **DESPITE** adequate resuscitation (CVP>12)

BONE Clinics in Chest Medicine, Volume 17, Issue 2, Pages 175-181 R.

Surviving sepsis in the tropics

4. Beyond medicine

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension

A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD

- Zambia: 1500 beds, but only 212 patients in 13 months?
- Mortality high: 48% / 33 %, only in <15% vasopressors (6 hrs)?
- Small study – in FEAST the results changed after 600 children
- 89 % HIV reactive (only 50% on treatment)
- Most malnourished (!) rr artificially low
- Dopamine, 208 not on ICU (!)
- Malaria?, 40% TB, long to enrollment, wann tod?
- Todesursachen?

a) Therapy of sepsis needs a “preemptive culture” :

- 1. Procurement :** Long, bureaucratic, complicated processes
- 2. Maintenance :** Knowledge, spare parts, efforts made
- 3. Replacement :** No communication, no accountability
- 4. Ressource-management :** bad for scarcity ressources
- 5. Prioritisation :** or the question „what is an emergency“
- 6. Centralisation :** No decisions on local level



b) Why do they present so late ?

Negligence, lack of education, low value of women

Who cares for the Maize - their only livelihood

A pregnant woman has five other children at home to care for

Transport is expensive (Minibus to hospital- a weekly wage !

Belief in witchcraft, Prolonged traditional treatment

- Great souls do suffer quitely“ (F.S.) -

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension

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Zambia: 1500 bed hospital.

Result:

Mortality high: 48% (4l in 6hrs) / 33 % (only 2l)

But:

More than 98% never saw ICU (!) Only 15% got a vasopressor.

Most patients were malnourished, 89 % HIV reactive.

Conclusion:

A predictable result: you administer 4 l fluids in malnourished patients with multiple comorbidities and you do not treat them adequately against sideeffects of volume - than they die.

In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute a new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less.

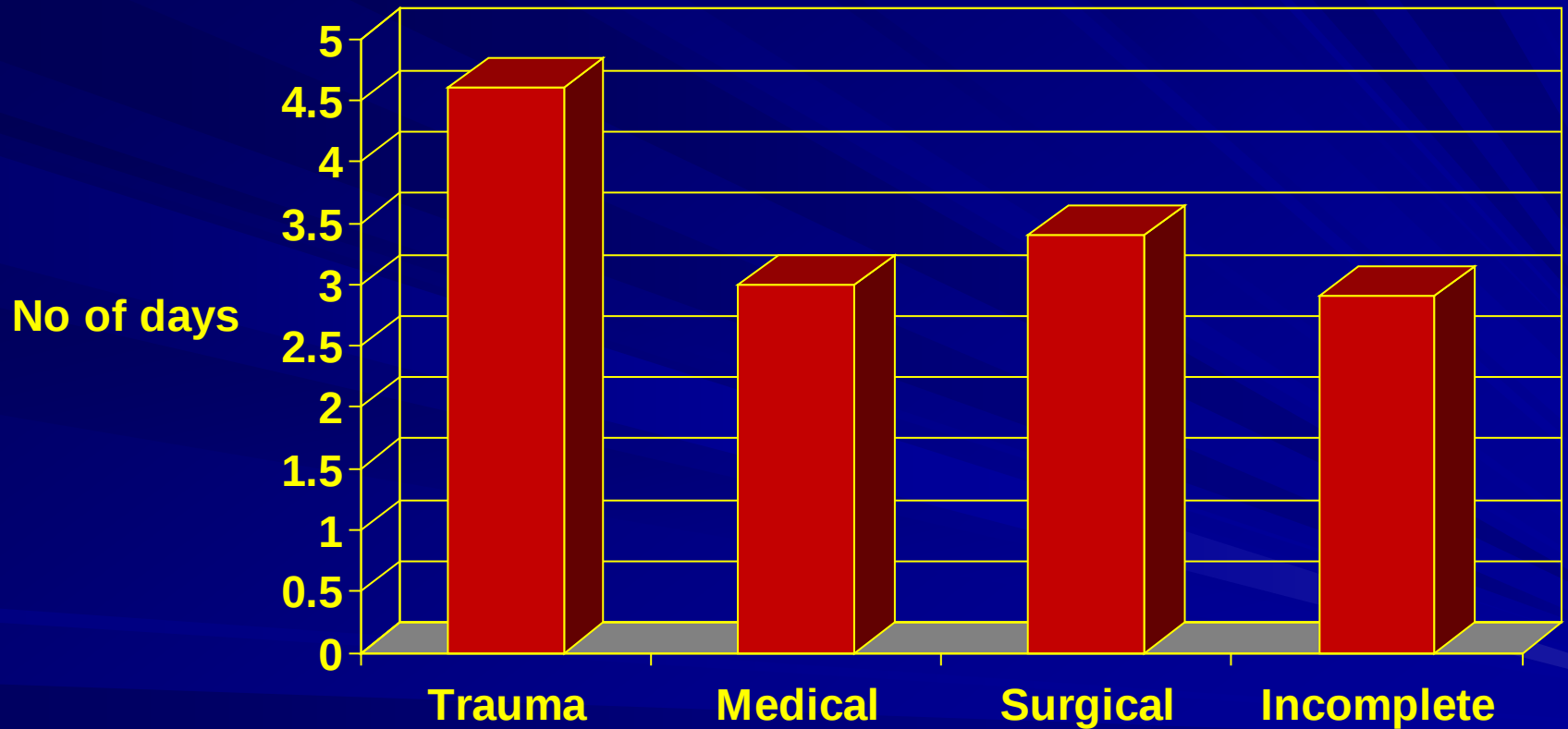
tion is consistent with the view that cellular defects underlie physiologic and biochemical abnormalities within specific organ systems. Under this terminology, "severe sepsis" becomes superfluous.

But:

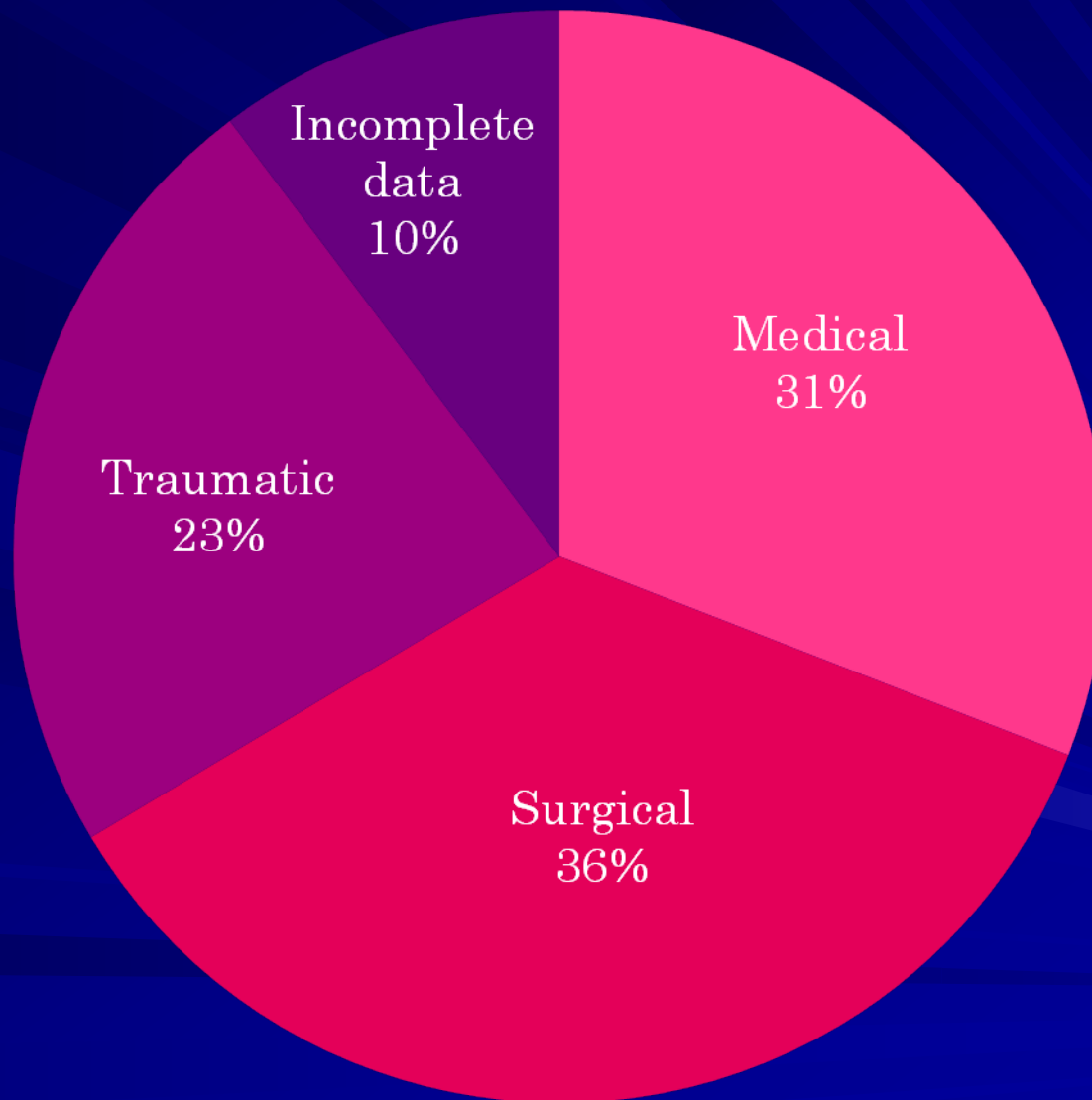
Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥ 2 points consequent to the infection.
 - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
 - A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.

