

# 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<sup>☆</sup>

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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

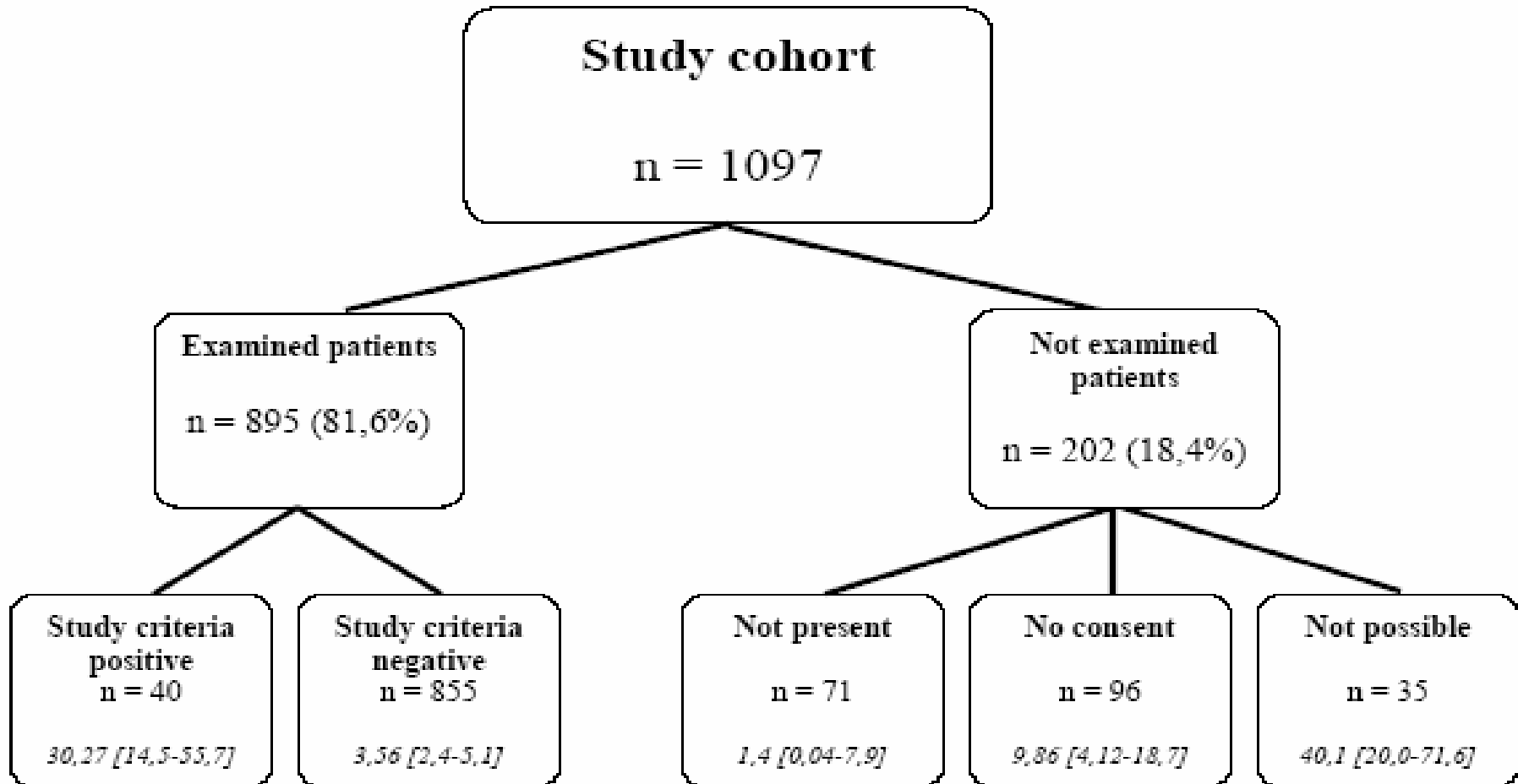
- Acute change in respiratory rate to  $<8$  or  $>30$  breaths/min
- Acute change in pulse oximetry saturation to  $< 90\%$ , despite oxygen administration
- Acute change in heart rate to  $<40$  or  $>130$ /min beats/min
- Acute change in systolic blood pressure to  $<90$  mm Hg
- Acute change in conscious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

