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Impact of Long Term Storage on Dried Blood Spot Assays

National Social Life, Health and Aging Project (NSHAP)

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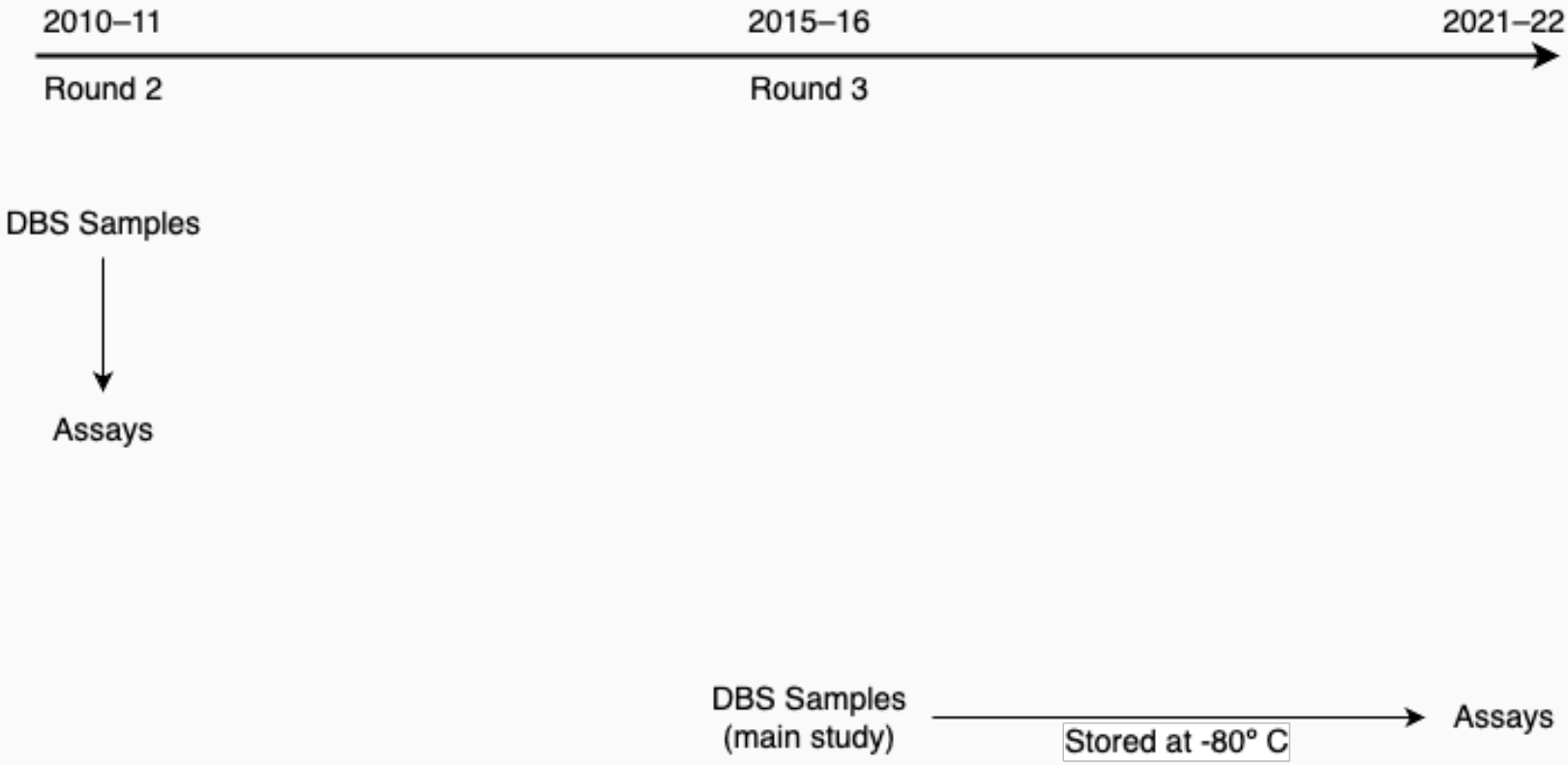
Overview

