

How to do your MET research

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The MET, *a complex intervention*

- Management of critically ill patients is complex
 - It involves multiple interventions and processes
 - Concomitant life-threatening pathologies require...
 - Numerous interactive therapies delivered by
 - ...a variety of health care providers
- Examples?
 - Medical emergency teams
 - Early goal directed therapy protocols
 - Advanced trauma life support (ATLS) systems

Evaluating a complex intervention

- Define an appropriate study population
- Define current treatments and outcomes in that population
- Define the intervention (for example, the MET) and the treatment to be used in the control group
- Deploy the intervention in a standardized manner

Evaluating a complex intervention (2)

- Study the potential **benefits**, and the
- **Adverse** effects of the intervention

Complex interventions, study design

- Observational studies
 - May provide insight into the effectiveness of treatment
- Randomized controlled trials
 - Can lead to causal inferences
 - However, RCTs usually study **single interventions** such as the benefits of a drug compared to placebo
 - It is difficult to use RCTs to test complex interventions (such as a MET)

Pretrial activities

- Literature review
- Retrospective studies; the use of existing databases may provide information on the study population, potential recruitment cases and **baseline patient outcomes**
- Pilot studies
- Prospective observational studies; may assist in defining “standard care” and expected outcome in the control patients
 - This allows for gauging realistic potential treatment effects
 - Allowing the determination of an appropriate sample size

Trial design

- All clinical research should be designed to answer a **clearly articulated question**
- Consider the **internal validity** (the extent to which systematic error has been avoided)
- Consider the **external validity** (the extent to which the results of the trial can be generalized to other circumstances)

Trial design (2)

- The population
 - All patients in the hospital? All surgical patients in the hospital?
 - The healthcare providers? The entire healthcare system?
- The intervention
 - Adherence to the protocol
 - Is the intervention (the MET) being used fully?

Trial design (3)

- Context dependence

- New processes of care may have different impacts on outcome depending on the background processes already in place
- Affects generalizability: test the protocol in different settings, various hospital types and locations

- Reproducibility

- Ensuring that the intervention is accurately and timely delivered
- A “learning curve”...improvement over time?
- “Trial fatigue”?

Trial design (4)

- The comparison group
 - “Wild type”=care as it happens now?
 - Regimented and commonly accepted care?
- The outcome
 - Should be robust and well defined in advance
 - Example (MET): all-cause mortality at a defined point in time, such as 30, 60 or 90 days

Trial execution

- Randomization
 - At hospital level, cluster randomization, avoids that the educational efforts of complex interventions will spill over into the control group
- Before- and after studies
 - Allows outcome measurements in a similar group of patients
- Blinding? It is difficult to conduct an RCT evaluating a complex intervention in a blinded fashion

Trial execution (2)

- Analysis

- An intention-to-treat analysis is recommended
- A pre-analysis statistical plan will ease concerns of post-hoc data manipulation and analytical bias

Trial reporting

- Focus on the description of the intervention
 - This allows it to be reproduced if so desired
- A description of the treatments delivered to the control group(s) is needed

Suggested reading

Bench-to-bedside review: The evaluation of complex interventions in critical care

Delaney et al. Critical Care 2008, 12:210

Complex intensive care unit interventions

Hillman et al. Crit Care Med 2009 Vol 37, No.1 (Suppl)

Pretrial activities: The Karolinska study

Resuscitation (2006) 70, 66–73



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Prevalence and sensitivity of MET-criteria in a Scandinavian University Hospital[☆]

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Testing the criteria, the Karolinska study

•Bell M et al, *Prevalence and sensitivity of MET-criteria in a Scandinavian University Hospital* Resuscitation 2006;70:66-73

- The study took place at two separate occasions, December 10th 2003 and March 24th 2004
- With the help of 50 nursing students from the Red Cross Nursing School, we set out to record *prevalent physiological data* on all adult patients treated in the hospital, excluding the intensive care- and psychiatric wards
- 1097 patients were treated at the wards during the two study periods
 - 81.6 % were included
- 40 patients (4.5%) fulfilled the study criteria
- 42 patients had a DNAR

