R-FACT Study

Risk Factors for Alloimmunization to Red Blood Cell Transfusion
A case control study
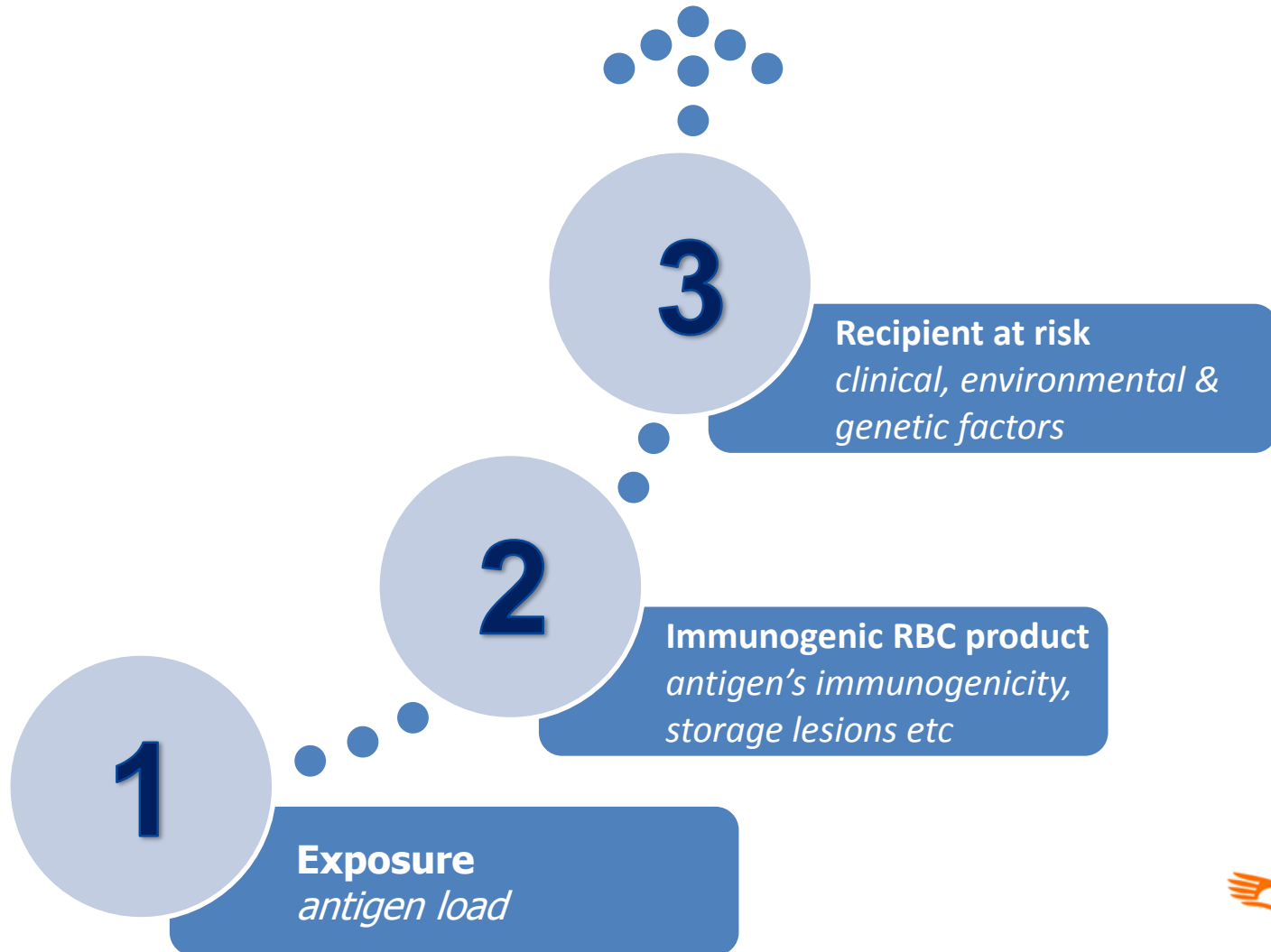
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Blood and Beyond