- NSHAP is a national, longitudinal study of older adults
- Data collection every 5 years (2005–6, 2010–11, 2015–16 and 2022–23)
- In home survey with broad range of bio-sampling (including dried blood spots (DBS)) and biomeasures
- Round 3 DBS samples not assayed at time of collection (funds diverted to support planned recruitment of new cohort)
- Round 3 samples assayed 5–6 years later

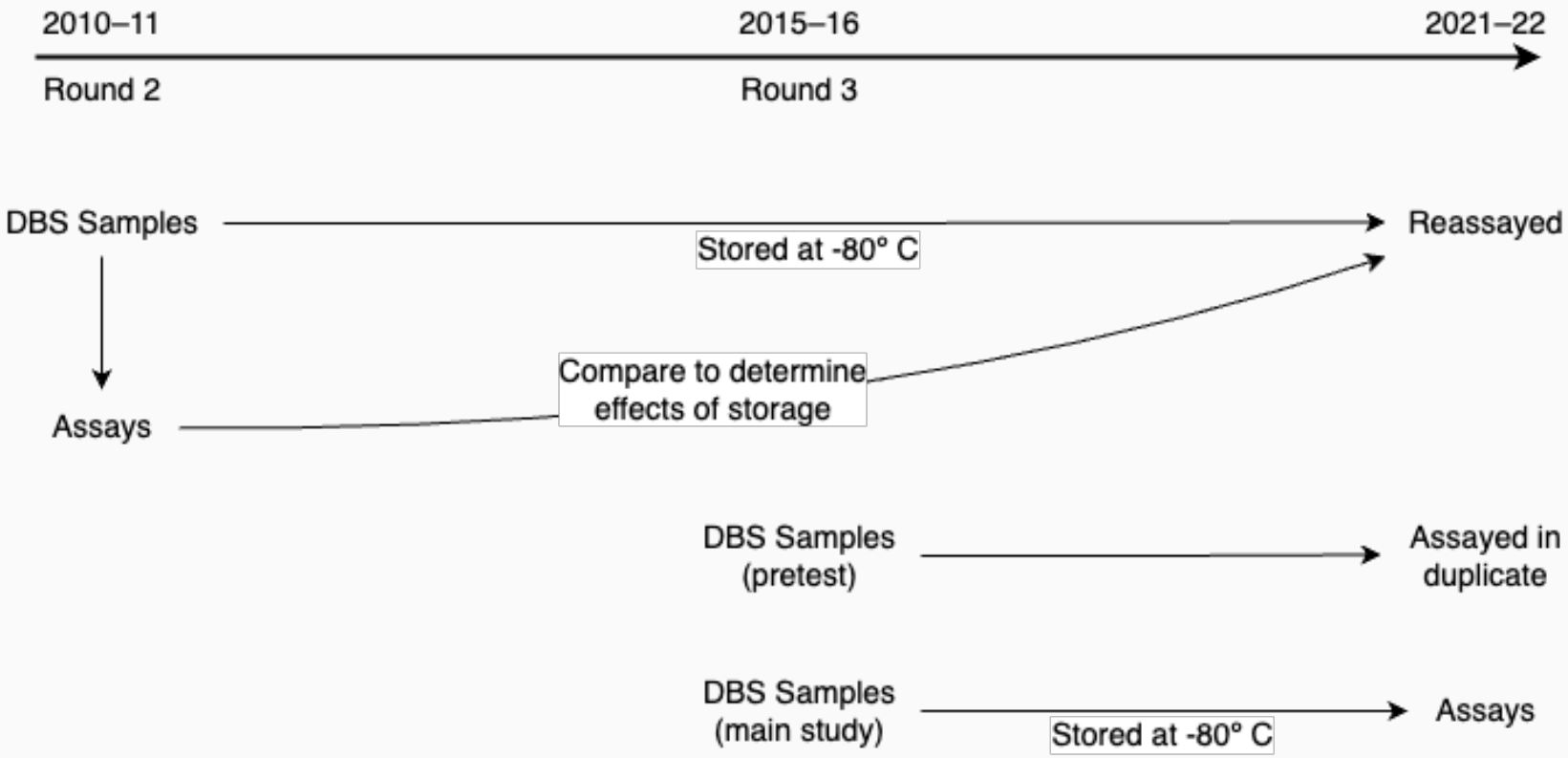
This work is relevant to:

- Decisions about when to assay samples
- Secondary use of stored samples

DBS Reassay Experiment



DBS Reassay Experiment



Statistical Model

Let y_{ij} be the log-transformed whole blood/plasma equivalent value of assay performed on sample from ith respondent at time j ($j = 1, 2$).

$$y_{ij} = \theta_i + \delta_i I_{[j=2]} + \epsilon_{ij}$$

where

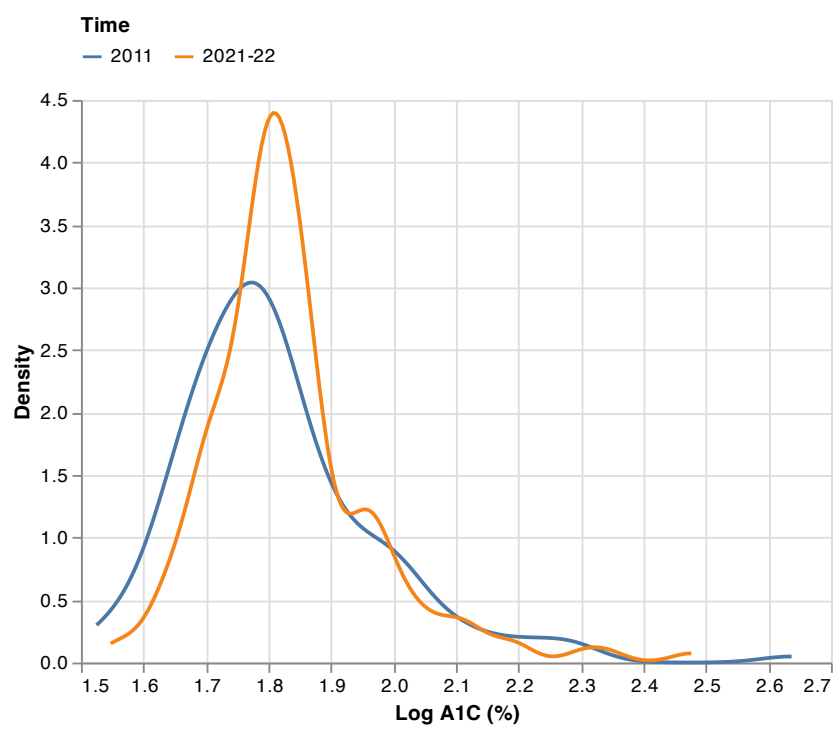
$$I_{[j=2]} = \begin{cases} 1, & \text{if } j = 2 \\ 0, & \text{otherwise} \end{cases}$$

