DIABETES
TECHNOLOGY & THERAPEUTICS

Diabetes Technology & Therapeutics: http://mc.manuscriptcentral.com/diabetestechnology

Assessing the utility of a capillary-adjusted oral glucose tolerance test for the early detection of type 1 diabetes in childhood

Journal:	*Diabetes Technology and Therapeutics*
Manuscript ID	DIA-2026-0492.R1
Manuscript Type:	Original Articles
Date Submitted by the Author:	n/a
Complete List of Authors:	Swaby, Rabbi; University of Oxford, Nuffield Department of Medicine Birks, Jacqueline; University of Oxford Nuffield Department of Surgical Sciences Dayan, Colin; University of Oxford, Nuffield Department of Medicine; Cardiff University Dunseath, Gareth; Swansea University, College of Medicine Gillespie, Kathleen; University of Bristol, Diabetes and Metabolism Unit, Translational Health Sciences Liu, Yuk-Fun; Guy's and St Thomas' Hospitals NHS Trust, Department of Diabetes and Endocrinology; King's College London, Diabetes Department; King's Health Partners, Institute of Diabetes, Endocrinology and Obesity Luzio, Steve; Swansea University, College of Medicine Shetty, Ambika; Noah's Ark Children's Hospital for Wales, Department of Paediatric Diabetes and Endocrinology Townson, Julia; Cardiff University, Centre for Trials Research Williams, Rachel; Nottingham Children's Hospital Willemsen, Ruben; Barts Health NHS Trust, Department of Paediatric Diabetes and Endocrinology, The Royal London Children's Hospital Besser, Rachel; University of Oxford, Nuffield Department of Medicine; University of Oxford, Department of Paediatrics
Keyword:	Type 1 diabetes, Autoimmunity, Adherence/Compliance, Pediatrics
Manuscript Keywords (Search Terms):	type 1 diabetes, staging, monitoring, management, early-stage

SCHOLARONE
MANUSCRIPTS

Title: Assessing the utility of a capillary-adjusted oral glucose tolerance test for the early detection of type 1 diabetes in childhood

Short running title: Utility of a capillary-adjusted OGTT.

Authors: Rabbi Swaby BMBS[1], Jacqueline Birks MA MSc[2], Colin Dayan PhD[1,3], Gareth Dunseath PhD[4], Kathleen Gillespie PhD[5], Yuk-Fun Liu PhD[6,7,8], Steve Luzio PhD[4], Ambika Shetty PhD[9], Julia Townson PhD[10], Rachel Williams PhD[11], Ruben H Willemsen PhD[12], Rachel E J Besser PhD[1,13]

Affiliations:

1. Diabetes and Inflammation Laboratory, Centre for Human Genetics, Nuffield Department of Medicine, Bukhman Centre for Research Excellence in Type 1 Diabetes, NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK.
2. Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK.
3. Clinical Diabetes and Metabolism, Cardiff University, School of Medicine, Cardiff, UK.
4. College of Medicine, Swansea University, Swansea, UK.
5. Diabetes and Metabolism Unit, Translational Health Sciences, University of Bristol, Bristol, UK.
6. Department of Diabetes and Endocrinology, Guy's and St Thomas' NHS Foundation Trust, London, UK.
7. Diabetes Department, School of Cardiovascular and Metabolic Medicine, King's College London, London, UK.
8. Institute of Diabetes, Endocrinology and Obesity, King's Health Partners, London, UK.

For Peer Review Only/Not for Distribution

9. The Noah's Ark Children's Hospital for Wales, Department of Pediatric Diabetes and Endocrinology, Cardiff and Vale University Health Board, Cardiff, UK.
10. Centre for Trials Research, Cardiff University, Cardiff, UK.
11. Nottingham Children's Hospital, Nottingham University Hospitals NHS Trust, Nottingham, UK.
12. The Royal London Children's Hospital, Barts Health NHS Trust, Department of Pediatric Endocrinology and Diabetes, London, UK.
13. Department of Pediatrics, University of Oxford, Oxford, UK.

Joint corresponding authors: Dr Rachel Besser, Centre for Human Genetics, Oxford NIHR Biomedical Research Centre, Roosevelt Drive. Oxford, OX3 7BN

Dr Rabbi Swaby, Centre for Human Genetics, Oxford NIHR Biomedical Research Centre, Roosevelt Drive. Oxford, OX3 7BN

Email: rachel.besser@well.ox.ac.uk, rachel.besser@ouh.nhs.uk; rabbi.swaby@nhs.net

Word Count: Abstract: 300 (300); Main text: 4559 (5000); 2 Tables, 4 Figures

Keywords: Type 1 diabetes, staging, monitoring, management, early-stage.

Prior presentation[1]

[1] An abstract of this study was an oral presentation at the British Society of Pediatric Endocrinology and Diabetes (BSPED), Sheffield, 12-14 November 2025 and in brief at the EDENT1FI meeting, Prague, 6-8 October 2025. It was also presented at the UK T1D Consortium Meeting, Cardiff, 20 May 2025. An abstract of this study was presented as a poster at the Diabetes UK Conference, 22-24 April 2026, and as an oral presentation at the Breakthrough T1D Congress, 9-11 October 2026.

For Peer Review Only/Not for Distribution

ABSTRACT

OBJECTIVE

The oral glucose tolerance test (OGTT) is the gold standard for staging and monitoring type 1 diabetes (T1D), but requires venous sampling in a healthcare setting, limiting its accessibility. We assessed the utility of a capillary-adjusted OGTT (cOGTT) method in children and young people (CYP).

METHODS

Study 1 – OGTT method comparison

CYP across the glycemic range underwent contemporaneous venous (vGluc) and capillary (cGluc) glucose sampling at 0-min, 60-min (subgroup), and 120-min, after a standard oral glucose load. Agreement between vGluc and cGluc was assessed using Bland-Altman between 3.5-15 mmol/L. Glycemic status was assessed using established thresholds, and acceptability by questionnaire.

Study 2 – At-home OGTT feasibility

CYP with early-stage T1D undertook home cOGTT testing (0, 120-min) and completed acceptability questionnaires.

RESULTS

For Peer Review Only/Not for Distribution

Study 1: Forty-five CYP participated (mean [SD] age 12.2 [3.2] years; range 5-17), with 20 undergoing additional 60-min sampling. cGluc and vGluc showed reasonable agreement across the glycemic range of 3.5–15 mmol/L, (bias, -0.22 mmol/L; 95% CI, -0.51-0.07; 95% limits of agreement, -2.91 to 2.47 mmol/L). cGluc performed well at normoglycemia: 21/22 (95% sensitivity; 95% CI, 77-100%), 14/17 (82% specificity; 57-96%); and hyperglycemia: 9/10 (90% sensitivity; 55-100%), 29/29 (100% specificity; 88-100%); but less well for dysglycemia: 4/7 (57% sensitivity; 18-90%), 30/32 (94% specificity; 79-99%). In 76% (32/42), cOGTT was preferred for future testing.

Study 2: Forty-five CYP participated (10.4 [3.1] years; range 4-17). In 91% (41/45), home cOGTT tests were completed successfully (3 device failures, 1 incomplete test). Home testing was acceptable in 98% (44 of 45). Two CYP were identified with stage 3 T1D with no evidence of DKA.

CONCLUSIONS

The cOGTT method is feasible and acceptable compared to venous OGTT in CYP, with promising performance for detecting hyperglycemia, but further assessment is needed before it can be used for glycemic staging.

(NCT06815081, https://clinicaltrials.gov/study/NCT06815081)

For Peer Review Only/Not for Distribution

INTRODUCTION

The oral glucose tolerance test (OGTT) is the gold standard test for staging and monitoring individuals with type 1 diabetes (T1D).[1] The OGTT is used to classify the early stages of T1D, where stage 1 and 2 are defined by the presence of two or more anti-islet beta-cell autoantibodies (IAb) and normoglycemia (stage 1), or dysglycemia (stage 2), and stage 3 by persistent hyperglycemia with or without symptoms of T1D.[2] The OGTT involves multiple venous blood draws, taken over two hours, in a healthcare setting. This is challenging, especially in children and young people (CYP), with studies showing high attrition rates (~45%) related to using the test for periodic monitoring.[3,4] Further, conducting an OGTT is sensitive to methodological error, particularly the process of glycolysis that occurs in the sample following collection, where it is estimated that 5-7% of glucose is degraded per hour, even when measured in an appropriate sample tube.[5,6] To address some of these limitations, a novel capillary-adjusted OGTT device (cOGTT) called the "GTT@home" has been developed to allow untrained individuals to perform an OGTT in the home or community setting. The GTT@home (Digostics Ltd, Didcot, UK) is an electronic device that is UKCA and CE marked (UK Conformity Assessed, Conformité Européene, or European Conformity marking) to collect, analyze and record capillary-adjusted glucose at the 0 and 120-min time points of an OGTT in adults and children under supervision.[7] Two previous studies have assessed this device for use in adults to detect type 2 and gestational diabetes, but there have been no studies to date in CYP.[8,9] Therefore, we investigated the agreement and diagnostic performance of the GTT@home device compared to the standard OGTT in CYP across a spread of glucose values, and the feasibility and acceptability of using the device in the home environment in CYP with early-stage T1D.