Research objective

Identifying (recipient and donor-related) factors associated with the risk of alloimmunization after RBC transfusion:

- ❑ insight into pathophysiological mechanisms of alloimmunization
- ❑ generate a risk score with cost effectiveness modeling
- ❑ extensive matching to those mostly profiting from this

Alloimmunization

3

Recipient at risk
clinical, environmental & genetic factors

2

Immunogenic RBC product
antigen's immunogenicity, storage lesions etc
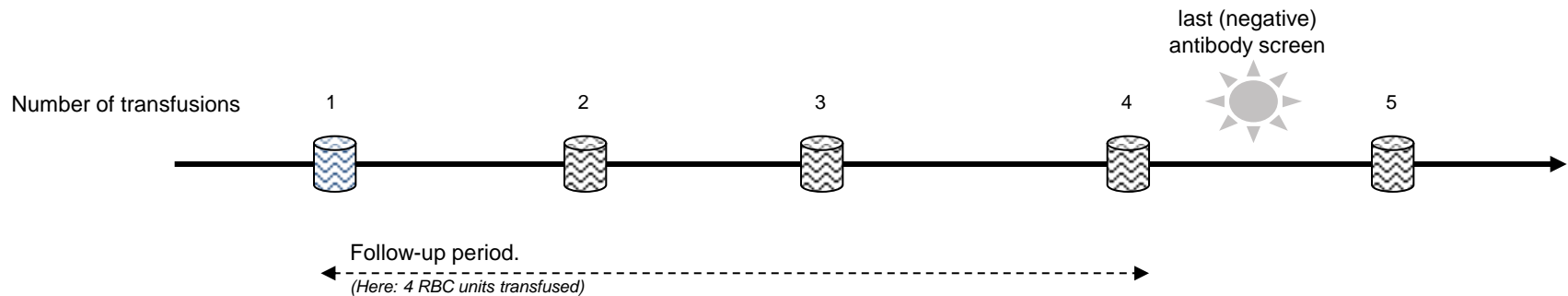
1

Exposure
antigen load

Methods

Incident new user cohort study: patients firstly transfused between 2005-2013

Follow-up until:
- ❏ non-immunized: last negative screen
- ❏ immunized: first-time alloantibody identification