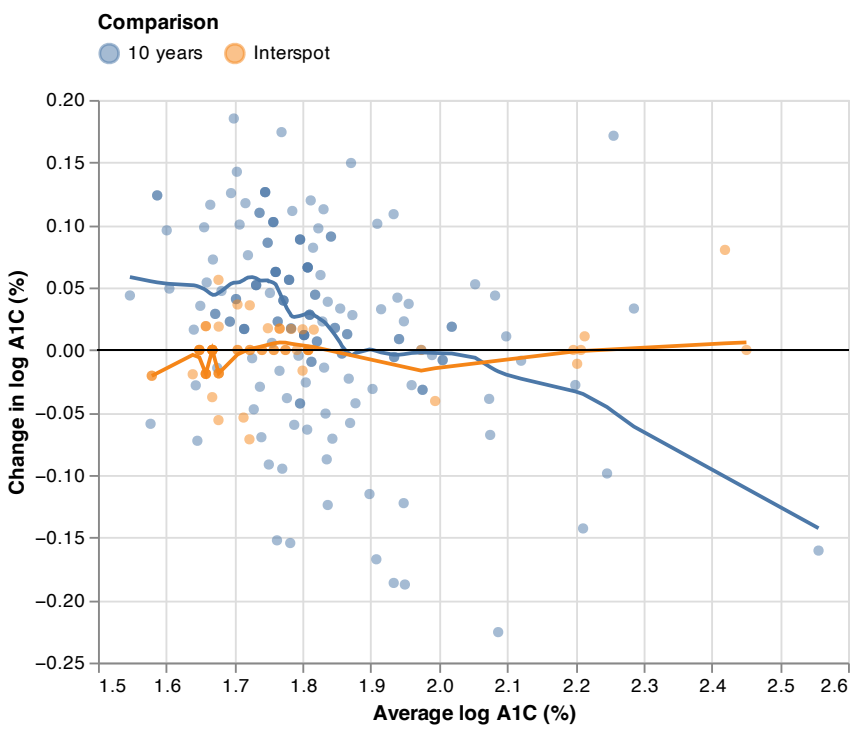
and

$$\begin{aligned} \theta_i &\sim \mathcal{N}(\mu_1, \sigma_1^2) \\ \delta_i &\sim \mathcal{N}(\mu_2, \sigma_2^2) \\ \rho &= \text{corr}(\theta_i, \delta_i) \\ \epsilon_{ij} &\sim \mathcal{N}(0, \sigma_3^2) \end{aligned}$$

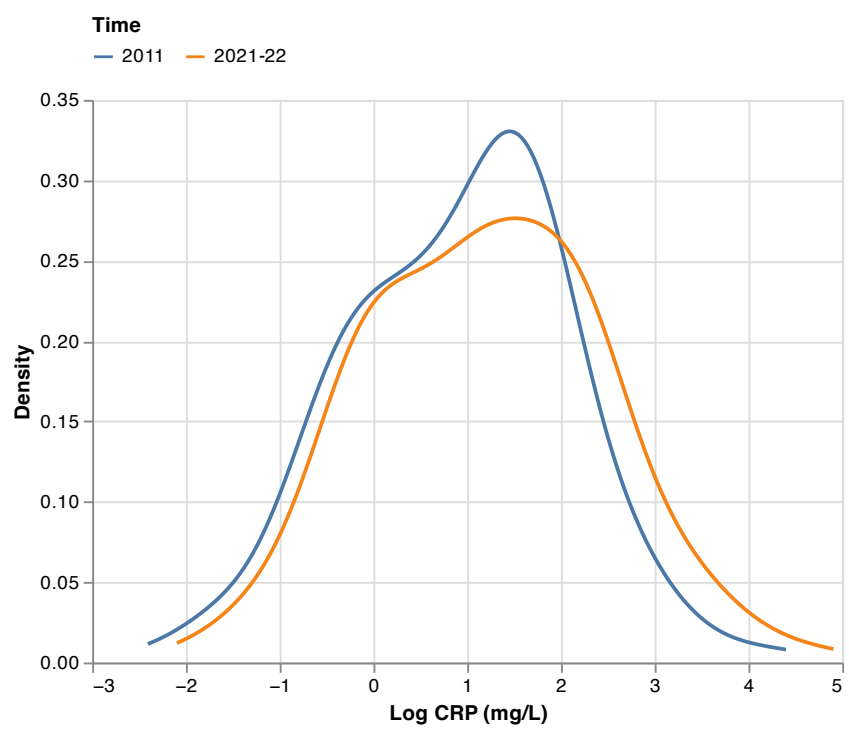
θ_i is the true value of the analyte in the sample, δ_j is the change due to freeze/thaw and 10 years of storage, and ϵ_{ij} is variation across spots.