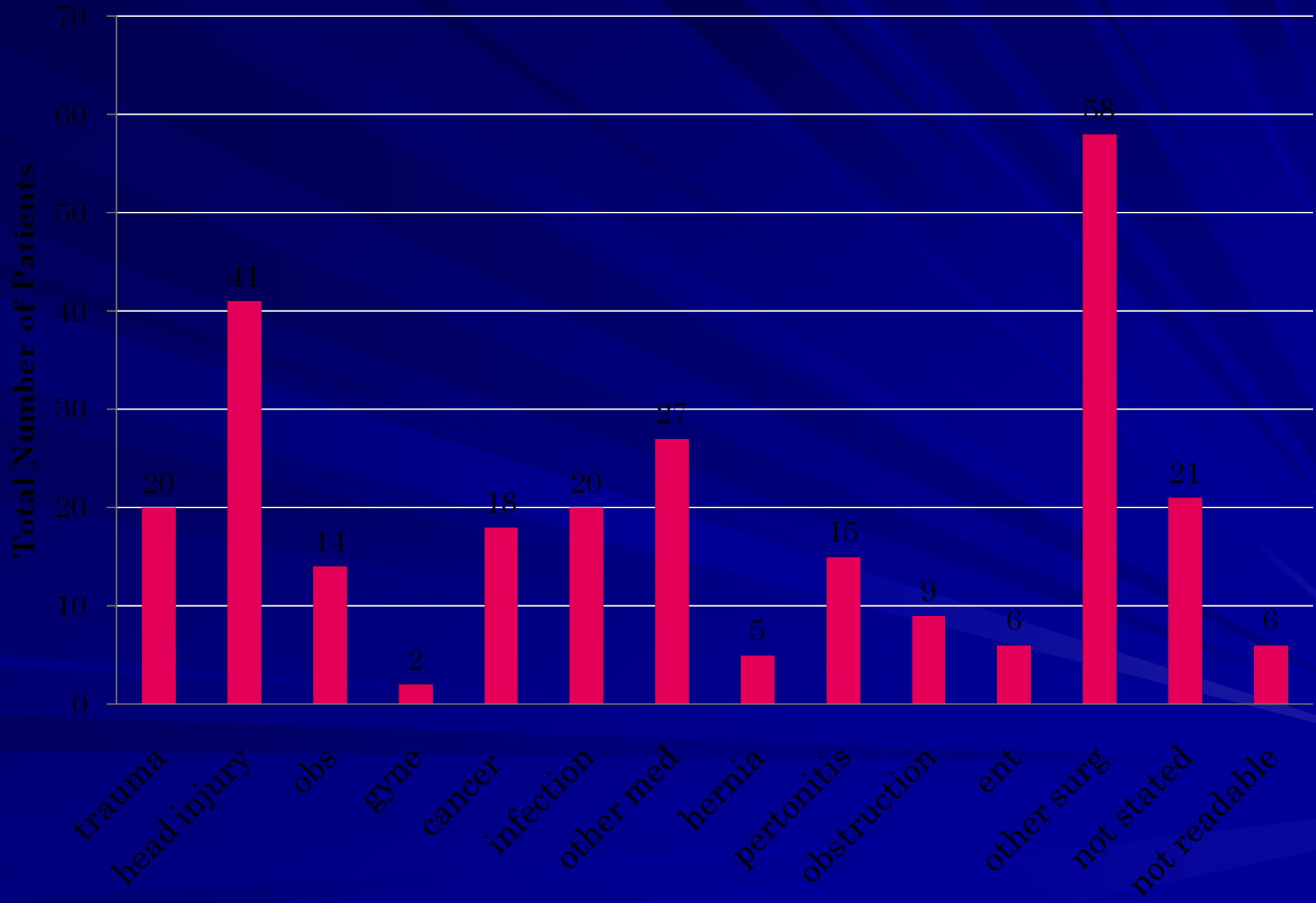
Length of stay



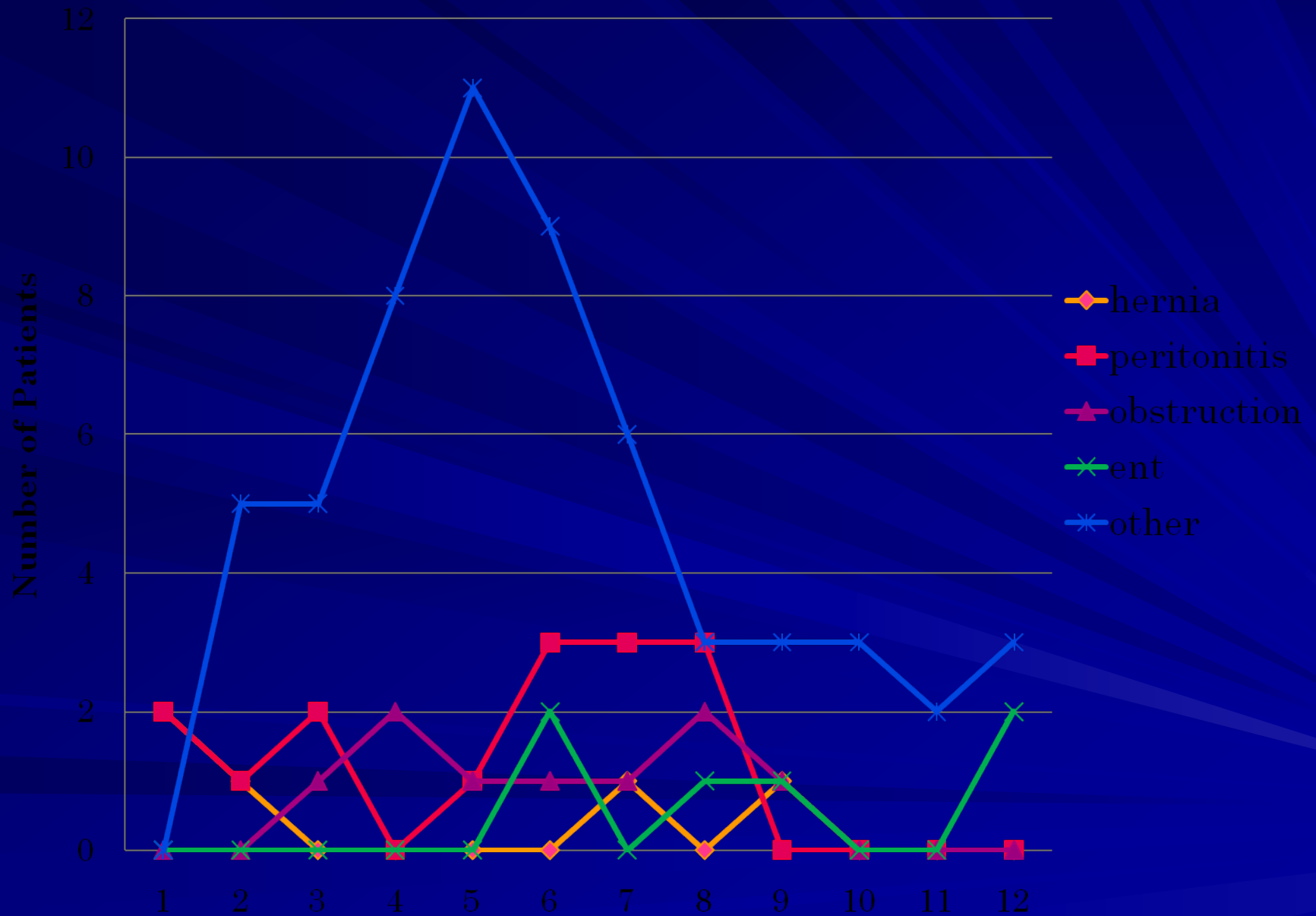
Total Admissions 06-07



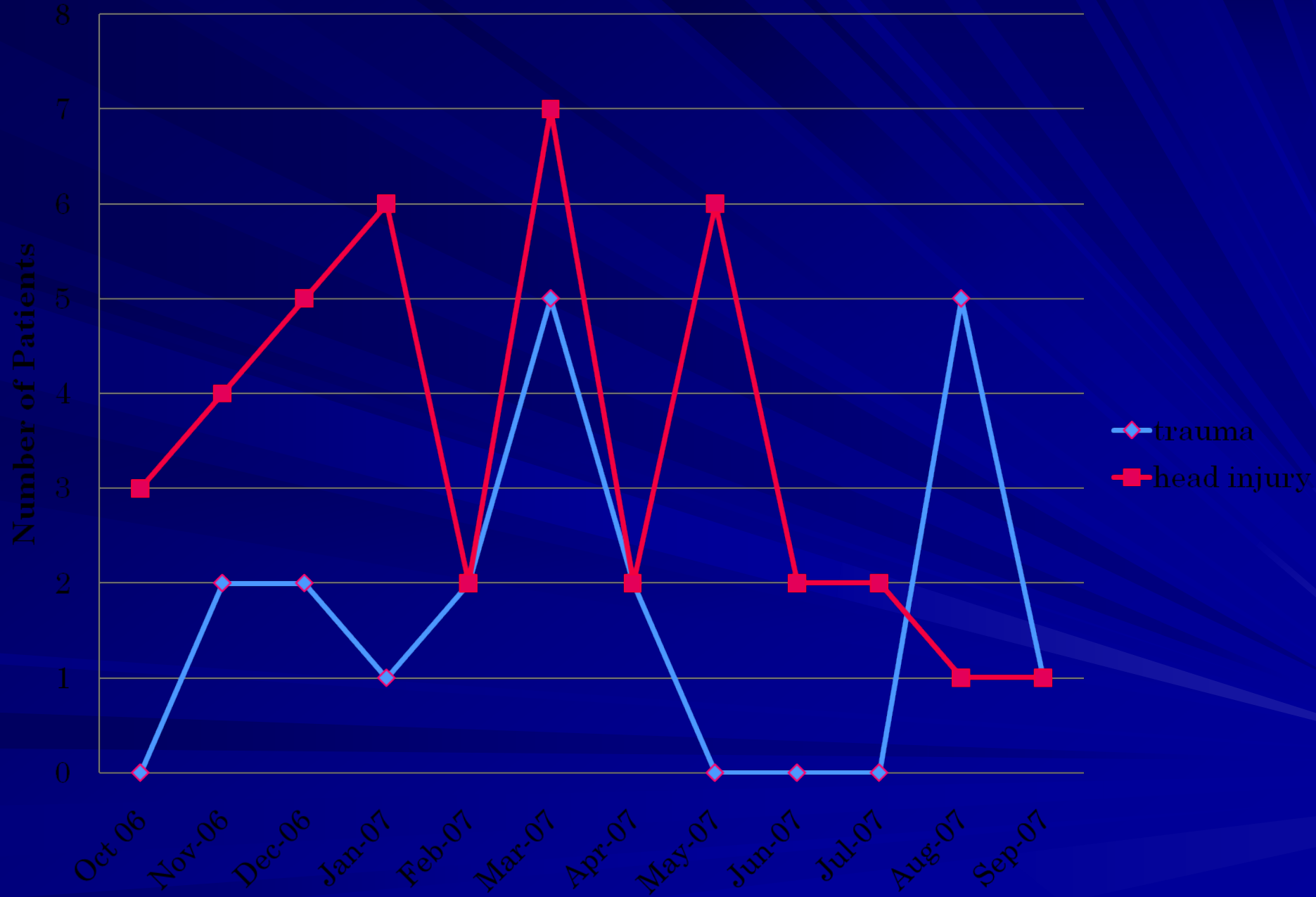
Reason for Admission 06-07



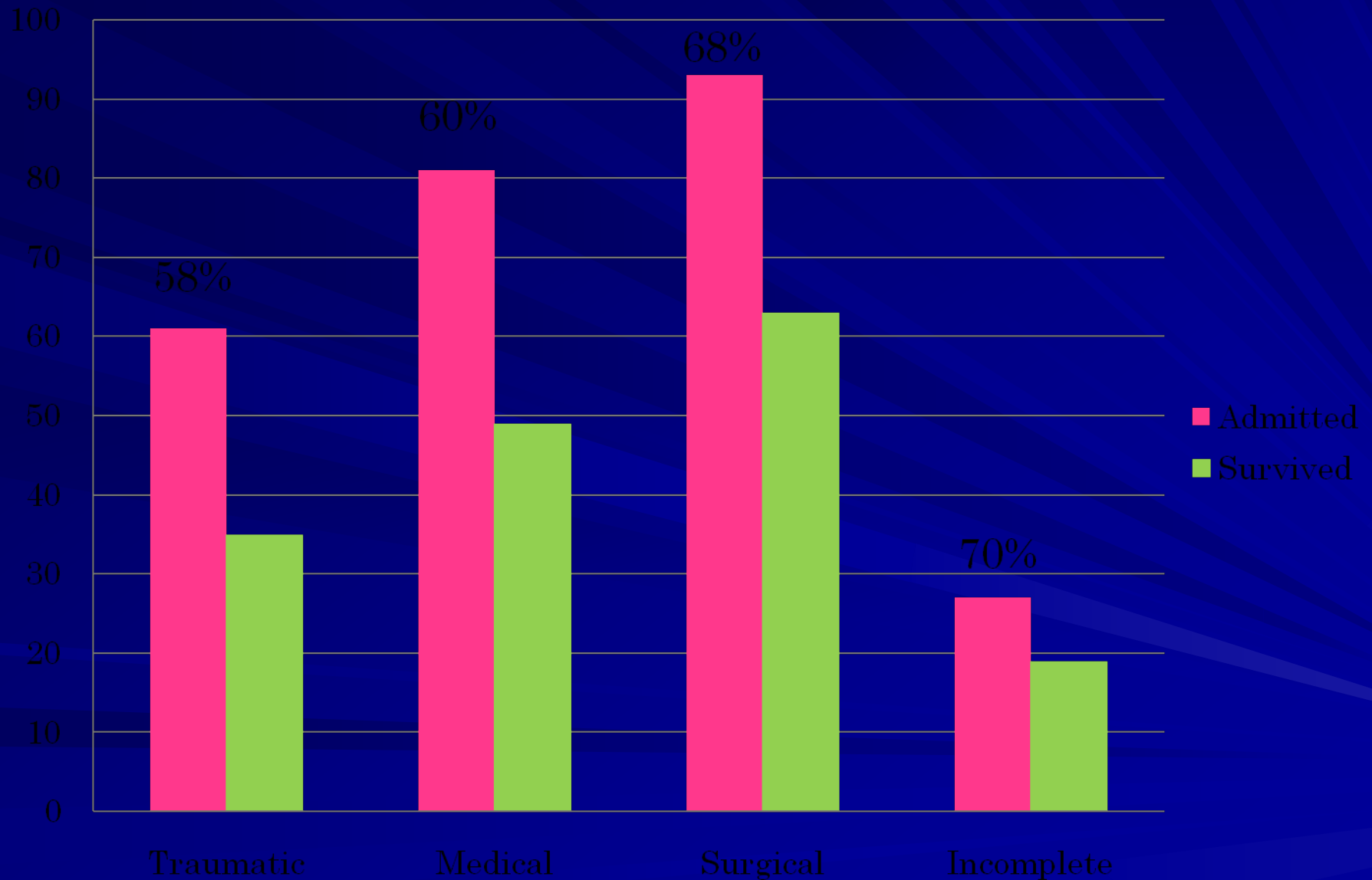
Surgical Admissions 06-07



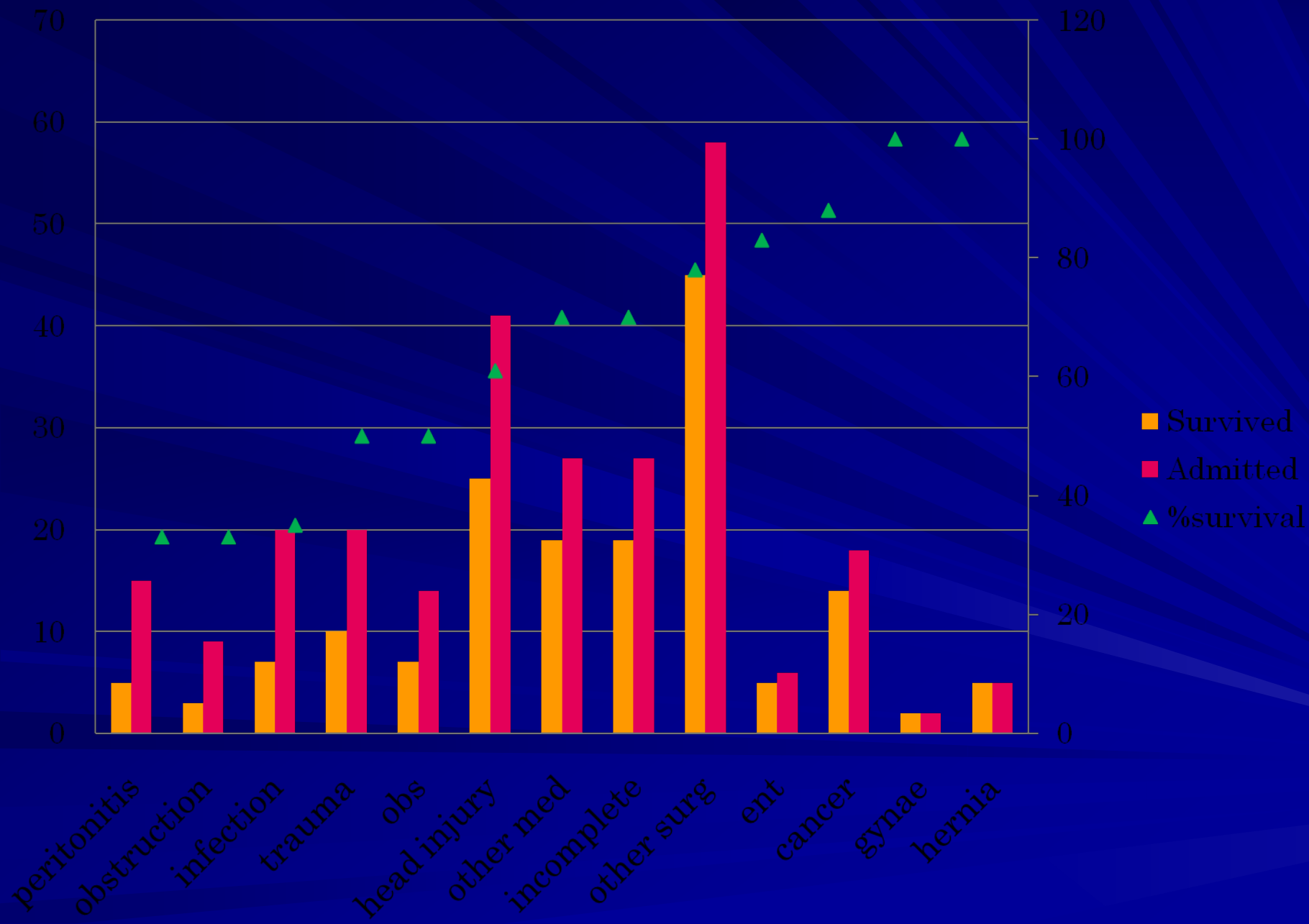
Traumatic Admissions 06-07



Survival Rates in Comparison to Admissions



Percentage Survival to Admission

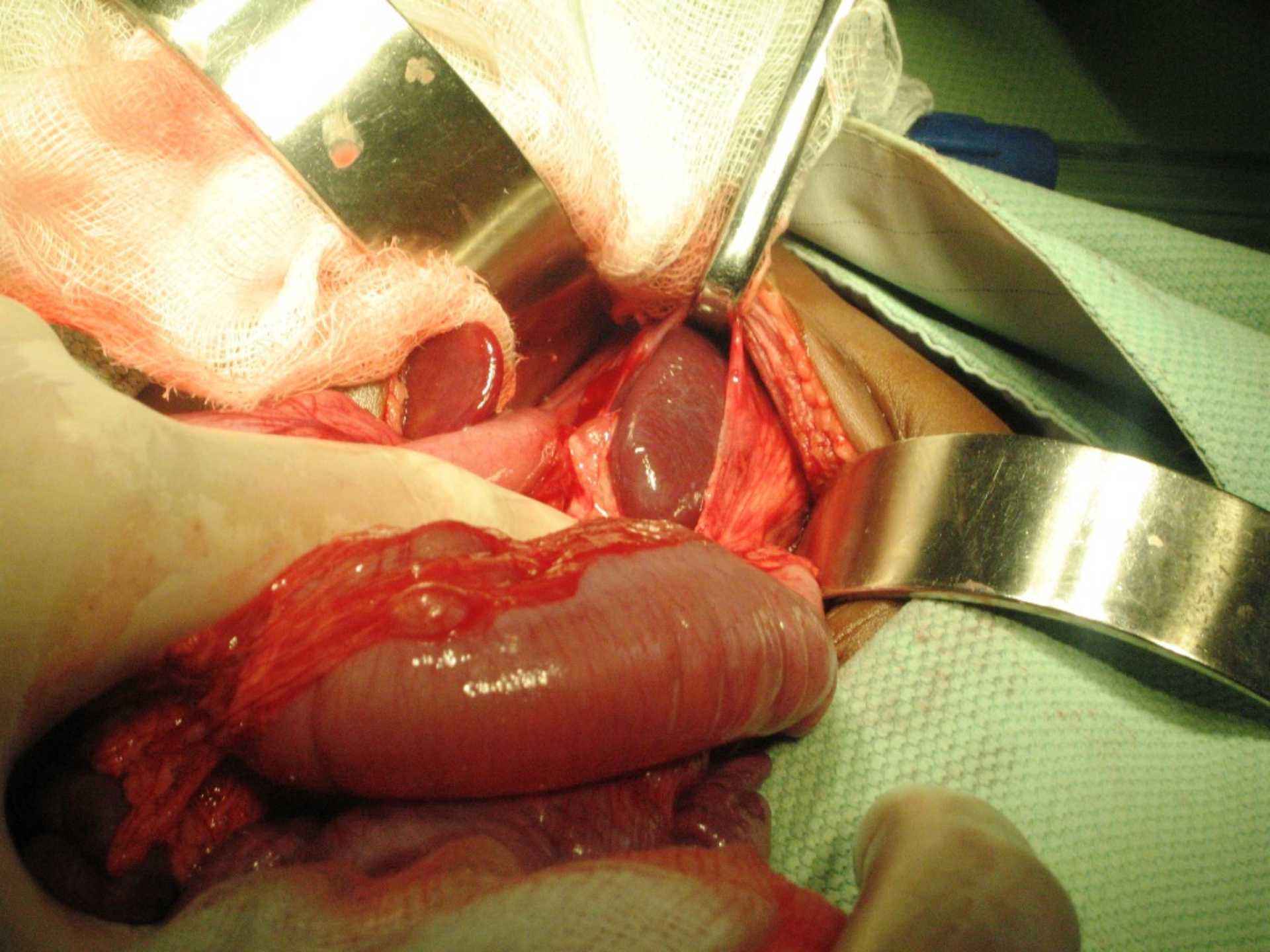


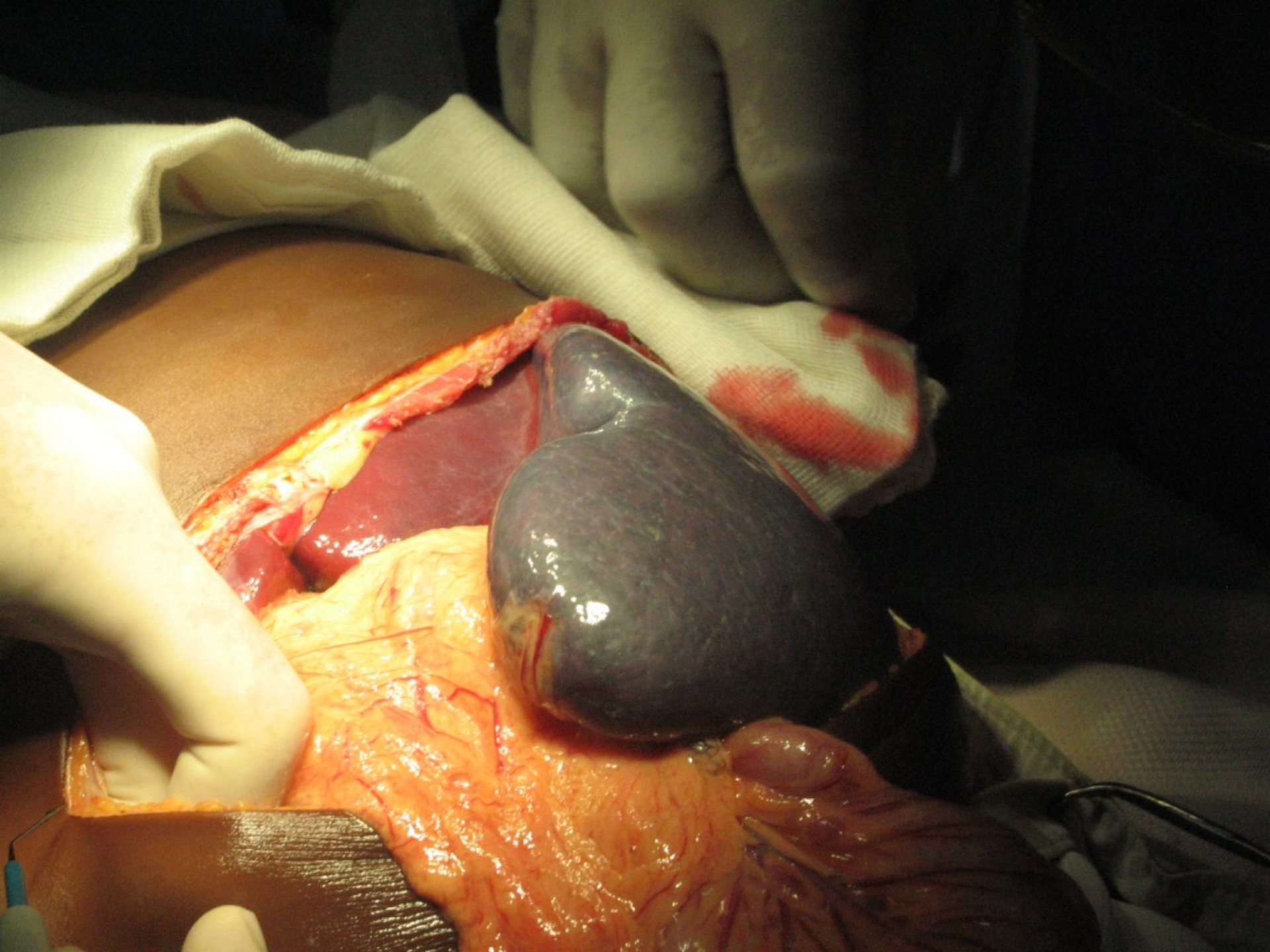
































Mitchell M. Levy
R. Phillip Dellinger
Sean R. Townsend
Walter T. Linde-Zwirble
John C. Marshall
Julian Bion
Christa Schorr
Antonio Artigas
Graham Ramsay
Richard Beale
Margaret M. Parker
Herwig Gerlach
Konrad Reinhart
Eliezer Silva
Maurene Harvey
Susan Regan
Derek C. Angus

The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis

Data from 15,022 subjects at 165 sites were analyzed to determine the compliance with bundle targets and association with hospital mortality.

Compliance with the entire resuscitation bundle increased linearly from 10.9% in the first site quarter to 31.3% by the end of 2 yrs ($p < .0001$).

Unadjusted hospital mortality decreased from 37% to 30.8% over 2 yrs ($p = .001$).

A reduction in reported hospital mortality rates was associated with participation







Established in 1895

'Justice demands that all people are equal'

Dealing with 'crosstutes in parliament—P5



'It is now clear that there is something fishy'

Ruling party ahead as rigging fears grow—P30



'The sheet the bank d its investm'

NBM dividend jum by 99% —Bus1

Parliament under British MPs' attack

BY VINCENT PHIRI

A GROUP of British MPs has attacked Malawi's Parliament for failing to hold government accountable on how it was spending donor money.

In a 69-page report released on Monday, the parliamentarians said foreign aid might have weakened Malawi's democracy by making government less accountable to the legislature.

"Historically, donors have tended to work over and around parliaments rather than with legislators themselves.

"Aid strengthens recipient governments and risks making them more accountable to donors and less accountable to their people," the report reads in part.

The British MPs observed that the situation has left civil society organisations

Turn to page 3

Residents burn, loot houses of 'witches'

BY FRANCIS TAYANJAH-PHIRI

SOME residents of Chanthomba location in Mzimba late last week went wild and destroyed property belonging to several elderly people named by some children as witchcraft instructors.

A fracas ensued when one child (name withheld) woke up last Wednesday with a swollen face and disclosed to her mother that she had fallen from a witchcraft plane.

Turn to page 3

WINDFALL K40bn aid from china



MUTHARIKA—This was my most successful trip

BY DEBORAH NYANGULU-CHIPOFYA

PRESIDENT Bingu wa Mutharika returned Monday night from his weeklong state visit to Mainland China and brought home a K40 billion aid package for Malawi.