last (negative)
antibody screen

Number of transfusions   1   2   3   4   5

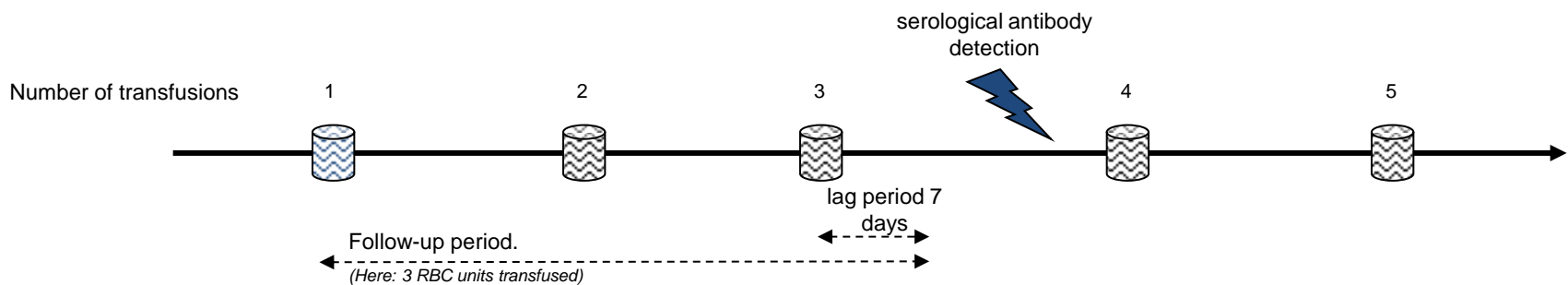Follow-up period.
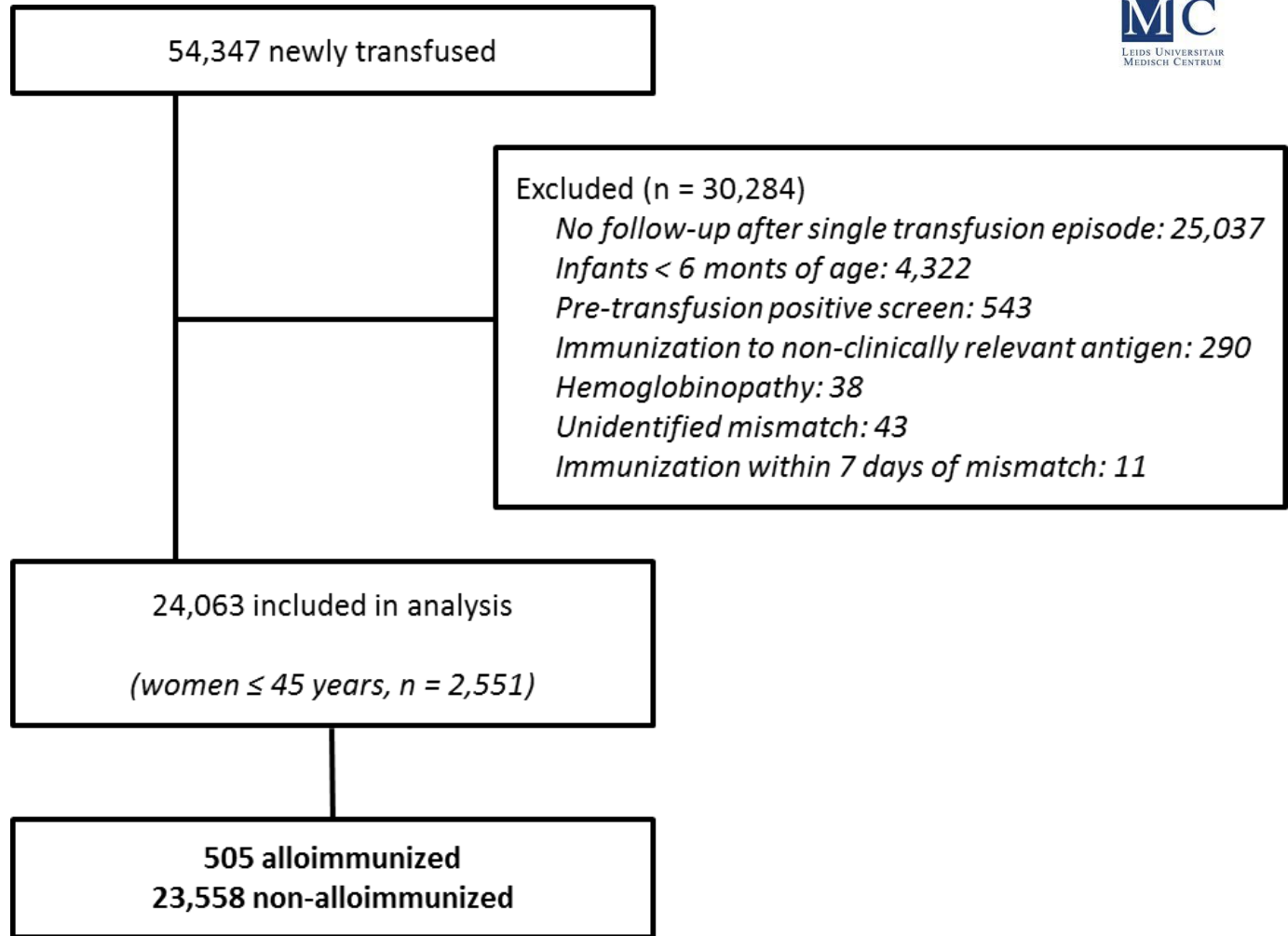*(Here: 4 RBC units transfused)*