Testing the criteria, the Karolinska study

The MET criteria

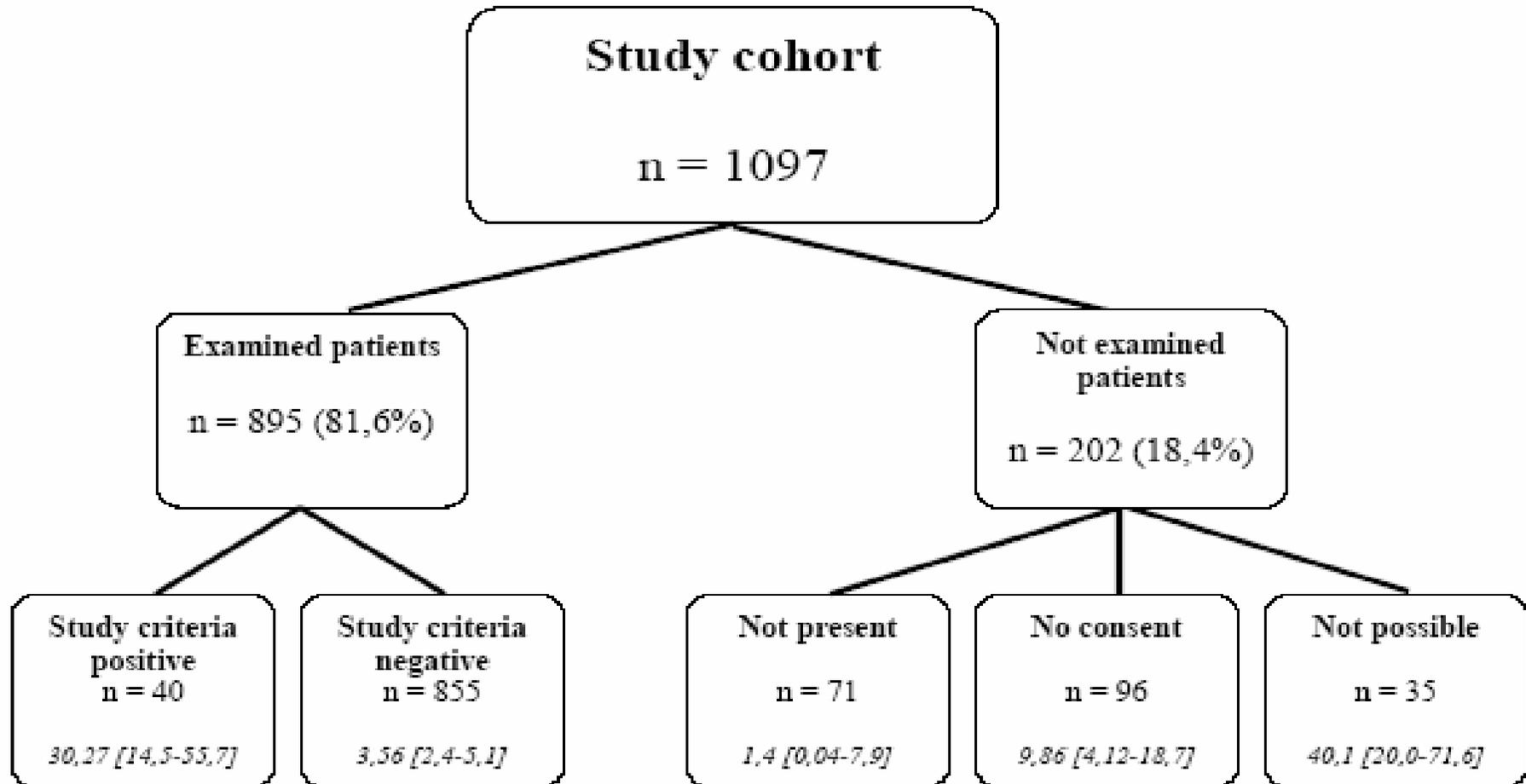
- Acute change in respiratory rate to <8 or >30 breaths/min
- Acute change in pulse oximetry saturation to $< 90\%$, despite oxygen administration
- Acute change in heart rate to <40 or >130 /min beats/min
- Acute change in systolic blood pressure to <90 mm Hg
- Acute change in conscious state as measured by a fall of GCS >2
- Staff member is worried about the patient

