DART – Reducing Treatment Burden

DBS PostAl remote immunoglobulin ReplacementT monitoring (DART)

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- DART Project
- Results
- Patient Feedback
- Health Economics
- Neurology
- Where next?

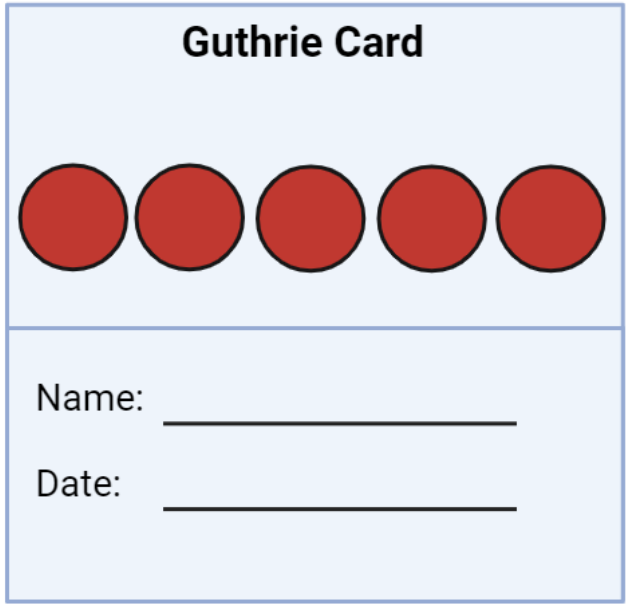
Dried Blood Spots (DBS)

DBS used in the Newborn Screening programme for early identification of 9 genetic disorders

Traditional Guthrie Card:

- **Semi-quantitative**

- Lack of volumetric control and haematocrit effect
- Risk of under- and over-fill
- Risk of sample contamination



Capitainer®B 50

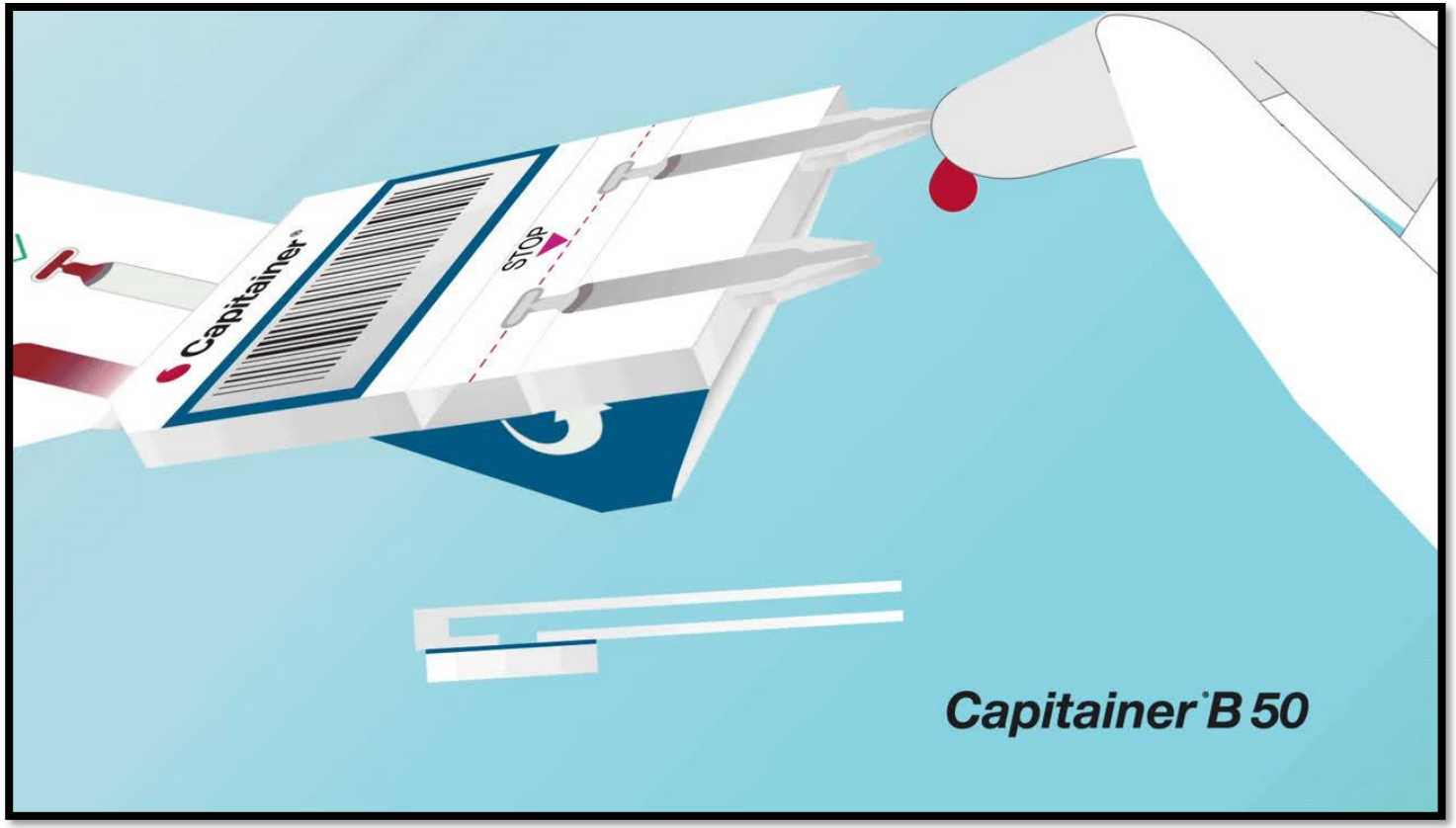
- **Quantitative**

- Accurately collects 50 µl whole blood from a finger prick
-Designed to minimize under- and over-fill

- No drying step required
- Protected from contamination
- Patients can see if correctly filled

Capitainer®B50

- 2x50µL of whole blood
- Volume precision < 3 %
- Sample protection
- Successful sampling indication
- Pre-cut sample discs
- Enables larger sample volume



Capitainer®B is CE-marked, registered as an IVD product according to the IVD Regulation (EU) 2017/746 and registered with the US FDA as a Device Class 1.

DART Aim:

To assess the **accuracy, ease of use and acceptability** of DBS sampling to monitor IgG levels of patients with antibody deficiency receiving immunoglobulin replacement therapy (IgRT).

		All patients (n=43)
Sex	Male	**20** (47%)
	Female	**23** (53%)
Age	20-29	**6** (14%)
	30-39	**6** (14%)
	40-49	**6** (14%)
	50-59	**10** (23%)
	60-69	**8** (19%)
	70-79	**5** (12%)
	80+	**2** (5%)
Immunological diagnosis	CVID	**26** (62%)
	Secondary antibody deficiency	**6** (14%)
	IgA deficiency	**3** (7%)
	XLA	**2** (5%)
	SCID	**1** (2%)
	Combined immunodeficiency	**2** (5%)
	Wiskott Aldrich Syndrome	**1** (2%)
	Other	**2** (5%)
Immunoglobulin replacement therapy administration	Subcutaneous	**42** (98%)
	Intravenous	**1** (2%)

vs

Traditional blood test

Capitainer blood spot

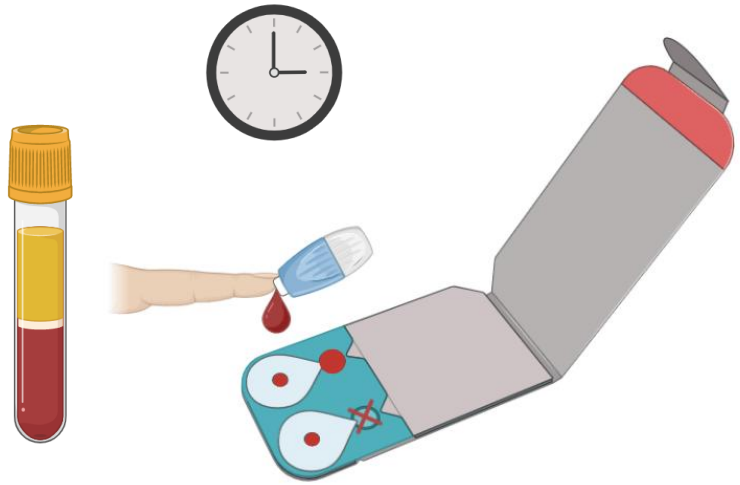
Standard of Care

- Monitoring of patients on IgRT – Hospital and Home
- Clinics 6 monthly – if unwell more frequent
- PID Clinics have a Nursing and Medical review
- Blood testing in clinic (may not time with trough for IVIg)
- Send in Blood testing
- Home IgRT – Immunology Nurse home visit every 2 years

