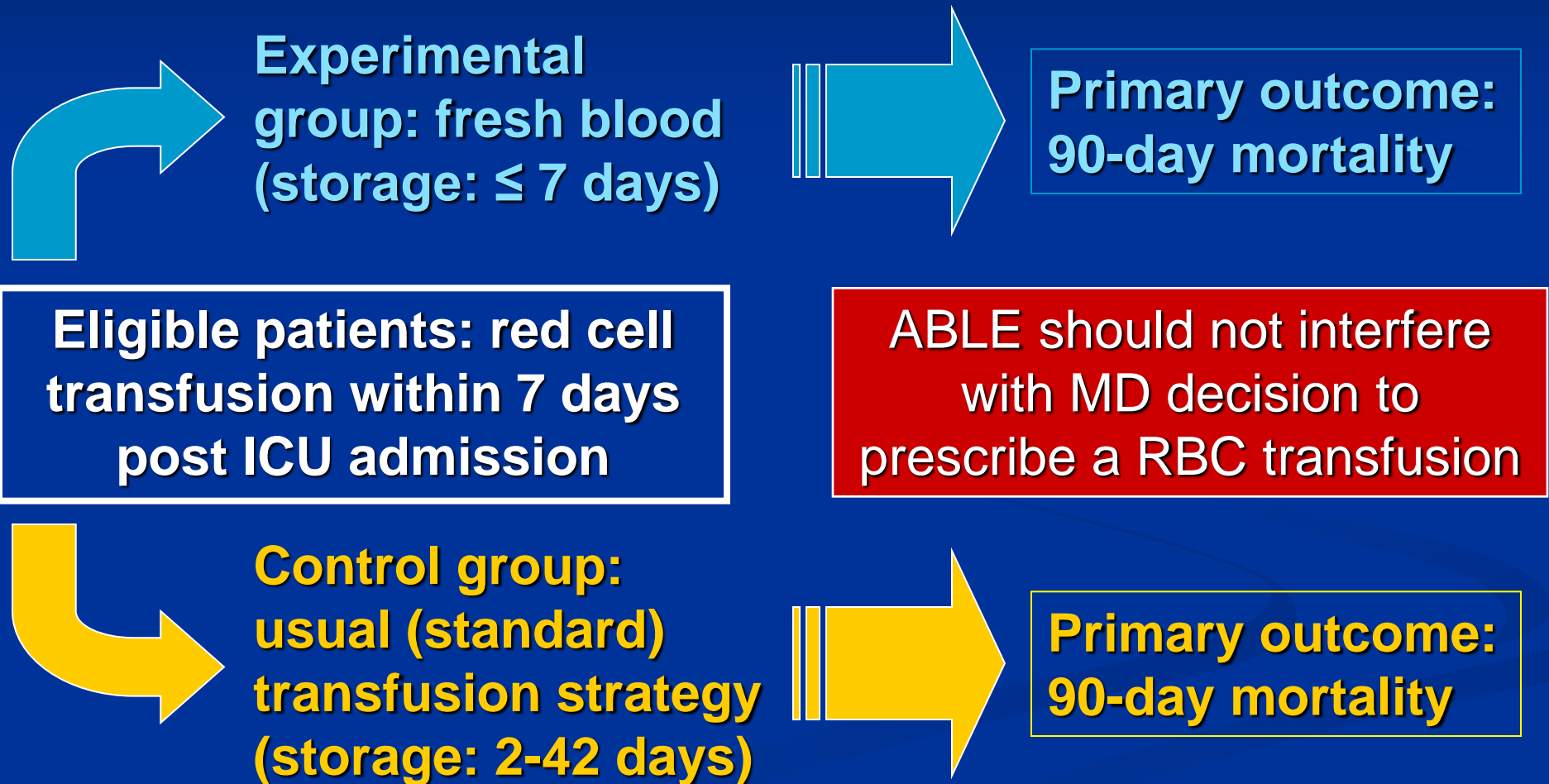


ABLE study: basic design

- The Age of Blood Evaluation (ABLE) trial is a double-blind, multicentre superiority randomized clinical trials:
 - Up to 40 academic & community centres (Canada, France, United Kingdom and Netherland).
 - Intensive care units for adults.
- Primary hypothesis: as compared to standard issue red cells (length of storage: 2 to 42 days), we expect to find that red blood cells (RBC) stored for 7 days or less decrease incidence of all-cause 90-day mortality, by an absolute risk reduction of 5% (20% relative risk reduction assuming a baseline mortality of 25%).

ABLE study: basic design

(2510 patients)