For Peer Review Only - Not for Distribution

METHODS

Study Populations

Study 1 - Method comparison of standard venous and capillary OGTT

To achieve a spread of glucose values, study 1 included CYP with early-stage (stage 1 or 2) or established stage 3 T1D, as well as CYP undergoing investigation for type 2 diabetes, aged < 18 years (Table 1). Participants were recruited from pediatric UK hospitals (John Radcliffe Hospital, Oxford; Barts Health Royal London Hospital, London; Nottingham Children's Hospital, Nottingham; Noah's Ark Children's Hospital, Cardiff).

Study 2 - At home OGTT feasibility and acceptability

Study 2 included CYP with early-stage T1D (stage 1 or 2), defined as being confirmed positive for ≥ 2 IAb, aged < 18 years. Participants were recruited through established UK research platforms: INNODIA (An Innovative Approach Towards Understanding and Arresting Type 1 Diabetes), TrialNet, Bart's-Oxford (BOX) Family Study and the UKT1D Research Consortium.[10–12]

Study Design

For Peer Review Only - Not for Distribution

Additional information on study design and procedures has been published.[13] This observational study included two separate study arms, inviting CYP to undertake a standard venous OGTT (study 1), or an OGTT at home using the GTT@home device (study 2). In both study arms, participants were advised to have a minimum 8-hour fast (preceded by a normal balanced diet), avoid exercise, and rest for the duration of the test. Both studies used a standard glucose load (1.75 g/kg, max 75 g). In study 1, significant hyperglycemia was observed in the first three participants with known stage 3 T1D. Therefore, for participant safety, a protocol amendment was introduced to reduce the glucose load in subsequent participants with known stage 3 T1D from 1.75 g/kg to 1 g/kg (max 75 g).

Study 1

Capillary glucose samples (using the GTT@home) were collected by research staff at 0 and 120 min contemporaneously with a venous glucose sample. Participants at the John Radcliffe Hospital also had an additional 60-min capillary and venous glucose sample collected contemporaneously using an additional cOGTT device (n=20) to compare capillary and venous glucose at an intermediate OGTT time point. At the end of the test, each device was scanned using a smartphone to capture the capillary glucose data (Supplementary Figure 1).

Study 2

Capillary glucose samples (using the GTT@home) were collected at 0 and 120 min by the participant (or parent) at home. Participants returned the test result by scanning the device with a smartphone or returning the detachable data record.

The capillary OGTT device

For Peer Review Only Not for Distribution

The cOGTT system (the GTT@home) is a handheld device that collects capillary blood samples and performs an immediate glucose test using the glucose dehydrogenase method at the 0- and 120-min time points. It is calibrated to convert capillary to venous plasma glucose results, using 0.6 microL of capillary blood and is validated from 3.5 to 15 mmol/L. Across this glucose range, the device has a coefficient of variation (%CV) of 3.4 to 6.1%. The cOGTT system uses a three-step calibration procedure: 1) the whole capillary blood glucose concentration is calculated from calibration algorithms within the server-based software; 2) the whole capillary glucose value is adjusted by the software for the recorded operating temperature at the time of each blood test procedure, to adjust for the effect of ambient temperature on the glucose value; 3) the temperature-adjusted glucose value is in turn adjusted using a proprietary algorithm that applies conversion factors for each test time point. These whole blood capillary to venous plasma conversions were determined experimentally during the development of the device. This process differs from the capillary to plasma conversion used in glucometers, which apply an 11% conversion to all test points to account for blood cell mass, as per previous recommendations.[14]

For Peer Review Only/Not for Distribution

The cOGTT device is designed to guide the user through a step-by-step process. After the 0-min glucose sample is taken and the glucose drink consumed, a built-in 120-min timer is initiated which ends with an audible alarm, prompting the participant to collect the 120-min glucose sample. The device does not allow the 120-min sample to be collected until the alarm has sounded. Glucose values are not displayed on the device. Instead, once the test is complete, the detachable data record is scanned using a smartphone to upload the glucose data to a secure cloud-based database. Alternatively, it can be removed and posted to the research team (Supplementary Figure 1).

Laboratory methods

Venous blood samples were processed within 30 min of sample collection, using fluoride oxalate sample tubes. Each sample was centrifuged at 4000 rpm for 5 min at 4°C, and a 1 ml aliquot of plasma was frozen and stored at -80°C. Plasma samples were batch couriered on ice and analyzed centrally at the Diabetes Research Group Laboratory, Swansea, UK (YSI 2500 Glucose Analyzer, Yellow Springs Instruments, Fleet, UK), and were considered the “reference” measure. The intra- and inter-assay %CVs for this device are less than 2% and 4% respectively, across a wide concentration range, covering both normal and elevated glucose ranges. Each participant had a complete blood count (or full blood count) measured, which was processed and analyzed locally at each site following routine procedures. The purpose of collecting this sample was to measure the hematocrit level, which when abnormal, can cause inaccuracies in capillary glucose readings.[15] Therefore, the hematocrit level was reported descriptively but not included in the statistical analysis.

Acceptability

For Peer Review Only/Not for Distribution

Study 1

Acceptability of the GTT@home device was assessed using a questionnaire adapted from Besser et al.[16] Questions related to pain associated with each sampling method (venous and capillary), the process of completing the test and participant preference for future OGTT testing. For participants aged ≥ 16 years, a traditional Likert pain scale graded 1 to 7 was used, where 1 was “not painful at all”, 4 was “moderately painful” and 7 was “very painful”. For participants aged < 16 years, a visual pain score (Wong-Baker FACES pain scale) was used, graded 0 to 10, where 0 was “no hurt”, and 10 was “hurts worst” (Supplementary Figure 2). To allow pain scores to be aligned on a common 0-10 numerical range, Likert pain scores were linearly transformed using a formula based on the percentage of maximum possible approach.[17]

Study 2

A similar questionnaire was used to assess acceptability of the GTT@home device in the home environment and data were collected on pain and the feasibility of home collection using a Likert scale (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree) (Supplementary Figure 3).

Recruitment and sample size

For Peer Review Only/NOT for Distribution

For study 1, the initial recruitment range was 30-50 participants, based on the feasibility of recruiting CYP undergoing OGTTs through clinical care and research platforms. Previous adult data[9] suggested that approximately 20% of our target population would have dysglycaemia. At the upper recruitment target of 50 participants, this would correspond to approximately 10 participants with dysglycaemia. If the sensitivity of the device was 100%, the 95% confidence interval for sensitivity would be 69%–100%. If sensitivity were 90%, the 95% confidence interval would be 55%–100%.[18,19] These estimates were used to assess the anticipated precision achievable within the feasible recruitment range. A pragmatic recruitment target of 45 participants was subsequently agreed.

To achieve a spread of glucose values, a midpoint review of recruitment was undertaken to determine if enrichment of specific glycemic groups was required.

For study 2, a recruitment target of 45 participants was based on the anticipated feasibility of recruiting CYP with early-stage T1D from established UK research platforms.

Statistical Analysis

For Peer Review Only Not for Distribution

Statistical analyses were conducted in R (version 4.4.3). Capillary glucose was compared to plasma glucose using paired samples from each participant that had both measures available. Participants with missing glucose data from the pair were excluded. Data were assessed for normal distribution using the Shapiro-Wilk test.[20] Agreement between the capillary and plasma glucose measures was assessed using a Bland-Altman plot,[21,22] and measures were compared within the 3.5 to 15 mmol/L range, as this covered both the diagnostic range and the lower and upper limits of the GTT@home device. Measures outside of this range (n=14) were not included. As a secondary analysis, agreement was reassessed using the Bland-Altman extension for multiple paired observations per individual, accounting for repeated measurements contributed by the same participant.[23] Mean absolute relative difference (MARD) was calculated to quantify the average absolute percentage difference between capillary and plasma glucose measurements. The 95% confidence interval was estimated using 10,000 participant-level bootstrap resamples to account for repeated measures within participants.[24] In addition, the relationship between capillary and plasma glucose was also assessed using the Spearman Rank correlation coefficient.[25] Diagnostic accuracy of capillary glucose measures was assessed against plasma glucose by calculating sensitivity and specificity for normoglycemia (0-min <5.6 mmol/L; 60-min <11.1 mmol/L; 120-min <7.8 mmol/L); dysglycemia (0-min 5.6-6.9 mmol/L; 60-min ≥11.1 mmol/L, 120-min 7.8-11.0 mmol/L) and hyperglycemia (0-min ≥7.0 mmol/L and/ or 120-min ≥11.1 mmol/L) using established thresholds.[1] For acceptability data, following transformation onto a common 0-10 scale, paired pain scores for capillary and venous glucose sampling were compared using the Wilcoxon signed rank test.[17,26] The preferred choice of future OGTT method (capillary versus venous) was

For Peer Review Only/Not for Distribution

assessed using the binomial test.[27] Otherwise, responses to Likert scale questions were reported descriptively.