Methods

Incident new user cohort study: patients firstly transfused between 2005-2013

Follow-up until:
- ❑ non-immunized: last negative screen
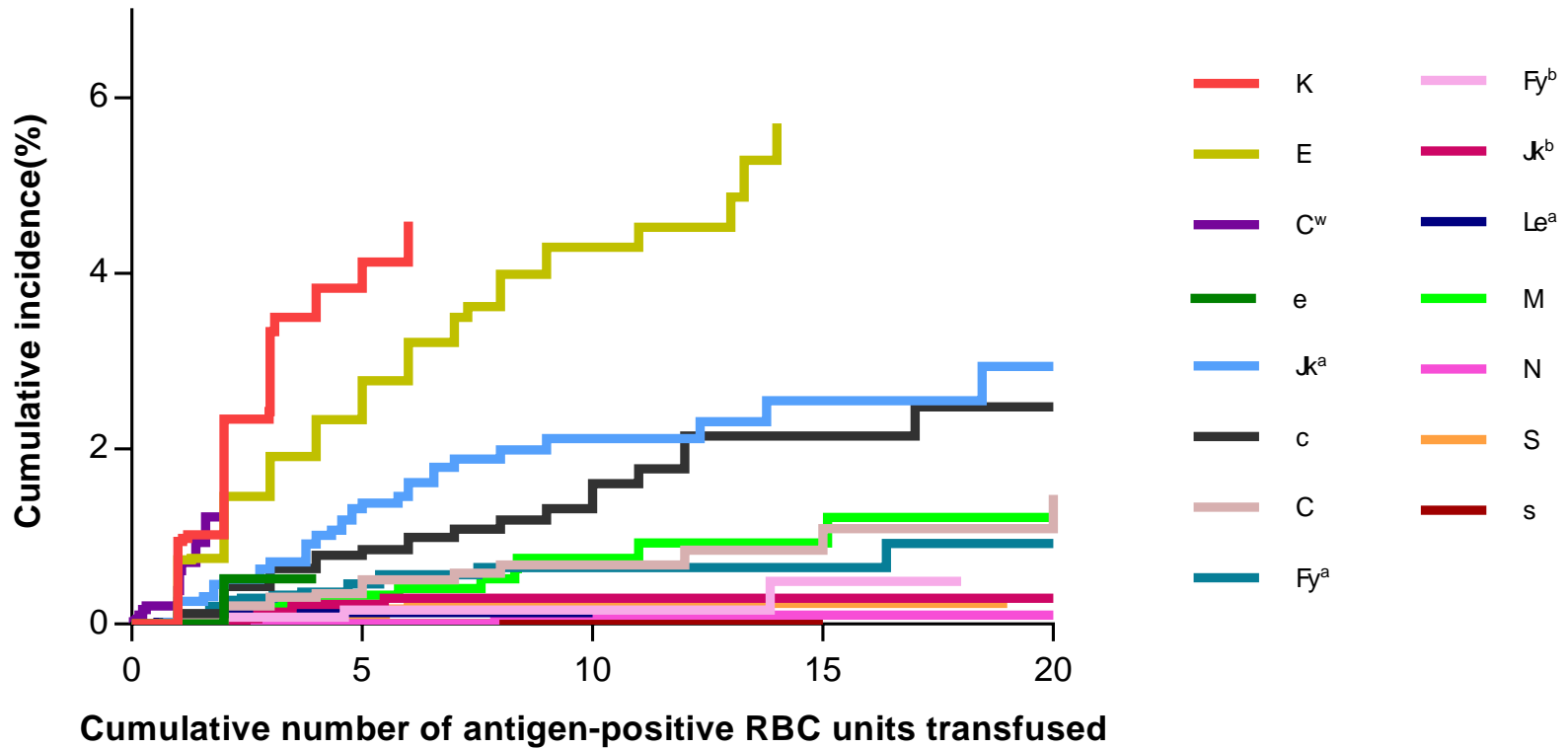- ❑ immunized: first-time alloantibody identification

serological antibody
detection

Number of transfusions   1   2   3   4   5

lag period 7
days

Follow-up period.