ABLE study: basic design

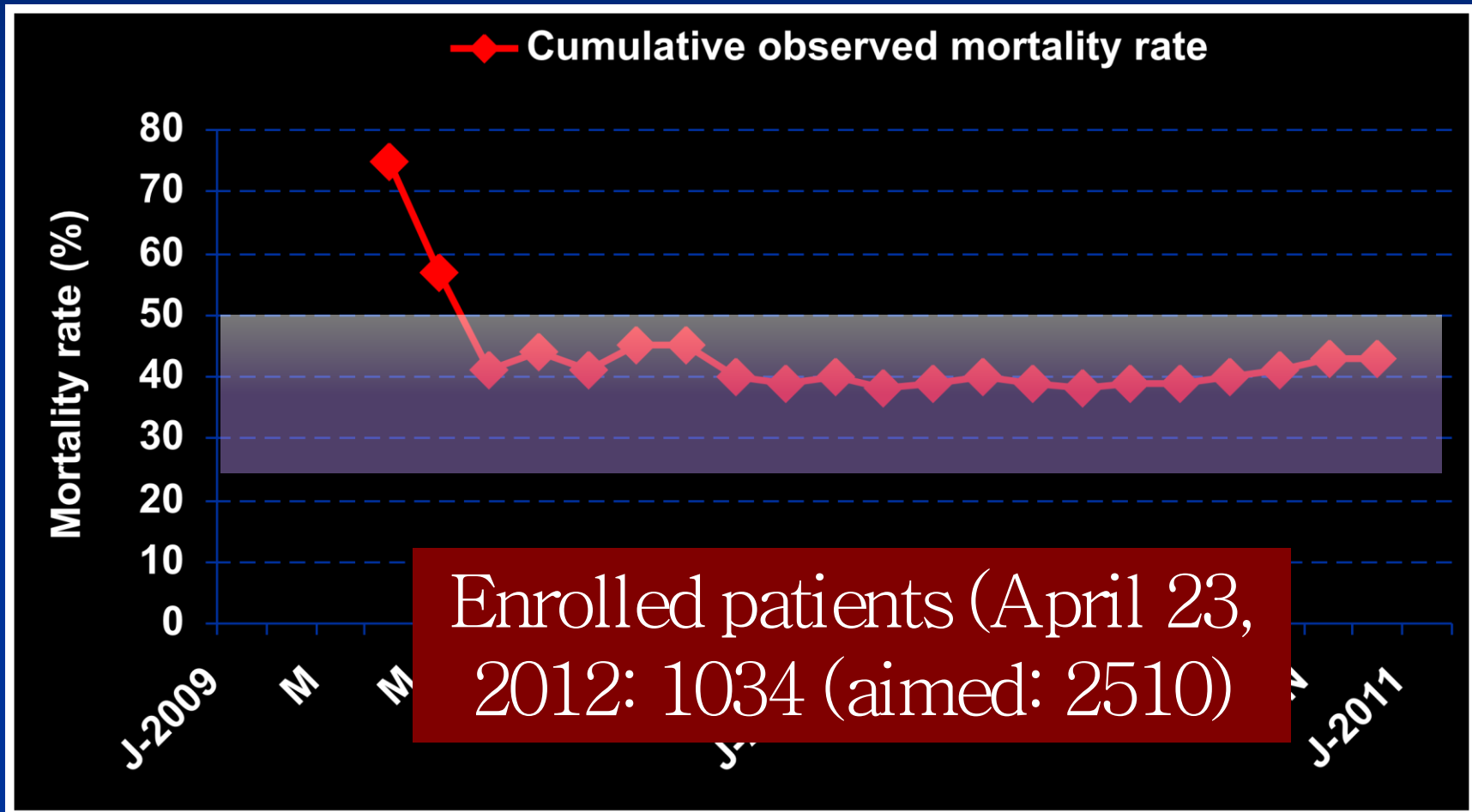
Inclusion criteria

■ Inclusion criteria:

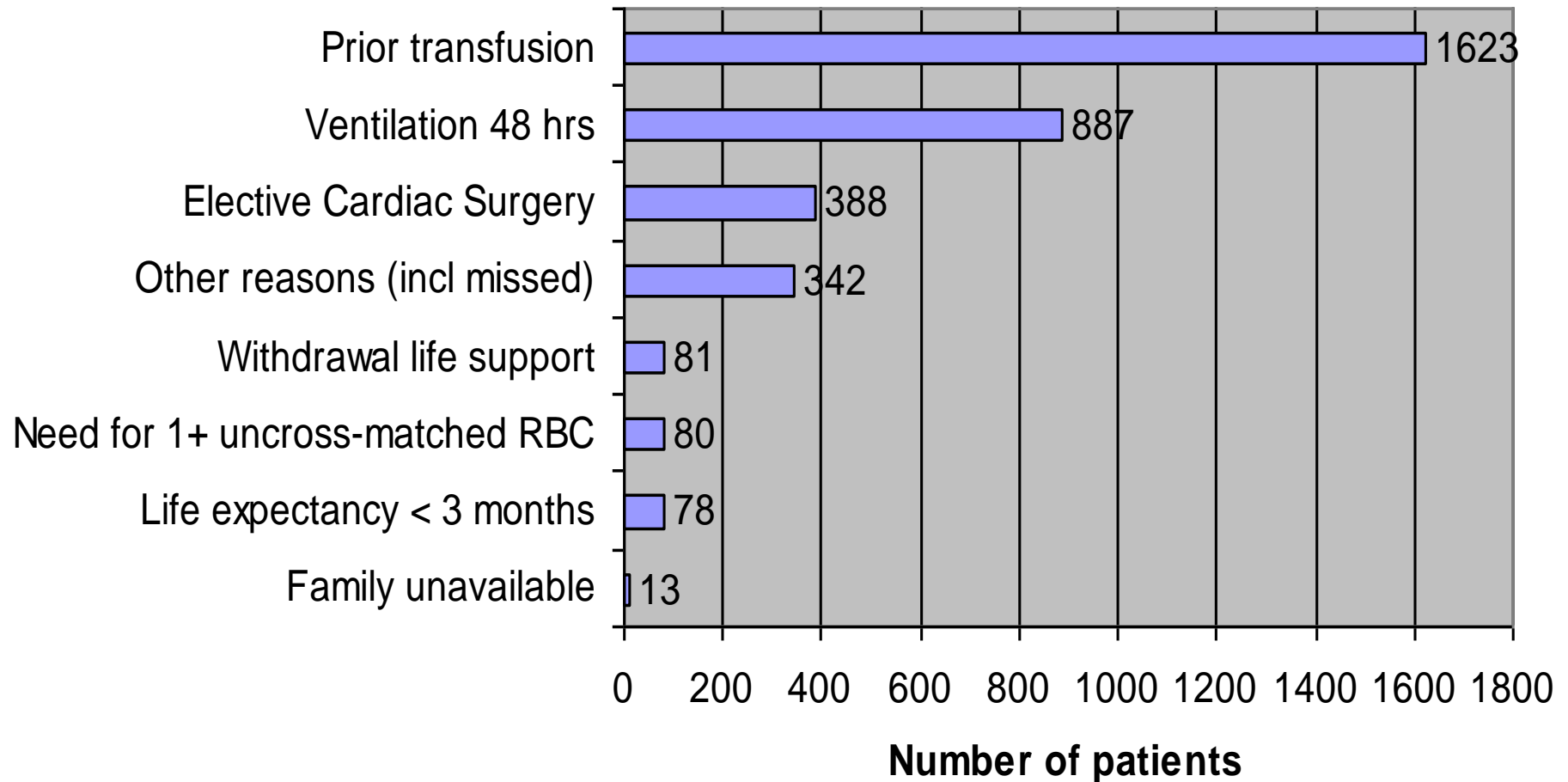
- At least one RBC transfusion is prescribed during the first 7 days in the ICU,
- *And* the patient has an anticipated length of mechanical ventilation exceeding 48 hours once enrolled.