Ethics

Ethical approval for this study was obtained from the UK Research Ethics Committee (reference: 23/WM/0184). The study was also registered with a clinical trials registry (NCT06815081). All participants, and for those under 16 years, their parent/guardian, gave informed written consent. Participants under 16 years provided informed written assent.

RESULTS

Study characteristics

Ninety-four CYP were recruited to the study (n=46 [study 1], n=48 [study 2]), of whom, 45 participants completed their study visit for each arm (Figure 1A, Figure 1B). Seven participants were recruited to both study arms. Participants in study 1 had a mean (SD) age of 12.2 years (3.2) (range 5-17) and 49% of participants were male. The majority (80%) were of White ethnicity, and 6.7% of participants were of Black, Asian or mixed ethnic backgrounds. Participants in study 2 had a mean (SD) age of 10.4 years (3.1) (range 4-17) and 67% of participants were male. The majority (93%) were of White ethnicity (Table 1).

For Peer Review Only/Not for Distribution

For study 1, 39 of 45 participants had both plasma and capillary glucose measures available for the 0- and 120-min time points. In total, there were 104 paired samples available (0-min, n=43; 60-min, n=20; 120-min, n=41). Of these, 90 paired samples were in the 3.5-15 mmol/L range. Missing data were due to errors collecting the capillary sample (n=5), or failed cannulation (n=1). For study 2, 41 of 45 participants had a capillary glucose measure available for both the 0- and 120-min time points (0-min, n=43; 120-min, n=41) (Figure 1A, Figure 1B).

Relationship between capillary and plasma glucose

Agreement and accuracy of capillary glucose measurement

There was no statistically significant bias observed between capillary (using the GTT@home device) and plasma glucose (reference measure using the YSI analyzer) over the diagnostic range of 3.5 – 15 mmol/L, with a small negative mean difference (bias) (-0.22 mmol/L; 95% CI, -0.51 to 0.07, n=90) and wide limits of agreement (LoA) (-2.91 to 2.47 mmol/L) (Figure 2). A secondary Bland-Altman analysis accounting for multiple paired observations per participant produced identical 95% limits of agreement (-2.91 to 2.47 mmol/L). When assessing agreement at each OGTT time point, a higher bias was observed at 0-min (-0.51 mmol/L; LoA, -2.95 to 1.94 mmol/L, n=43) (Supplementary Figure 4). The bias was lower at the 60-min (0.19 mmol/L; LoA, -3.25 to 3.63 mmol/L, n=15) and 120-min time points (0.07 mmol/L; LoA, -2.66 to 2.81 mmol/L, n=33) (Supplementary Figure 5, Supplementary Figure 6). The MARD between capillary and plasma glucose measurements was 16.9% (95% CI, 14.20 to 19.64).

Spearman's Rank correlation

For Peer Review Only/Not for Distribution

Capillary glucose also demonstrated a moderate positive correlation with plasma glucose over the diagnostic range (Spearman's Rho = 0.74, p<0.0001, n=90) (Supplementary Figure 7).

Classification by glycemic status

Overall, 87% (34 of 39) participants were correctly classified according to glycemic category using the cOGTT method. Using the 0- and 120-min time points, of those that were misclassified: 7.7% (3 of 39) were reported as normoglycemia, instead of dysglycemia; 2.6% (1 of 39) were reported as dysglycemia, instead of normoglycemia; 2.6% (1 of 39) were reported as dysglycemia, instead of hyperglycemia.

Normoglycemia: capillary glucose had a sensitivity of 95% (21 of 22; 95% CI, 77 to 100%) and a specificity of 82% (14 of 17; 95% CI, 57 to 96%) for detecting normoglycemia (Table 2).

Dysglycemia: capillary glucose had a sensitivity of 57% (4 of 7; 95% CI, 18 to 90%) and a specificity of 94% (30 of 32; 95% CI, 79 to 99%) for detecting dysglycemia (Table 2).

Hyperglycemia: capillary glucose had a sensitivity of 90% (9 of 10; 95% CI, 55 to 100%) and specificity of 100% (29 of 29; 95% CI, 88 to 100%) for detecting hyperglycemia (Table 2). Of the eight participants with known clinical T1D who received a modified glucose load, seven were classified as hyperglycemic by both capillary and venous methods, while one participant was classified as hyperglycemic by venous testing but dysglycemic by the capillary method.

Classification by time point

For Peer Review Only/Not for Distribution

The sensitivity and specificity of capillary glucose was also assessed per OGTT time point. At the 60-min time point, capillary glucose had a sensitivity of 86% (6 of 7; 95% CI, 42 to 100%), and specificity of 92% (12 of 13; 95% CI, 64 to 100%) for detecting dysglycemia. The 0- and 120-min time points were also analyzed (Supplementary Table 1).

Acceptability

Study 1: Capillary versus venous glucose testing

Pain experience

The median pain score rating was significantly lower for capillary (median, 2; IQR, 0-2) compared with venous testing (median, 3; IQR, 2-5.5, p = 0.001) (Figure 3).

Test process

The process of completing the OGTT was tolerated well by most participants, with 76% (32 of 42) of participants stating that the time taken to complete the test was acceptable, and 66% (28 of 42) agreeing that the time taken to travel to and from the hospital for the test was acceptable (Supplementary Figure 8).

Patient preference

Seventy-six percent (32 of 42, p = 0.00094) chose the cOGTT as their preferred method for future glycemic assessment, compared to 24% (10 of 42) who chose the standard venous OGTT (Supplementary Figure 9). Of the ten participants who chose the venous OGTT, 70% (7 of 10) rated the pain from capillary sampling as the same or worse than the venous method (age range 7-17 years).

Study 2: Home testing

For Peer Review Only/Not for Distribution

Feasibility

Ninety-one percent (41 of 45) of OGTTs attempted in the home environment measured both 0- and 120-min time points successfully. Of the four unsuccessful tests, three involved device failures. Two devices failed to give any capillary glucose readings and one failed to measure a 120-min glucose. In one test, the participant vomited shortly after ingesting the glucose load, so the test was abandoned. Thirteen percent (6 of 45) of CYP gave written feedback stating they disliked the glucose drink.

Hyperglycemia was identified during home cOGTT testing in 11% (5 of 45) of CYP with early-stage T1D. All were asymptomatic at testing and were referred to their local hospital diabetes teams for further management. Two of the five CYP required insulin therapy within a few weeks of referral and were not in DKA at the initiation of treatment. The remaining three children were started on 3-monthly monitoring using HbA1c and sensor glucose by their local clinical teams (Figure 1B).

Acceptability

All participants (n=45) who completed a home cOGTT responded to the post-test questionnaire, which assessed acceptability relating to pain experience and the testing process.

Pain experience

Pain associated with capillary sampling was reported as mild (median pain score, 2; IQR, 0-2) and was similar to that seen in study 1.

Test process

For Peer Review Only Not for Distribution

The process of completing the OGTT at home was tolerated well by most participants, with 98% (44 of 45) agreeing that completing the test without a healthcare professional was acceptable. The self-collection of blood samples was acceptable in 87% (39 of 45) of participants (Supplementary Figure 10).

DISCUSSION

In the first published pediatric study, we found the cOGTT method to be feasible and acceptable for home use, and sensitive for detecting hyperglycemia. However, before this device can be adopted more widely as a staging tool, more work is needed to determine its use in identifying thresholds of dysglycemia. Currently, it offers the potential to be useful as an adjunct to the venous OGTT, by facilitating testing between formal OGTTs, helping to avoid a delayed diagnosis of stage 3 T1D and subsequent DKA (Figure 4).

The capillary method as a potential adjunct to the gold standard venous OGTT

The cOGTT method classified normoglycemia and hyperglycemia with high accuracy and correctly classified glycemic status in 87% of participants overall. Misclassification occurred in 13% (5 of 39) of participants and was confined to the dysglycemic range (3 false negatives and 2 false positives for dysglycemia). Although few participants had dysglycemia, the pattern of misclassification suggests the method may have a reduced sensitivity for intermediate glycemic abnormalities, while appearing to perform better at the extremes of glycemia.

