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Preventing Alloimmunization using a New Model for Matching Extensively Typed Red Blood Cells

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Conflict of interest

No conflict of interest to declare

Introduction

Red blood cells (**RBC**): most common transfused blood product.

transfusion with phenotype-incompatible RBC units
→ production of alloantibodies by the patient's immune system (**alloimmunization**)
→ hemolytic transfusion reaction on future transfusions

Alloimmunization can be prevented by transfusing fully compatible RBC units.
Genotyping → extensive typing
- donors: increase in the availability of typed RBCs
- patients: preventive matching on minor antigens

large-scale extensive matching → reducing alloimmunization

number of possible phenotype profiles increases exponentially with the number of antigens
→ need for **software-driven solution** to select the best RBC unit for a given patient

aim: Minimize the expected number of alloimmunizations over all transfused patients by providing them with suitable RBC units, without introducing any additional shortages or outdating of RBCs.

Methods

novel flexible **issuing strategy** for assigning RBC units to patients
- penalty-based approach for preventing mismatches
  - **penalty** determined by antigen **immunogenicity**[2]
- 11 minor antigens: representing 95% of clinically relevant alloantibodies resulting from alloimmunization

virtual **RBC inventory**: direct patient requests, resupplied with random units

baseline for comparison: FIFO/MROL for ABO, RhD-matching (ABOD)[1]:
(comparable to current strategy in the Netherlands)

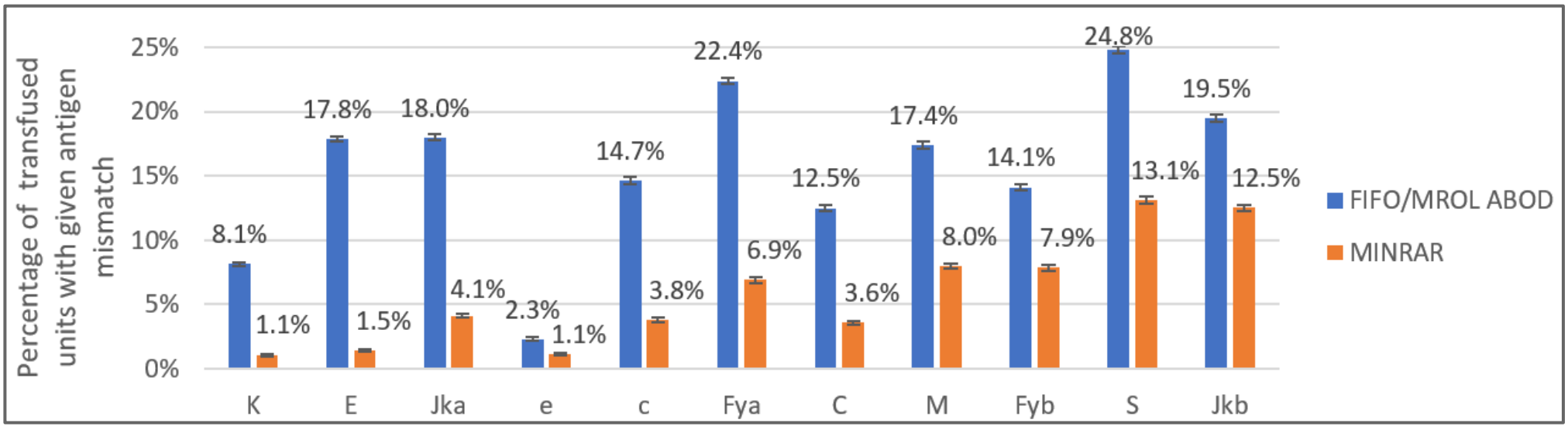
level of antigen exposure not considered
→ proportion of patients without exposure is maximized.

integer linear programming (ILP) model: **MINRAR** (MINimize Relative Alloimmunization Risks)
iterative solving → decisions affect matching potential for the next day(s)

Number of alloimmunizations per 1000 patients exposed to 2 mismatching units	
C	2.1
c	4.3
E	14.6
e	5.1
K	23.4
Fy^a	2.7
Fy^b	0.8
Jk^a	5.1
Jk^b	0.2
M	1.8

[1] Van Sambeeck JHJ, Van Brummelen SPJ, Van Dijk NM, Janssen M. Blood group specific issuing policies to improve inventory management of red blood cells. Eur J Oper Res. 2021.
[2] Evers D, Middelburg RA, de Haas M, et al. Red-blood-cell alloimmunisation in relation to antigens' exposure and their immunogenicity: a cohort study. Lancet Haematol. 2016;3(6):e284-e292.