Expected mortality:
 $\geq 25\%$.

ABLE: observed versus expected mortality rate (25-50%, whitish strip)



More frequent causes of exclusion



ABLE study: basic design

Interventions and co-interventions

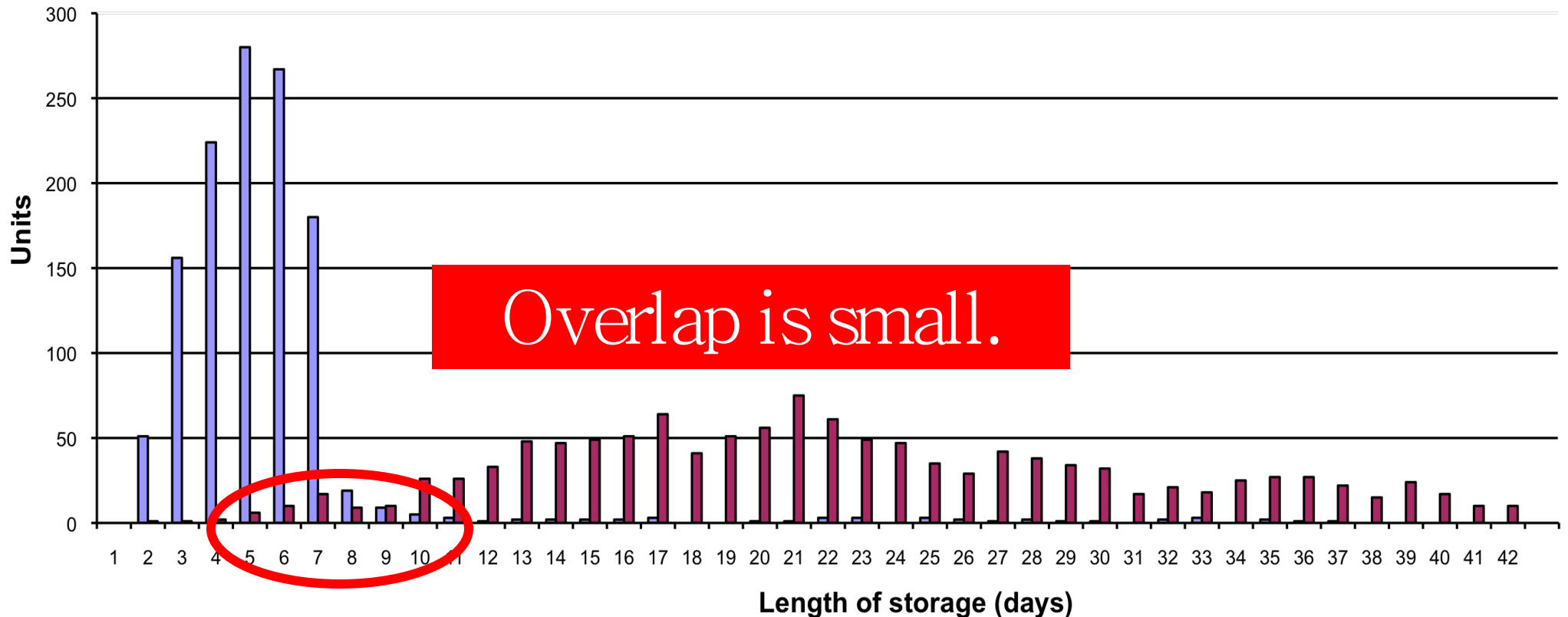
- Intervention:
 - **Experimental group:** RBC units that will be as fresh as possible (length of storage must be ≤ 7 days if possible).
 - Expected average length of storage: **about 5 days.**
 - **Control group:** standard RBC delivery strategy (length of storage: 2 to 42 days). Blood will be delivered as it would be in normal circumstances, which means that patients will receive the oldest available blood first.
 - Expected average length of storage: **≥ 15 to 21 days.**
- Co-interventions (volume/kg): platelets and plasma.