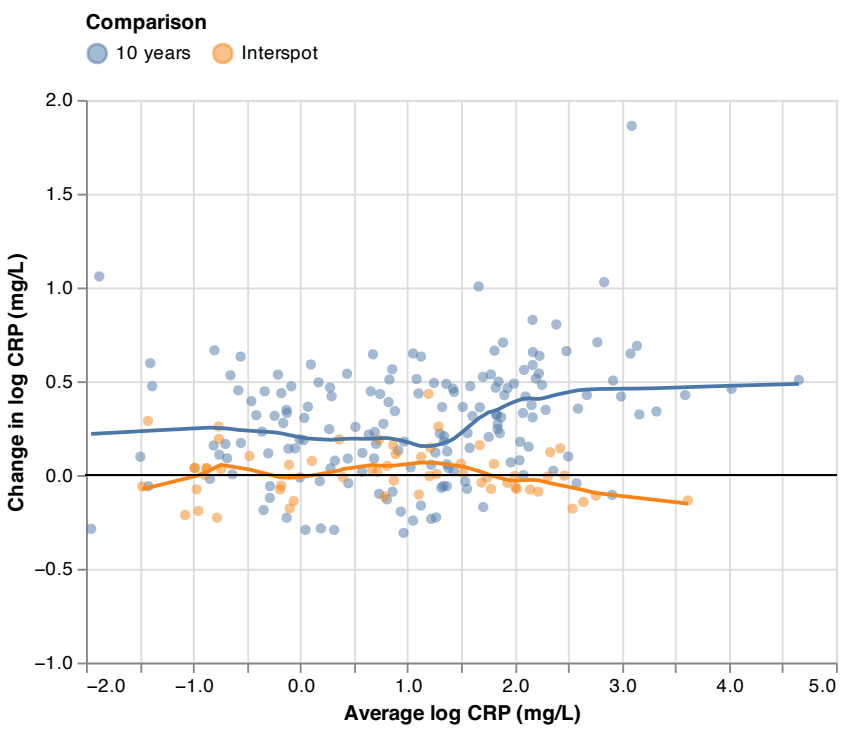
Results: A1C


Time
2011
2021-22
Density
Log A1C (%)

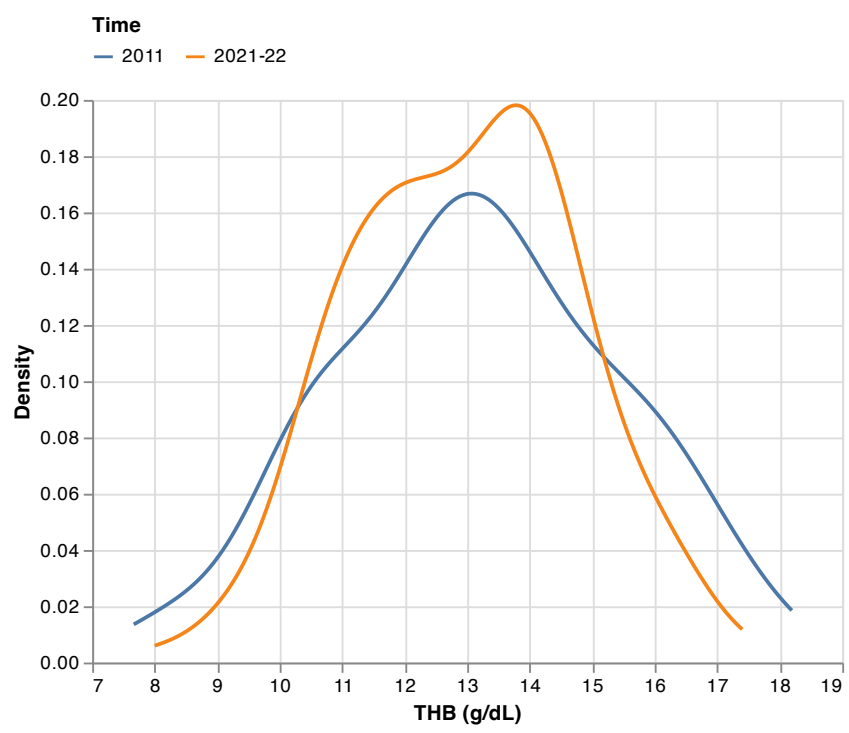

Comparison
10 years
Interspot
Change in log A1C (%)
Average log A1C (%)