Mutharika briefed the press on his visit yesterday at the New State House in Lilongwe.

Reading the President's communique, Deputy Foreign Affairs Minister Henri Mumba said the K40 billion includes a K12.2 billion grant, which would, among other projects, be used for construction of the Karonga/Chitupa road and the new Parliament building in Lilongwe.

The package also includes K26.6 billion for a five-year period for concessionary loans for various development projects, K426 million for defence cooperation and K213 million for construction of two rural schools.

Mutharika described the trip as one of his most successful state trips to date.

"I am happy to be the first Malawian head of state to visit the People's Republic of China. I hope Malawians in the private sector will take advantage of my trip to forge partnerships with their Chinese counterparts," he said.

The Pre relationship whole new bilateral rel most impor world.

"China economic happy to be said Mutha

He said Malawi co whose su volumes all hard work

"Let n nobody w but us. O can only i in the d teamwork of our ef Muthari

Agar economi Preside would a resource China scholar

The Malaw promise between Ma week











More to mention - streets...



Staffing problems 2

5. Continouus staff rotation : No capacity building is possible

6. Brain drain : Externally and internally

7. Education and training : Maths and anaesthesia

8. Ability or certificate? : Political careers, abilities neglected no clear career path,

Thats it on ethics ?

No

-

Should we do anything against sepsis before
we did non solve the challenges of good
governance?

-

Corruption, centralisation, patronage,
intransparency, no rule of law, allowances,
allocation of funds...

Planned study to help us :

1. controlling ICU resource utilisation for septic patients by a straight forward cardiac output measurement in the HDUs through Doppler :

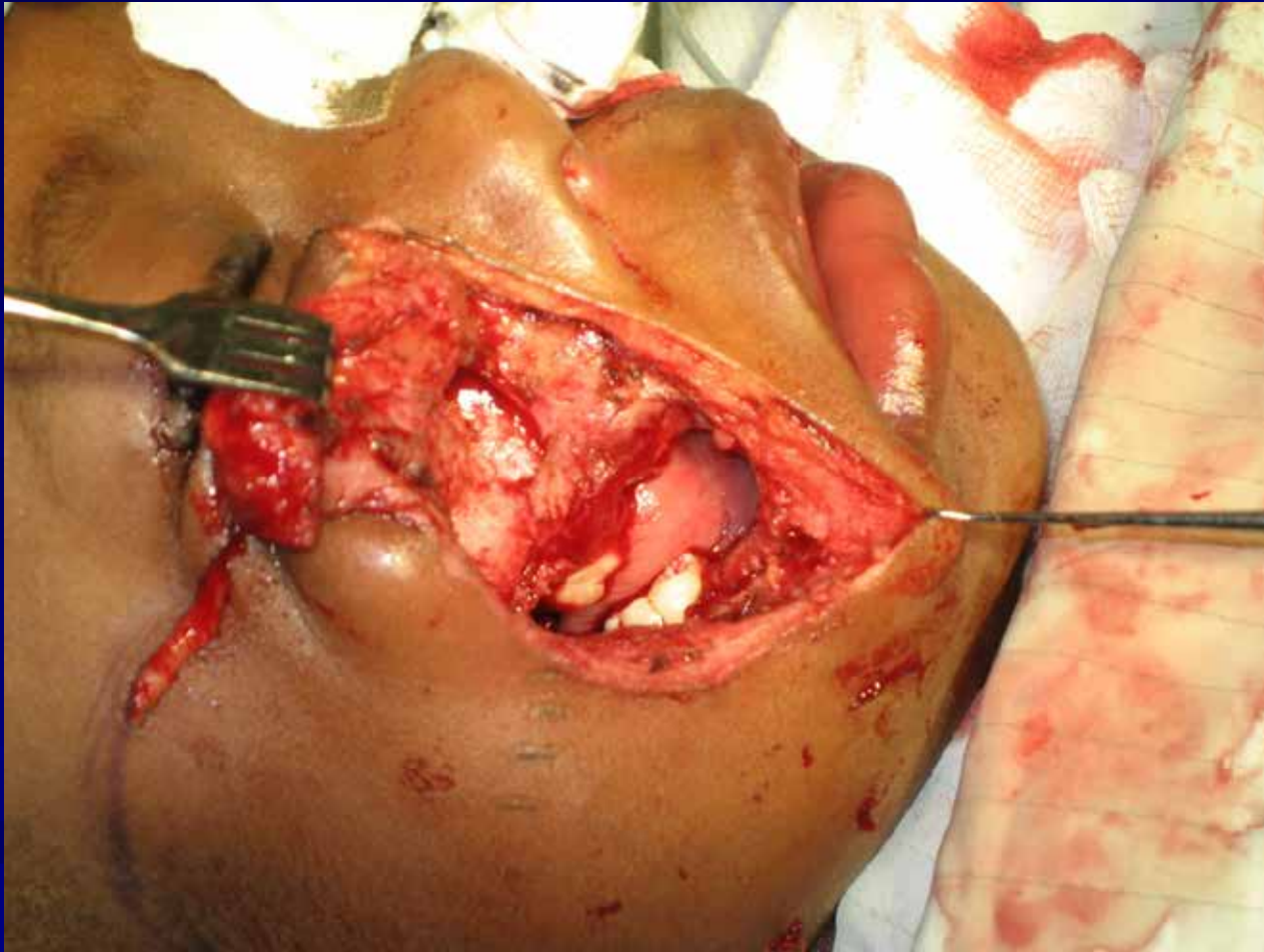
as a minimal invasive, quick and continuous estimation of CO

in order to prevent tissue oxygen debt and early organ failure by adequate fluid resuscitation already on HDU.

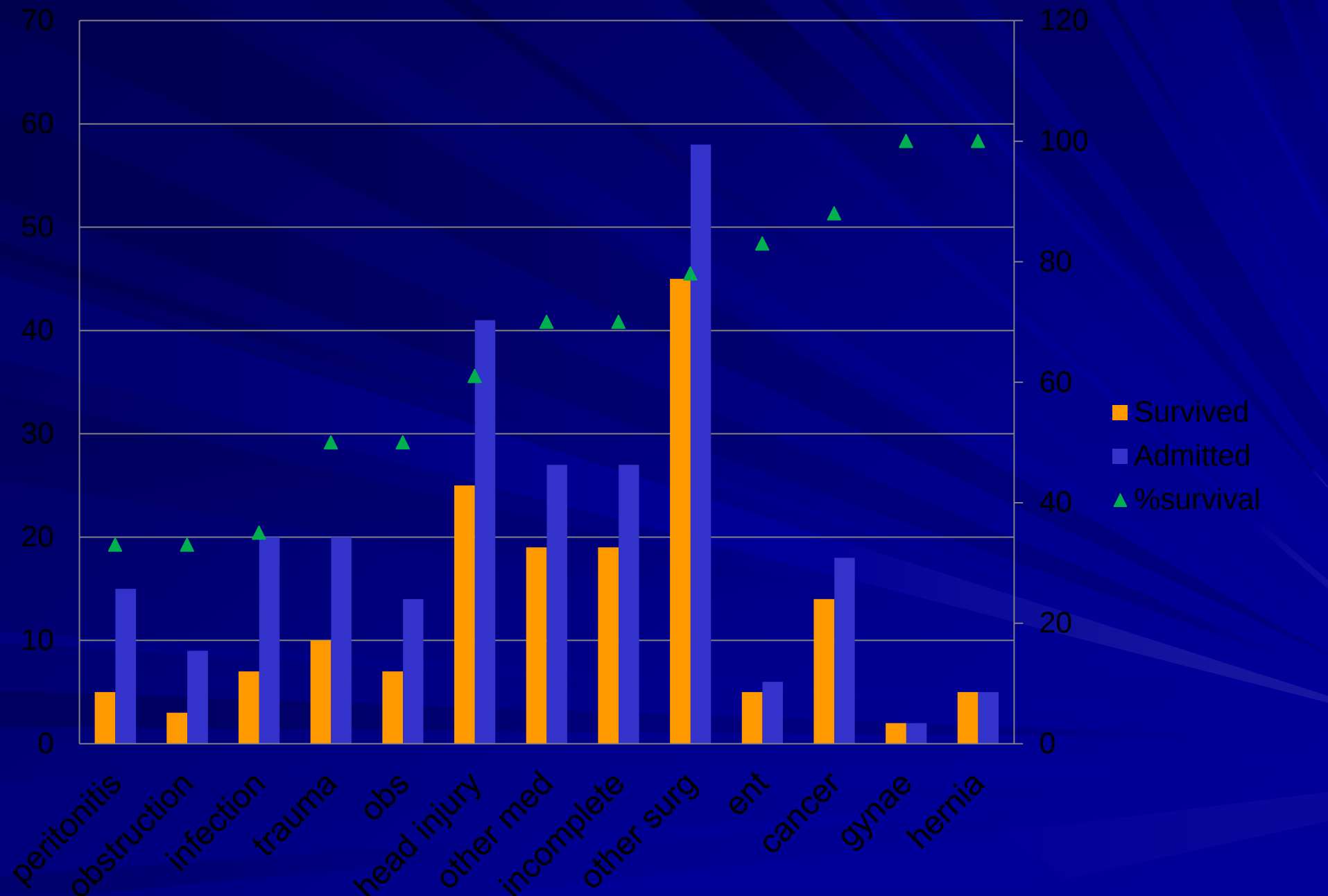
2. in decisionmaking : who can stay on HDU / who needs ICU



Noma



Percentage Survival to Admission



- CONCLUSIONS AND RELEVANCE
- These updated definitions and clinical criteria should replace previous definitions, offer greater consistency for epidemiologic studies and clinical trials, and facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing sepsis.

It's daily work on the ground...

Sometimes hard



Sometimes not



Surviving sepsis and its ethics 4

A more recent dilemma :

Should we ignore even public health and give all available money to female (!) education?

-

Because this is the only point in development aid where everybody (in theory) agrees that it is useful.

Surviving sepsis and Ethics 2



- Different concepts of death in some african societies
 - treat a brain dead or a septic patient -
 - can be a major problem !



