more high-quality comparative studies are needed to evaluate the effectiveness of different smartphone-based AI models in real-world clinical settings.

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Soluble receptor for advanced glycation end products and CVD risk in T1D individuals with resistant hypertension

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Background: Elevated concentrations of soluble receptor for advanced glycation end products (sRAGE) have been reported in T1D in relation to endothelial cell damage and left ventricular hypertrophy in subjects with hypertension.

Aim: To investigate the association of sRAGE with incident coronary artery disease (CAD) and stroke in T1D individuals with resistant hypertension (RH).

Method: We included 237 individuals with T1D who had RH at baseline. RH was defined as uncontrolled BP with ≥3 antihypertensive drugs from different classes, one of which was a diuretic or controlled BP with ≥4 drugs. During the median of 12.3 years follow-up time, 53 individuals developed incident CAD and 33 individuals developed incident stroke. Association of sRAGE with incident CAD or stroke event was assessed by Cox regression and Kaplan-Meier survival analysis with minimum follow-up time of half a year. Models were adjusted for age, sex, HbA1c, waist-to-hip-ratio or BMI, current smoking, LDL cholesterol, and eGFR, when applicable.

Results: In fully adjusted Cox models, sRAGE concentrations were associated with incident CAD (HR 1.05 [95% CI 1.01, 1.09], $p = 0.01$), but not with incident stroke ($p = 0.2$). The highest quartile was not associated with CAD in the unadjusted model, but was associated (HR 2.61 [95% CI 1.07, 6.37], $p = 0.04$) after adjusting for clinical variables (age, sex, HbA1c, waist-to-hip-ratio, current smoking, LDL cholesterol), except eGFR. The highest quartile of sRAGE was not associated with incident stroke ($p \geq 0.3$). In Kaplan-Meier survival analysis, in the highest sRAGE quartile, the 10-year cumulative risk of CAD was 28.2% [95%CI 13.8–40.2, $p = 0.003$] when compared with quartile two, and for stroke 12.2% [95%CI 1.5–21.7, $p = 0.3$] when compared with the lowest quartile.

Conclusion: Our findings suggest an independent association of sRAGE with the risk of incident CAD in T1D and baseline RH. The highest sRAGE quartile showed increased risk of CAD, but the nature of this relationship needs further investigation.

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Association of Diabetes with COVID-19 Mortality: A Systematic Review and Meta-Analysis of 118 Observational Studies

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Background: Despite a growing body of scholarly research on the risks of severe COVID-19 associated with underlying chronic diseases [1, 2], there is still a need for pooled risk estimates, particularly in the global context, with adjustment for confounding effects.

Aim: We conducted a systematic review and meta-analysis to estimate the pooled adjusted risk ratios on the association of diabetes with COVID-19 mortality.

Method: We searched 16 literature databases for original studies published between Jan 1, 2020, to Dec 31, 2020. Pooled adjusted risk ratios (PRR) were estimated using random-effects meta-analysis to account for the uncertainty in residual heterogeneity [3]. Subgroup analysis and meta-regression were conducted to assess the impact of country- and study-level characteristics on PRR. We used contour-funnel plots and Egger's test to assess possible publication bias.

Results: We reviewed 34,830 records identified in the literature, of which 118 original studies were included in the meta-analysis. PRR for diabetes on COVID-19 mortality was 1.43 (95% CI 1.32 to 1.54). There was considerable heterogeneity for PRR of diabetes associated with COVID-19 mortality ($I^2 = 94\%$). Subgroup analysis showed a higher PRR in countries from the WHO Western Pacific Region, with a lower Global Health Security Index (GHSI) score, with a lower-middle income level as defined by the World Bank, and in studies with a higher risk of bias as assessed by adapted Newcastle-Ottawa Scale. Meta-regression showed a negative association between the mean age of the participants ($P = 0.02$) and GHSI score ($P = 0.02$) with the risk ratios. There was no evidence of a funnel plot asymmetry in the association between diabetes and COVID-19 mortality (Egger's test $P = 0.29$).

Conclusion: Diabetes was associated with an increased risk of COVID-19 mortality independent of other known risk factors. This association was more pronounced in low-resource settings, highlighting the importance of addressing diabetes for global pandemic preparedness and prevention of severe outcomes.

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Associations of CR1 with mild cognitive impairment in type 2 diabetes mellitus

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Background: Type 2 diabetes mellitus (T2DM) has been known as an important risk factor for cognitive impairment and the liver plays a central role in the development of T2DM and insulin resistance.

