

# ACCEPTED VERSION

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## **A Prospective Cohort Study to Develop and Validate a Multivariable Prediction Model for Transient Ischaemic Attack (TIA) Diagnosis Using Proteomic Discovery and Candidate Lipid Mass Spectrometry, Neuroimaging and Machine Learning: Study Protocol**

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**Page 72 held our abstract for an [electronic poster](#) and [video](#) presented at this conference.**

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## **APSC ABSTRACT**

**Note:** Section headings follow APSC recommendations  
400-word limit to abstract; our word count = 400.

**Title:** A prospective cohort study to develop and validate a multivariable prediction model for Transient Ischaemic Attack (TIA) diagnosis using proteomic discovery and candidate lipid mass spectrometry, neuroimaging and machine learning: study protocol.

**Purpose:** Urgent evaluation and diagnosis of TIA is important as early treatment can prevent subsequent strokes, but TIA is difficult to differentiate from small stroke and TIA mimics. Current advanced mass spectrometer (MS) technology allows quantification of many plasma proteins and lipids, resulting in large datasets needing sophisticated analysis. We aim to (1) identify and validate plasma protein, lipid and/or radiological biomarkers and develop a panel with the most significant biomarkers as a diagnostic tool to differentiate TIA from small stroke and TIA mimics; (2) assess our results using different techniques including statistical analysis and machine learning.

**Methods:** Patients with TIA/small stroke/TIA-like symptoms who attend the TIA Clinic, Emergency Department or Stroke Ward at the Royal Adelaide Hospital will be recruited consecutively (allowing for logistical limitations) for our prospective cohort study of at least 518 patients (80% power, alpha=0.05 allowing 20% for potential mismatches). Patients will provide written informed consent to participate in this grant-funded ethics-approved study. Non-contrast CT and CT-angiography/multi-modal MRI (diffusion, T1, T2 and MR-angiography) will be performed on each patient with images independently assessed by three stroke-neurologists.

Venous blood samples will be collected within the first 48-hours of onset of symptoms along with demographic and clinical data: medical history, modified Rankin Score and ABCD2 stroke-risk stratification score. Advanced MS will be used for discovery plasma proteomic and candidate lipid analysis. Using MS-software, Principal Component Analysis and hierarchical cluster analysis will be undertaken and output files analysed for biomarker differences between the three groups. We will also apply machine learning to the data, including deep learning with neural networks. Advanced radiological neuroimaging will be included and excluded in machine learning models to develop algorithms appropriate for medical centres with neuroimaging capabilities, and also for rural and remote regions without neuroimaging capacity.

**Results:** Twenty-seven of 29 potential TIA candidates have been enrolled (range 48-94 years; 15 female), blood samples collected and plasma frozen – these have not been analysed – the study is suspended due to COVID-19 restrictions.

**Conclusion:** We have designed a new TIA biomarker study protocol. Using plasma protein, lipid and radiological biomarkers, our study will develop and validate predictive algorithms for differentiating TIA, small stroke and TIA mimics, with analysis by conventional statistical methods and also machine learning.

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