1. The big five !



- 1. Good governance
- 2. Sustainability
- 3. Capacity building
- 4. Facility management
- 5. Better Implementation

3. Try new ways to fight old problems - the next will be :



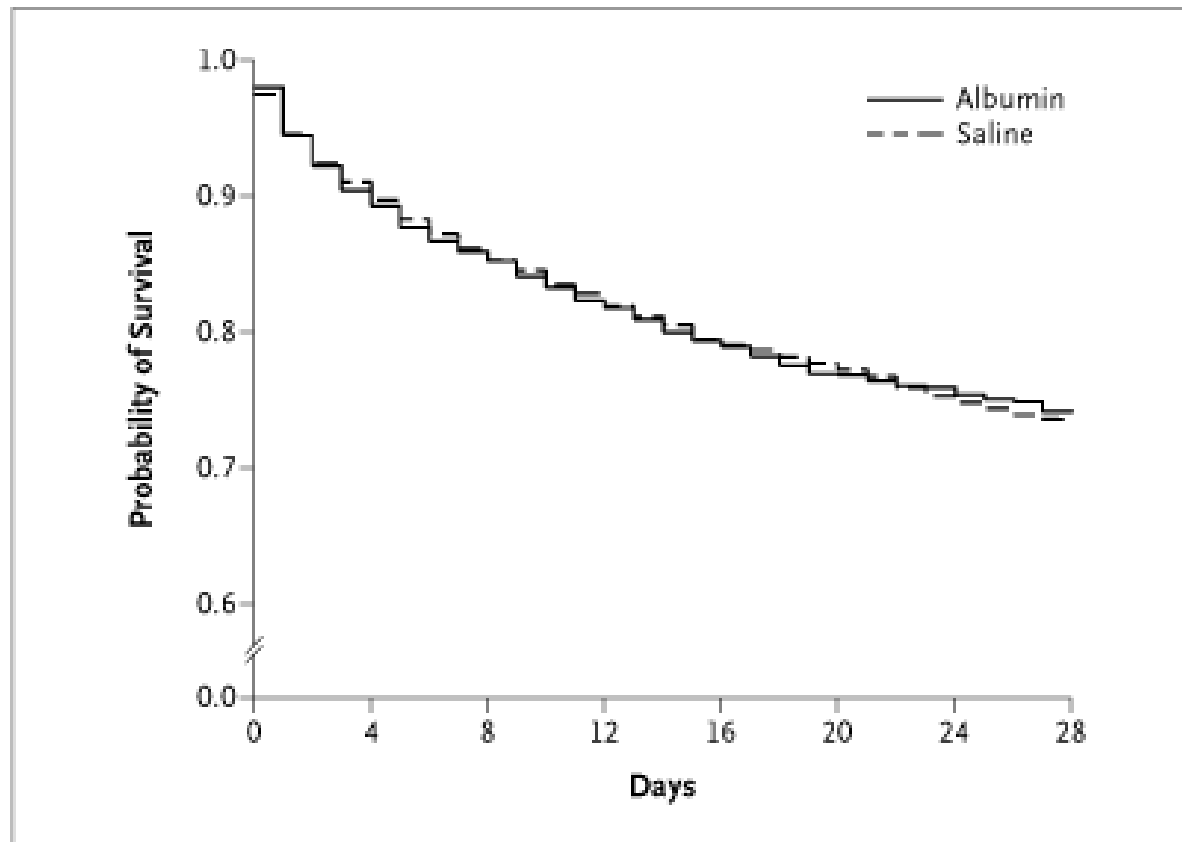
Our pilot study with 40 patients will use oesophageal/supra-sternal doppler and is targeted :

At the use of EGDT already on HDU

At an outcome measurement via Apache

At decisionmaking : who can stay on HDU / who needs ICU

Surviving Sepsis -Update



The SAFE Study Investigators 350 (22): 2247, Figure 1 NEJM May 27, 2004

- Critical Care is poorly developed and resourced in Malawi. We are battling against the multiple problems. Poor infrastructure produces erratic supplies of essential drugs, limited qualified personnel and little attention of educators to the triage and optimisation of the critically ill produces delays in referral and advance disease at presentation, both at referral health centres and within the tertiary hospitals. The situation is compounded with the twin epidemics of HIV/AIDS and road traffic accidents, with approximately 30% of our admissions being HIV positive and 30% of our workload is in the management of severe head injury.
- As Malawi tertiary care develops more trained doctors are returning with an increasing vision to possible medical intervention. Such increasing sophistication inevitably requires a higher degree of support care. Unfortunately critical care is perceived as a luxury that cannot be afforded in a poor country, and as a consequence the country's investment in new specialists will never be fully realised.
- The intensive care ward at Queen Elizabeth Central Hospital has 4 beds for a 1000 bedded hospital and admits all patients from neonates to the elderly from all specialities. The hospital has high dependency units, but these are not adequately staffed, or resourced. Due to delays in patients seeking treatment and referrals we perform many laparotomies on sick patients, if ventilation is not required due to the pressures outlined patients usually miss out on critical care. We are convinced that many patients die as a direct consequence of inadequate fluid monitoring post operatively on over stretched wards. Due to lack of resources ICU outreach is not a realistic possibility so alternative solutions must be found.
- We propose to validate a protocolised intraoperative fluid replacement regime guided by the oesophageal Doppler and establish whether this reduces mortality of those high risk patients denied critical care. We believe this will be the first such study undertaken in such a resource poor setting.

African Context

- 1,243,000 babies die before reaching one month of age in Sub-Saharan Africa (about 40% of global burden)
- Most deaths occur within the first week of life; and at home due to various cultural practices
- Neonatal sepsis is one of the three major causes of newborn death – contributes about 30%
- Management of neonatal sepsis is restricted to tertiary and secondary health facilities -
- MDG 4 will not be reached in most African countries without increasing access to prevention and treatment of neonatal sepsis



- Plus: RIVERS et al.

But :

Control the timeline

Supervise your collaborators

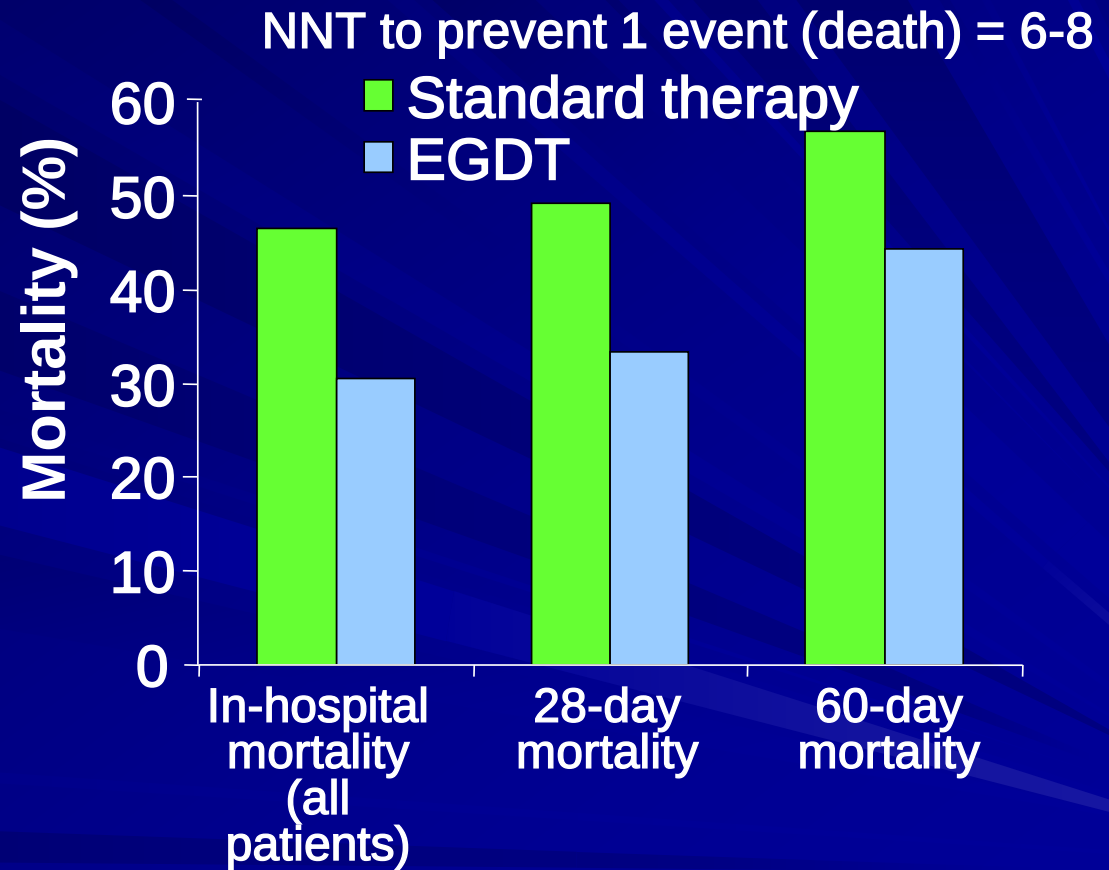
Repeat measurements

Be consequent in therapy

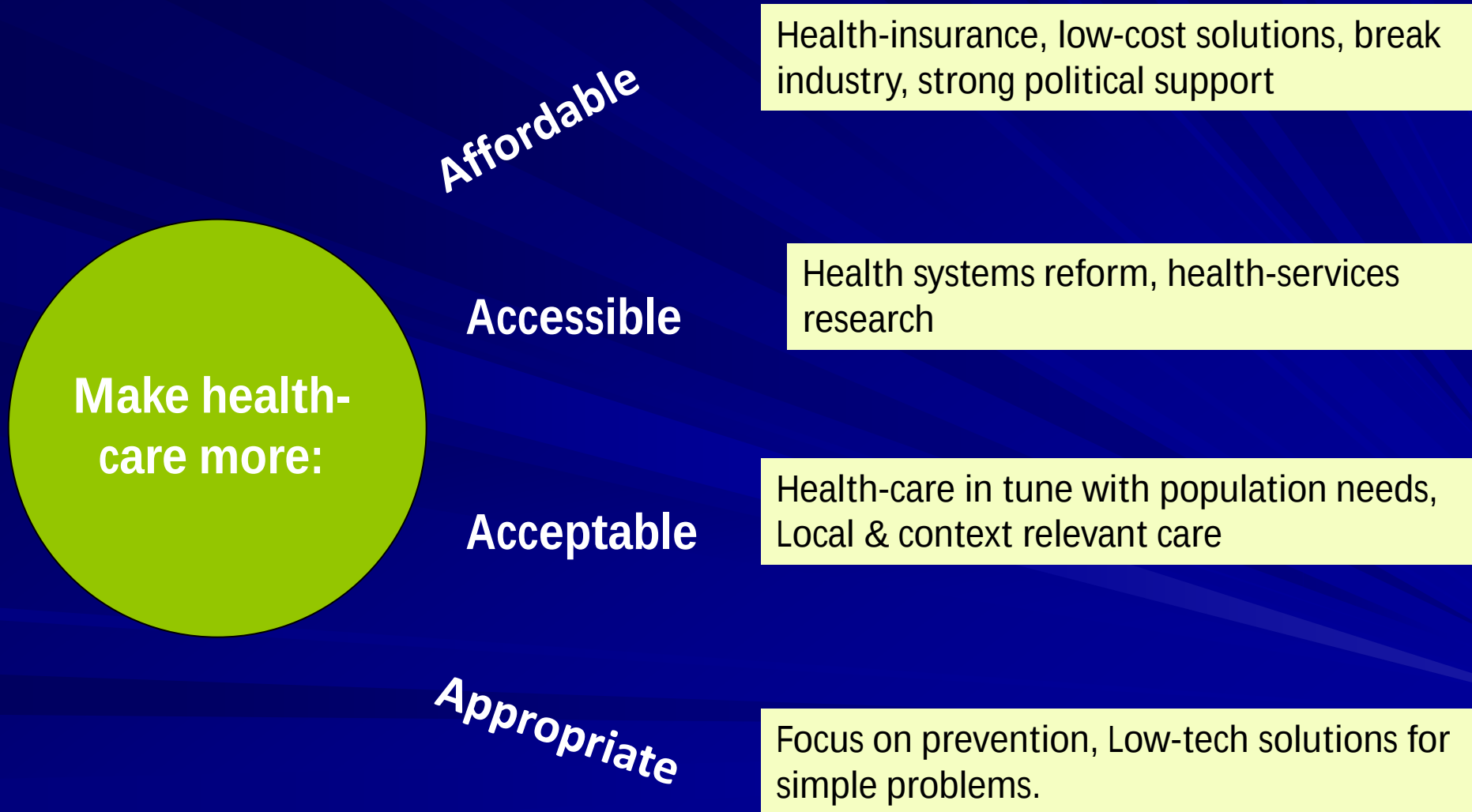
Try to Keep dedication up

and

adjust to the tropical setting

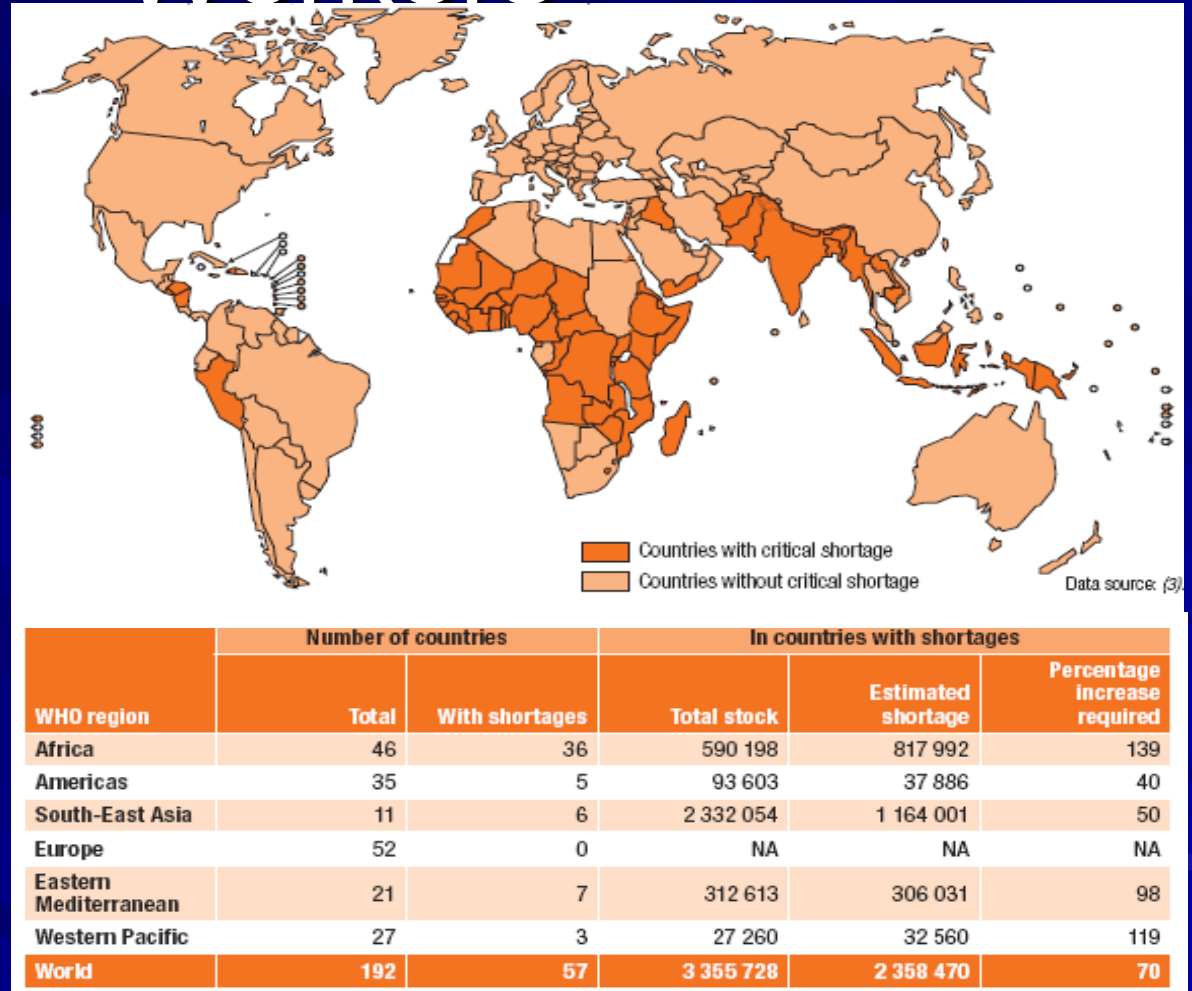


The 4A Solution



Global Shortage of Health Workers

- Using that definition:
 - 57 countries have a critical shortage
 - 36 of which are in the SSA region



