

# Preoperative Cerebrospinal Fluid and Plasma Markers of Inflammation and Neurodegeneration Predict Mortality Eight Years Later in an Observational Cohort

## Study of Postoperative delirium in an Older Elective Arthroplasty Population

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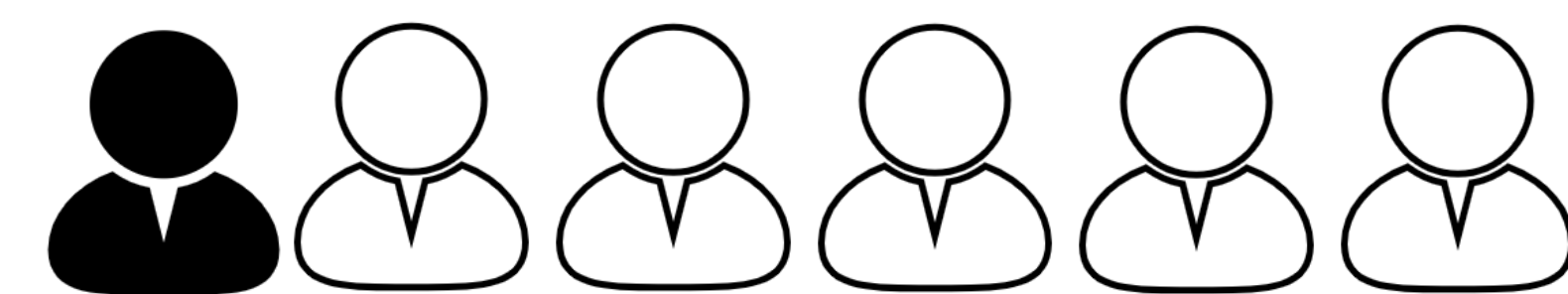
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### Background

#### Postoperative Delirium

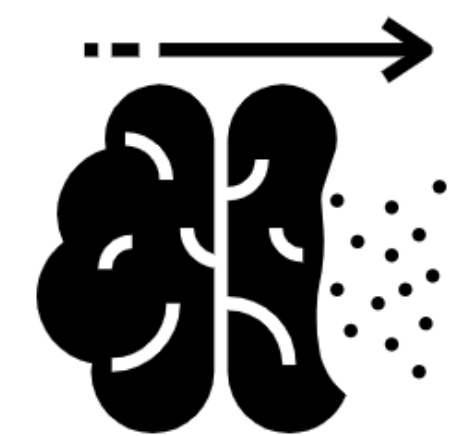
Delirium is an acute change in consciousness, which is fluctuating in nature and accompanied by disturbances in attention, perception and cognition [1]. Postoperative delirium (POD) is a common complication in older adults undergoing elective surgery, with an estimated incidence of 17% in elective orthopaedic surgery [2].

**1 in 6**  
Post-operative



Delirium is associated with a host of long-term complications, including dementia [1]. It is not yet clear to what extent POD is due to underlying neurodegeneration.