(Here: 3 RBC units transfused)

54,347 newly transfused

Excluded (n = 30,284)
  No follow-up after single transfusion episode: 25,037
  Infants < 6 monts of age: 4,322
  Pre-transfusion positive screen: 543
  Immunization to non-clinically relevant antigen: 290
  Hemoglobinopathy: 38
  Unidentified mismatch: 43
  Immunization within 7 days of mismatch: 11

24,063 included in analysis

(women ≤ 45 years, n = 2,551)

505 alloimmunized
23,558 non-alloimmunized

Exposure and antigen immunogenicity
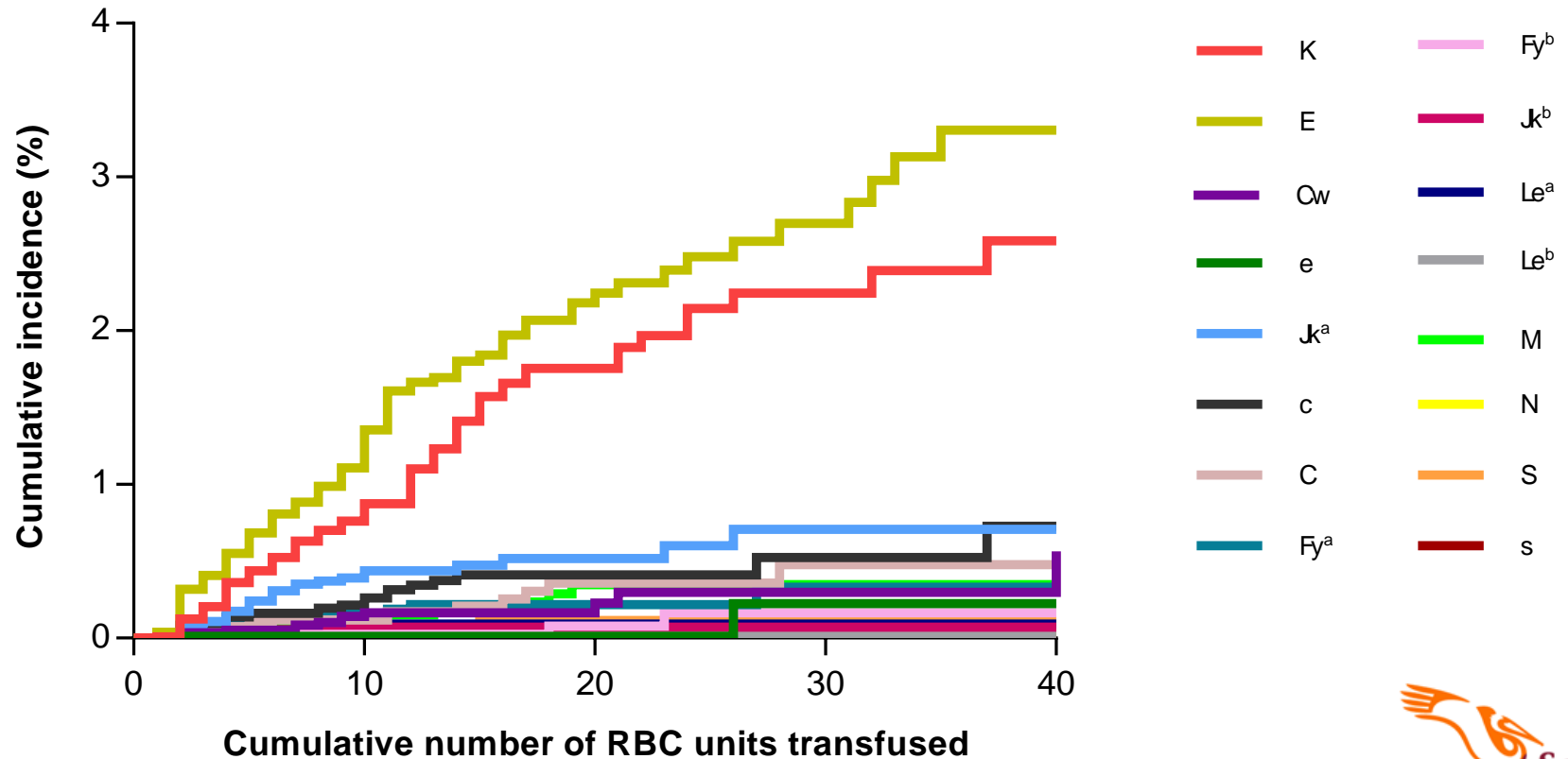
Exposure and antigen immunogenicity