ICU

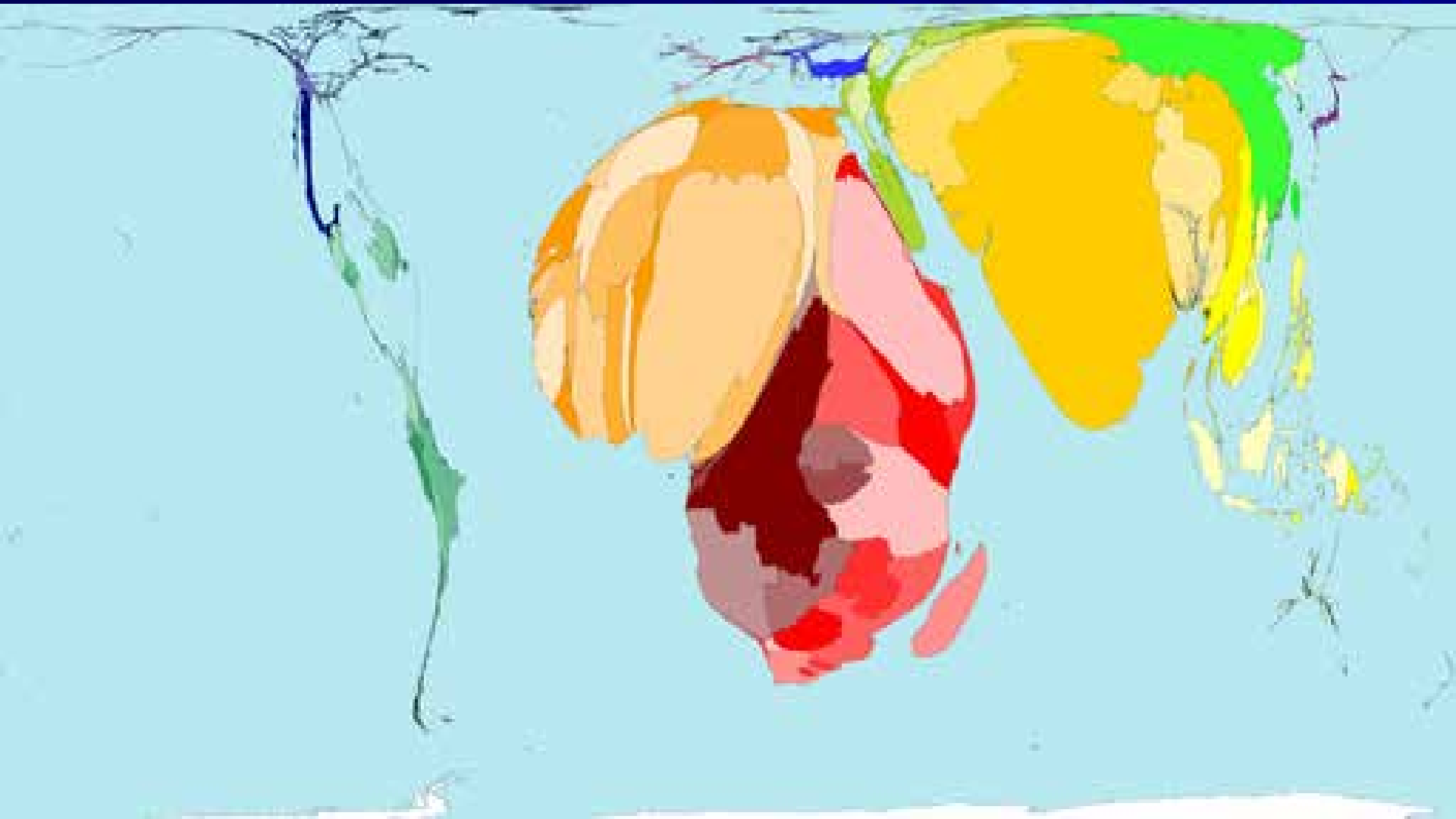
MALAWI – some data of poverty

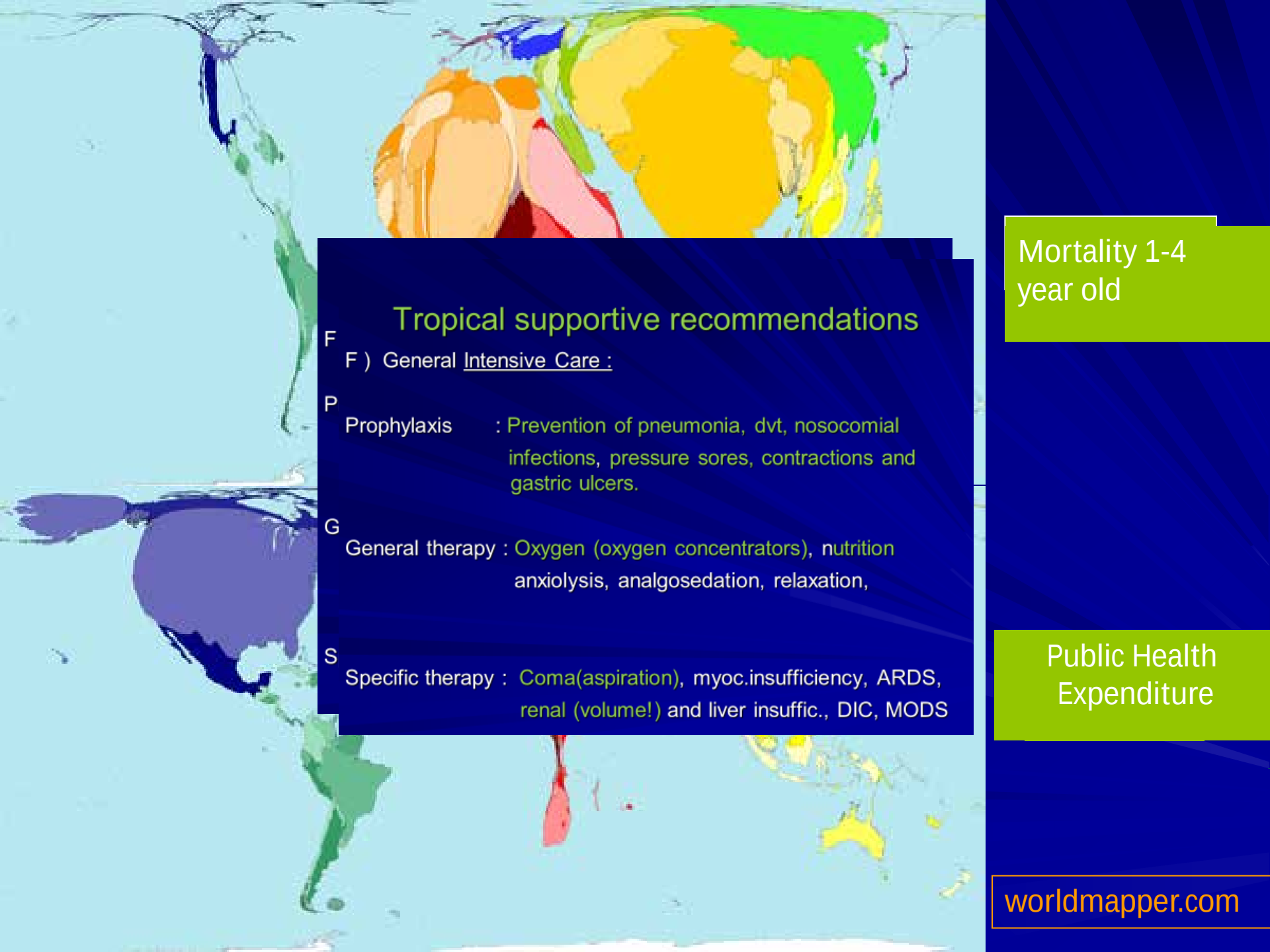
- Per capita income around 170-200 US \$ / y
- One doctor for 70 – 100000 inhabitants
- Life expectancy : 38 – 45 years
- ½ bis 1 million orphans (14 million inhabitants)
- Periods of hunger for 50% of the population

Health

- 1 doctor for 70 - 100.000 inhabitants
- QECH : 540.000 patients / year
- Maternal deaths : 60 / y at QECH !

Neonatal Mortality





Tropical supportive recommendations

F) General Intensive Care :

P Prophylaxis : Prevention of pneumonia, dvt, nosocomial infections, pressure sores, contractions and gastric ulcers.

G General therapy : Oxygen (oxygen concentrators), nutrition, anxiolysis, analgosedation, relaxation,

S Specific therapy : Coma(aspiration), myoc.insufficiency, ARDS, renal (volume!) and liver insuffic., DIC, MODS

Mortality 1-4
year old

Public Health
Expenditure

Tropical supportive recommendations

F) General Intensive Care :

Prophylaxis : Prevention of pneumonia, dvt, nosocomial infections, pressure sores, contractions and gastric ulcers.

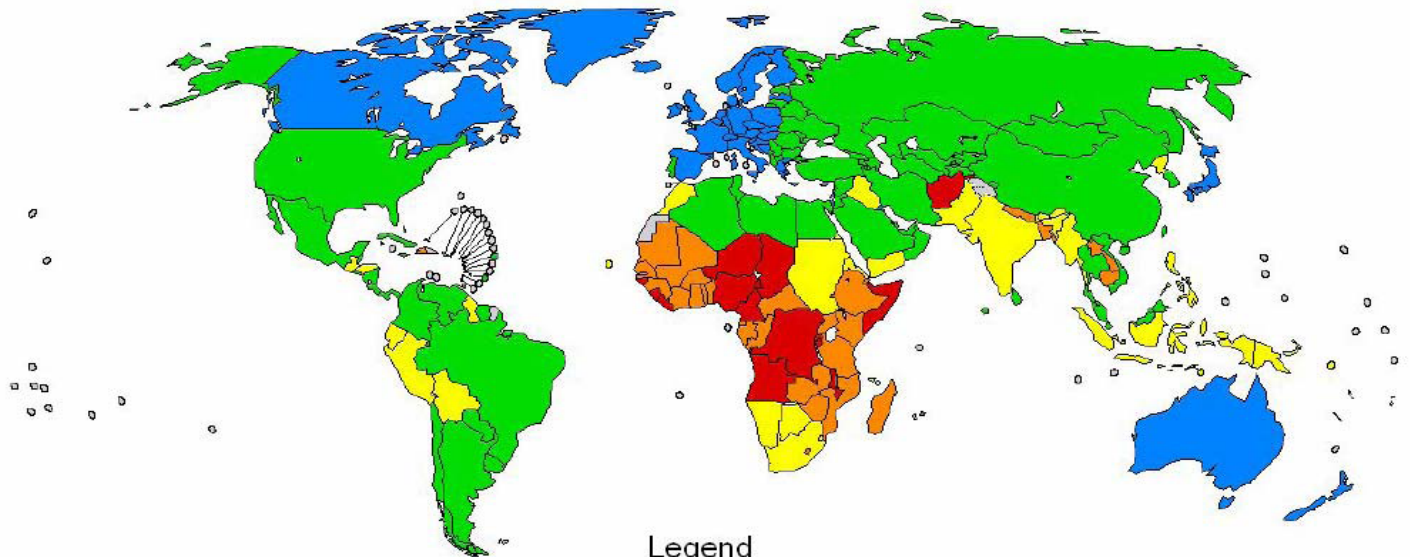
General therapy : Oxygen (oxygen concentrators), nutrition
anxiolysis, analgosedation, relaxation,

Specific therapy : Coma(aspiration), myoc.insufficiency, ARDS,
renal (volume!) and liver insuffic., DIC, MODS

MDG – Maternal Mortality

§ 550,000 women die in childbirth related incidents/year

Maternal mortality ratio per 100 000 live births

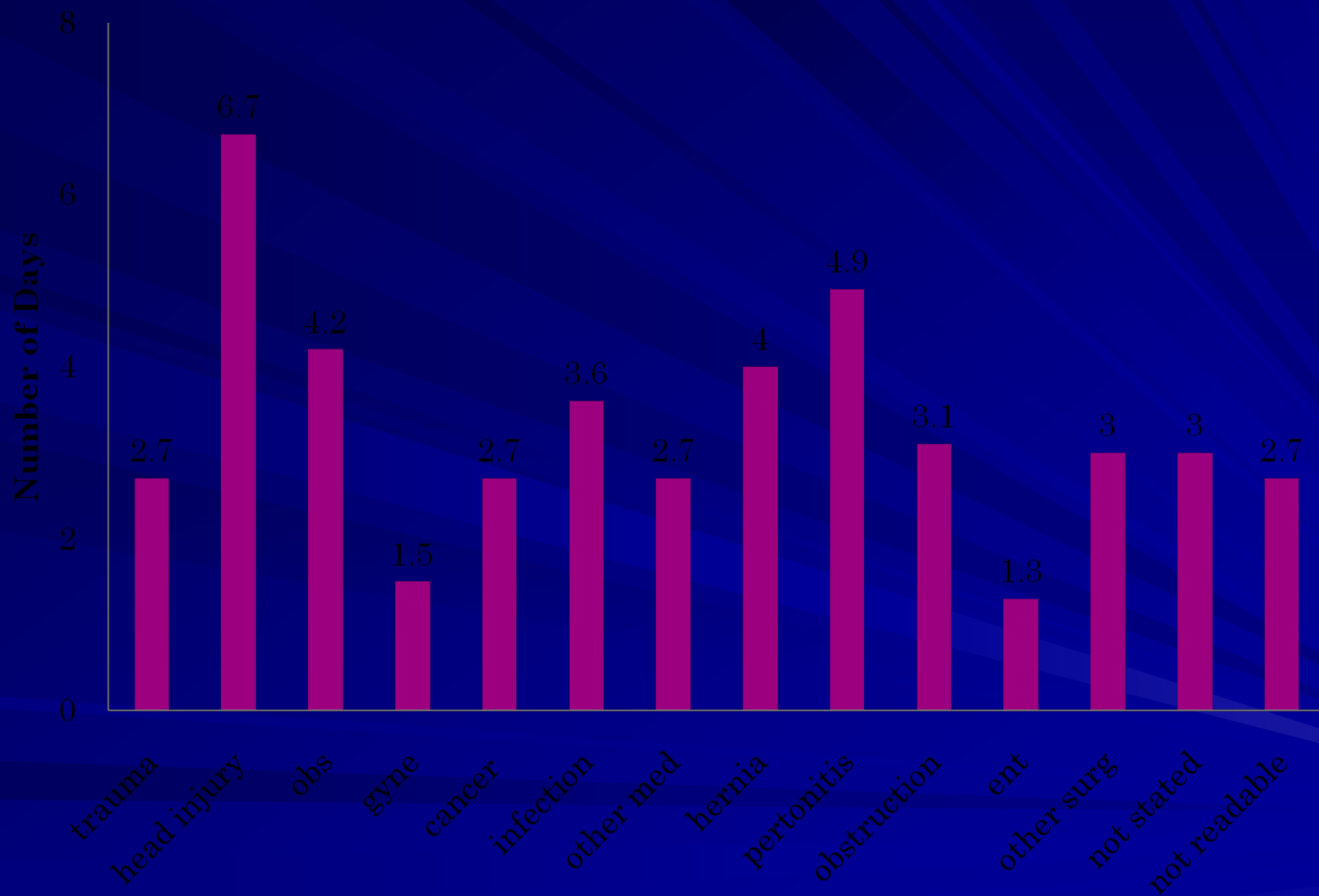


Legend

- Less than 10 deaths per 100000
- 10 - 199 deaths per 100000
- 200 - 499 deaths per 100000
- 500 - 999 deaths per 100000
- greater than or equal to 1000 deaths per 100000
- Data not available

The boundaries and names shown, and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Average Length of Stay



MINISTRY OF HEALTH

QUEEN ELIZABETH CENTRAL HOSPITAL
P.O. BOX 95, BLANTYRE, MALAWI

CONSENT FOR OPERATION

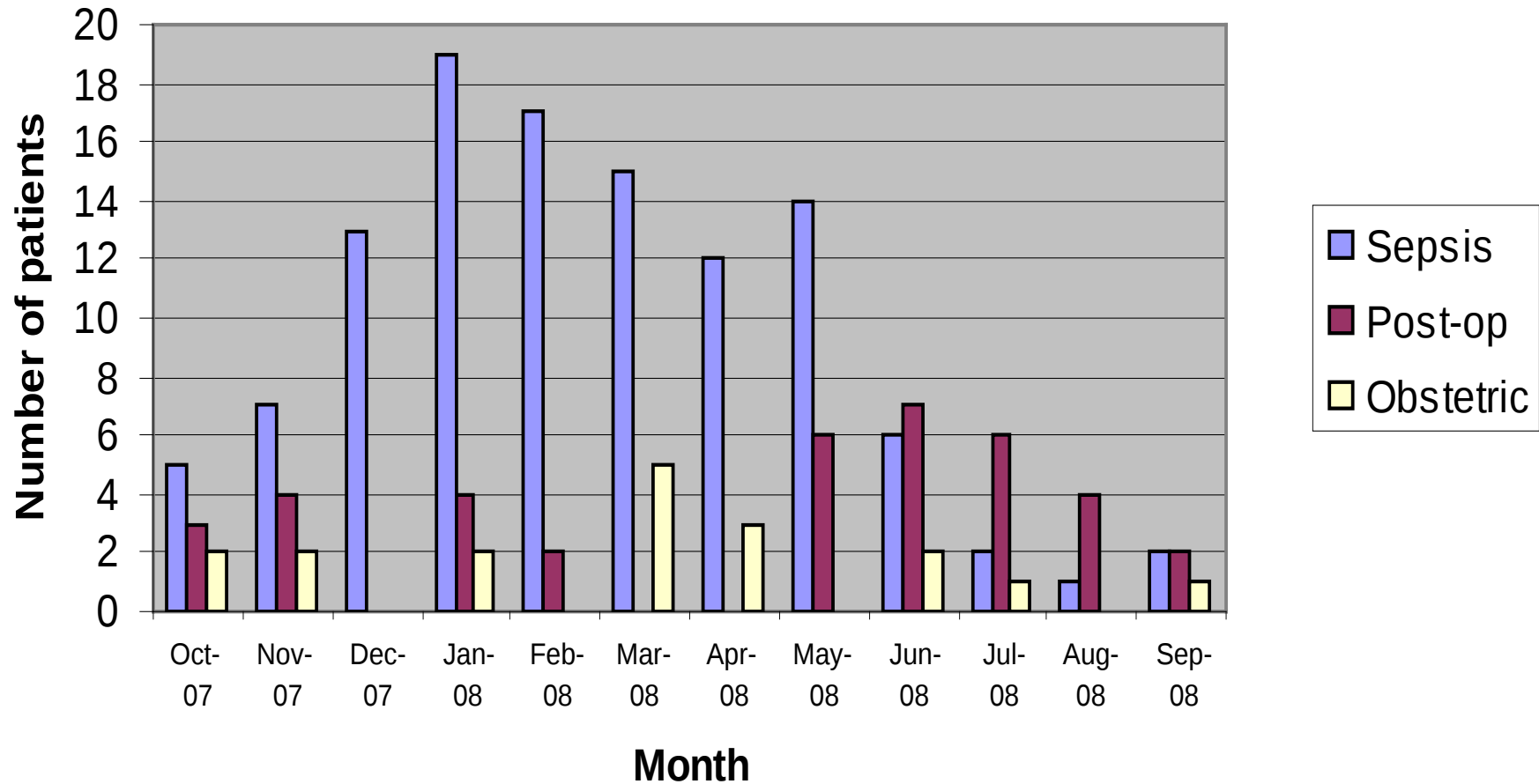
I, here by _____ give my full consent for
administration of anaesthesia and a cardiac surgery to be performed on my body
_____ which the Doctor(s) may consider
necessary.