#### This study



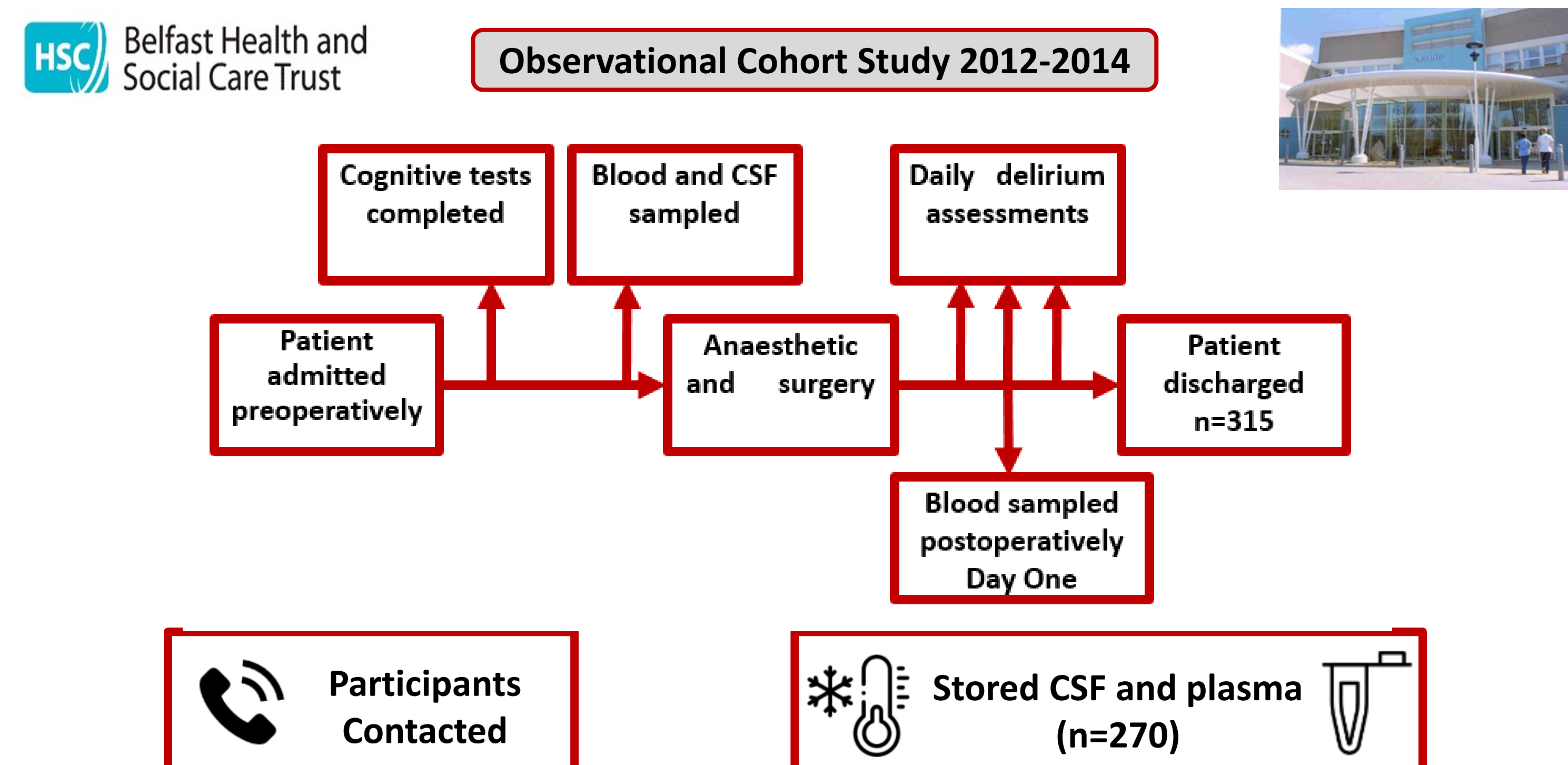
In 2012-2014, an observational cohort study of postoperative delirium (POD) in an elective arthroplasty population recruited 315 individuals without a diagnosis of dementia aged over 65. We are now conducting a follow-up study to determine what effect POD has on cognition eight years later.

### Aims



- Contact all surviving participants and **recruit** them to our follow-up study.
- Determine what factors **predict mortality** in our cohort eight years later.