DART - what we did in clinic

- Patients were recruited from Immunodeficiency Clinic appointments
- Training in the use of the Capitainer took place in clinic
- First parallel samples Capitainer and Liquid blood collected
- Patients were provided with the standard of care blood collection kits and also the Capitainer kits
- Routine monitoring 3-4 monthly of both methods for 1 year
- Questionaires with each send in of samples
- Early feedback from the training enabled modification including ‘finger tourniquet’ and milking technique

1



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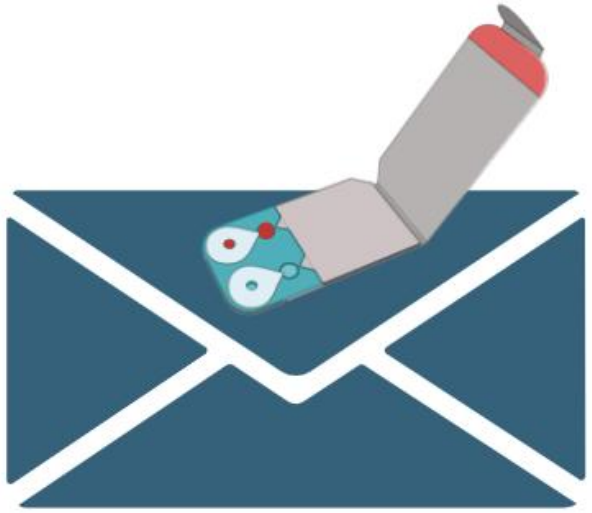

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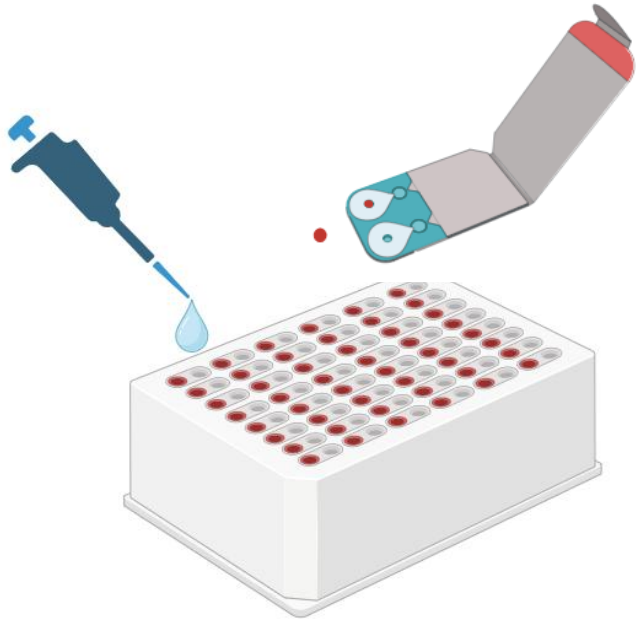

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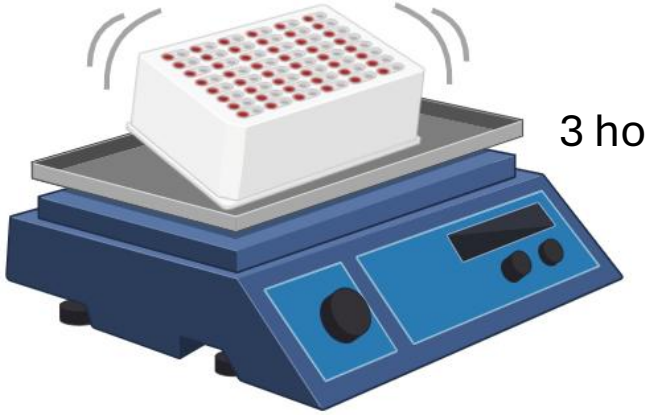
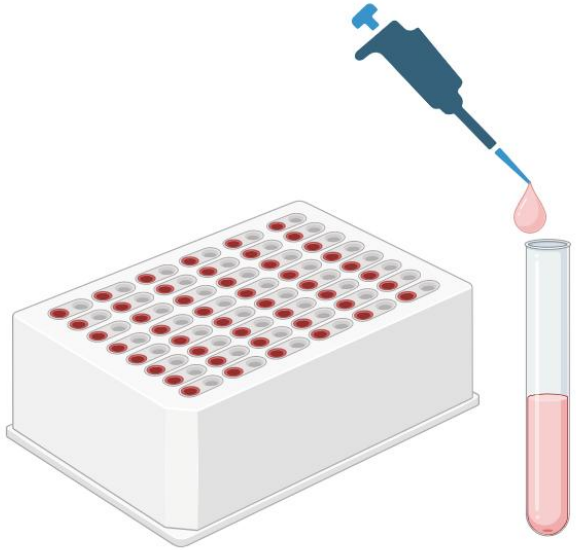