For Peer Review Only/Not for Distribution

Studies in other populations have demonstrated that routine OGTT procedures may result in substantial misclassification when recommended pre-analytical protocols are not followed. Jamieson et al estimated that 62% of women were misclassified, with a 1.8-fold increase in gestational diabetes (GDM) diagnosis when recommended protocols were implemented.[28] Similarly, Daly et al reported a 2.7-fold increase in GDM diagnosis when sample handling procedures recommended by the American Diabetes Association were followed.[29] Although these findings are not directly from CYP with early-stage T1D, they highlight the substantial impact of pre-analytical processing on OGTT performance and demonstrate the importance of strict sample handling procedures.[5]

The pre-analytical phase of an OGTT includes physiological (stress, exercise, hydration status) and procedural factors (collection tube, sample handling and storage, glucose load) and has been estimated to account for 46-68% of glucose error during a standard OGTT.[30,31] The cOGTT method removes several pre-analytical handling steps, which may reduce this source of variability and support its use as an adjunct to venous OGTT testing. In our study, all plasma samples were centrifuged and stored at -80ºC within 30 min of collection and batch analyzed to minimize processing-related error. However, maintaining this level of sample handling outside the research setting may be challenging, raising questions regarding whether this standard can be achieved in routine clinical practice.[28]

For Peer Review Only/Not for Distribution

Other studies have also highlighted the challenge of identifying dysglycemia. A recent study in CYP and adults at risk of dysglycemia reported a 20% discordant classification rate across two OGTT visits in CYP.[32] In our study, the ability of the cOGTT method to detect dysglycemia improved at the 60-min time point (with the use of an additional device), consistent with previous studies that have shown intermediate glucose time points to be useful in detecting dysglycemia.[33,34]

Overall, the cOGTT method was perceived as less painful than the standard venous OGTT, with 76% preferring the GTT@home for future testing. However, 24% still preferred the venous method. This may reflect the routine use of topical anesthetic cream for venous sampling, as several participants who preferred venous testing (n=5) reported greater discomfort with the capillary method, which likely influenced their future test preference.

The utility of the GTT@home in the home environment

Our findings demonstrate that most participants could independently complete the cOGTT procedure at home, and preferred it as an option for future testing, although a minority preferred venous sampling. There were three (7%) device failures which was slightly higher than the 3% seen in an early study in adults.[9] This previous study was conducted in a controlled clinical setting, with samples taken by healthcare professionals, which could explain the higher success rate. Participants in our study found the overall experience of the capillary method, including the time taken to complete the test, collect the blood sample, consume the glucose drink and scan the device, highly acceptable, which aligns with adult studies.[8,9]

Alternative approaches to the OGTT

For Peer Review Only Not for Distribution

Current recommendations state that an OGTT should be based on the measurement of venous plasma glucose.[5] In earlier attempts to find capillary alternatives to venous glucose measurement, glucometers have been studied. Glucometers are widely available, often report plasma-equivalent glucose values from whole capillary blood, and adhere to the ISO 15197 criteria, that specifies accuracy standards.[35] However, studies comparing some of the commonly used commercially available glucometers, as an alternative OGTT method, have been disappointing. This includes two studies in pregnant/ postpartum women that found varied agreement between glucometers (Accu-Chek [Aviva-Roche], Contour Next One and HemoCue 201+) and plasma glucose, with a low bias at 0-min (0.15 – 0.2 mmol/L), and a high bias at 120-min (1.5 – 1.9 mmol/L).[36,37] These reported biases are larger than those observed in our cOGTT data, which demonstrated a low overall bias of -0.2 mmol/L, with lower variation between time points (0-min, 0.5 mmol/L; 120-min, 0.07 mmol/L), although direct comparisons should be made cautiously. This improved performance could be explained in part by the method each device type uses to convert capillary glucose to plasma equivalent. Glucometers commonly multiply capillary glucose by approximately 1.11 (11%), as per previous recommendations.[14] However, capillary glucose has been shown to differ from venous glucose, particularly at the 120-min time point, and this plasma conversion factor could further widen the observed difference.[38] The GTT@home does not apply a constant conversion factor, instead using a proprietary algorithm based on differences seen in contemporaneous capillary and venous glucose at both the 0- and 120-min time points (see methods).

For Peer Review Only/Not for Distribution

Inconsistency between different glucometers has also been described. One study comparing 17 commercially available devices to plasma glucose across the glycemic range demonstrated wide variation in accuracy (mean absolute relative difference, 5.6 - 20.8%).[39] The varied accuracy between devices could be explained by the inconsistent use of reference methods to calibrate different glucometers.[40] In a separate study testing the agreement of 18 different glucometers with plasma glucose using two reference methods to analyze glucose (glucose-oxidase and hexo-oxidase), authors demonstrated that only 66% of glucometers met the ISO 15197 criteria on both methods.[40] In contrast, the GTT@home device is calibrated using a singular reference method (YSI 2500, glucose-oxidase method), allowing for improved consistency compared to a group of different glucometers. Current evidence does not support the use of glucometers as an alternative to venous glucose testing.

Recent evidence suggests that continuous glucose monitoring (CGM) may offer comparable performance to OGTT-derived measures for predicting progression to stage 3 T1D in CYP,[41] although some studies have demonstrated superior predictive performance with the OGTT.[42] Comparative studies directly comparing cOGTT and CGM are needed to determine their relative utility for glycemic staging and monitoring progression to stage 3 T1D.

Strengths

For Peer Review Only/Not for Distribution

The study included a range of glucose values and age ranges, making the results translatable to pediatric settings. The home study was undertaken in a population of CYP with early-stage T1D, individuals who typically have regular venous OGTTs, sometimes over many months or years. This allowed assessment of the device under "real-world" conditions, where previous studies focused on its use by trained professionals within controlled environments.[8,9]

Limitations

For Peer Review Only/Not for Distribution

Our method comparison analysis found no statistically significant bias comparing the cOGTT with the venous method. However, the limits of agreement were wide enough to cross glycemic thresholds. Although the venous glucose samples were processed within 30 min of collection, bedside YSI analysis would been advantageous to further reduce the chance for measurement error. Therefore, the lack of bedside YSI measurement in our study could represent a limitation. Furthermore, the number of participants with dysglycemia, as determined by the venous 0- or 120-min time points was small (n=7), representing a significant limitation of this study. The poor sensitivity seen in the dysglycemic group needs further investigation, especially as our findings indicated that there may be improvement in the detection of dysglycemia at the 60-min time point, collected using an additional device (Supplementary Table 1). Given the cOGTT device does not collect a 60-min capillary glucose, the opportunity to detect dysglycemia at an intermediate glucose time point would be missed.[33] Therefore, further assessment is needed to determine if this device, or a modified version, can be used for glycemic staging. Finally, the cost of the cOGTT is £65 per test for use in the NHS in the UK. We did not conduct a health economic evaluation, therefore we are unable to compare the costs between the two methods. However, it is likely that a home administered test would be cheaper than a test conducted in a healthcare setting. This emphasizes the need for cost-effectiveness analyses in the context of early-stage T1D monitoring.

Implications

For Peer Review Only/Not for Distribution

Large T1D population screening studies have seen high drop-out rates of up to 45%, with the invasiveness of the standard OGTT considered a contributing factor.[3,4] Any alternative OGTT method needs to improve acceptability, whilst maintaining accuracy and precision.

The cOGTT method showed promising performance for identifying individuals in stage 3 T1D and may have a role in several situations (Figure 4). The first, to allow more frequent home testing to identify more precisely the onset of stage 3 disease, the timing of which is often recorded according to the date of a planned venous OGTT. This could reduce the risk of DKA through prompt recognition of stage 3 T1D and enable investigators to track more subtle changes over time and reduce inter-test variability. The second, to alert clinicians or researchers to those who need formal OGTT testing. This supports the recent emphasis on a pragmatic approach to monitoring that reduces test burden and improves adherence to follow-up,[1,43,44] but could miss some individuals in stage 2. Also, it could facilitate confirmatory testing that is required for some studies. In the clinical setting, it could preclude the need for a formal OGTT if stage 3 is detected by other means, such as random venous glucose, HbA1c or CGM. The third, to avoid over-reliance on the HbA1c, which is cheap and accessible, but known to have low sensitivity for detecting stage 3 (23.7 – 33.3%) compared to an OGTT at a single time point, and may be less reliable in some disease states, such as anemia.[45,46]

This “light touch” monitoring approach could encourage individuals to remain in follow-up. In addition to reducing invasiveness and improving adherence, the cOGTT method could also reduce the number of hospital visits needed for individuals under follow-up, creating potential cost savings for healthcare systems, and patients.

For Peer Review Only Not for Distribution

Conclusions

The cOGTT method offers a feasible and acceptable adjunct to the gold standard venous method in CYP. The reliability of the method to accurately stage individuals in the early stages of T1D needs further investigation, particularly in the dysglycemic range, and is already planned in the pan-European study EDENT1FI (European action for the Diagnosis of Early Non-clinical Type 1 diabetes For disease Interception).[47] This additional work could support the refinement of the proprietary algorithm used by the device. Further testing is also required in other populations, such as pre-type 2 diabetes, where barriers to patient engagement pose an ongoing challenge.[48] It is also possible that this method could be paired with other biomarkers that require minimal equipment, such as C-peptide, and future studies could assess the implications of combining these tests. Expansion of the device to include intermediate time points would also be beneficial.

ACKNOWLEDGEMENTS

We would like to thank John Todd for supporting the study and review of the manuscript. We would also like to thank Claire Scudder for supporting the setup and delivery of the study, and the research nurses/ staff within the pediatric diabetes research teams at the John Radcliffe Hospital, Oxford, UK; Bart's Health Royal London Hospital, London, UK; Nottingham Children's Hospital, Nottingham, UK; Noah's Ark Children's Hospital, Cardiff, UK; University of Bristol, UK; UK Type 1 Diabetes Research Consortium, UK., for recruitment.