ABLE: observed length of storage

	Fresh group	Standard group
Average age of blood (days)	4.95 ± 1.4	22.41 ± 8.7
Number of patients with length of storage collected in case report form	388	392
Delta: 17.46 days		

Last update: January 1, 2012

Length of storage of the RBC units given to ABLE participants



ABLE study: basic design

Outcome measures

- Primary outcome measure: 90-day mortality
- Secondary outcome measures:
 - Mortality: 28-day, 6-month, ICU & hospital discharge, survival.
 - MODS: frequency and severity (MODS score).
 - Nosocomial infections (incidence rate).
 - Length of ICU and hospital stays.
 - Length of need for cardiovascular (vasoactive drugs).
 - Length of respiratory (mechanical ventilation).
 - Length of renal organ support (renal replacement therapy) .
 - Adverse events, acute reactions to RBC transfusion.

ABLE study:

Statistical analysis

- Sample size: 2510 patients.
- Interim analyses: each 500 patients.
 - Aim: for safety and benefit.
- Final analysis:
 - Superiority (alpha at 0.05, power at 0.9).
 - Intention-to-treat.
 - Subgroup analyses:
 - Severe sepsis/septic shock vs other.
 - Trauma vs other.
 - Perioperative vs other.
 - One to 3 RBC units vs more than 3 units.
 - Patients with APACHE II score < 20 vs high ≥ 20 .

ABLE study: members of the Executive Committee

■ Principal investigators:

- Jacques Lacroix
- Paul C. Hébert
- Dean Fergusson
- Alan Tinmouth



■ Co-investigators:

- Morris Blachman
- Jeannie Callum
- Gilles Capellier
- Deborah Cook
- John Marshall
- Loralyn McIntyre
- Pierre Tiberghien
- Alexis Turgeon

■ Study manager:

- Lucy Clayton



Conclusion

Age of blood: does it matter?

- “There is strong laboratory evidence suggesting that prolonged RBC storage may be deleterious.”

Tinmouth et al. Transfusion 2006.