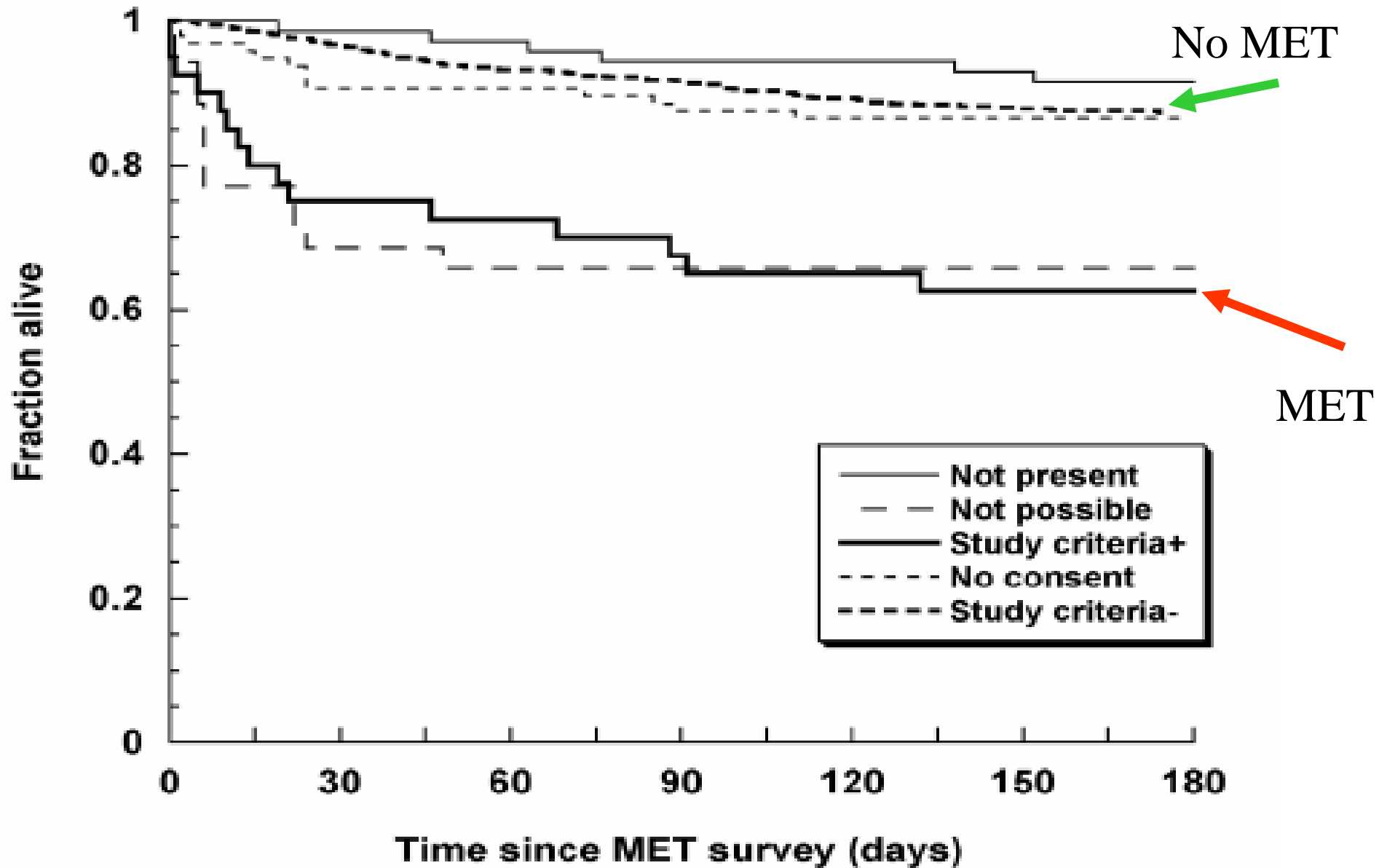
## Study Criteria

- 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  $\leq 10$  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  $\leq 6$  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....**