AUTHORS' CONTRIBUTIONS

For Peer Review Only Not for Distribution

R.S. developed the protocol, recruited participants, researched data, wrote and edited the manuscript. J.B. researched data and edited the manuscript. C.D. developed the protocol, researched data and edited the manuscript. G.D. undertook sample analysis and edited the manuscript. K.G. recruited participants and edited the manuscript. Y.F.L. recruited participants and edited the manuscript. S.L. undertook sample analysis and edited the manuscript. A.S. recruited participants and edited the manuscript. J.T. supported the design of the questionnaires and edited the manuscript. R.W. recruited participants and edited the manuscript. R.H.W recruited participants and edited the manuscript. R.E.J.B conceptualized the study, developed the protocol, recruited participants and edited the manuscript. All authors reviewed and agreed to the final version of the manuscript. R.S. and R.E.J.B. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

STATEMENTS AND DECLARATIONS

Ethical Considerations

Ethical approval for this study was obtained from the UK Research Ethics Committee (reference: 23/WM/0184). The study was also registered with a clinical trials registry (NCT06815081). All participants, and for those under 16 years, their parent/guardian, gave informed written consent. Participants under 16 years provided informed written assent.

Consent to participate

All participants, and for those under 16 years, their parent/guardian, gave written informed consent prior to participation.

For Peer Review Only/Not for Distribution

Consent for publication

Not applicable

Funding Statement

This study was supported by the Novo Nordisk UK Research Foundation, which funded R.S. through a research fellowship. R.E.J.B. is funded by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), and by the Innovative Health Initiative Joint Undertaking and its members and contributing partners, under grant agreement 101132379, with additional funding through the UK Research and Innovation (UKRI) Guarantee Fund. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. Additional support is provided by the Diabetes and Inflammation Laboratory from Wellcome (091157/Z/10/Z and 107212/Z/15/Z), Breakthrough T1D (4-SRA-2017-473-A-N) and the European Association for the Study of Diabetes-Novo Nordisk Foundation Diabetes Prize for Excellence 2021).

Declaration of conflicting interest

For Peer Review Only Not for Distribution

R.S. has received speaker honoraria and conference attendance reimbursement from Sanofi. R.E.J.B. reports receiving speaker honoraria from Eli Lilly and Springer Healthcare, reports sitting on the Novo Nordisk UK Foundation Research Selection Committee on a voluntary basis, acting as an independent advisor for Provent Bio, and received speaking honoraria from Sanofi and Medscape, which were donated to an education research fund. RHW has received speaker honoraria from Insulet and Sanofi, consultancy fees and conference attendance reimbursement from Sanofi, and an honorarium to act as an independent advisor in a Spex Capital interview for Digostics.

Data availability

Deidentified individual participant data that underpins the results presented in this manuscript (tables, figures, text and supplementary material) can be made available on reasonable request, with permission from the University of Oxford. Requests should be directed to the corresponding author(s) via email.

REFERENCES

1. Phillip M, Achenbach P, Addala A, et al. Consensus guidance for monitoring individuals with islet autoantibody–positive pre-stage 3 type 1 diabetes. *Diabetes Care,* 2024; 47(8):1276–1298.

2. Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: A scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. *Diabetes Care,* 2015; 38(10):1964–1974.

For Peer Review Only/Not for Distribution

3. Sims EK, Geyer S, Johnson SB, et al. Who is enrolling? The path to monitoring in type 1 diabetes TrialNet's Pathway to Prevention. *Diabetes Care,* 2019; 42(12):2228–2236.

4. Driscoll KA, Tamura R, Johnson SB, et al. Adherence to oral glucose tolerance testing in children in stage 1 of type 1 diabetes: The TEDDY study. *Pediatr Diabetes,* 2021;22(2):360–368.

5. Sacks DB, Arnold M, Bakris GL, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem,* 2023; 69(8):808–868.

6. Bruns DE, Metzger BE, Sacks DB. Diagnosis of gestational diabetes mellitus will be flawed until we can measure glucose. *Clin Chem,* 2020; 66(2):265–267.

7. Medicines and Healthcare products Regulatory Agency. 2025. Public access registration database. Available from: https://pard.mhra.gov.uk/manufacturer-details/44830

8. Bethel MA, Price HC, Sourij H, et al. Evaluation of a self-administered oral glucose tolerance test. *Diabetes Care,* 2013; 36(6):1483–1488.

9. Dunseath GJ, Bright D, Jones C, et al. Performance evaluation of a self-administered home oral glucose tolerance test kit in a controlled clinical research setting. *Diabetic Medicine,* 2019; 36(7):862–867.

10. Dunger DB, Bruggraber SFA, Mander AP, et al. INNODIA master protocol for the evaluation of investigational medicinal products in children, adolescents and adults with newly diagnosed type 1 diabetes. *Trials,* 2022; 23(1):414.

For Peer Review Only/Not for Distribution

11. Jacobsen LM, Felton JL, Nathan BM, et al. Type 1 diabetes TrialNet: leading the charge in disease prediction, prevention, and immunotherapeutic mechanistic understanding. *Diabetes Care,* 2025; 48(7):1112–1124.

12. Gillespie KM, Fareed R, Mortimer GL. Four decades of the Bart's Oxford study: improved tests to predict type 1 diabetes. *Diabetic Medicine,* 2021; 38:e14717.

13. Swaby R, Scudder C, Randell T, et al. A study to determine a capillary alternative to the gold standard oral glucose tolerance test - Protocol. *Wellcome Open Res,* 2024; 9:601.

14. D'Orazio P, Burnett RW, Fogh-Andersen N, et al. Approved IFCC recommendation on reporting results for blood glucose (abbreviated). *Clin Chem,* 2005; 51(9):1573–1576.

15. Tang Z, Lee JH, Louie RF, et al. Effects of different hematocrit levels on glucose measurements with handheld meters for point-of-care testing. *Arch Pathol Lab Med,* 2000; 124(8):1135–1140.

16. Besser REJ, Long AE, Owen KR, et al. Transdermal blood sampling for C-peptide is a minimally invasive, reliable alternative to venous sampling in children and adults with type 1 diabetes. *Diabetes Care,* 2024; 47(2):239–245.

17. Cohen P, Cohen J, Aiken LS, et al. The problem of units and the circumstance for POMP. *Multivariate Behav Res,* 1999; 34(3):315–346.

18. Kohn M, Senyak J. 2026. Sample Size Calculators. Available from: https://sample-size.net/confidence-interval-proportion/

For Peer Review Only/Not for Distribution

19. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. *Biometrika,* 1934; 26(4):404–413.

20. Royston P. Remark AS R94: A remark on algorithm AS 181: The W-test for Normality. *Appl Stat,* 1995; 44(4):547.

21. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet,* 1986; 1(8476):307–310.

22. Giavarina D. Understanding Bland Altman analysis. *Biochem Med,* 2015; 25(2):141–151.

23. Bland JM, Altman DG. Agreement between methods of measurement with multiple observations per individual. *J Biopharm Stat,* 2007; 17(4):571–582.

24. Field CA, Welsh AH. Bootstrapping clustered data. *J. R. Statist. Soc. B*, 2007; 69(3):369–390.

25. Schober P, Boer C, Schwarte LA. Correlation coefficients: appropriate use and interpretation. *Anesth Analg,* 2018; 126(5):1763–1768.

26. Rosner B, Glynn RJ, Lee MT. The Wilcoxon signed rank test for paired comparisons of clustered data. *Biometrics,* 2006; 62(1):185–192.

27. GraphPad. 2026. The binomial test. Available from:

28. Jamieson EL, Spry EP, Kirke AB, et al. Real-world gestational diabetes screening: problems with the oral glucose tolerance test in rural and remote australia. *Int J Environ Res Public Health,* 2019; 16(22):4488.

For Peer Review Only/Not for Distribution

29. Daly N, Flynn I, Carroll C, et al. Impact of implementing preanalytical laboratory standards on the diagnosis of gestational diabetes mellitus: a prospective observational study. *Clin Chem,* 2016; 62(2):387–391.

30. Bogdanet D, O'Shea P, Lyons C, et al. The oral glucose tolerance test - is it time for a change? A literature review with an emphasis on pregnancy. *J Clin Med,* 2020; 9(11):3451.

31. Plebani M. The detection and prevention of errors in laboratory medicine. *Ann Clin Biochem,* 2010; 47(2):101–110.

32. Tjaden AH, Edelstein SL, Arslanian S, et al. Reproducibility of glycemic measures among dysglycemic youth and adults in the rise study. *J Clin Endocrinol Metab,* 2023; 108(10):e1125–e1133.

33. Simmons KM, Sosenko JM, Warnock M, et al. One-hour oral glucose tolerance tests for the prediction and diagnostic surveillance of type 1 diabetes. *J Clin Endocrinol Metab,* 2020; 105(11):e4094–e4101.

34. Sosenko JM, Skyler JS, Dimeglio LA, et al. A new approach for diagnosing type 1 diabetes in autoantibody-positive individuals based on prediction and natural history. *Diabetes Care,* 2015; 38(2):271-276.