Matching is profitable
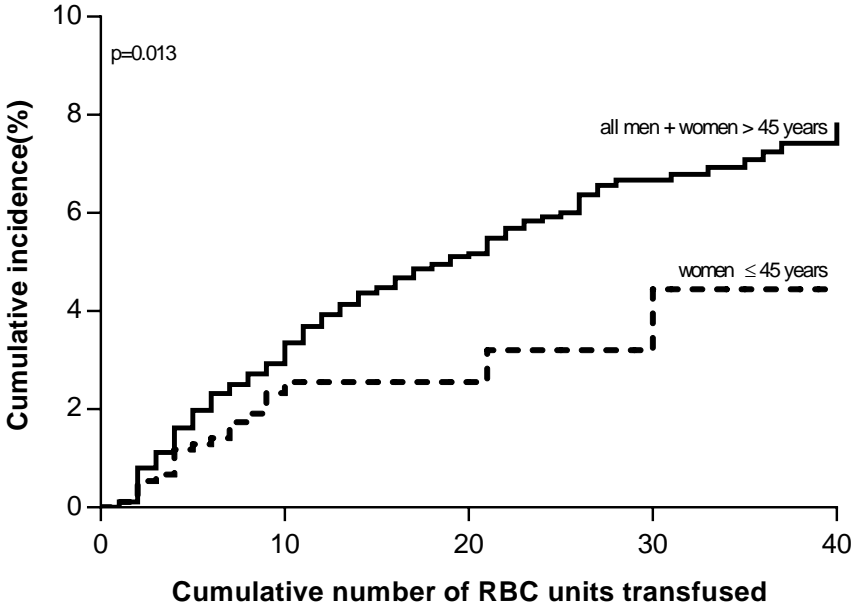
Matching is profitable

ALL	cE	cEK	CcEK	CcEK + Jk^a	CcEK + Jk^a + Fy^a	CcEK + Jk^a + Fy^a + C^w
100%	45%	69%	76%	83%	86%	88%
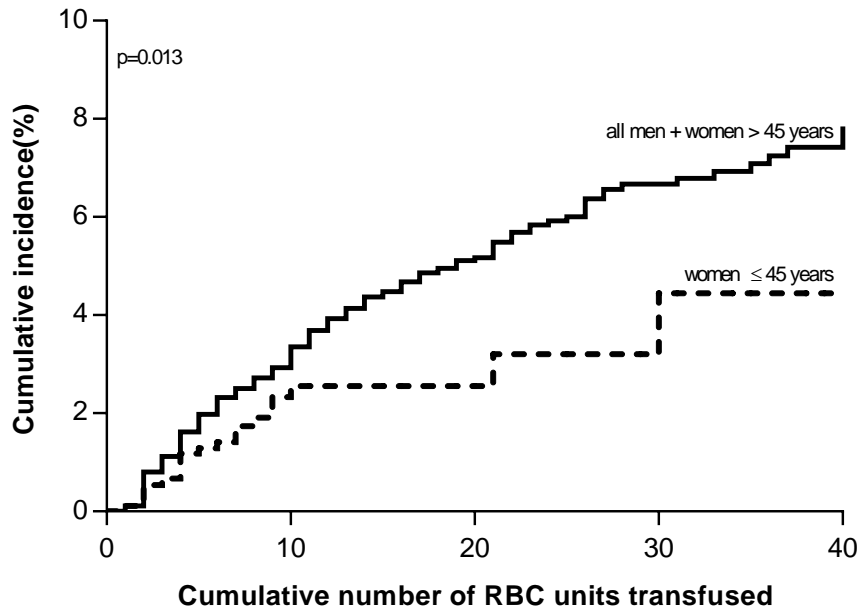
Clinical Risk Factors
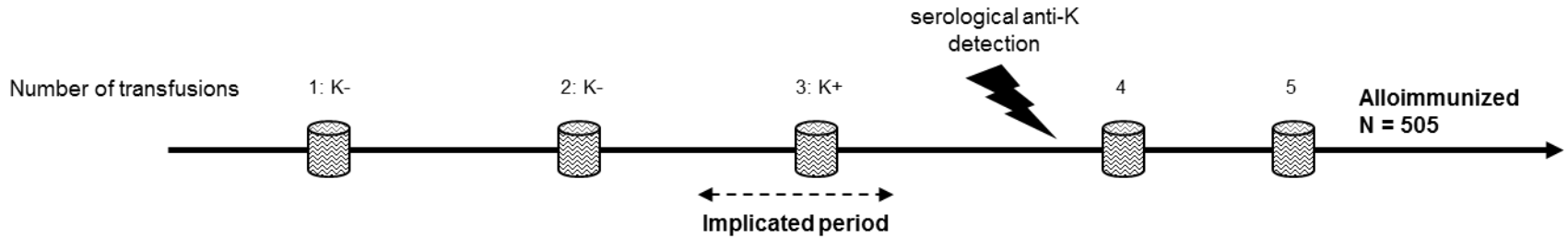
Implicated period = 4 weeks before up till 1 week after implicated transfusion.