Date 6/7/02

Pl finger print

Guardian (Father/Mother)

General sepsis as reason for admission on ICU



Malaria can be acquired on (!) ICU

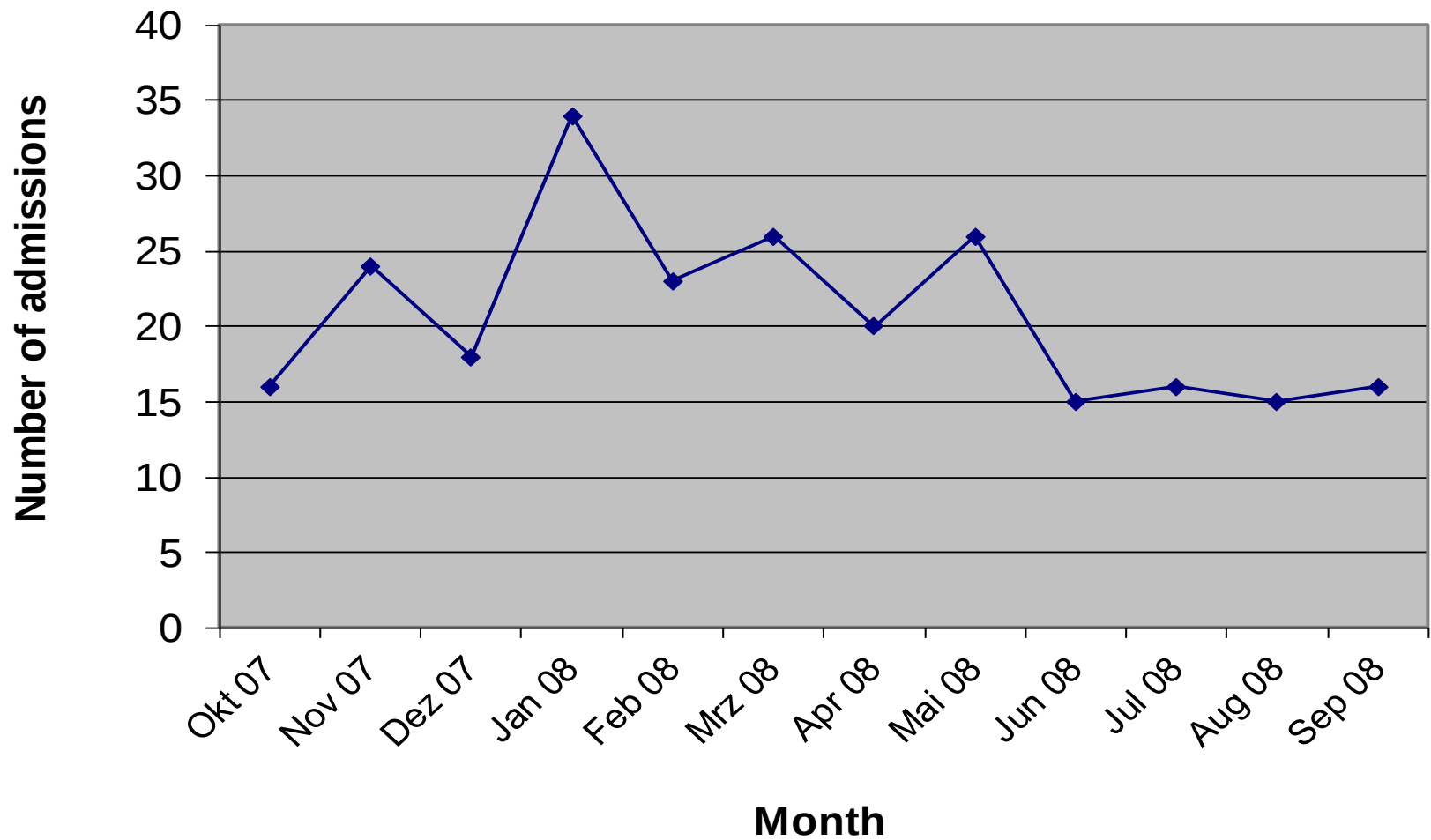


The Third International Consensus Definitions for Sepsis & Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP¹; Clifford S. Deutschman, MD, MS²; Christopher Warren Seymour, MD, MSc³;
Manu Shankar-Hari, MSc, MD, FFICM⁴; Djillali Annane, MD, PhD⁵; Michael Bauer, MD⁶; Rinaldo Bellomo, MD⁷;
Gordon R. Bernard, MD⁸; Jean-Daniel Chiche, MD, PhD⁹; Craig M. Coopersmith, MD¹⁰; Richard S. Hotchkiss, MD¹¹;
Mitchell M. Levy, MD¹²; John C. Marshall, MD¹³; Greg S. Martin, MD, MSc¹⁴; Steven M. Opal, MD¹²; Gordon
D. Rubenfeld, MD, MS^{15,16}; Tom van der Poll, MD, PhD¹⁷; Jean-Louis Vincent, MD, PhD¹⁸; Derek C. Angus, MD,
MPH^{19,20}

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

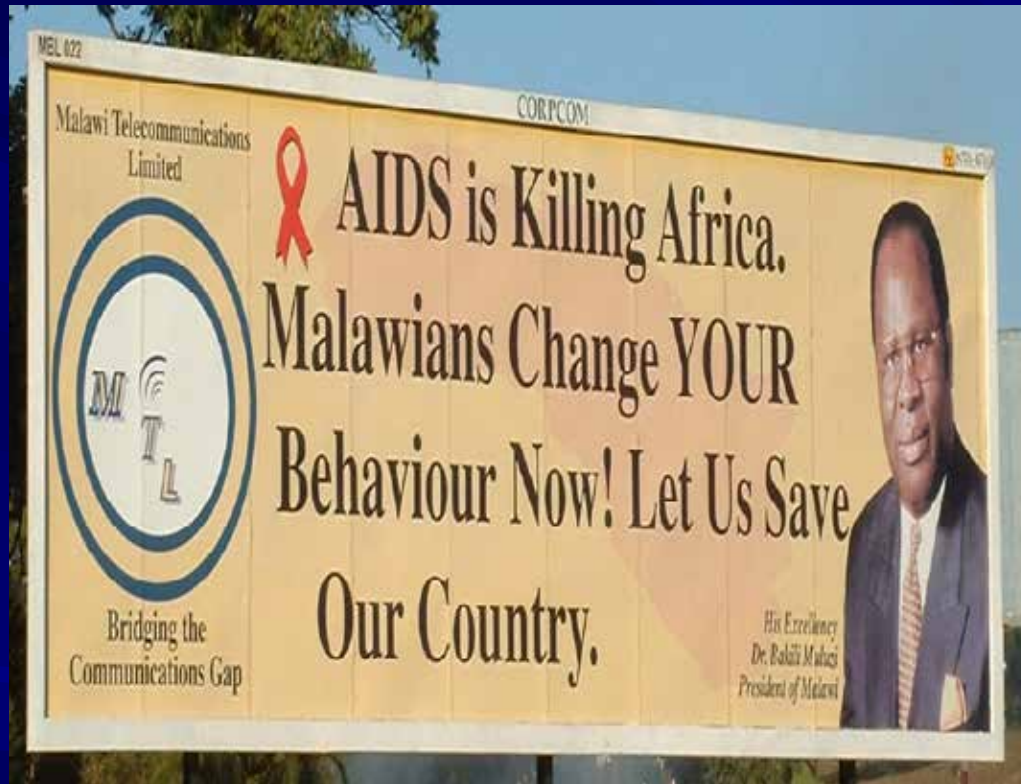
Demographics



Road traffic accident !



AIDS



- AIDS changes Intensive care !
- Malawi : 14 % HIV
- QECH : surg. 30-40 %
med. >70 % (!)

A small german part in tropical intensive care...



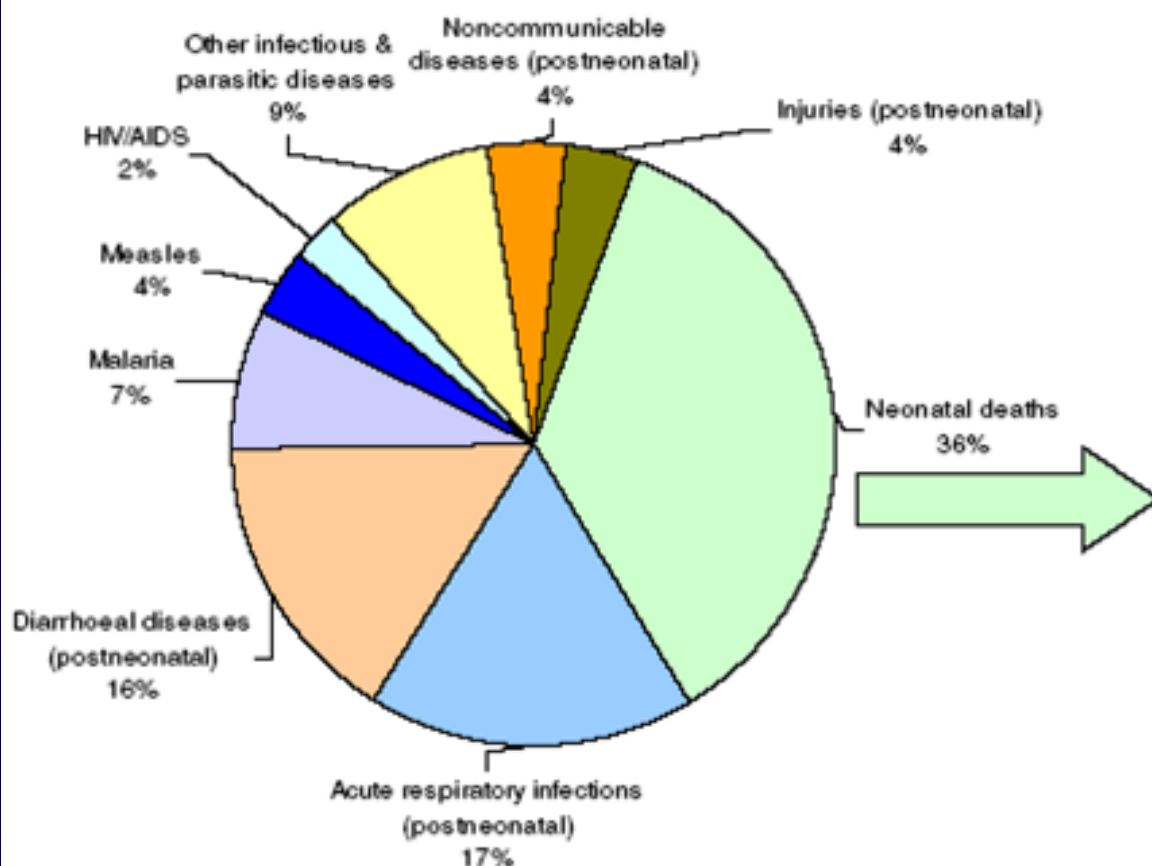
- Plus peds wichtig in tropen an d peds sofa?
- Normwerte für afrikaner
- Normwerte für malnourished erwachsenen und kinder?
- Sept schock möchte ich ja auch nicht!

Is India Ready for Intensive Care?

- An infant undergoes complex cardiac surgery at 2 days of life and was discharged after 2 weeks in the ICU that cost 2 lakhs (\$4000)
- 40 days later, re-admitted to the ICU with diarrhoea & severe dehydration resulting in shock and death.

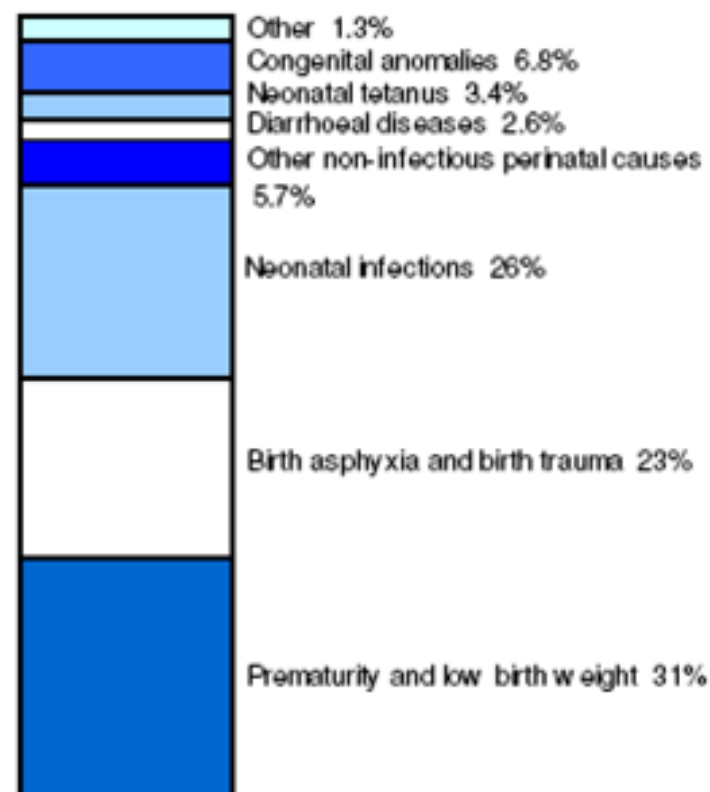


Deaths among children under five



35% of under-five deaths are due to the presence of undernutrition⁽²⁾

Neonatal deaths



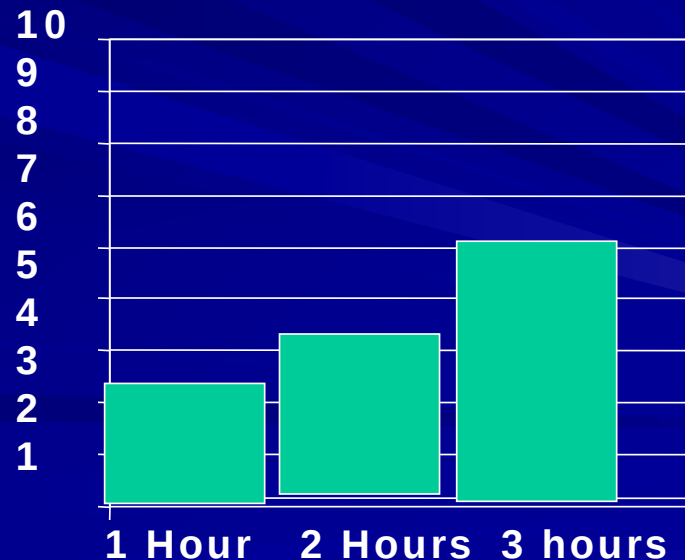
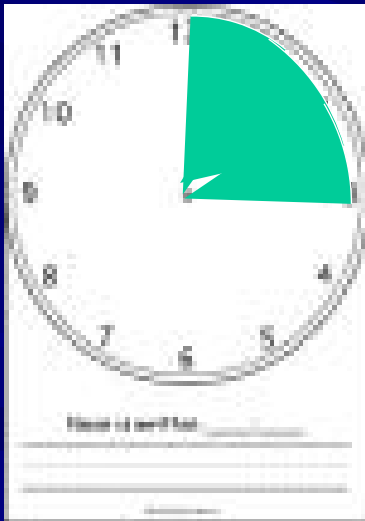
Long-Term Impacts of Poor Maternal Health and Survival Rates

- The chronic suffering or tragic death of mothers significantly impacts the health and survival of the newborn and any of her previous children.
- Among those infants who survive the death of their mother, only 10% live beyond their first birthday (Jowett, 2000).
- Measham and Gillespie (1998) found that the death of a mother is likely to be followed by the death of approximately 50% of her children under the age of five.