3 hours

5



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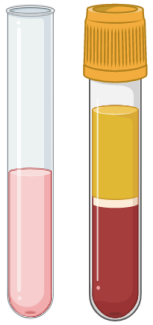
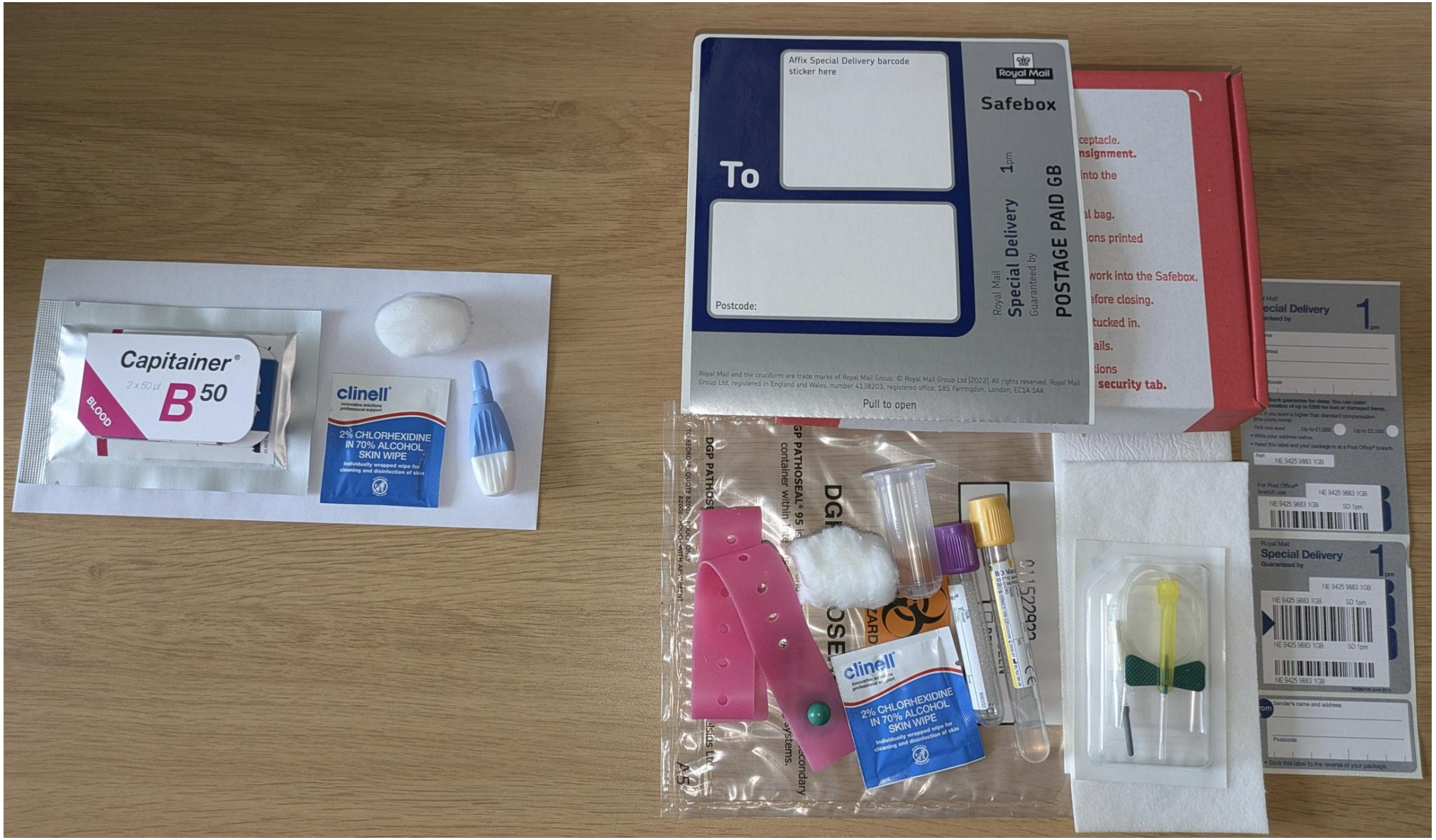