### Methods



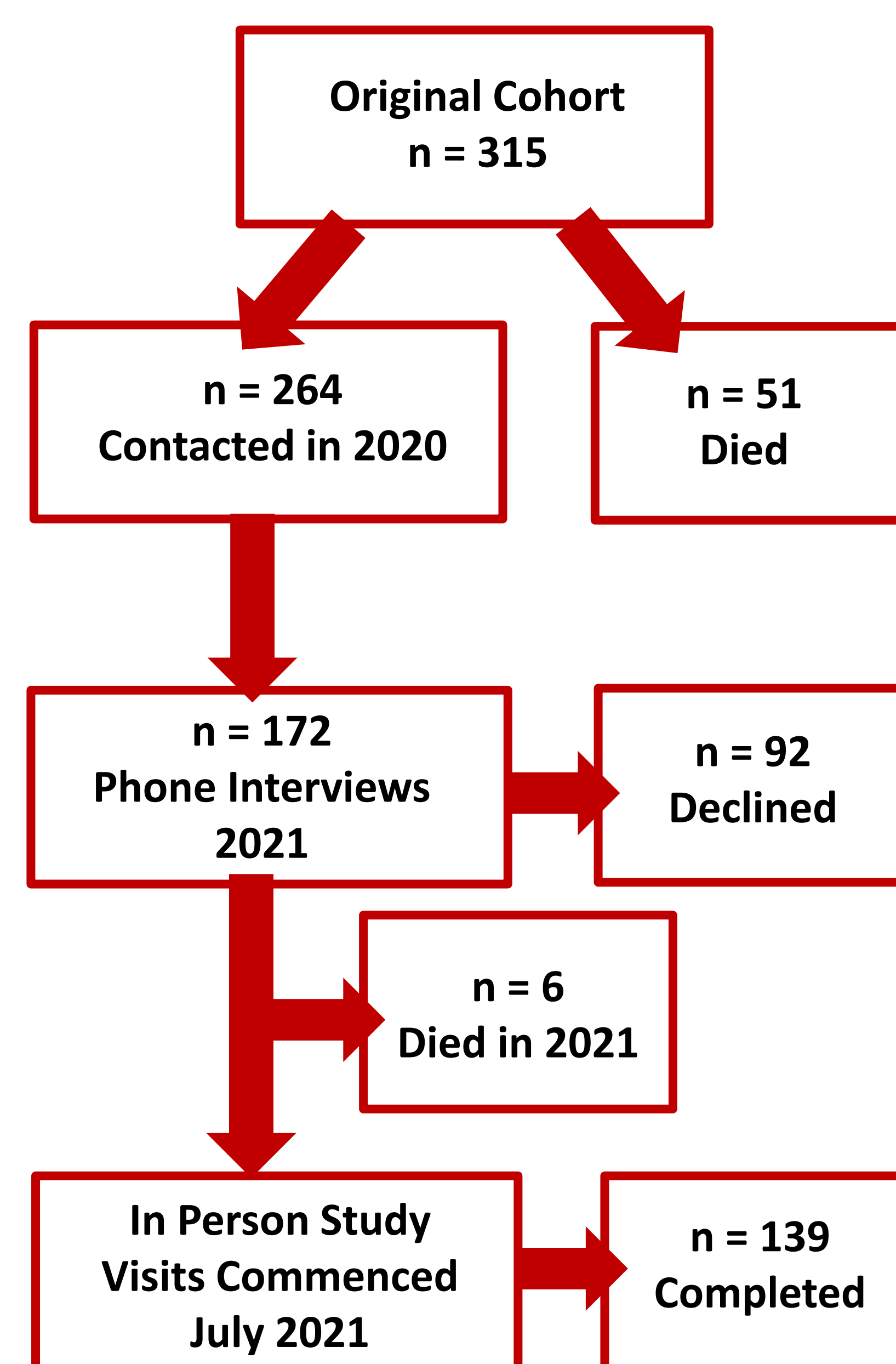
#### Inflammatory Markers

- Interleukin-1 $\beta$
- Interleukin-6
- Interleukin-8
- Tumour Necrosis Factor- $\alpha$

#### Neurodegenerative Markers

- A $\beta$ 40 and A $\beta$ 42
- Neurofilament Light (NFL)
- Glial Fibrillary Acidic Protein (GFAP)
- Triggering Receptor Expressed on Myeloid Cells 2 (sTREM2) (CSF only)
- Phosphorylated Tau-181 (plasma only)