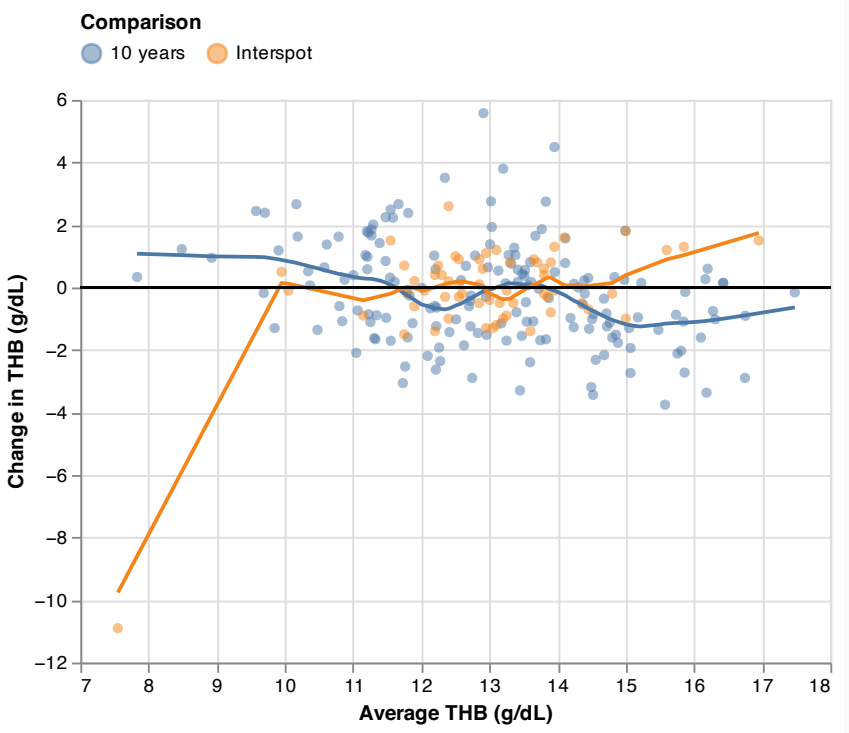
Results: CRP


Time
2011
2021-22
Density
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
−3
−2
−1
0
1
2
3
4
5
Log CRP (mg/L)

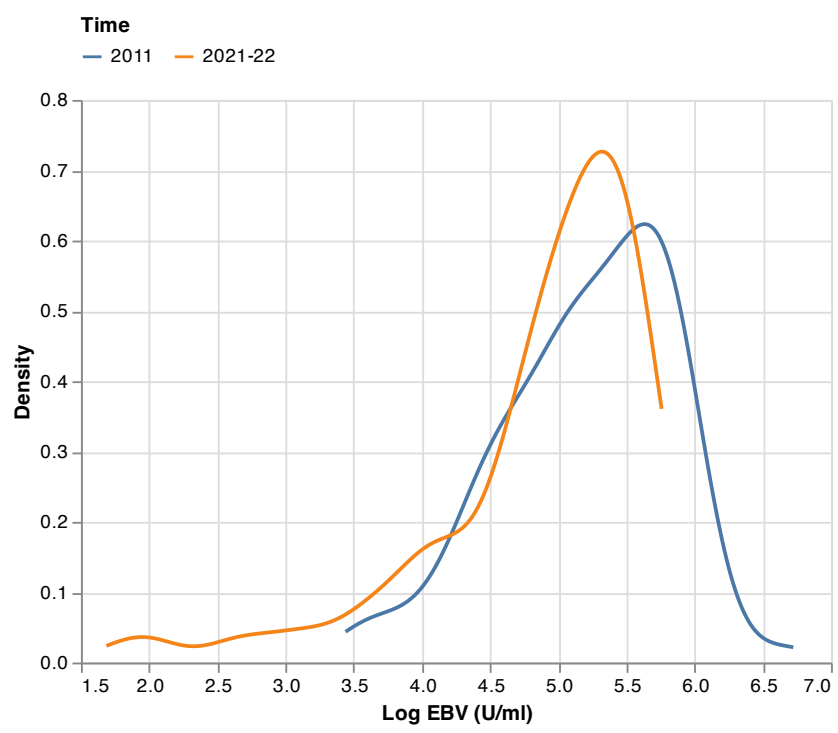

Comparison
10 years
Interspot
Change in log CRP (mg/L)
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
−2.0
−1.0
0.0
1.0
2.0
3.0
4.0
5.0
Average log CRP (mg/L)