35. Breitenbeck N, Brown A. Accuracy assessment of a blood glucose monitoring system for self-testing with three test strip lots following ISO 15197:2013/EN ISO 15197:2015. *J Diabetes Sci Technol,* 2017; 11(4):854–855.

For Peer Review Only/Not for Distribution

36. García-Claver A, Ramos-Corral R, Laviña-Fañanás C, et al. Capillary glucose concentration during oral glucose tolerance test for the diagnosis of gestational diabetes. *International Journal of Gynecology and Obstetrics,* 2020; 150(2):234–240.

37. Ignell C, Berntorp K. Evaluation of the relationship between capillary and venous plasma glucose concentrations obtained by the HemoCue Glucose 201+ system during an oral glucose tolerance test. *Scand J Clin Lab Invest,* 2011; 71(8):670–675.

38. Colagiuri S, Sandbæk A, Carstensen B, et al. Comparability of venous and capillary glucose measurements in blood. *Diabet Med,* 2003; 20(11):953–956.

39. Ekhlaspour L, Mondesir D, Lautsch N, et al. Comparative accuracy of 17 point-of-care glucose meters. *J Diabetes Sci Technol,* 2017; 11(3):558–566.

40. Freckmann G, Baumstark A, Jendrike N, et al. Impact of two different reference measurement procedures on apparent system accuracy of 18 CE-marked current-generation blood glucose monitoring systems. *J Diabetes Sci Technol,* 2022; 16(5):1076–1088.

41. Steck AK, Dong F, Pyle L, et al. Continuous glucose monitoring has similar predictive performance to OGTT for monitoring early-stage type 1 diabetes. *The J Clin Endocrinol Metab*, 2026.

42. Ylescupidez A, Speake C, Pietropaolo SL, et al. OGTT metrics surpass continuous glucose monitoring data for T1D prediction in multiple-autoantibody-positive individuals. *J Clin Endocrinol Metab*, 2023; 109(1):57-67.

For Peer Review Only/Not for Distribution

43. Hendriks AEJ, Marcovecchio ML, Besser REJ, et al. Clinical care advice for monitoring of islet autoantibody positive individuals with presymptomatic type 1 diabetes. *Diabetes Metab Res Rev,* 2024; 40(2):e3777.

44. Besser REJ, Campbell F, Damazer K, et al. UK best practice recommendations for children and young people <18 years with pre-stage 3 type 1 diabetes, on behalf of the British Society for Paediatric Endocrinology and Diabetes (BSPED). *Diabet Med,* 2025; 42(11):e70117.

45. Alzahrani BA, Salamatullah HK, Alsharm FS, et al. The effect of different types of anemia on HbA1c levels in non-diabetics. *BMC Endocr Disord,* 2023; 23(1):24.

46. Vehik K, Rewers MJ, Cuthbertson D, et al. Performance of HbA 1c as an early diagnostic indicator of type 1 diabetes in children and youth. *Diabetes Care,* 2012; 35(9):1821–1825.

47. Hoffmann L, Kohls M, Arnolds S, et al. EDENT1FI master protocol for screening of presymptomatic early-stage type 1 diabetes in children and adolescents. *BMJ Open,* 2025; 15(1):e088522.

48. Shah AS, Barrientos-Pérez M, Chang N, et al. ISPAD clinical practice consensus guidelines 2024: type 2 diabetes in children and adolescents. *Horm Res Paediatr,* 2024; 97(6):555–583.

For Peer Review Only/Not for Distribution

For Peer Review Only/Not for Distribution

TABLES

Table 1: Participant characteristics.

	Study 1	Study 2
N	45	45
Male, n (%)	22 (49)	30 (67)
Age, years (SD); range	12.2 (3.2); 5-17	10.4 (3.1); 4-17
Hematocrit, % (SD)	38 (3)	-
Diabetes type, n		
Early-stage T1D*	23	45[a]
Stage 1 T1D[b]	16	34
Stage 2 T1D[b]	7	2
Stage 3 T1D[b]†	10	5
Preclinical T2D‡	11	0
Other	1	0
Ethnicity, n (%)		
White	36 (80)	42 (93)
Black	3 (6.7)	0 (0)
Asian	3 (6.7)	0 (0)
Mixed	3 (6.7)	2 (4)
Other	0 (0)	1 (2)

Data are presented as mean (standard deviation) unless otherwise stated.

SD, standard deviation; T1D, type 1 diabetes; T2D, type 2 diabetes.

* Participants with early-stage T1D under OGTT monitoring. † Participants with known stage 3 T1D, or under monitoring for early-stage T1D and identified with stage 3 T1D. ‡ Participants investigated for suspected type 2 diabetes. [a] Four participants in cohort 2 were not staged. [b] Cohort 2 staging based on capillary-adjusted oral glucose tolerance test measures.

For Peer Review Only/Not for Distribution

Table 2. Sensitivity and specificity of the capillary OGTT device for the classification of glycemic status at pre-defined cut-offs, using reference plasma glucose as the standard (n=39).

Glycemic Status	N	Sensitivity (95% CI)	N	Specificity (95% CI)
Normoglycemia 0-min <5.6 mmol/L 60-min <11.1 mmol/L 120-min <7.8 mmol/L	21/22	0.95 (0.77 – 1.00)	14/17	0.82 (0.57 – 0.96)
Dysglycemia 0-min 5.6 – 6.9 mmol/L 60-min ≥11.1 mmol/L 120-min 7.8 – 11.0 mmol/L	4/7	0.57 (0.18 – 0.90)	30/32	0.94 (0.79 – 0.99)
Hyperglycemia 0-min ≥7.0 mmol/L 120-min ≥11.1 mmol/L	9/10	0.90 (0.55 – 1.00)	29/29	1.00 (0.88 – 1.00)

For Peer Review Only/Not for Distribution

FIGURE LEGENDS

Figure 1A. A flow diagram of participants included in study 1.

Figure 1B. A flow diagram of participants included in study 2.

Figure 2. A Bland-Altman plot comparing capillary and venous glucose measurements within the diagnostic range (3.5-15 mmol/L) in 90 paired samples. The solid line indicates the bias (-0.22 mmol/L). The dashed lines represent the 95% limits of agreement (-2.91 to 2.47 mmol/L).

Figure 3. A box plot showing the median pain score ratings for capillary (median, 2; interquartile range, 0-2) and venous testing (median, 3; interquartile range, 2-5.5), p = 0.001). The dashed line represents paired ratings.

Figure 4. A flowchart showing a clinical pathway of early-stage type 1 diabetes monitoring, integrating the capillary OGTT method (S2 = stage 2 type 1 diabetes, S3 = stage 3 type diabetes). Suspected stage change e.g. S1 to S2, or S2 to S3 (≥10% rise in HbA1c, consecutive HbA1c >42 mmol/mol, a fasting glucose above 5.6 mmol/L, stimulated >7.8 mmol/L, or >10% of time spent above 7.8 mmol/L on CGM*). † Stage 2 and asymptomatic stage 3 type 1 diabetes require confirmatory testing.

For Peer Review Only Not for Distribution

Assessing the utility of a capillary-adjusted oral glucose tolerance test for the early detection of type 1 diabetes in childhood

Objective

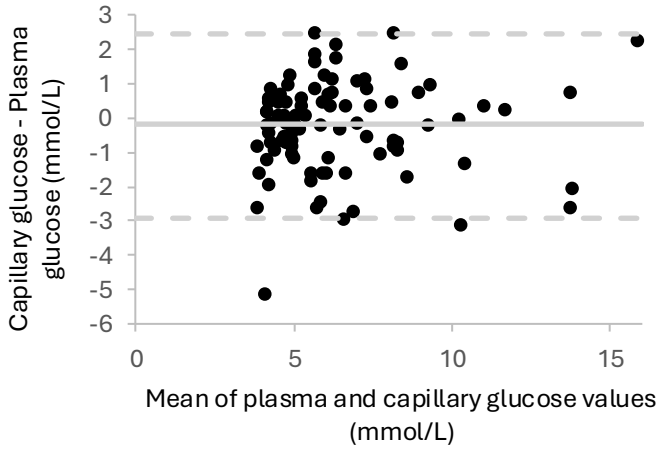
To assess the utility of a capillary-adjusted OGTT (cOGTT) method in children and young people.