### Follow-Up Recruitment



Participant numbers correct as of July 2022

### Other Predictors of Mortality

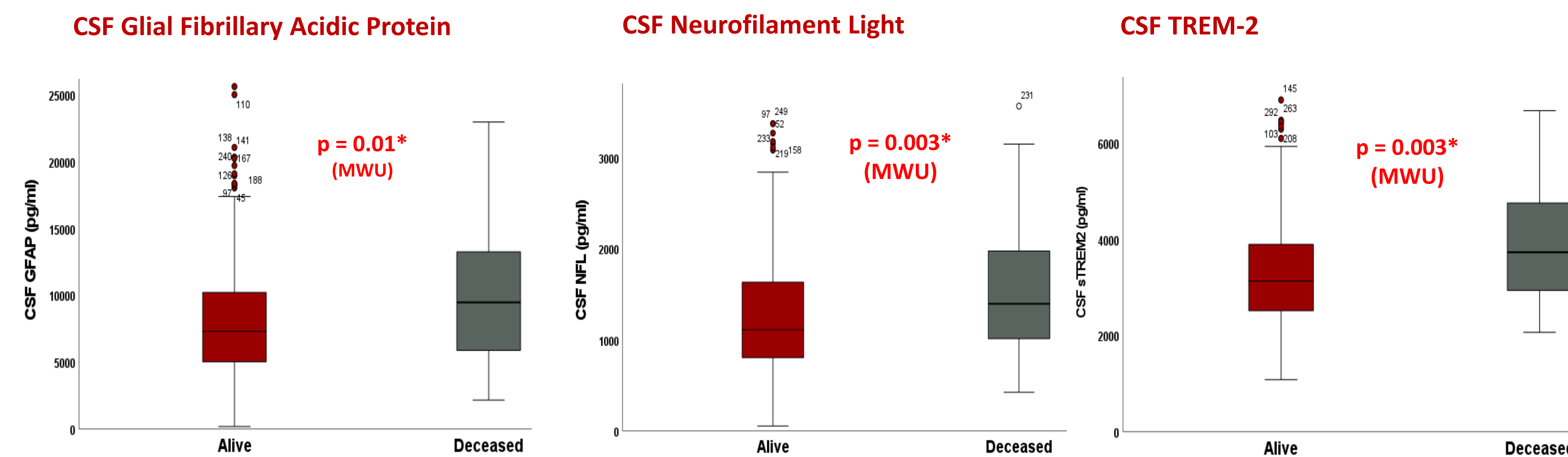
Older age at surgery ( $p < 0.001$ ), multimorbidity (Charlson Comorbidity Index;  $p = 0.007$ ) and lower performance on an executive function task (Colour Trails 2;  $p < 0.001$ ) were all predictive of mortality at eight years in this cohort.

Higher mortality was observed in those who had developed POD ( $n = 12/44$ ) compared to those who did not ( $n = 45/271$ ) but did not reach statistical significance ( $p = 0.09$ ).

Since abstract submission, plasma analyses which yielded results which were too low to be detected have been replaced with the minimum value detected for that plasma marker to avoid biased results. Participant mortality has also increased. The results are therefore different than those reported in the abstracts. The authors are happy to discuss – please see contact details.