A little something for the Planet

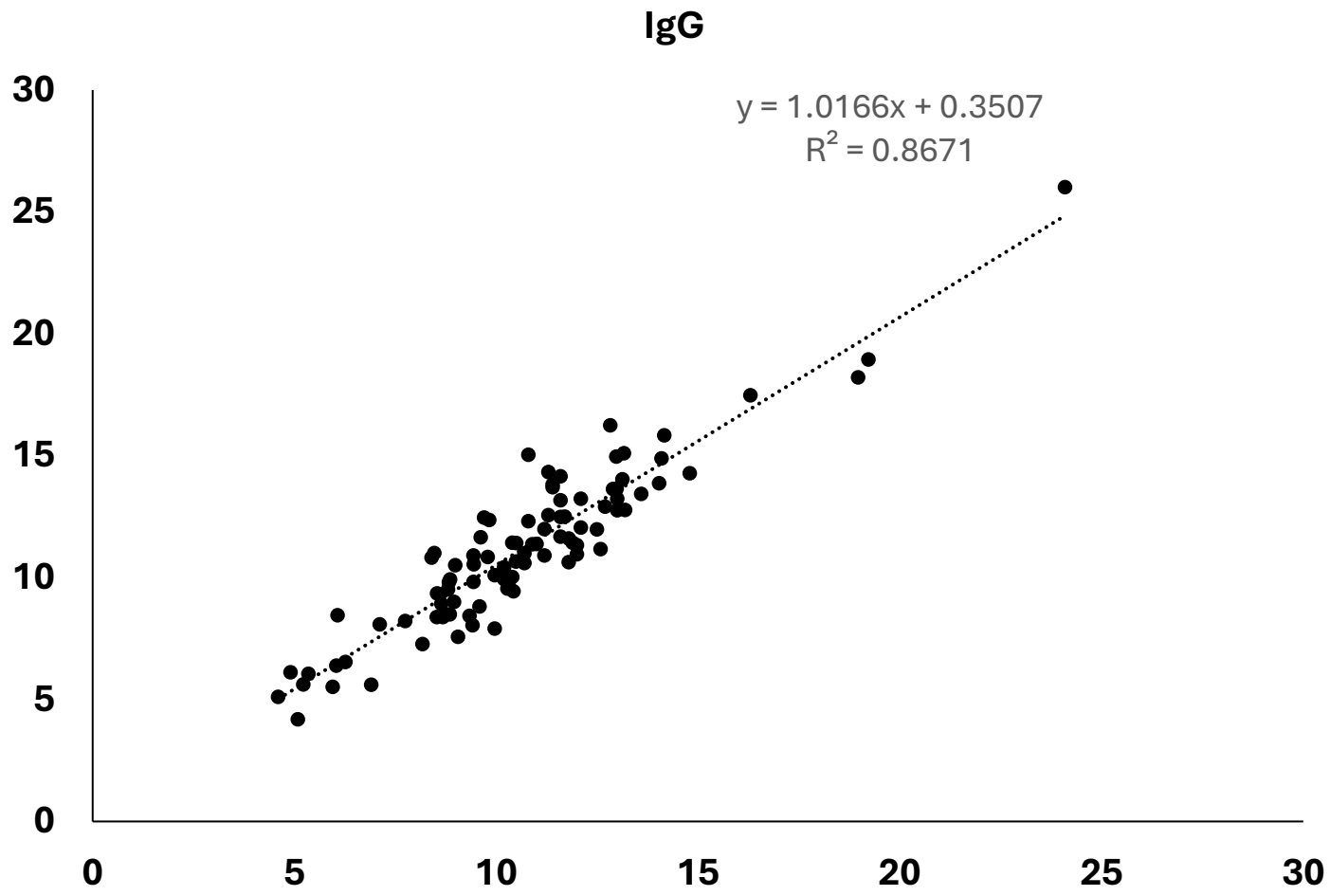


Modified Optilite Protocol

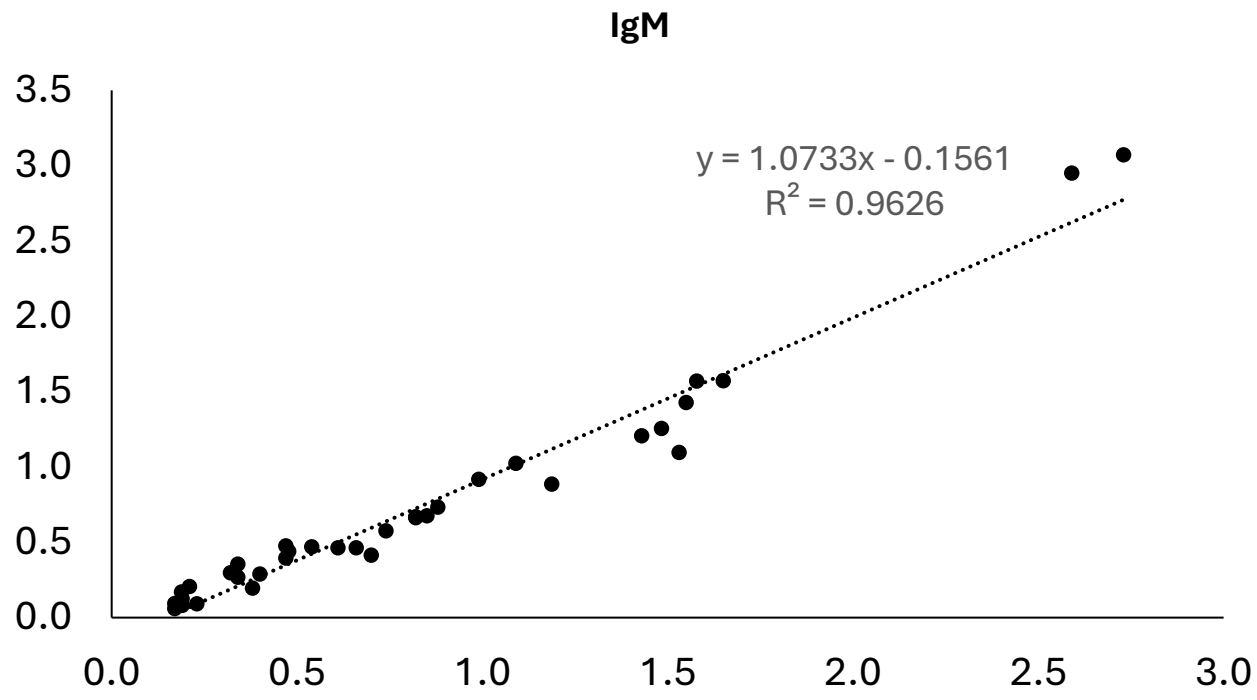
- Capitainer spot dilution means that normal Ig protocol can't be used
- Need to limit on board dilution
- Optilite CSF protocol was used for IgG, IgA and IgM

Results Capitainer vs Liquid Blood

Capitainer vs Liquid Blood - IgG



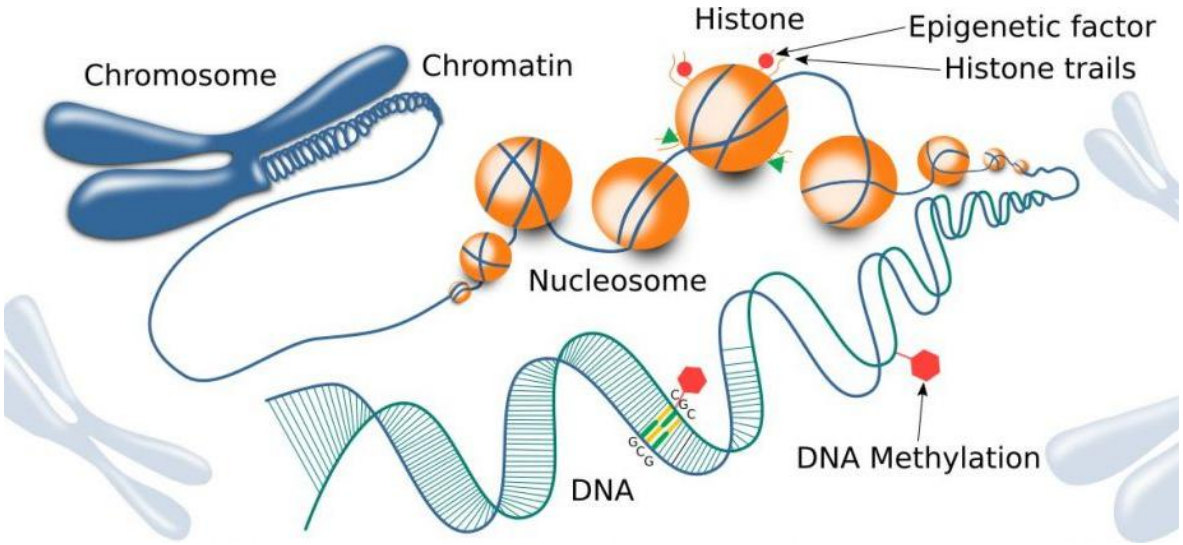
Capitainer vs Liquid Blood - IgM

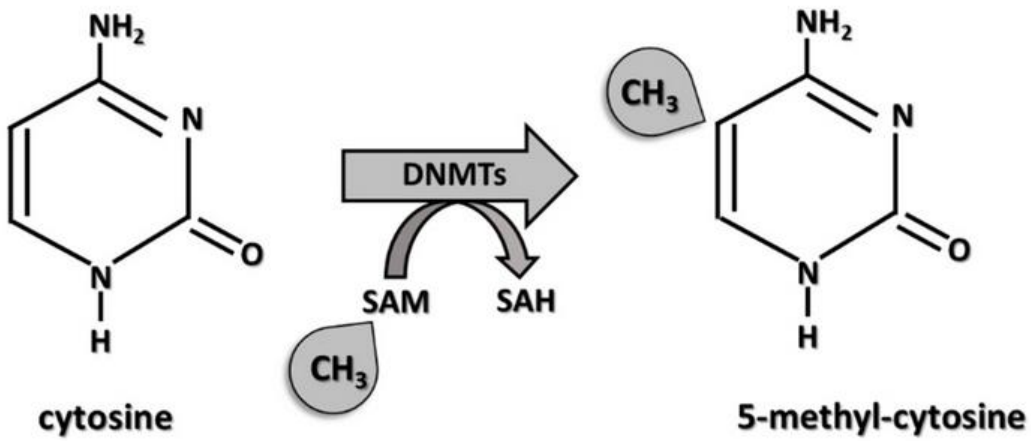


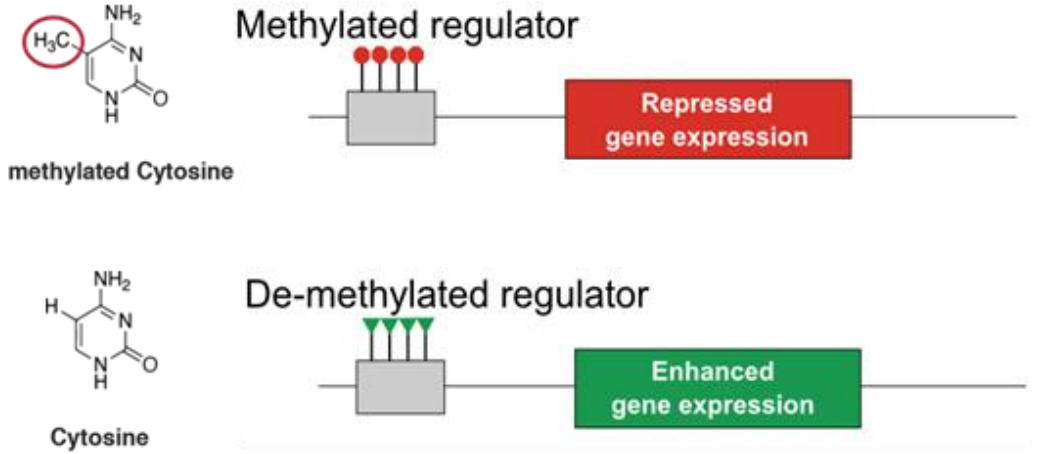
Epigenetic Immune Cell Quantification

Technology is based on DNA methylation:

- CpG dinucleotides
- Stable, long-term modification of DNA
- Regulatory function of gene expression