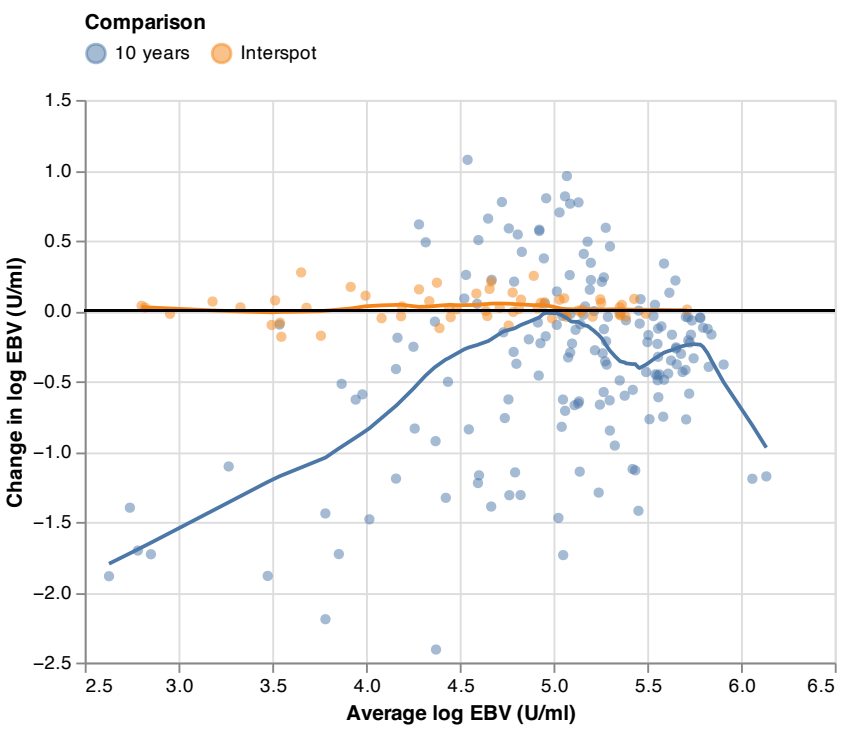
Results: THB


Time
2011
2021-22
Density
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
7
8
9
10
11
12
13
14
15
16
17
18
19
THB (g/dL)


Comparison
10 years
Interspot
Change in THB (g/dL)
6
4
2
0
−2
−4
−6
−8
−10
−12
7
8
9
10
11
12
13
14
15
16
17
18
Average THB (g/dL)

Results: EBV


Time
2011
2021-22
Density
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
Log EBV (U/ml)


Comparison
10 years
Interspot
Change in log EBV (U/ml)
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
−2.5
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
Average log EBV (U/ml)

Model Estimates (SEs in parentheses)

Parameter	Log A1C (%)	Log CRP (mg/L)	THB (g/dL)	Log EBV (U/ml)
σ_1^2	0.170 (0.008)	1.198 (0.057)	1.90 (0.10)	0.708 (0.033)
μ_2	0.023 (0.006)	0.281 (0.024)	-0.18 (0.12)	-0.317 (0.050)
σ_2^2	0.072 (0.005)	0.277 (0.020)	1.25 (0.12)	0.647 (0.037)
ρ	-0.58 (0.06)	0.19 (0.09)	-0.58 (0.06)	-0.19 (0.09)
σ_3^2	0.017 (0.001)	0.093 (0.009)	0.66 (0.06)	0.067 (0.006)

Conclusions

- Storage of DBS samples *does* matter, and effect varies across analytes
- Effects may vary depending on initial level of analyte
- Additional variability due to storage was least for CRP and A1C
- If you're planning to store samples, consider incorporating experiment to assess storage effects
- Adjusted Round 3 DBS values (based on model) will be added to public dataset