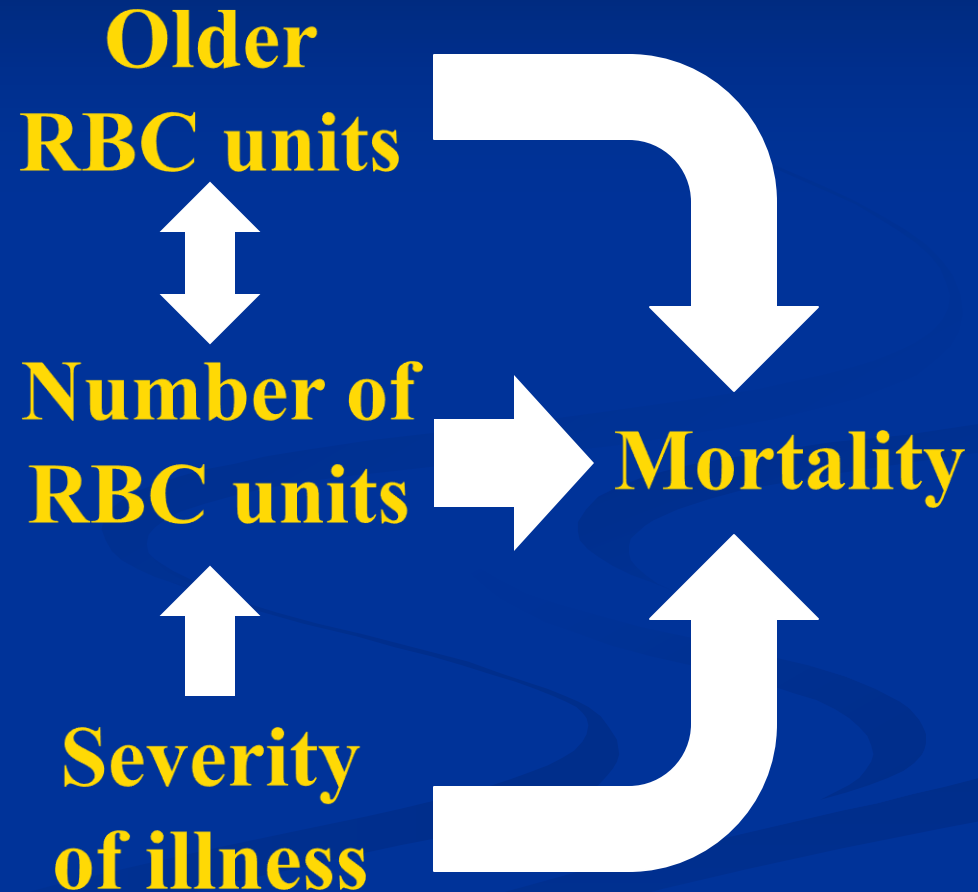
- There is some clinical evidence that an association exists between length of storage and outcome.
- However, observational studies overestimate the real benefit — or harm — of a treatment by 30 to 60%.

Deeks. Health Technol Assess 2003;7:1-173.

- Data are equivocal: the number of positive observational studies is almost similar to the number of negative studies.
- Moreover, finding an association does not mean that there is a cause-effect relationship.

Age of blood: does it matter?

- An association is described between age of blood (AOB) and mortality in ICU patients.
 - The same association is observed with number (#) of RBC units and severity of illness
 - AOB, # and severity of illness are associated together.
- Thus, there is **confounding by indication** (Middelburg et al. Transfusion 2010;50:1881-3).
 - **Multivariate analysis cannot deconstruct this relationship.**
 - Actually, it is unknown if storage lesions really cause clinically significant problems.



Why ABLE and other RCTs on AOB must be done

- Only RCT like the ABLE study can uncouple the relationship and the interaction between severity of illness, number of transfusions, and age of blood, and prove that there is a cause-effect relationship between length of storage and outcome of transfused ICU adults.

Back to the future: large RCTs

- 3 large RCTs on length of storage of RBC units are presently ongoing:
 - ABLE study (ISRCTN44878718).
 - RECESS (NCT00991341; M Steiner, USA & NIH):
 - Patients: 1600 cases of coranoplasty with cardio-pulmonary bypass.
 - Outcome measure: MODS score.
 - Published protocol: Transf Apher Sci 2010;43:107-16
 - The “Red Cell Storage Duration and Outcomes in Cardiac Surgery” (NCT00458783): Koch et al, Cleveland .
 - Patients: 2800 cases.
 - Outcome: morbidity post-surgery.
- 3 large RCTs may start quite soon:
 - INFORM.
 - TRANSFUSE.
 - ABC-PICU study (Tucci, Spinella): under review.