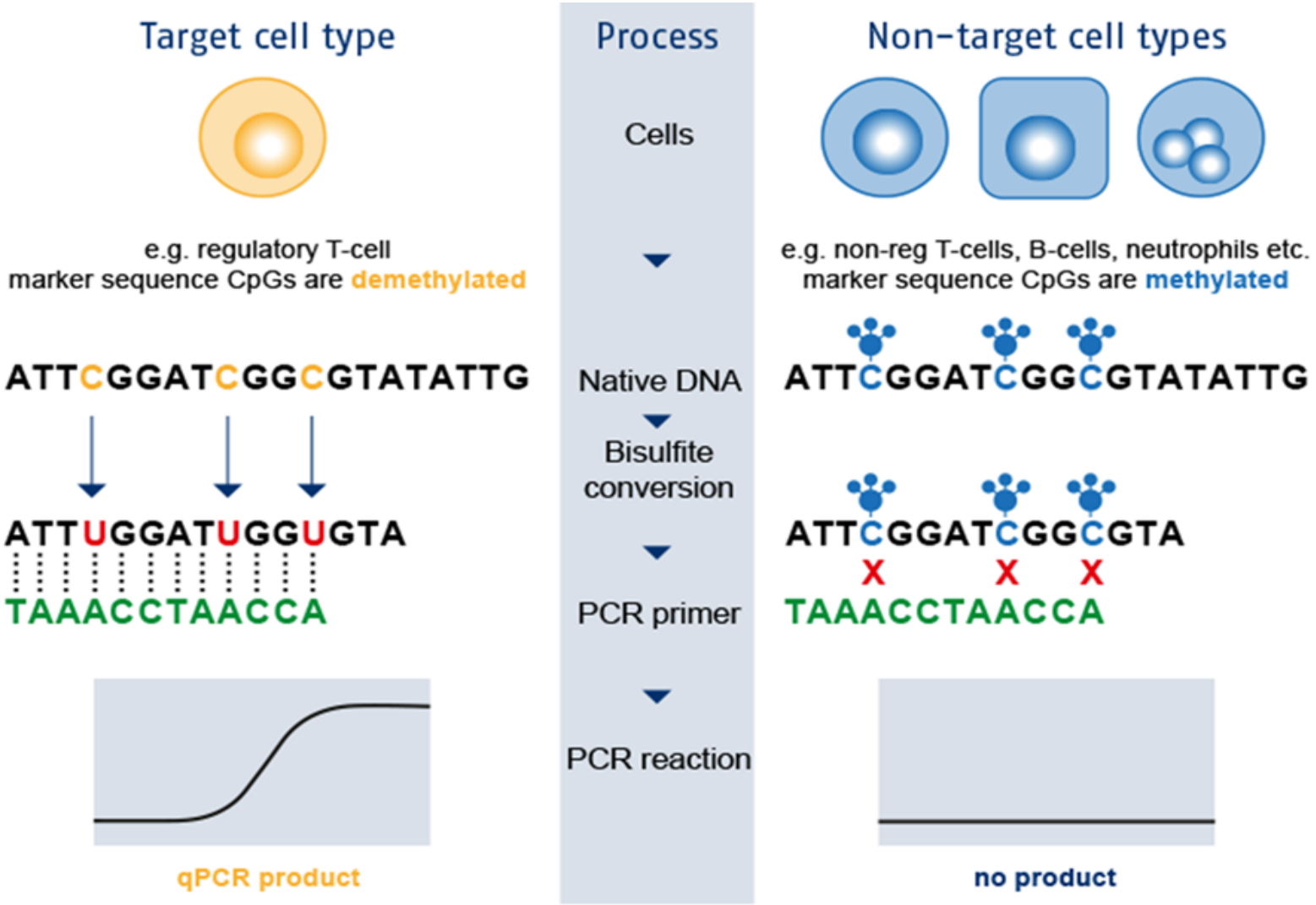






DNA methytransferase DNMT, S adenosyl L methionine SAM

Epigenetic Immune Cell Quantification



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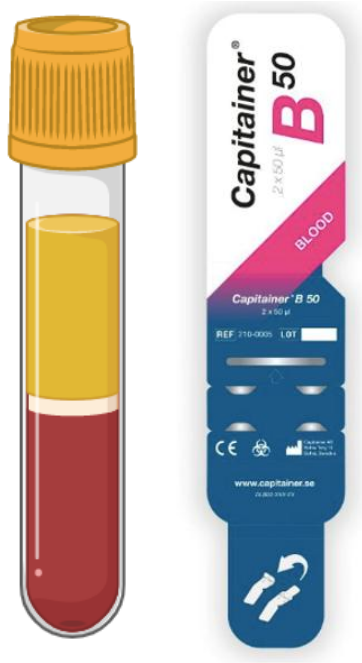
i.Mune TBNK – Overview of Test Procedure

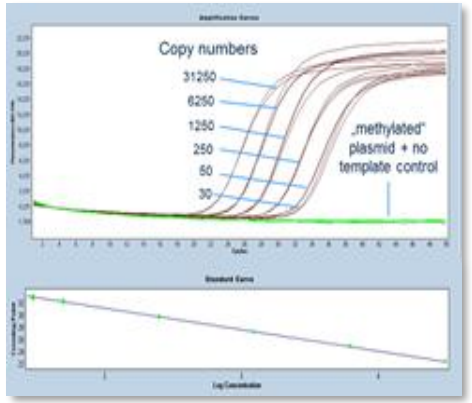
Sample Types



Lysis/ Bisulfite Conversion/ DNA Isolation

qPCR

Quantification



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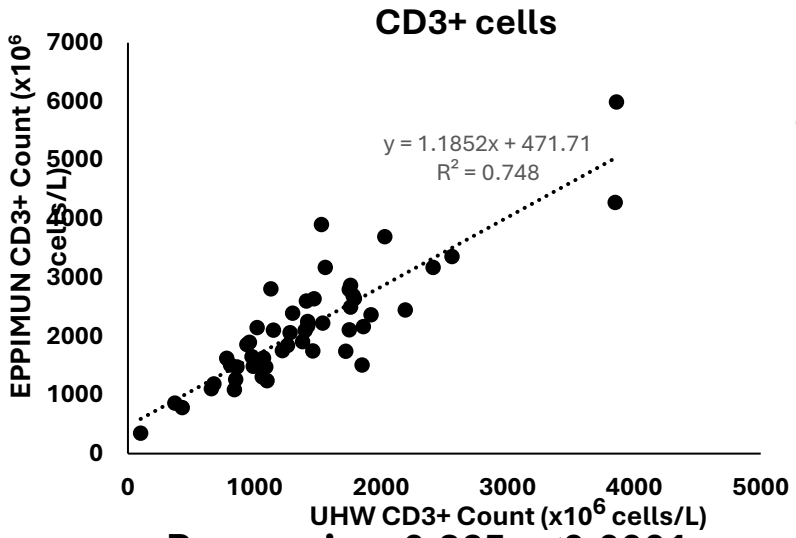
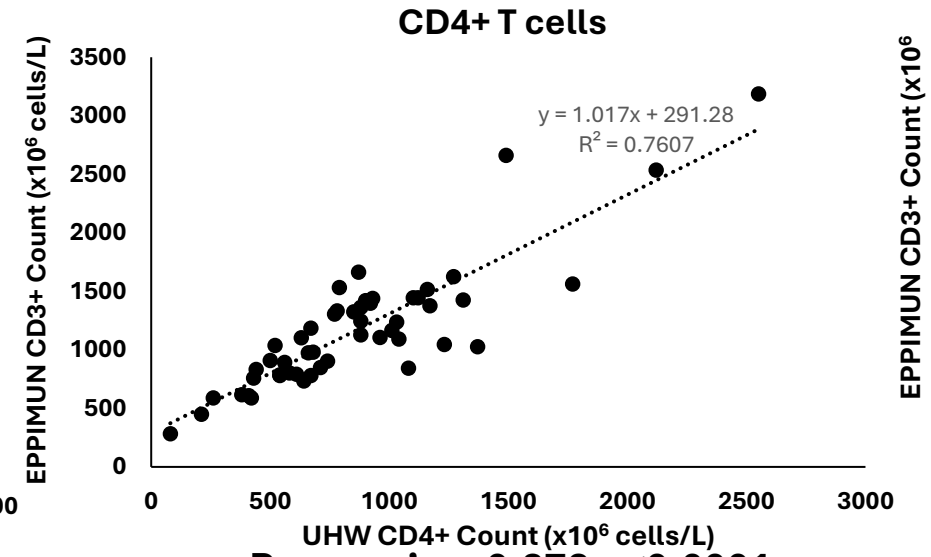
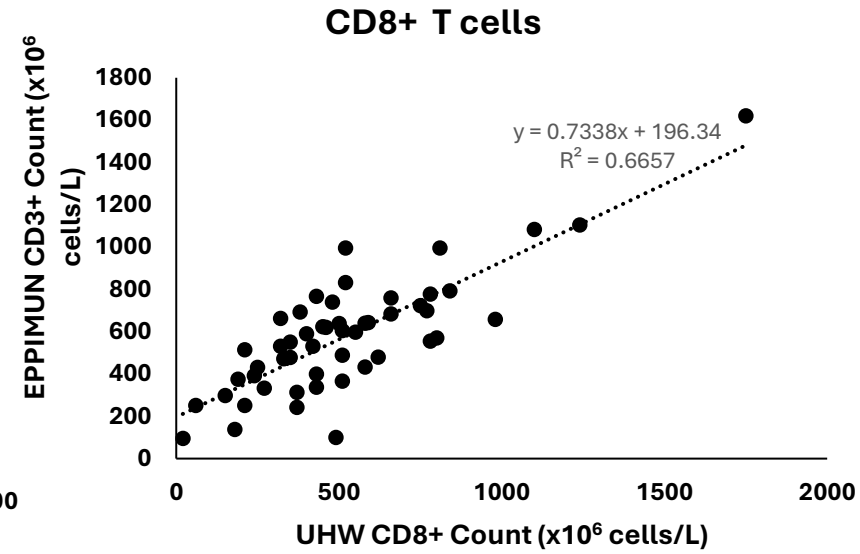
Lymphocyte subsets



