ISPAD–Breakthrough Research Fellowship Interim Progress Report

Project Title: Exploring the role of Lipoprotein(a) in the development of vascular complications in youth with type 1 diabetes

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Type of Report: Interim Progress Report

1. Background

Vascular complications remain a leading cause of morbidity in youth with Type 1 Diabetes (T1D) [1]. In both adolescents and adults with T1D, increases in albumin excretion- even within the normal range- during the first years after diagnosis can predict the future risk of microalbuminuria [2,3]. Adolescence represents a critical period for identifying early renal risk factors and developing preventive strategies. The Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT) demonstrated that adolescents with higher-normal urinary albumin excretion are more likely to develop microalbuminuria, a precursor to diabetic nephropathy, which is typically observed in adulthood [3,4]. As AdDIT participants now enter early adulthood, this longitudinal cohort provides an opportunity to investigate the outcomes to detect renal injury in T1D.

As AdDIT participants now transition into early adulthood, this longitudinal cohort provides a valuable opportunity to investigate early renal changes and their clinical implications. This fellowship project builds upon the AdDIT database to refine early risk stratification and generate evidence that will guide future studies focused on preventive strategies for young people with T1D.

2. Aims and Objectives

Primary Objectives:

- To investigate associations between early renal alterations and subsequent renal dysfunction using long-term AdDIT follow-up data.
- To examine the long-term impact of cumulative exposure to modifiable and non-modifiable risk factors on renal outcomes during young adulthood.

Secondary Objectives

- To assess renal outcomes and their evolution from adolescence to young adulthood.
- To determine the prevalence of renal complications (micro- and macroalbuminuria) in early adulthood according to ACR stratification in adolescence.

3. Study Design and Population

The AdDIT study is a longitudinal, multi-center, international cohort designed to track cardio-renal outcomes in adolescents with T1D. For the current analyses, data from 301 participants (comprising 903 urine samples) were extracted and harmonized from the AdDIT follow-up dataset. All analyses are being conducted in the Wellchild Laboratory, St. Thomas' Hospital, London, UK, ensuring methodological consistency with the original study.

Renal outcomes—including glomerular filtration rate and albumin-to-creatinine ratio (ACR)—are being re-evaluated to identify long-term renal trajectories across previously defined ACR categories (high vs. low). These outcomes are analyzed alongside demographic, biochemical, and renal variables to identify early markers of vascular injury.

4. Progress During the Reporting Period (15 May–15 October 2025)

Statistical and Methodological Training

The fellow completed multiple biostatistics and bioinformatics courses at the University of Cambridge, gaining proficiency in multivariate regression modeling, mixed-effects modeling, and time-to-event analyses. These skills are now actively applied to the AdDIT dataset evaluation.

Completion of an Independent Study and Manuscript Preparation:

A complementary study investigating 24-hour ambulatory blood pressure monitoring and pulse wave velocity in adolescents with T1D from Türkiye has been completed.

Statistical analysis and manuscript drafting are finalized, and the paper is currently under preparation for submission to a peer-reviewed journal. This study enhances the fellow's knowledge in assessing the risk of micro- and macrovascular complications.

Data Extraction and Quality Assurance:

Final renal outcome data from AdDIT were successfully extracted, cleaned, and validated. The dataset now integrates renal outcomes with corresponding demographic, metabolic, and clinical parameters, ensuring high data fidelity for the upcoming analyses.

Urinary Sample Analysis and Integration:

Follow-up urine samples were analyzed and merged into a unified database. Rigorous quality control checks were completed in September 2025, ensuring consistency with prior AdDIT datasets.

Preliminary Analyses and Early Findings:

Initial analyses have begun, focusing on the relationships between renal function indices and demographic and clinical features. Early models adjusting for age, diabetes duration, and HbA1c are currently being refined, providing preliminary insights into renal trajectories across the cohort.

Research Communication and Professional Development:

The fellow has strengthened academic writing and data presentation skills through active participation in research seminars and abstract preparation. Preliminary findings are being prepared for presentation at the ISPAD Annual Congress 2026, with a concurrent manuscript planned for submission to a peer-reviewed journal.

During this reporting period, several research outputs have been prepared and submitted, reflecting ongoing progress related to the fellowship project: A review article, *currently under review*, focuses on the prevention and management of vascular complications in adolescents with Type 1 Diabetes, summarising current evidence and highlighting future research directions. In addition, two abstracts have been submitted, including one to the Diabetes UK Annual Professional Conference.

As we have not yet received sufficient funding to initiate the laboratory analyses for Lipoprotein(a), we have focused on advancing other key analyses within the AdDIT dataset, while awaiting external funding to support the laboratory component of the project. Including renal function trajectories, risk factor modeling, and data integration

across multiple variables. Detailed research about the role of “Lp(a) in the development of vascular complications in youth with Type 1 Diabetes” will commence once the necessary funding for laboratory work becomes available.

5. Next Steps

Complete Full Statistical Modeling:

Finalize regression, mixed-model, and time-to-event analyses to evaluate longitudinal associations between ACR trajectories, renal outcomes, and key risk factors.

Validate Findings and Conduct Sensitivity Analyses:

Continue collaborative validation with UCL and the Wellchild Laboratory to ensure robustness and reproducibility of findings.

Disseminate Findings:

Prepare and submit an abstract for the ISPAD 2026 Congress. Draft the first manuscript based on finalized results for submission to a high-impact peer-reviewed journal.

Expand Literature Review:

Conduct an in-depth literature synthesis on Lipoprotein(a) as a potential mediator of vascular injury in T1D, integrating recent advances in Lipoprotein(a) outcomes and diabetic complications.

6. References

[1]- Marcovecchio, M. L., Tossavainen, P. H., & Dunger, D. B. (2010). Prevention and treatment of microvascular disease in childhood type 1 diabetes. British Medical Bulletin, 94(1), 145–164.

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[3]- Dunger, D. B., Schwarze, C. P., Cooper, J. D., et al. (2007). Can we identify adolescents at high risk for nephropathy before the development of microalbuminuria? Diabetic

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