ICU

CAVE: Children : “Han / Carcillo” or “FEAST” ?

After adjustment for Patient Severity:
Every hour without appropriate resuscitation and
restoration of capillary refill < 2 s and normal
blood pressure increases mortality risk by 40%!
(Han et al Pediatrics 2003)







A randomised trial of fluid resuscitation strategies in African children with severe febrile illness and clinical evidence of impaired perfusion

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JUNE 30, 2011

VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

Why do we have to deal with „FEAST“ ?

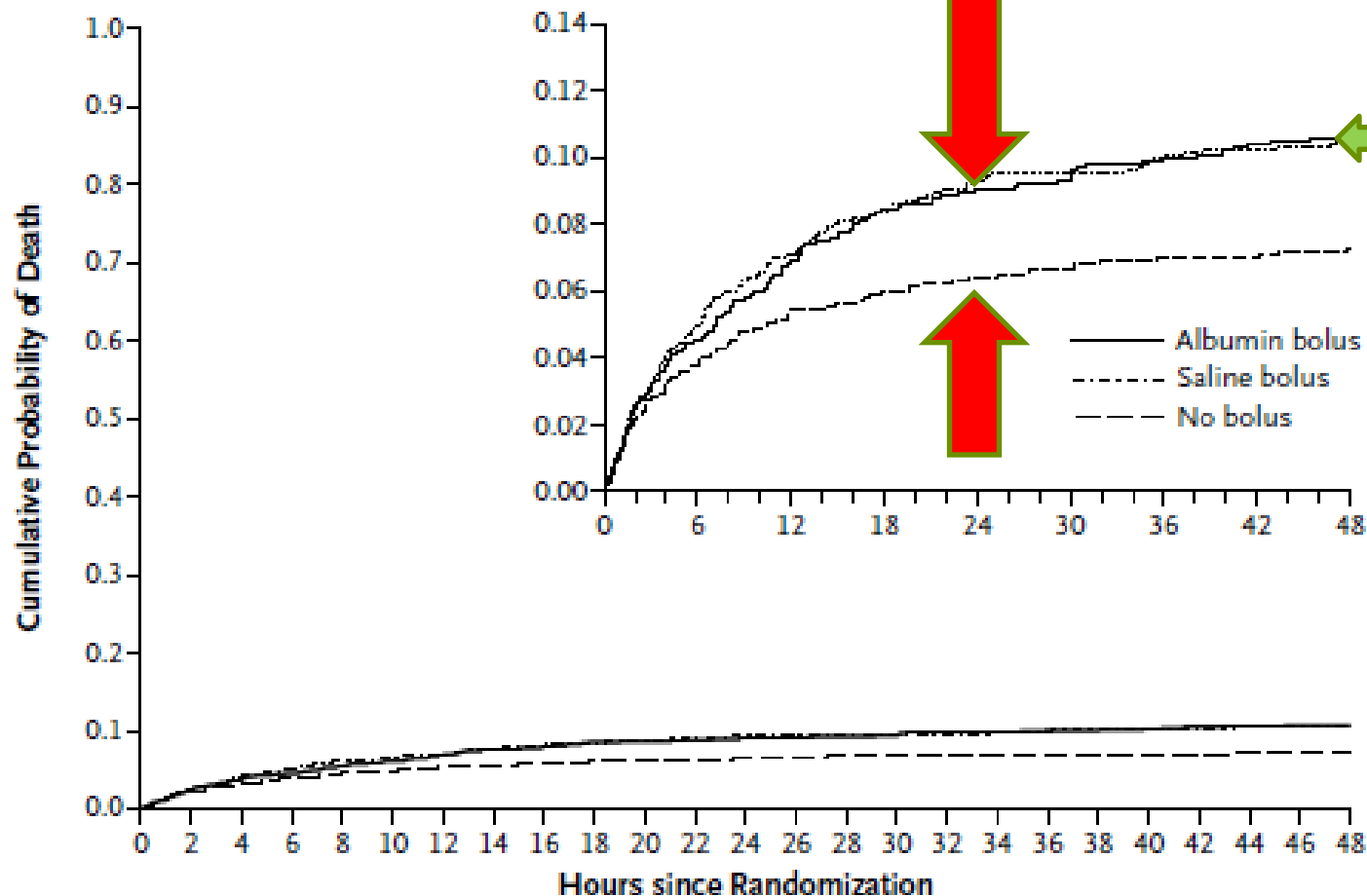
overall) and clinical severity were similar across groups. The 48-hour mortality was 10.6% (111 of 1050 children), 10.5% (110 of 1047 children), and 7.3% (76 of 1044 children) in the albumin-bolus, saline-bolus, and control groups, respectively (relative risk for saline bolus vs. control, 1.44; 95% confidence interval [CI], 1.09 to 1.90; $P=0.01$; relative risk for albumin bolus vs. saline bolus, 1.01; 95% CI, 0.78 to 1.29; $P=0.96$; and relative risk for any bolus vs. control, 1.45; 95% CI, 1.13 to 1.86; $P=0.003$).

Even worse:

2B). The excess mortality associated with the bolus groups as compared with the control group was consistent across all prespecified subgroups (Fig. 3), and there was no evidence supporting a benefit from bolus fluid infusion in any subgroup. At 4 weeks, neurologic sequelae were

A Mortality at 48 Hours

Primary
End
point:
48 hrs
mortality



	Hr 1			Hr 2			Hr 3			Hr 4			Hr 5-8			Hr 9-24			Hr 24-48		
No. at Risk	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
Died	13	12	14	13	15	9	8	7	6	6	9	4	17	20	14	38	34	20	16	13	9
%	1.2	1.1	1.3	1.3	1.5	0.9	0.8	0.7	0.6	0.6	0.9	0.4	1.7	2.0	1.4	3.8	3.5	2.0	1.7	1.4	0.9

From the study protocol:

	ALBUMIN-BOLUS			
	all fluids	Bolus	Blood	Maintenance
Total number enrolled.	1050	1050	1050	1050
Total fluid received in first 1 hour				
number of children that received fluid (%)	1045 (99%)	1045 (99%)	26 (2%)	10 (1%)
median amount of fluid (IQR) mls/kg/hr in those that received fluid	20 (20,20)	20 (20,20)	0.1 (0.07, 1.5)	0.06 (0.06, 2.2)
mean amount of fluid (sd) mls/kg/hr in those that received fluid	22.2 (6.6)	22.2 (6.5)	1.7 (4.0)	1.0 (1.7)
median amount of fluid (IQR) mls/kg/hr in all children alive	20 (20,20)	20 (20,20)	0 (0, 0)	0 (0,0)
mean amount of fluid (SD) mls/kg/hr in all children alive	22.1 (6.7)	22.1 (6.7)	0.04 (0.7)	0.01 (0.2)
Total fluid received in second hour				
number alive at beginning of second hour	1032	1032	1032	1032

NO BOLUS CONTROL			
all fluids	Bolus	Blood	Maintenance
1044	1044	1044	1044
640 (61%)	2* (0.2%)	207 (20%)	439 (42%)
2.2 (1.4, 3.2)	28.3 (12.8, 43.7)	2.8 (1.6, 4.4)	1.9 (1.3, 2.7)
2.7 (2.9)	28.3 (21.8)	3.2 (2.2)	2.3 (2.3)
1.2 (0, 2.5)	0 (0,0)	0 (0,0)	0 (0, 1.8)
1.7 (2.6)	0.05 (1.4)	0.6 (1.6)	1.0 (1.9)
1031	1031	1031	1031

The guidelines: 6 hours - and our streets?



Surviving Sepsis in Malawi – a.) money !



Budgets : 1

- GNP Malawi : 4,5 billion euros
- Turnover Boehringer Ingelheim: 10 billion euros

Budgets 2 :

- Germany : Budget ICU's : 5 billion US \$
- Malawi : GNP : 4,5 billion euros

b) Staffing or „can you react quick in sepsis?“

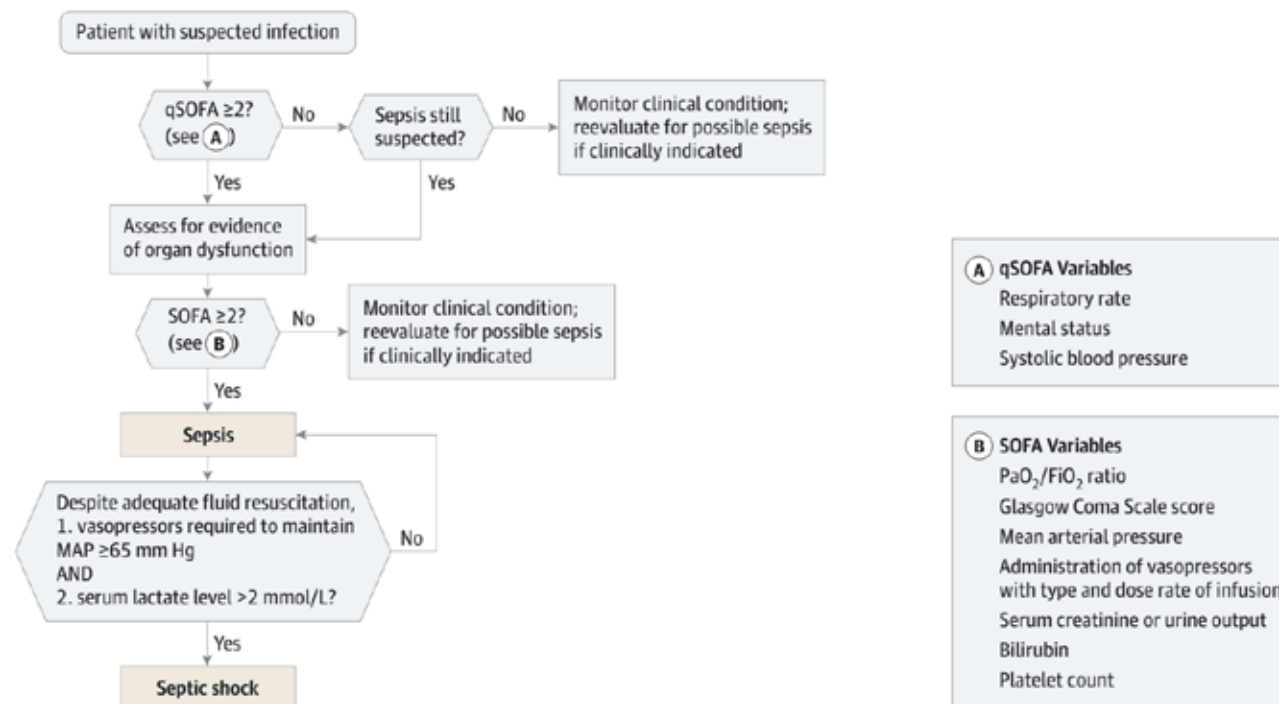
- 1. Numbers :** Doctors, Clinical Officers and Nurses incredibly low.
- 2. Renumeration :** Which dedication can you expect for 160 Euro/month ?
- 3. Dedication :** Early (!!) Goal Directed Therapy is very difficult to achieve.
- 4. Morbidity :** Around 20 % are HIV pos.

Surv. sepsis and its ethics

The old struggle :
Primary health care and public health
vs.
Clinical medicine

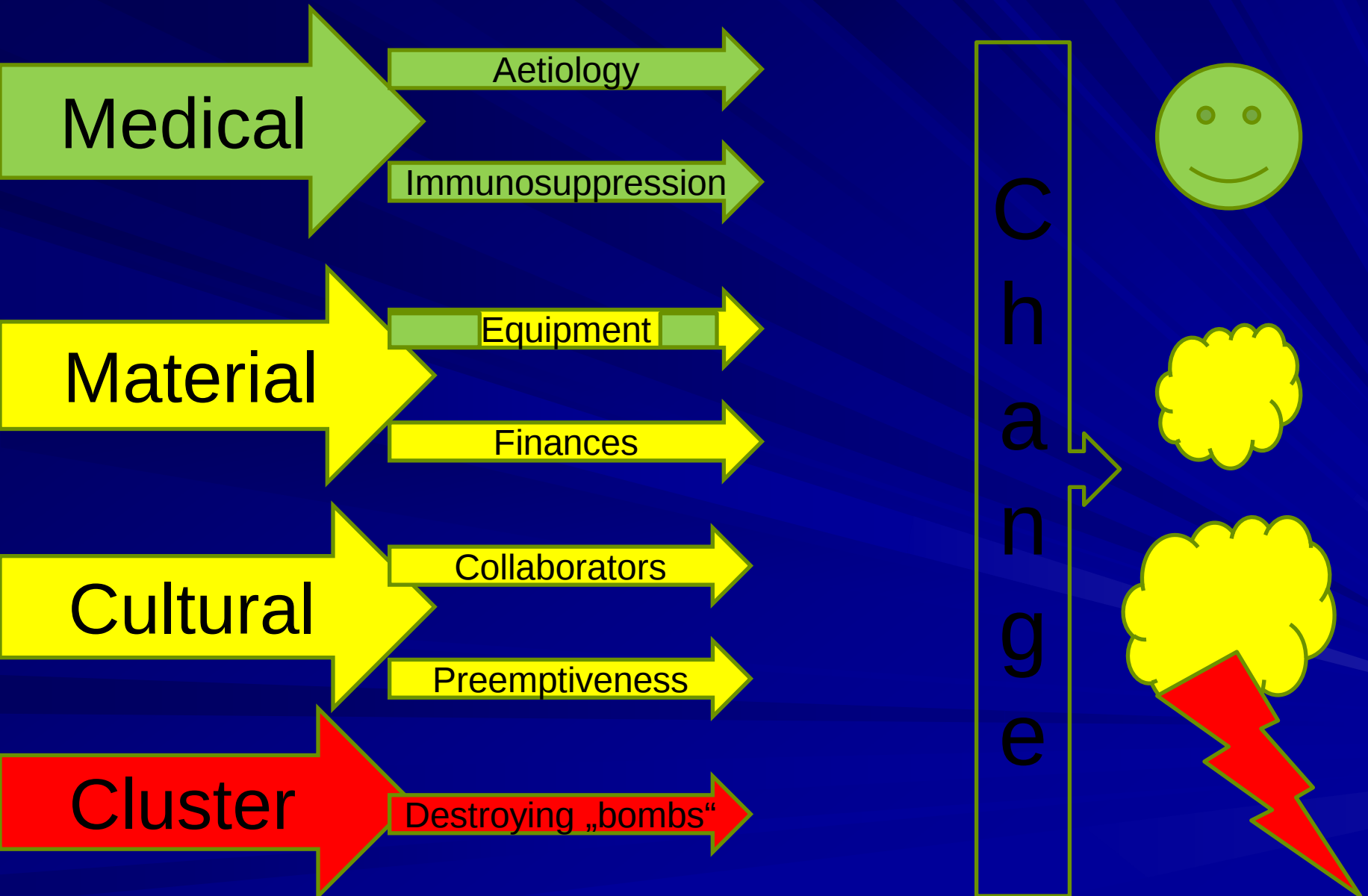
(cheap nets and vaccinations or expensive sepsis treatment)

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

3.African Bundle implementation – was their focus right?



Cluster bombs on sepsis bundles



The guidelines and us

Focus-erradication : Quality of surgeons : extremely variable

6 hours – a time limit in africa (contradictio in adjecto?)

d) Why do they present so late ?

Transport is expensive (Minibus to hospital- a weekly wage !

Villages are far away (some even in Mocambique)

Atmosphere in hospitals is frightening

They learn that people die in hospitals (which is true...)

You always need a guardian (which doubles all problems)

Surviving sepsis and it's ethics



Ventilation in 4-5 beds for a hospital with 1000 beds.

These beds are for newborns as well as for young mothers or elderly people.