Results

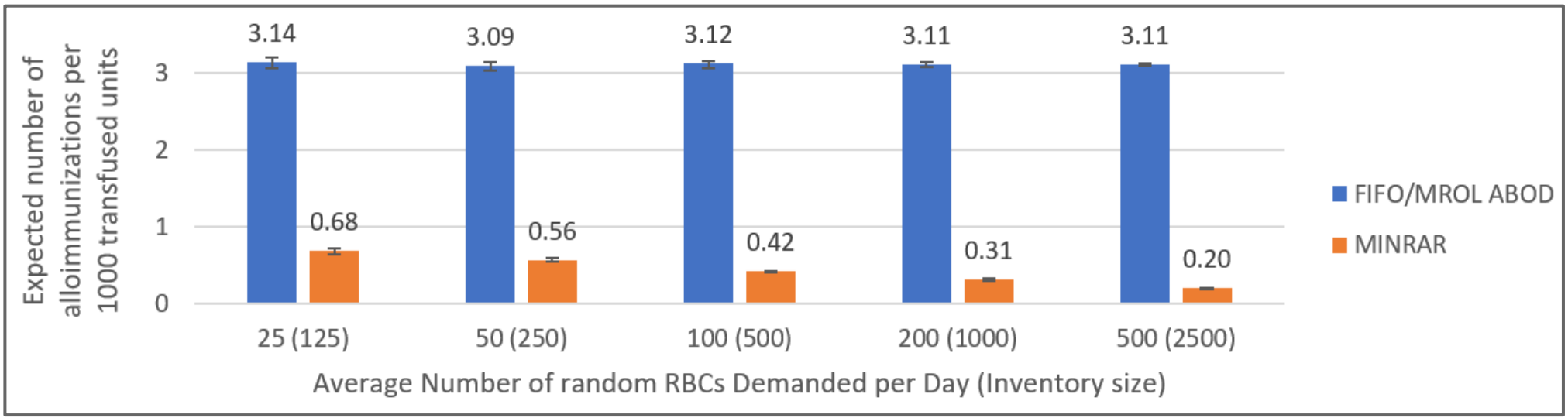


average of one-year simulations

- Inventory: 500 units
- average daily demand: 100 units

→ **reduction** in **mismatches** for every antigen.

Results



→ substantial **reduction** in number of **alloimmunizations**:

– reduced by 78%* when matched locally

– reduced by 94%** when matched centrally

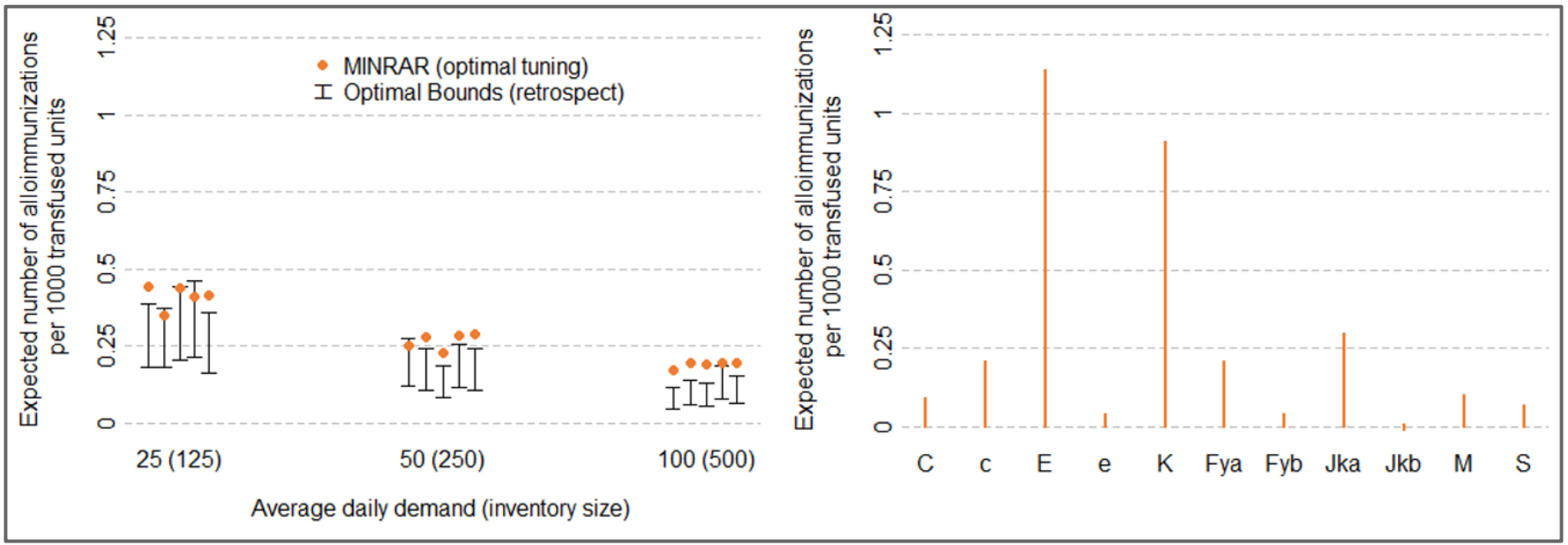
without increase in shortages or outdating