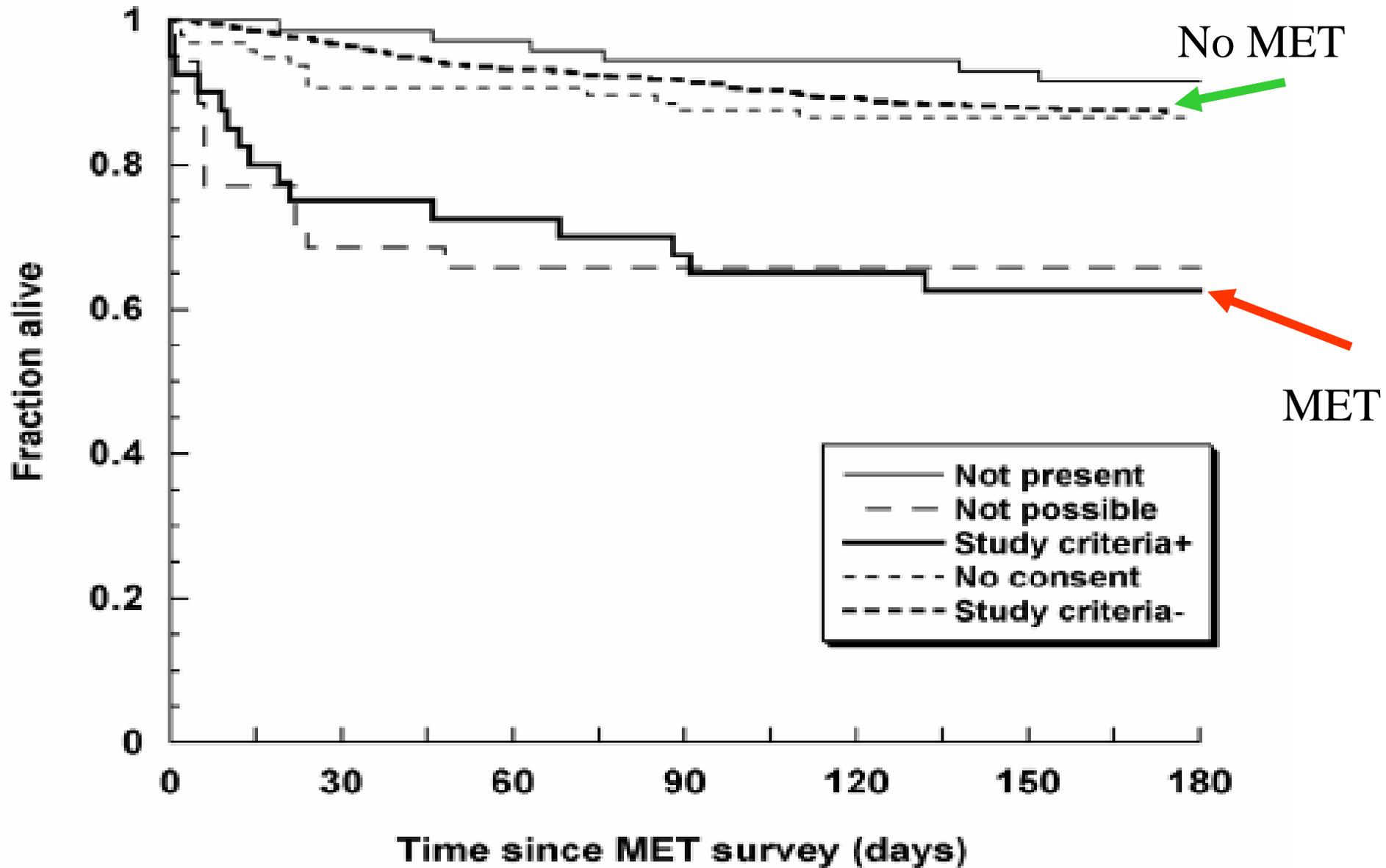
Study Criteria

- Respiratory rate of <8 or >30 breaths/min
- Heart rate of <40 or >130 /min beats/min
- Systolic blood pressure of <90 mm Hg

Testing the criteria, the Karolinska study

Flow diagram describing the distribution of the cohort. 30-day mortality rates and CI in italics





Testing the criteria, the Karolinska study

The extended criteria

- Respiratory rate of ≤ 10 or > 28 breaths/min
- Heart rate of < 50 or > 120 /min beats/min
- Systolic blood pressure of < 100 mm Hg

The restricted criteria

- Respiratory rate of ≤ 6 or > 32 breaths/min
- Heart rate of < 35 or > 140 /min beats/min
- Systolic blood pressure of < 80 mm Hg

Testing the criteria, the Karolinska study

- 4,5% (40) of the scored patients fulfilled the study criteria
 - 30-day mortality: 25% (CI 12.7-41.2)
- The patients *not* fulfilling the study criteria
 - 30-day mortality: 3.5% (CI 2.4-5)
- *Extended criteria* resulted in 13.8 % of the cohort (123) fulfilling these criteria
 - 30 day mortality: 14.6 % (CI 8.9-22.1)
- *Restricted criteria*: 2,2 % (20) fulfilled these criteria
 - 30 day mortality: 20 % (CI 5.7-43.7)

Our pretrial conclusions

- Do crisis criteria detect patients at risk?
 - Well, yes, but are our criteria good enough? Are they optimized?
 - Trade-off: work load vs risk of missing patients?
 - Trade-off: simplicity vs sensitivity?
- If the afferent limb of the MET could be sold as a spray....**