- 680,000 Patients a year

The guidelines and us

Initial therapy : -Measurements : CVP (not HDU), SpO2 and MAP available

Scvo2, ph and gases not available

-Volume : Crystalloids +, (colloids +/-) , blood (+), (FFP, platelets +))

-Catecholamines : Only adrenalin always available

The guidelines and us

Vasopressors : No noradrenalin, sometimes dopamine

Inotropes : Adrenalin, sometimes dobutamine

Corticoids : Hydrocortison available, dexamethasone

A. Protein C : ~~Not available~~

Sugar Control : -Realistically not more often than 1-2 times a day

Renal Replacement : -CVVH : available but seldom used because it is in our setting extremely staff consuming (a pity), (similar for peritoneal Dialysis)

Haemodialysis : (5 hours drive with ambulance) 2 years ago, now available to a degree



**Surviving
Sepsis
Campaign**

Current supportive recommendations 1

C) Intensive Care :

- Prophylaxis : Prevention of pneumonia, dvt, nosocomial infections, pressure sores, contractions and gastric ulcers
- Renal replacement : Not prophylactic, but in acute renal ins.
- General therapy : Oxygen, analgosedation, relaxation, anxiolysis, nutrition
- Specific therapy : Coma, myocardial insufficiency, ARDS, renal and liver insufficiency, DIC, MODS

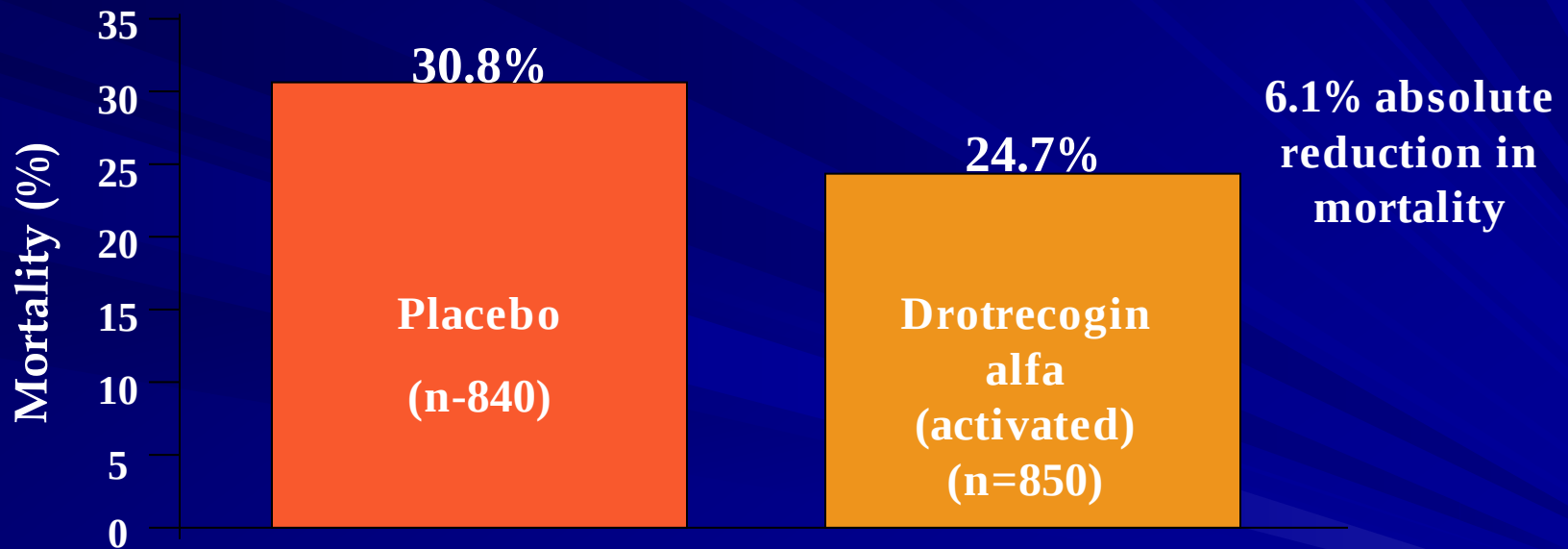
Current supportive/adjunct recommendations

2

OUT (not only of Africa) :

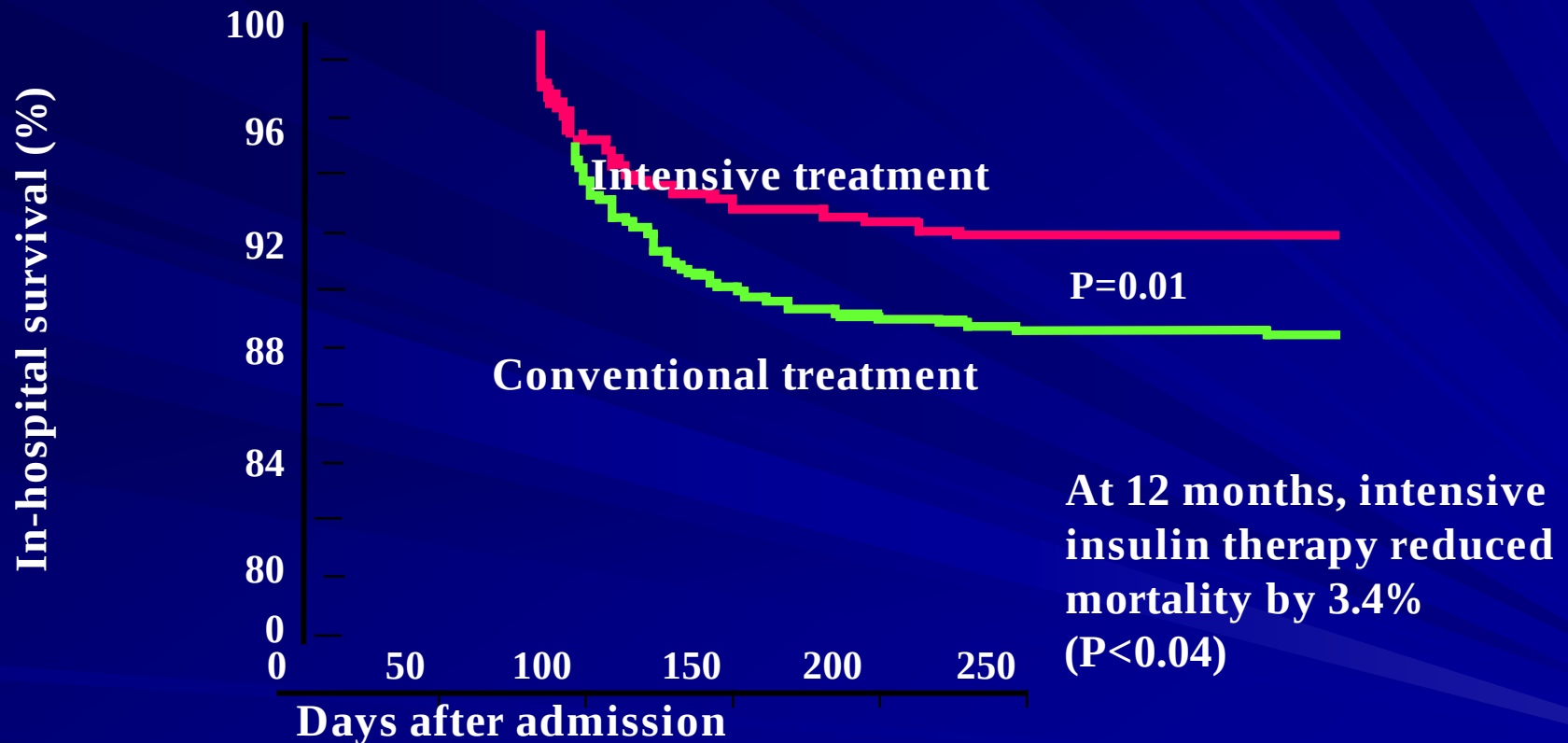
- a) Steroids : Annane et al. JAMA 02 (for more than 2-3 days)
- b) Others : AT3, Se, NAC, Pentoxifyllin, ... : no proof !

Supportive recommendations :- rAPC – ~~out for Africa~~



Bernard GR, Vincent JL, Laterre PF, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001; 344:699-709

Supportive recommendations : Insulin – out for Africa



van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001;345:1359-67

Traditional healing and witchcraft



You are called on ICU :

- 6 years, male, very weak, not moving much, laying on left side
- Belly pain since 3 days (later: 3 weeks)
- No med. history, no medication
- Mother is accompanying the child and behaves strangely desinterested, not really answering medical questions despite good understanding
- Urine output in the next hours deteriorating
- After 2 hrs nurses turn the boy to right side -

Conclusion

What are the suggestions for the management of
sepsis in a resource poor setting :

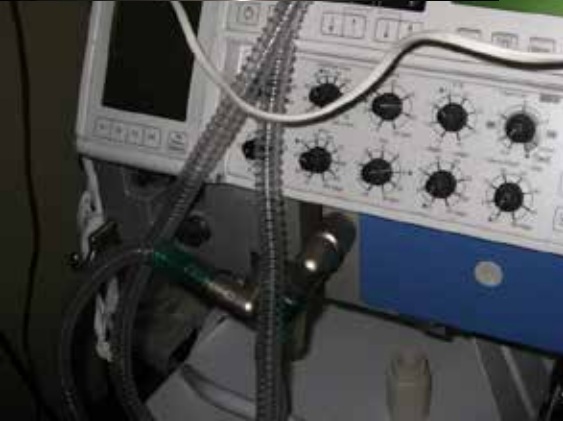
Consequences for the tropics:

- I fear they are detrimental for our decisions on whom to admit to our few precious Intensive Care units.
- „Sepsis ist die Gesamtheit der lebensbedrohlichen klinischen Krankheitserscheinungen und pathophysiologischen Veränderungen als Reaktion auf die Aktion pathogener Keime und ihrer

ICU-Beatmung: Ein großes Problem für uns:

2011: 40. Geburtstag!

- ž Keine Ersatzteile
- ž Keine Instandhaltung
- ž O₂ als Antriebskraft
- ž Kein Handbuch
- ž oder auf Chinesisch
- ž Alt und kurzlebig
- ž Wie ausbilden ?
- ž Eigenes Geld?





Diagnosis ?

Trias

- Strange behaviour of mother
- Belly pain and signs of vasoconstriction
- Quick deterioration

Think about intoxication by traditional treatment with ????

Sepsis bundles in Africa

What is possible / practicable ?



See: homepage of the German Sepsis Society:

<http://www.sepsis-gesellschaft.de/DSG/Deutsch/Kongress/Workshops/WS2>

ProMlse (2015): wait...

- Third part of the saga: 2016
- EGDT worse in several points – but 90 day mortality = (!!)
- That's it with nice studies?
- No ! The worst is yet to come!!

QECH: Medical admissions septic shock 190 patients a year – 4/5 ICU beds

(Pollach G; Downie P, 2009)

Although existing published data suggest that sepsis causes about 10 % of all maternal deaths and 26 % of neonatal deaths, these are likely to be considerable underestimates because of methodological limitations.”

Seale AC, Mwaniki M, Newton CR, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009

A small german part in tropical intensive care...



Even worse:

2B). The excess mortality associated with the bolus groups as compared with the control group was consistent across all prespecified subgroups (Fig. 3), and there was no evidence supporting a benefit from bolus fluid infusion in any subgroup. At 4 weeks, neurologic sequelae were

Cross infections ?



Tb - pulmonary



Surviving sepsis – the guidelines and us:

(some examples from Q.E.C.H)

Diagnosis :

-Bloodcultures and other cultures only selectively available

X-ray, ultrasound, CT(!), MRI(!!) partly available

Scoring (APACHE) : No blood gases, crea difficult
sometimes no urea or e'lytes



A randomised trial of fluid resuscitation strategies in African children with severe febrile illness and clinical evidence of impaired perfusion

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JUNE 30, 2011

VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

Importance & Incidence

- severe sepsis -

- Worldwide incidence: 18 Million patients/y
1400 people a day die

(Galeski)

- Although existing published data suggest that sepsis causes about 10 % of all maternal deaths and 26 % of neonatal deaths, these are likely to be considerable underestimates because of methodological limitations.”

- In the western world at least as common as MI

QECH: Medical admissions septic shock 190
patients a year – 4/5 ICU beds

(Pollach G; Downie P, 2009)



- Mortality 10% in children / up to 38% >85yrs

Seale AC, Mwaniki M, Newton CR, Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009; 9: 928-934

Angus DC et al. Crit Care Med 2001; 29: 1303-10
R. P. H. Peters et al. Tropical Medicine & International Health 2004; 9; 8:

The guidelines and us

Antibiotics : - Ceftriaxon, (Cefotaxim), Gentamicin
Chloramphenicol, Penicillin G,
Metronidazol,
Ciprofloxacin + Erythromycin (oral)

Test for sensitivity : erratic..... ..

(SDD?: not an option)

- Eine Sepsis liegt dann vor, wenn sich innerhalb des Körpers ein Herd gebildet hat, von dem kontinuierlich oder periodisch pathogene Bakterien in den Kreislauf gelangen und zwar derart, dass durch diese Invasion subjektive und objektive Krankheitserscheinungen ausgelöst werden.“
- – klassische Formulierung von Hugo Schottmüller (1914)[5]
- „Sepsis ist die Gesamtheit der lebensbedrohlichen klinischen Krankheitserscheinungen und pathophysiologischen Veränderungen als Reaktion auf die Aktion pathogener Keime und ihrer Produkte, die aus einem Infektionsherd in den Blutstrom eindringen, die großen biologischen Kaskadensysteme und spezielle Zellsysteme aktivieren und die Bildung und Freisetzung humoraler und zellulärer Mediatoren auslösen.“
- – moderne Definition von Schuster und Werdan (2005)[6]
- „Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.“
- „Sepsis ist definiert als lebensbedrohliche Organdysfunktion verursacht durch eine fehlregulierte Wirtsantwort auf eine Infektion.“
- – Mervyn Singer et al. für die Task Force der Society of Critical Care Medicine und der European Society of Intensive Care Medicine: Dritte Internationale Konsensus-Definition der Sepsis und des septischen Schocks (Sepsis-3)[7]

- unktesystems bestimmt werden. Bei diesem Sequential [Sepsis-related] Organ Failure Assessment, kurz: SOFA, werden jeweils bis zu 4 Punkte für die Funktionseinschränkung der folgenden Organsysteme vergeben:

- Atmung (Horovitz-Quotient, $\text{PaO}_2/\text{FiO}_2$)
- Gerinnung (Thrombozytenzahl)
- Leber (Bilirubinwert)
- Herzkreislauf (Blutdruck bzw. Katecholaminbedarf)
- Gehirn (Glasgow Coma Scale)
- Niere (Kreatininwert bzw. Urinmenge)

- Zusätzlich wurde ein vereinfachter quick SOFA (qSOFA) mit nur drei Kriterien eingeführt, der helfen soll, die Patienten zu identifizieren, die eine besonders hohe Sterblichkeit im Rahmen einer Sepsis aufweisen. Dabei müssen zwei der drei folgenden Kriterien erfüllt sein:

- Atemfrequenz $\geq 22/\text{min}$
- eingeschränktes Bewusstsein
- systolischer Blutdruck $\leq 100 \text{ mmHg}$.

Wonderful – we know what to do !



A randomised trial of fluid resuscitation strategies
in African children with severe febrile illness and
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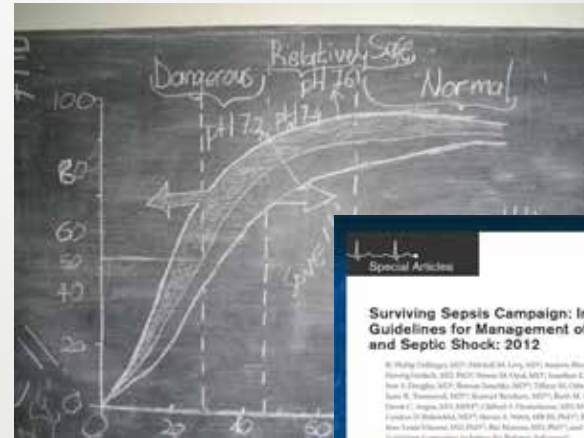
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Sepsis in the tropics

– a constantly changing and challenging topic –



UNIVERSITY OF MALAWI
Department of Anaesthesiology and Intensive Care

Humanitarian Symposium Munich 2018

Gregor Pollach (Assoc. Prof. M.A.,M.A.,FCAI hon.)

Why do we have to deal with „FEAST“ ?

overall) and clinical severity were similar across groups. The 48-hour mortality was 10.6% (111 of 1050 children), 10.5% (110 of 1047 children), and 7.3% (76 of 1044 children) in the albumin-bolus, saline-bolus, and control groups, respectively (relative risk for saline bolus vs. control, 1.44; 95% confidence interval [CI], 1.09 to 1.90; $P=0.01$; relative risk for albumin bolus vs. saline bolus, 1.01; 95% CI, 0.78 to 1.29; $P=0.96$; and relative risk for any bolus vs. control, 1.45; 95% CI, 1.13 to 1.86; $P=0.003$).

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension

A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwangi Bwalya, MBChB; Gordon R. Bernard, MD

- Zambia: 1500 beds, but only 212 patients in 13 months? One group sepsis protocol 4 l in 6h, second group 2 l.
- Mortality high: 48% / 33 %, only in <15% vasopressors (6 hrs)?
- Small study – in FEAST the results changed after 600 children
- 89 % HIV reactive, only half on treatment.
- Dopamine used.
- Long time to (1 h) to enrollment.
- Timeline of deaths and reasons for death? Malaria prevalence?
- **More important:**
- More than 98% never saw ICU (!)
- Most patients were malnourished.
- **Conclusion:**
- A predictable result: you administer 4 l fluids in malnourished patients with multiple comorbidities and you do not treat them adequately against possible sideeffects of volume - than they die.