Clinical Risk Factors

Number of transfusions

1: K-   2: K-   3: K+   serological anti-K detection   4   5   **Alloimmunized N = 505**

Implicated period

Number of transfusions

1.   2.   3.   4.   last (negative) antibody screen   5.   **Non-alloimmunized N = 1010**
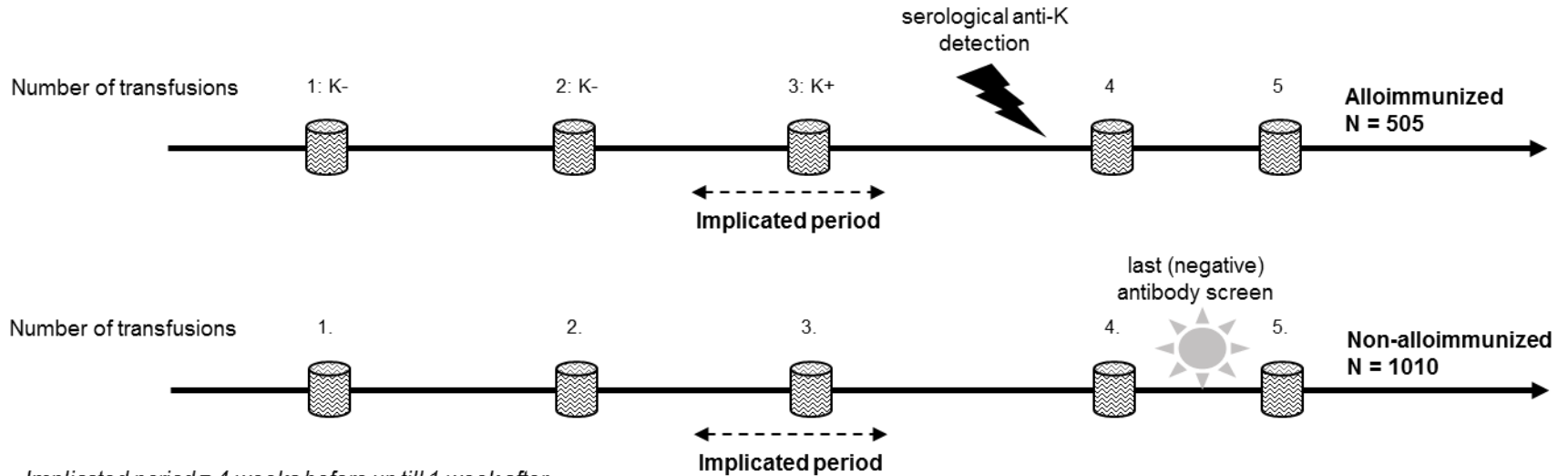
Implicated period

Implicated period = 4 weeks before up till 1 week after implicated transfusion.