Aim: This study attempted to develop and validate the associations of liver insulin resistance-related genes with mild cognitive impairment inT2DM.

Method: We obtained IR-related differentially expressed genes (DEGs) of human liver tissue from the Gene Expression Omnibus (GEO) database and captured MCI-related genes from the GeneCards database. The limma package in R software was used to identify differentially expressed genes (DEGs).These genes were compared to obtain the overlapping targets in T2DM and MCI, and based on them, enrichment analysis was carried out, and the least absolute shrinkage and selection operator (LASSO) logistic regression and support vector machine-recursive feature elimination (SVM-RFE) algorithms were used to identify the specific genes. Finally, real-time polymerase chain reaction in vitro verification was performed.

Results: In this study, 44 DEGs were totally identified between MCI and T2DM, and the enrichment analysis indicated that they were much related to the function of AGE-RAGE signaling pathway in diabetic complications and neuroinflammatory response. CR1 and NCAPH2 were identified as the marker genes in both diseases. Based on the validation of RT-qPCR from 20 T2DM patients with MCI(MCI group) and 22 T2DM patients with non-MCI(NC group), CR1 in peripheral blood mononuclear cells was found to be significantly upregulated in MCI group($P < 0.01$), and NCAPH2 was found to be downregulated but no significant difference between the two groups. Their clinical significances were further analyzed.

Conclusion: Discovering and exploring the marker genes that are dysregulated in both 2 diseases could help us better comprehend the intrinsic relationship between T2DM and MCI, which may inspire us to develop new strategies for facing the dilemmas of clinical or basic research in cognitive dysfunction.

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Digital Delivery of T2D Remission Program: Clinically Significant Weight Loss and Improved Glycemic Control

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Background: The UK National Health Service type 2 diabetes (T2D) Remission Program supports people living with T2D to lose weight, improve glycaemic control, reduce medication, and achieve remission. This improvement can reduce diabetes complications and cardiovascular (CVD) risk (1). The program consists of a 12 weeks of 900 Kcal total diet replacement, 6 weeks of food reintroduction followed by 8 months of behaviour change support.

The program is delivered remotely via the Liva app, with live group-based webinars and video calls led by a health coach. Liva has proved significant success in inspiring lifestyle changes among this population (2, 3).

Aim: To assess if a digitally delivered T2D remission program can lead to longterm weight loss and CVD risk reduction.

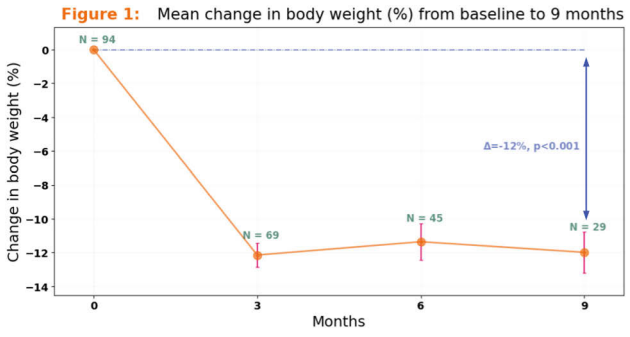
Method: We conducted a mid-point service evaluation of the Liva program using routine service delivery data. Our primary and secondary outcomes were changes in weight and HbA1c, respectively.

Results: Between May 2022 and June 2023, 243 patients were referred, of which 94 were eligible and enrolled. 60% were female, with mean baseline demographics of 51 years old, 104.3 kg weight, 36.9 kg/m^2 BMI, 2.8 years after T2D diagnosis, and 59 mmol/mol HbA1c.

At present, 29 participants have reached the 9-month milestone and registered their weight, with 10 self-reporting their HbA1c level at 6 months.

Mean weight loss at 9 months was 12.7 kg (12%) (figure 1) with 83% losing >5%, 55% losing >10%, 34% losing >15% and 10% losing >20% body weight. The mean reduction in HbA1c after 6 months was 14 mmol/mol, with 70% achieving HbA1c levels within the non-diabetic range.

Figure 1: Mean change in body weight (%) from baseline to 9 months



Conclusion: Our assessment demonstrates that a digitally delivered T2D remission program can result in clinically significant weight loss and improvements in glycaemic control. By focusing on weight loss in this population, we promote the