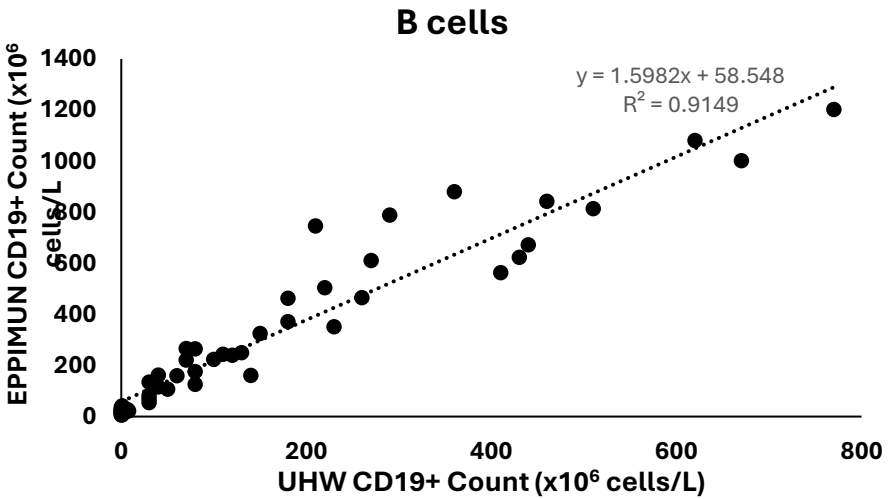
Pearson's r=0.865 p<0.0001



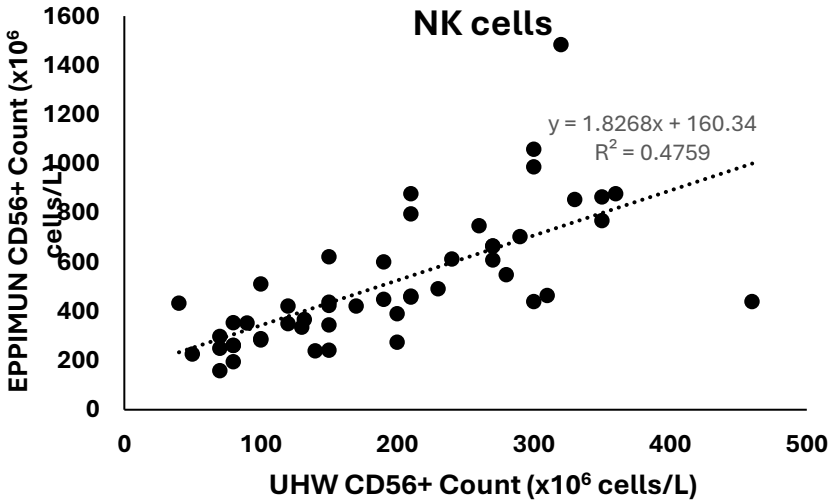
Pearson's r=0.872 p<0.0001



Pearson's r=0.816 p<0.0001



Pearson's r=0.96 p<0.0001



Pearson's r=0.864 p<0.0001

Neurology Multiple Sclerosis (MS) Project

- The Neurology Unit at UHW looks after around 1000 MS patients
- There is increasing use of B cell ablative therapies eg Ocrelizumab
- Dosing is usually every six months
- B cells are usually absent
- Ongoing collaboration with Neurology on SAD

Neurology (MS – antiCD20) and Immunodeficiency

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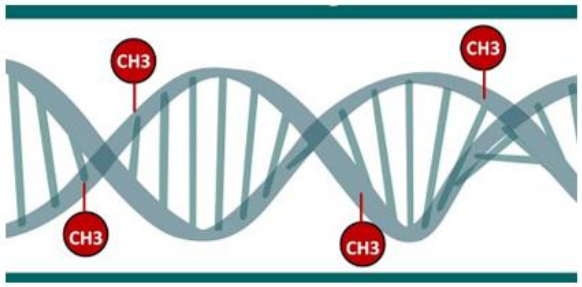
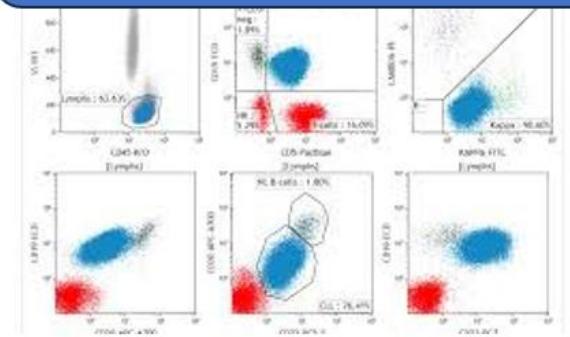
Capitainer samples

