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Title: R-fact study: risk factors for alloimmunization after red blood cell transfusions:

methodology, risk factors and challenges in transfusion medicine research

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## STELLINGEN (PROPOSITIONS)

- 1. The incident new-user cohort design provides a more reliable estimate of alloimmunization risk than a cohort that starts with a cross-section of prevalent users. (This thesis)
- 2. A case-referent design is equipped to provide valid evidence on an etiologic transfusion research question only if referent patients are matched to the case-patients on transfusion history. (This thesis)
- 3. Risk of developing alloantibodies increases with the cumulative number of red blood cell transfusions and reaches a "plateau" around 40-45 transfusions. (This thesis)
- 4. Risk of developing alloantibodies does not differ for men and women. (This thesis)
- 5. Storage time of red blood cells, within the clinically relevant ranges of 7-28 storage days does not modulate the risk of alloimmunization. (This thesis)
- 6. Concomitant immunosuppressive use should be incorporated in a risk score identifying high or low risk patients for clinical alloimmunization. (This thesis)
- 7. Use of prediction methods to answer etiologic (causal) questions has led to misinterpretation of the notion of "independent risk factors" and in consequence, possibly insufficient treatment of patients requiring red cells for their oxygen deprived tissues. (This thesis)
- 8. We need to identify potential confounding to be able to eliminate it; that is different from defining some variables as confounders.
- 9. Power calculations are not necessary in observational studies, except very globally to know whether it is worthwhile to start the study at all; confidence intervals are telling what precision one has obtained in the research, and suffice for interpretation.
- 10. Thinking about matching in a case-control study can become quite a complicated process, as witnessed in chapters 2, 4 and 6 of this thesis.
- 11. The immune system by necessity has evolved into having the capacity to mount a vigorous response against some foreign antigens, but not against others antigens. (adapted: Dr. J. Zimring in Transfusion Clinique et biologique, 2012)
- 12. If you want to be more dramatic, just add another zero. (source: R.A. Middelburg, 2012)
- 13. Study the past if you want to define the future. (source: Ancient Vedic scriptures, circa 4 BC)
- 14. Wikipedia is the first place I go when I'm looking for knowledge; or when I want to create some. (source: Stephen Colbert, 2007)
- 15. If you don't stick to your values when they're being tested, they're not values: they're hobbies. (source: Jon Stewart, 2009)