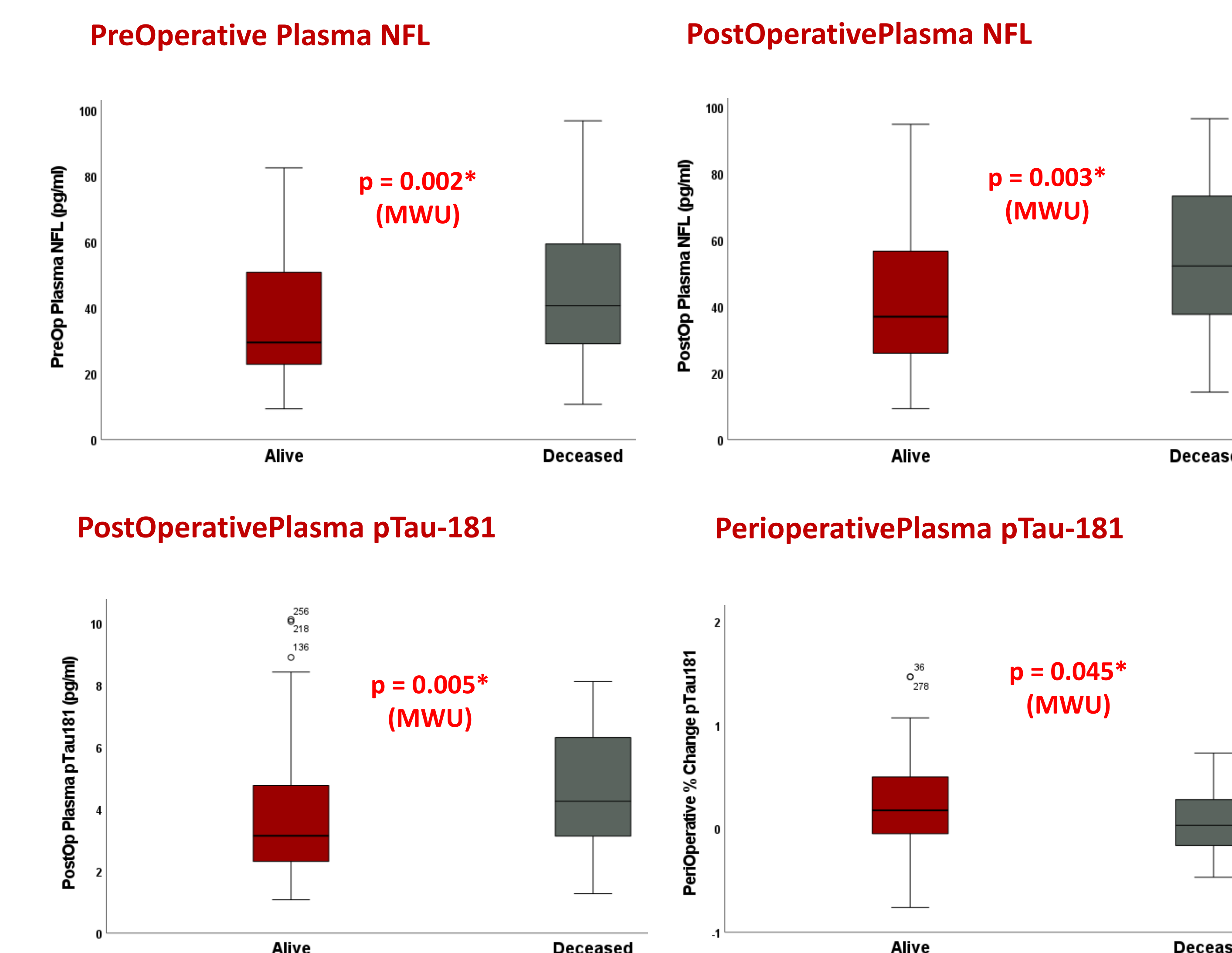
### Results

#### CSF Predictors of Mortality



CSF Interleukin-1 $\beta$ , Interleukin-6, Interleukin-8, Tumour Necrosis Factor- $\alpha$ , A $\beta$ 40 and A $\beta$ 42 were not predictive of mortality at eight years.

#### Plasma Predictors of Mortality



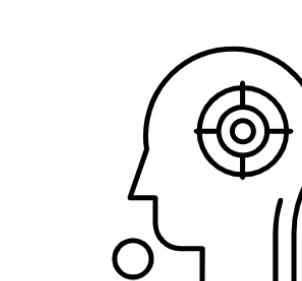
Plasma Interleukin-1 $\beta$ , Interleukin-6, Interleukin-8, Tumour Necrosis Factor- $\alpha$ , A $\beta$ 40, A $\beta$ 42 and Glial Fibrillary Acidic Protein were not predictive of mortality at eight years.

Perioperative change in most plasma markers were not predictive of mortality.

### Conclusions



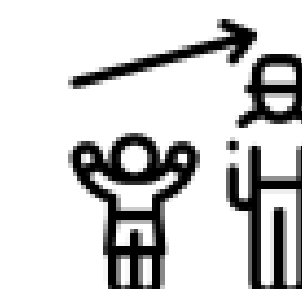
The majority of participants in this elective arthroplasty observational cohort are still alive eight years later.



Increased preoperative CSF measures of neurodegeneration were associated with mortality in adults eight years following elective orthopaedic surgery.



Perioperative plasma markers in keeping with neurodegeneration were also associated with mortality at eight years in this cohort.



Older age at time of surgery, multimorbidity and lower neuropsychological performance with mortality in adults eight years following elective orthopaedic surgery.

### References

- Psychiatric AA. Diagnostic and Statistical Manual of Mental Disorders. In: 5th ed. Washington, DC: American Psychiatric Association; 2013.
- Scott JE, Mathias JL, Kneebone AC, 2015. Incidence of delirium following total joint replacement in older adults: a meta-analysis. *Gen Hosp Psychiatry*, 2015, 37(3), pp.223-9.

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