Methylated DNA



Whole blood samples

Flow cytometry



Immunodeficiency Patient Questionnaires

Dried blood vs whole blood comparison

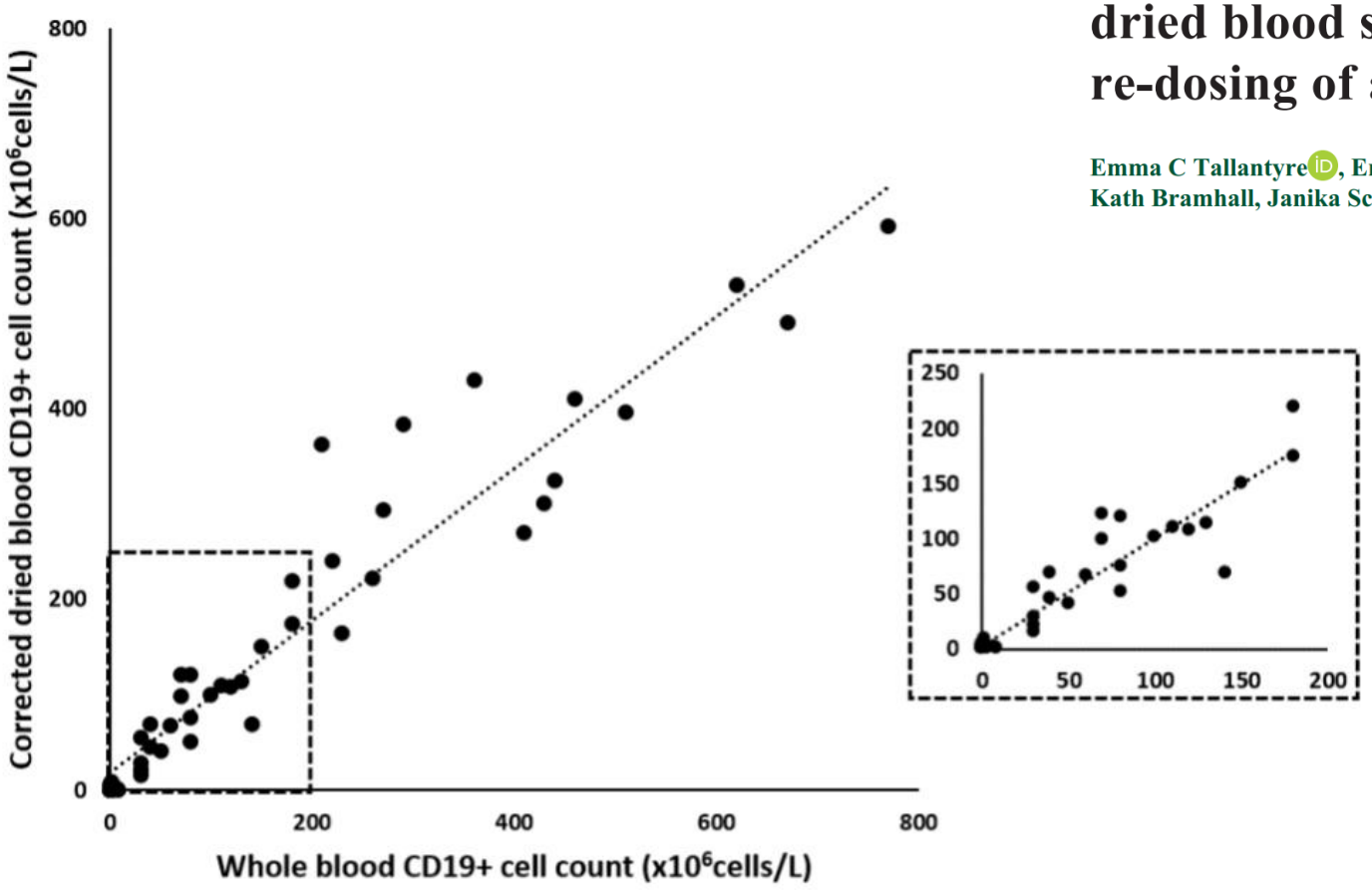
MULTIPLE SCLEROSIS JOURNAL | MSJ

Short Report

Home-sampling of B cells using quantitative dried blood spots to enable tailored therapeutic re-dosing of anti-CD20 therapies

Emma C Tallantyre, Emily Jacob, Laura Davies, Samantha Loveless, Emily Carne, Kath Bramhall, Janika Schulze, Stuart J Moat* and Stephen Jolles*

Multiple Sclerosis Journal
1–4
DOI: 10.1177/13524585251330962



[normal range 50 – 500 x10^6 cells/L]

		Dried blood spot CD19 ≤10 Yes	No	Total	
Whole blood CD19 ≤10	Yes	14	0	**14**	Sensitivity = 100%
	No	0	36	**36**	Specificity = 100%
	Total	**14**	**36**	**50**	

Personalised dosing of antiCD20

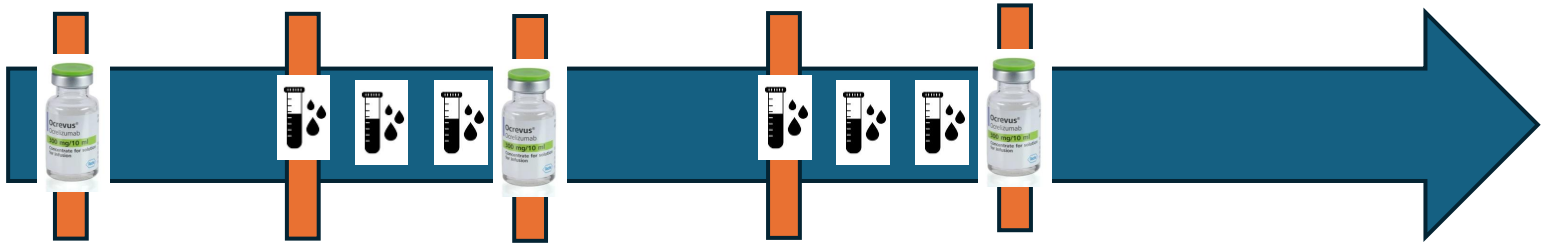
Ocrevus

Standard dosing

Drug cost ~£40k

0 months | 6 months | 12 months | 18 months | 24 months

Personalised dosing



~£20k

0 months | 6 months | e.g. 11 months | 17 months | e.g. 22 months

Blood tests of B-cells 4-6 weekly (once dose due) every cycle

Other Neurological uses of rituximab

- Vasculitis
- Neuromyelitis optica
- MOG antibody disease
- Autoantibody mediated encephalitis
- Immune mediated neuropathy

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Other Specialties use of B cell ablation

- Rheumatology
- Respiratory
- Renal
- Haematology
- Other

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Combined B cell and SAD monitoring

