Hypothesis-generating simulation of personalized immune surveillance based on molecular matching

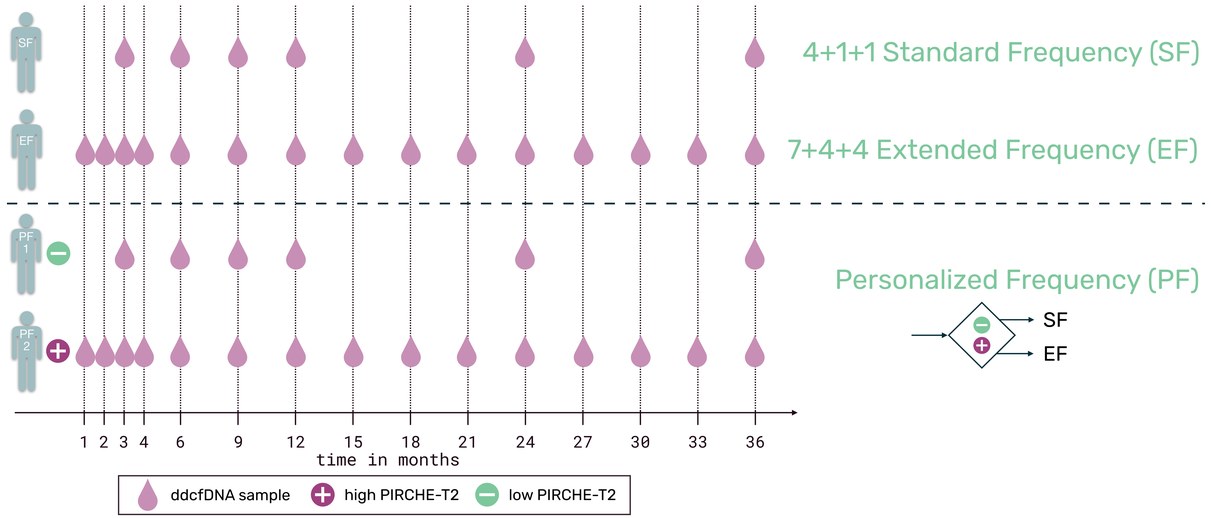
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Purpose

Long-term kidney graft survival is impaired by allo-immune responses. A number of biomarkers are indicated for post-transplant immune surveillance, such as donor-specific HLA antibodies (DSA), donor-derived cell-free DNA (cfDNA), gene-expression panels or cytokines. **Frequent monitoring** of these markers **increases costs** and requires facilitating the logistics of handling large volumes of samples within short timeframes. However, **patients at high risk may benefit** from extended surveillance, **suggesting personalizing surveillance protocols**. To quantify the effect of personalized immune monitoring, we simulated occurrence and detection of rejection events stratifying patient monitoring strategies by the PIRCHE-T2 histocompatibility metric.

Methods



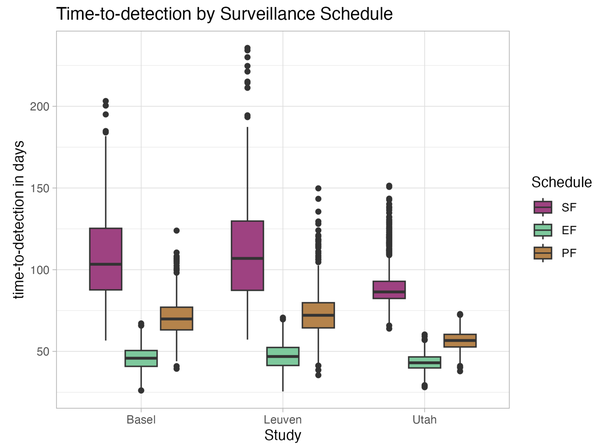
- Repeated simulations, 200 patients per simulation
- Simulated uniform cfDNA surveillance
  - 4+1+1 = 6 tests / 3y (SF)
  - 7+4+4 = 13 tests / 3y (EF)
- Simulated personalized surveillance (PF)
  - Low PIRCHE-T2 -> SF surveillance
  - High PIRCHE-T2 -> EF surveillance
- Proportions and hazards derived from previous publications (Table 1)
- Evaluated metrics:
  - Median Time-to-Detection (TTD)
  - Mean Normalized Testing Burden and TTD (MNT)

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Results

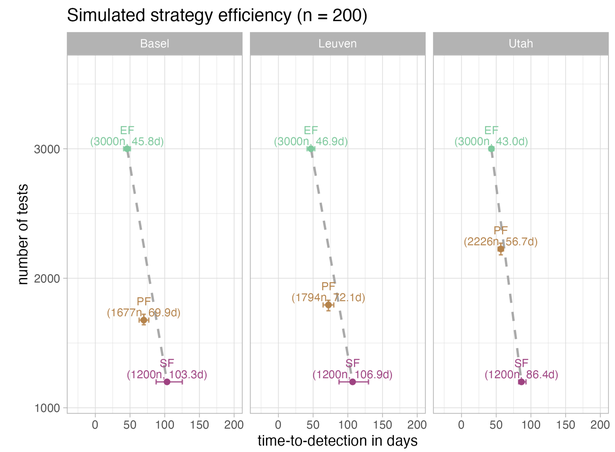
Dataset	High PIRCHE-T2 Proportion	Baseline Hazard at y1	Hazard Ratio
Salt Lake City, Utah, 10.3389/fimmu.2026.1858108	57 %	32.3 %	1.40
Leuven, Belgium, 10.1053/j.ajkd.2022.04.009	33 %	9.7 %	1.28
Basel, Switzerland, 10.1111/tan.15748	27 %	10.7 %	2.19

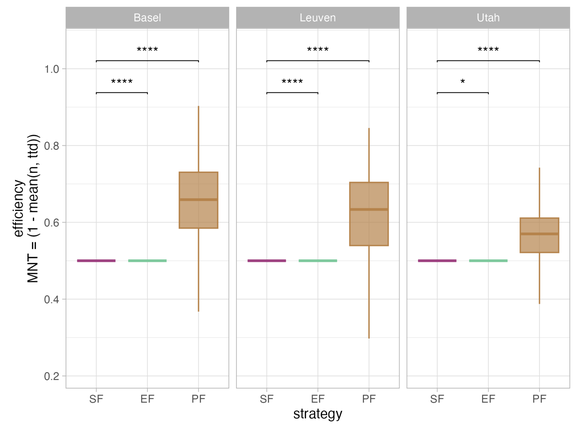
Table 1: Considered reported HR and PIRCHE-T2 distribution of three published articles.



- Time-to-detection reduces with more testing
  - 50%-56% with EF surveillance (vs. SF)
  - 32%-34% with PF surveillance (vs. SF)
- Number of cfDNA tests increases
  - 250% tests with EF surveillance (vs. SF)
  - 140%-186% tests with PF surveillance (vs. SF)
- Linear correlation of tests vs. TTD in uniform surveillance (SF and EF)

- Personalized surveillance simulations show improved efficiency
- Over-proportional reduction in TTD for invested tests
- Over-proportional reduction in tests for accepted TTD
- 59% of the effect for 27%-57% of the additional testing





Conclusion

Our simulations indicate that **personalized surveillance** monitoring protocols may provide a **reduced time to detection** relative to performed test count compared to uniform testing schedules. As a next step, we plan to perform a **target trial emulation** in retrospective datasets to validate our findings.

Disclosures: MN, BM, and BG are employees of PIRCHE AG, publishing the TxPredictor® web service.

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