concentrated on the more immunogenic antigens such as K, E and Jk[a]

* 1-(0.68/3.14)≈0.78

** 1-(0.20/3.11)≈0.94

Results

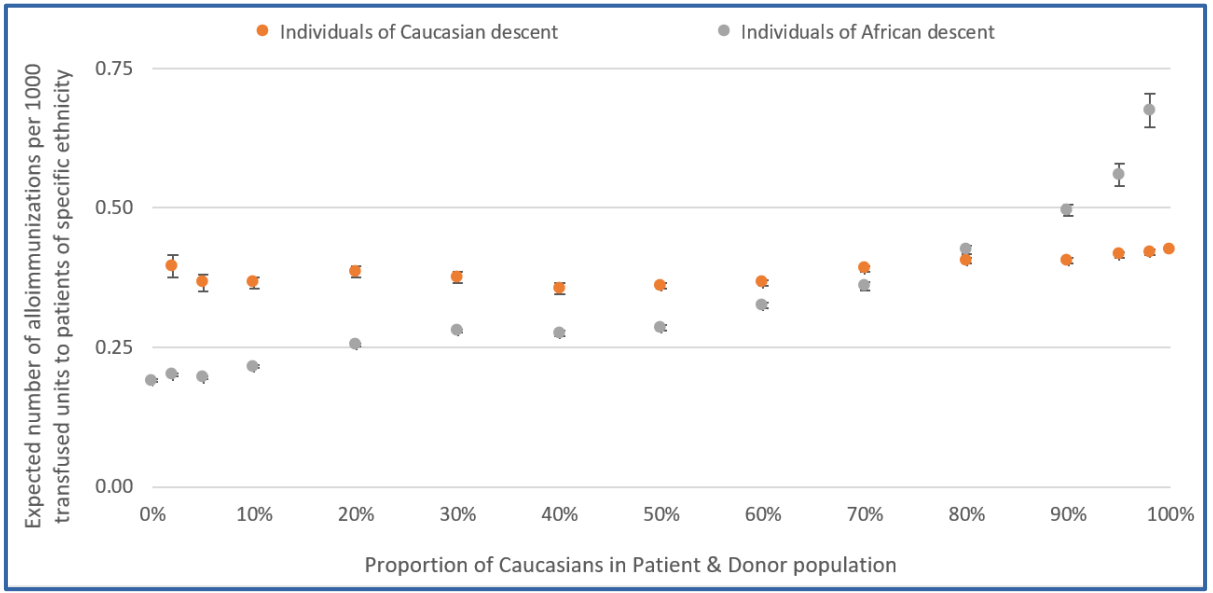


What would have been the **best possible allocation** in retrospect?

prevented alloimmunization with retrospective issuing ≈ alloimmunization induced by ignoring antigens M, S or C

→ MINRAR strategy provides **a near-optimal solution**.

Results



How is matching affected by **heterogeneity** of donor and patient **populations**?

→ alloimmunization risk for individuals of African descent

– increases up to 60% if population is 98% Caucasian

– increases only 4.9% if population is 80% Caucasian, 20% African descent

Conclusion

Compatible matching on all clinically relevant antigens can **reduce** the risk of **alloimmunization** by almost **94%** compared to matching on antigens A, B and RhD alone.
Without any increase in outdating or shortages!

practical feasibility of extended matching → **improved safety** of future RBC transfusions

continuing research
- financial viability of large-scale extensive matching
- operational and organizational challenges resulting from changes in matching policy