- B cells
- IgG, IgA and IgM
- Functional antibodies

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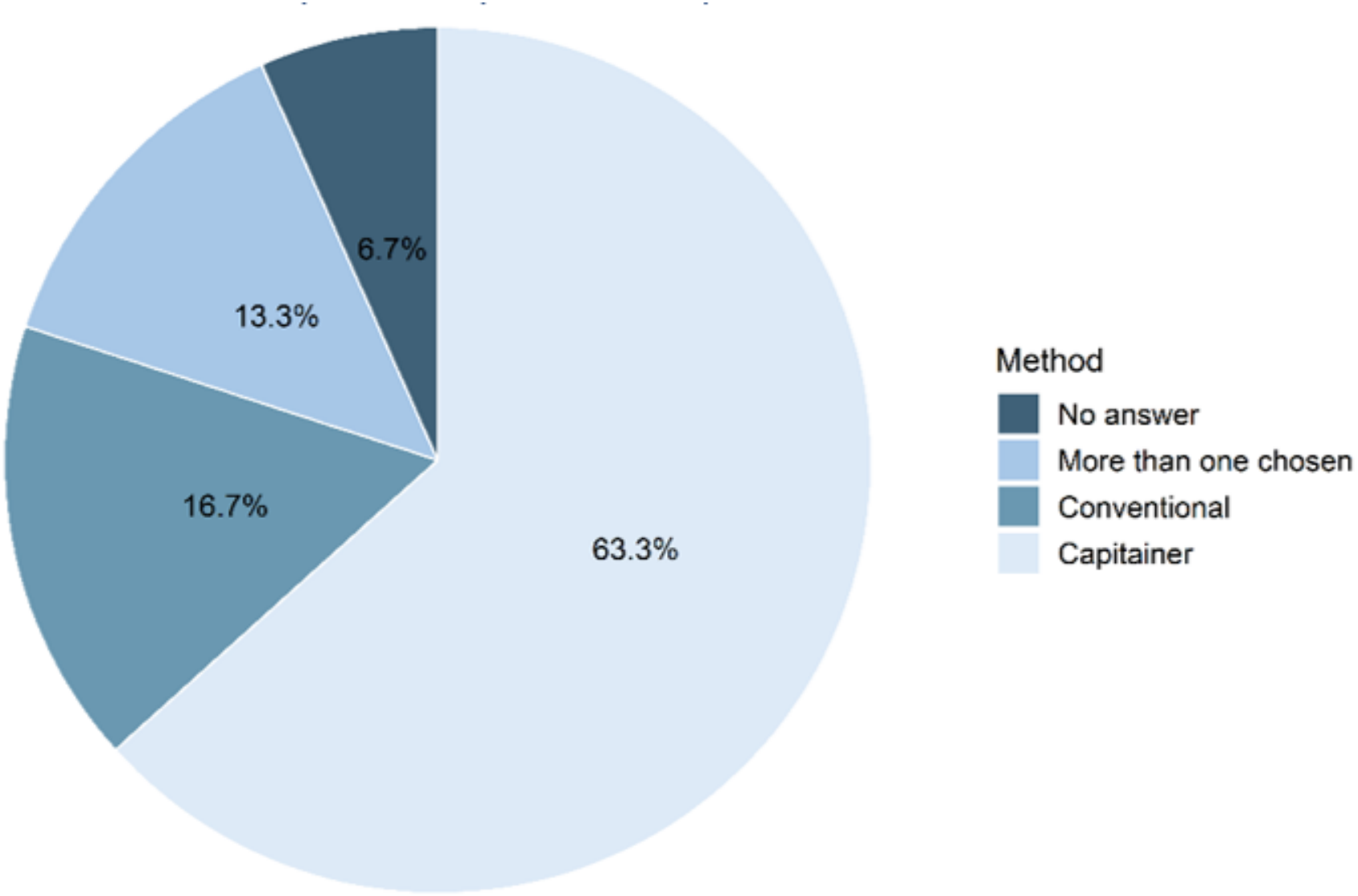
Preferred method of blood sampling



But - most of it was

"It is less intrusive in regards to the needles, less risk of infections I wouldn't have to sit in the GP waiting rooms or travel on public transport or get a lift from a family member."

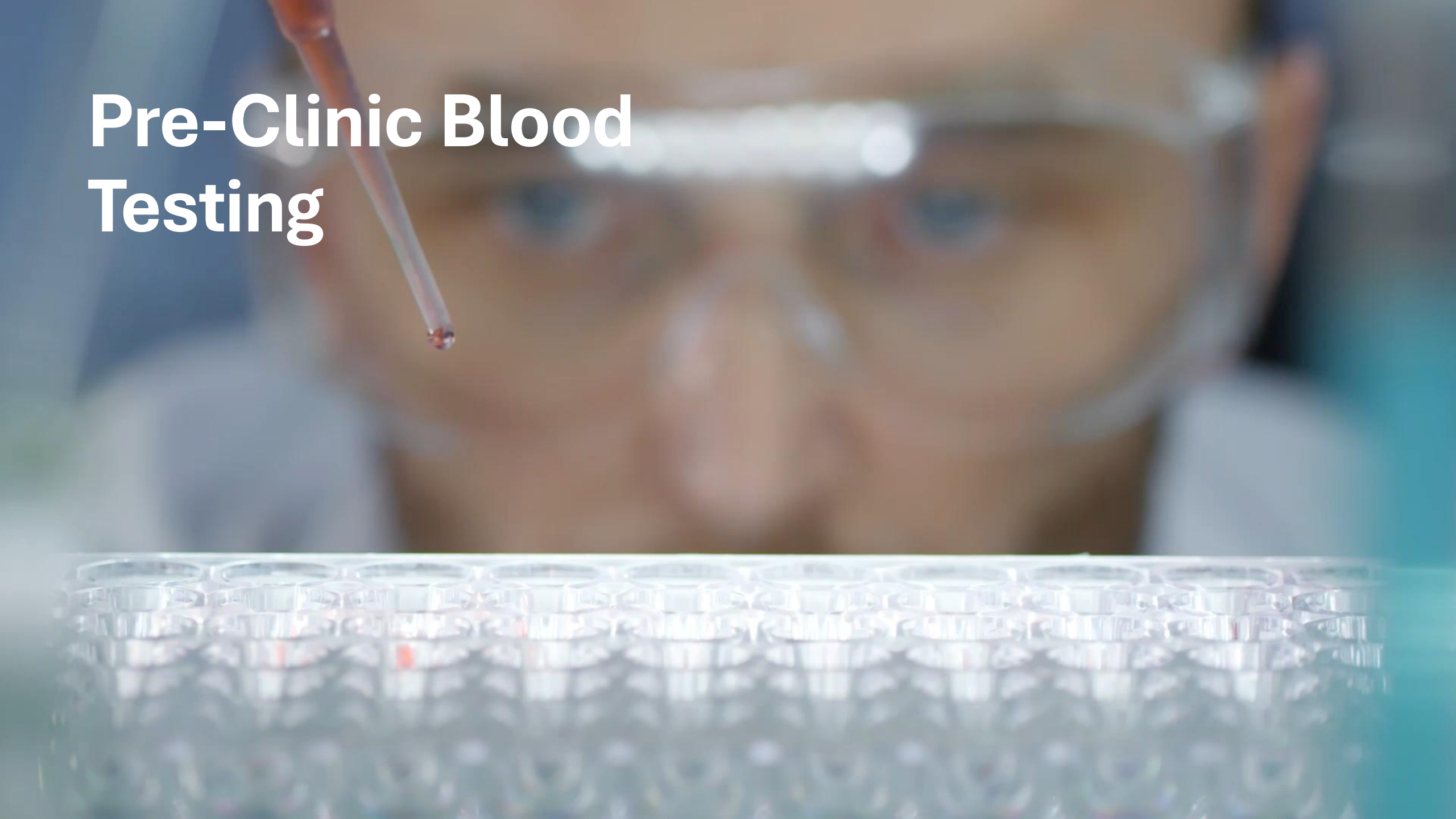
Participant 5

"Today feeling anxious as I set off for my bloods to be done as I am thinking about what problems will occur as usual".

Participant 15

Lost in Translation

- Challenges in translating an approach into the routine service
- Requires capital and staff investment
- Remember service contracts
- Initial cost per sample may be higher as numbers are smaller
- Difficult to persuade if savings are made elsewhere eg in primary care or a neurology drug budget
- Or are less tangible ie for patients



Pre-Clinic Blood Testing

Pre Clinic Bloods

- For new referrals into Immunodeficiency clinic
- If appropriate – blood boxes and request forms are sent to patients
- This allows the results to be assessed and vaccinations with follow up bloods to be arranged ahead of clinic
- The results and next steps can then be discussed with the patient in clinic
- Aims to speed up the diagnostic/assessment process and reduce clinic appointment burden

Conclusions

- The combination of quantitative DBS linked to mDNA and protein assays may enable Immunoglobulin and lymphocyte analysis in both Immunology and other settings
- Potential for reduced treatment/monitoring burden for patients
- Initial study was overall well received by patients
- Savings to drug costs may be made in Neurology (other)
- Potential reduction in the numbers of patients with secondary antibody deficiency
- Translation and service change has its challenges

Thank you