Immunosuppressants

TABLE 3. RR of alloimmunization in patients using only corticosteroids, only other immunosuppressants, and both compared to using none of these*

Immunosuppressive therapy	Case patients	Control patients	Crude RR† (95% CI)	Adjusted RR‡ (95% CI)
None	93	150	1 (ref)	1 (ref)
Only corticosteroids	43	99	0.68 (0.43-1.08)	0.70 (0.42-1.16)
Only immunosuppressants	1	3	0.45 (0.04-5.00)	0.51 (0.04-7.1)
Both	10	51	0.28 (0.13-0.59)	0.19 (0.07-0.53)

† Adjusted for the matching variables (number of matched transfusions and hospital).
‡ Adjusted for matching variables (number of matched transfusions and hospital); sex, age, COPD, infection, fever, transplants, allergies autoimmune diseases, leukemia, lymphoma, chemotherapy, surgeries, trauma, diabetes Type 1, and diabetes Type 2.

Corticosteroids and/or immunosuppressants: adjusted RR 0.55 (0.34-0.91)

**TABLE 1. Immunosuppressive medication use (n = 207 patients) among total study population of 468 patients**

Medication	Number (%)
Prednisolone/prednisone	104 (50.2)
Dexamethasone	97 (46.9)
Hydrocortisone	50 (24.1)
Methylprednisolone	34 (16.4)
Other	1 (0.5)
Cyclosporine	34 (16.4)
Mycophenolate mofetil	37 (17.9)
Azathioprine	5 (2.4)
Antithymocyte globulin	9 (4.3)
Basiliximab	16 (7.7)
Tacrolimus	22 (10.6)
Thalidomide	3 (1.4)
Other	1 (0.5)

Preliminary results

Dialysis

	Crude OR	Crude OR 95%	Adjusted OR	Adjusted OR 95%
Dialysis	0.616	0.402-0.943	0.620	0.390-0.985
eGFR<30 ml/min gedurende ≥ 1 week	1.027	0.968-1.089	1.028	0.964-1.095
Kreat > 500 µmol/L (minimaal 1-malig)	0.630	0.425-0.933	0.621	0.406-0.949
Kreatinin > 500 µmol/L (≥ 1 measurement) without dialysis	0.929	0.422-2.044	0.872	0.386-1.971

Adjusted OR: adjusted for age, gender, DM2, cardiac morbidity, ICU admission, CABG, surgery, use of immunosuppressants.
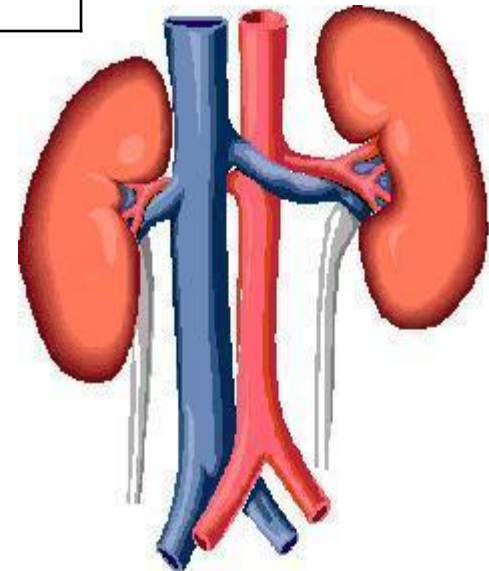
Other potential associated factors

- Inflammation: fever, infection (and type e.g. bacterial vs viral), (coronary) atherosclerosis, COPD, leucopenia / -cytosis, CRP values
- Auto-immune diseases (and type)
- Malignancies: type, dissseminated, treatment (chemo- / RTx, SCT)
- Surgery, ICU admission
- ……

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