Research Design & Methods

	Study 1 In-hospital comparison	**Study 2** At home feasibility/ acceptability
Sample	n = 45, across glucose range	n = 45, early-stage type 1 diabetes
Design	vs	
Outcome	1. Agreement 2. Acceptability	1. Successful tests (%) 2. Acceptability

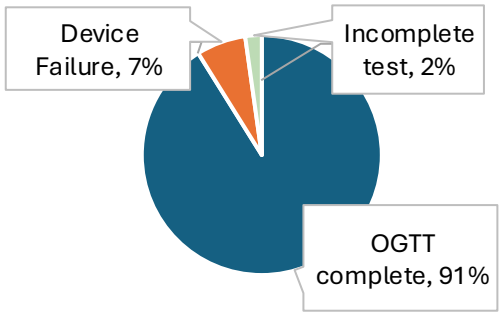
Results

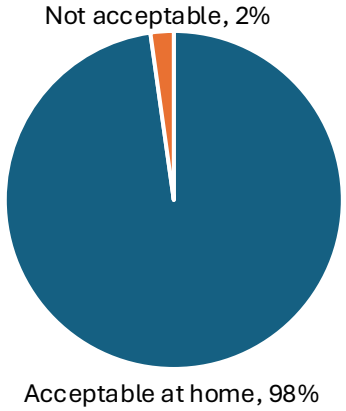
Study 1



Normoglycemia	Sensitivity 95% Specificity 82%
Dysglycemia	Sensitivity 57% Specificity 94%
Hyperglycemia	Sensitivity 90% Specificity 100%

Study 2



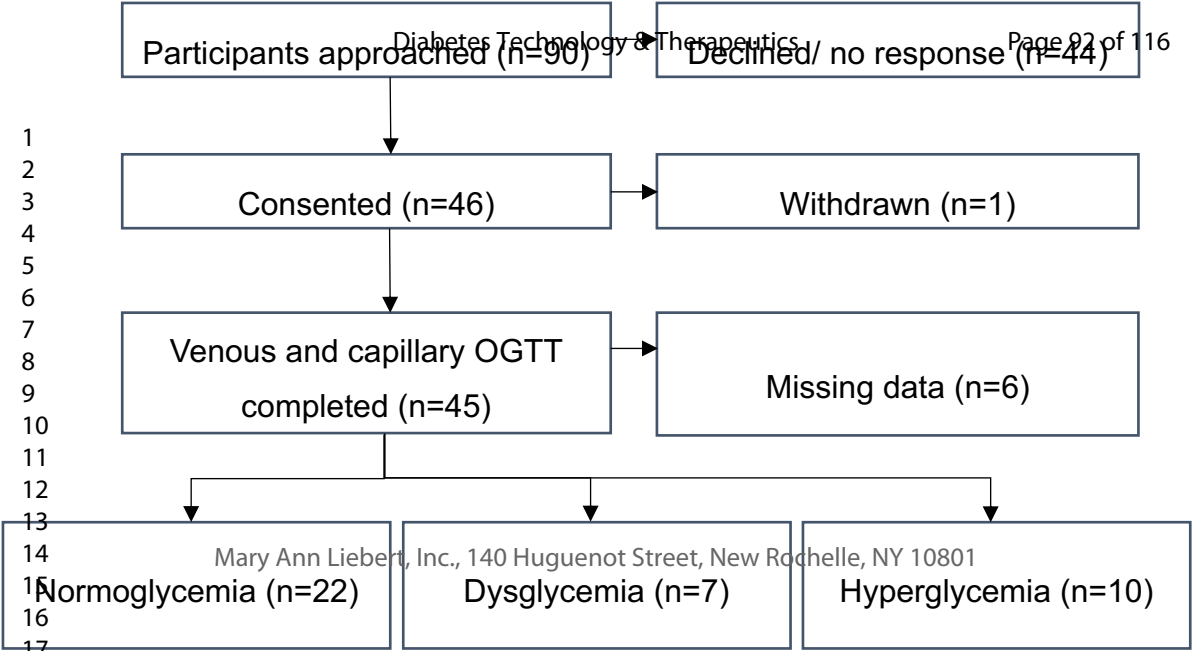


Conclusions

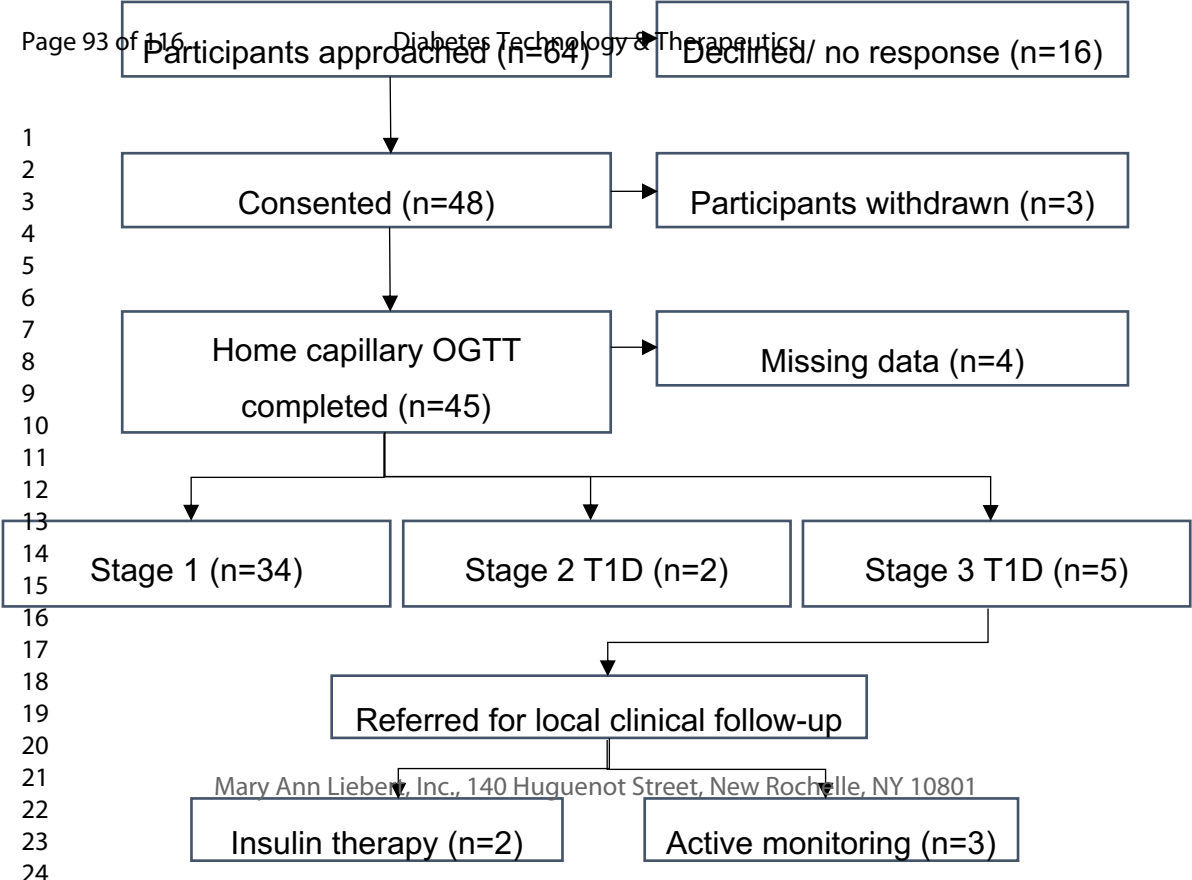
The cOGTT method is a feasible and acceptable adjunct to venous sampling in CYP to detect hyperglycemia and can be undertaken at home. Further work is needed before it can be used for glycemic staging.

Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801

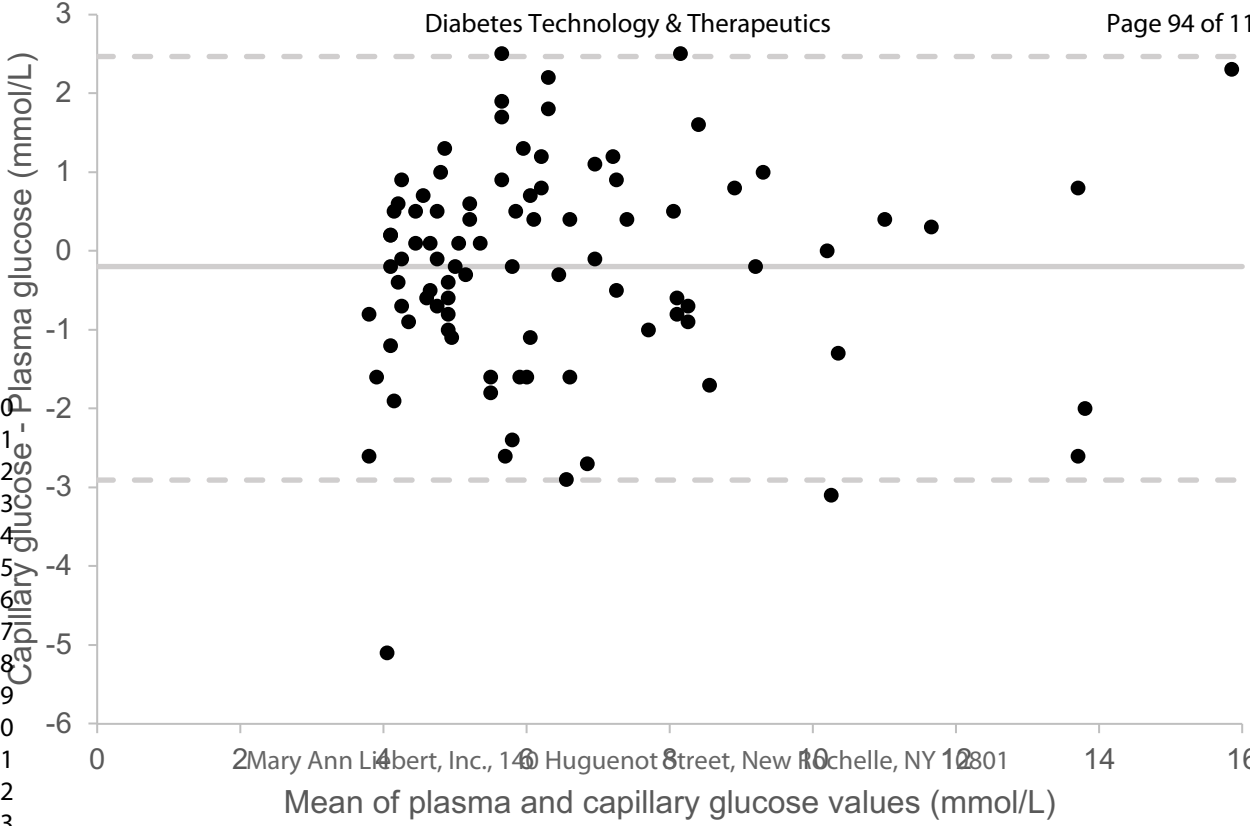
Graphical abstract created by: R Swaby



Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801



Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801


Capillary glucose - Plasma glucose (mmol/L)
3
2
1
0
-1
-2
-3
-4
-5
-6
0
2
4
6
8
10
12
14
16
Mean of plasma and capillary glucose values (mmol/L)

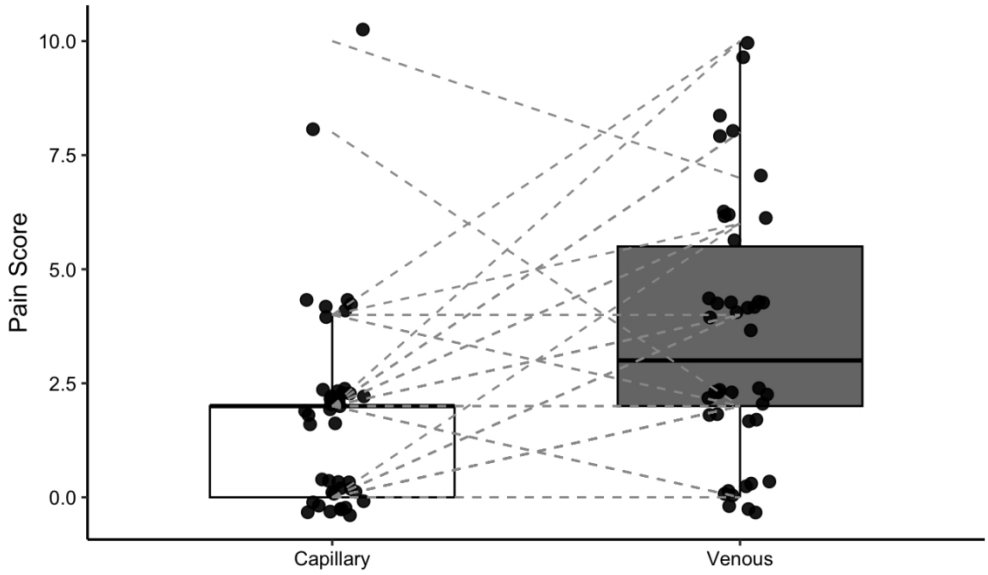
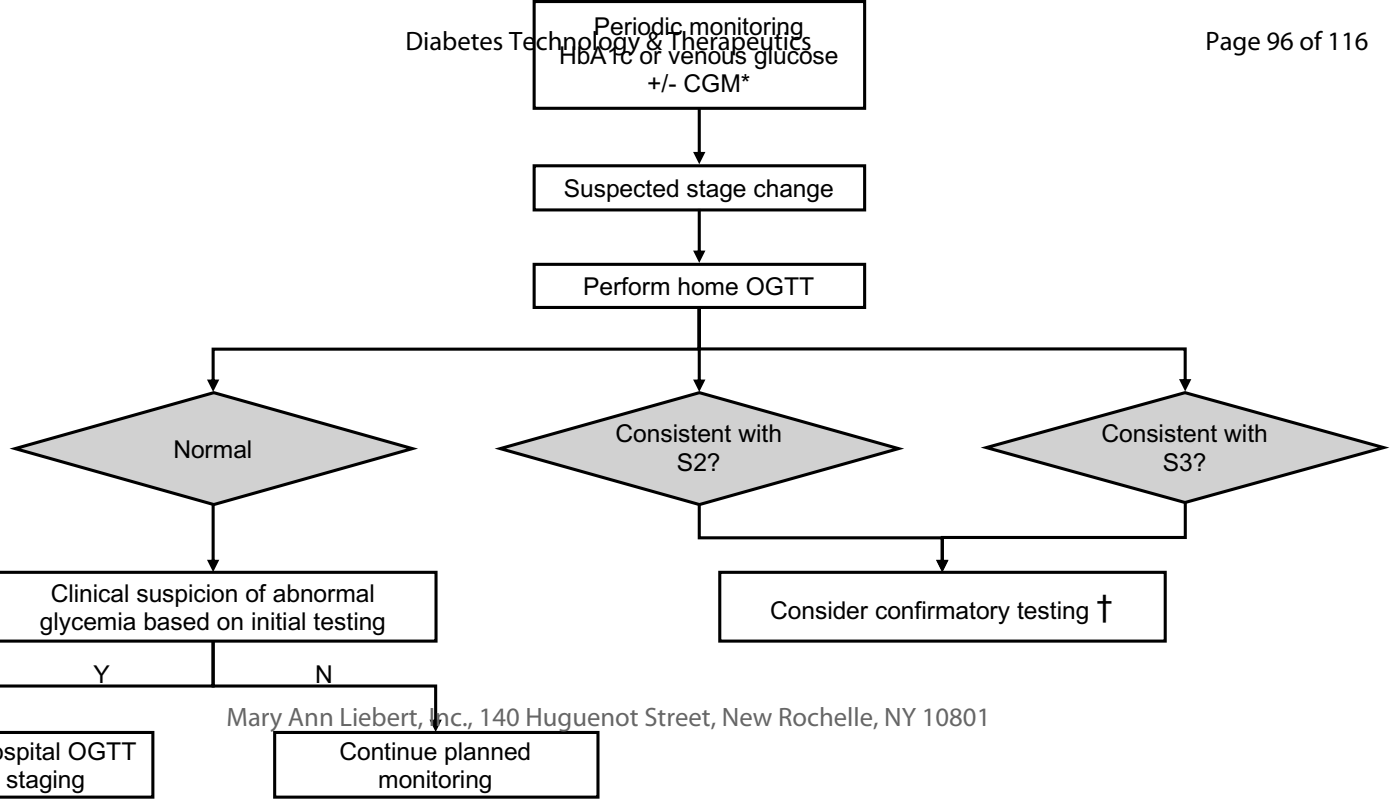


Figure 3. A box plot showing the median pain score ratings for capillary (median, 2; interquartile range, 0-2) and venous testing (median, 3; interquartile range, 2-5.5), p = 0.001). The dashed line represents paired ratings.

458x282mm (72 x 72 DPI)



Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801

For Peer Review Only/Not for Distribution

SUPPLEMENTARY MATERIAL

Supplementary Table

Supplementary Table 1. Sensitivity and specificity of the capillary OGTT device for the classification of glycemia status at pre-defined cut-offs, using reference plasma glucose at fasting, 60-min and 120-min time points.

Supplementary Figures

Supplementary Figure 1. A picture of the GTT@home device.

Supplementary Figure 2. An example questionnaire used to assess acceptability in study 1.

Supplementary Figure 3. An example questionnaire used to assess acceptability in study 2.

Supplementary Figure 4. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 0-min OGTT time point in 43 paired samples. The solid line indicates the bias (-0.51 mmol/L). The dashed lines represent the 95% limits of agreement (2.95 to 1.94 mmol/L).

Supplementary Figure 5. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 60-min OGTT time point in 15 paired samples. The solid line indicates the bias (0.19 mmol/L). The dashed lines represent the 95% limits of agreement (-3.25 to 3.63 mmol/L).

Supplementary Figure 6. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 120-min OGTT time point in 33 paired samples. The solid line indicates the bias (0.07 mmol/L). The dashed lines represent the 95% limits of agreement (-2.66 to 2.81 mmol/L).

Supplementary Figure 7. A scatter plot showing the relationship between capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) in 90 paired samples (Spearman's Rho = 0.74, p <0.001). Dotted line presents line of best fit.

Supplementary Figure 8. A stacked bar chart indicating the responses to questions 3 and 4 of the acceptability questionnaire for participants in study 1. Percentages are grouped strongly disagree and disagree (left), neither agree nor disagree (middle), agree and strongly agree (right).

Supplementary Figure 9. A bar chart showing participant preference for future glycemic assessment, comparing capillary with venous OGTT.

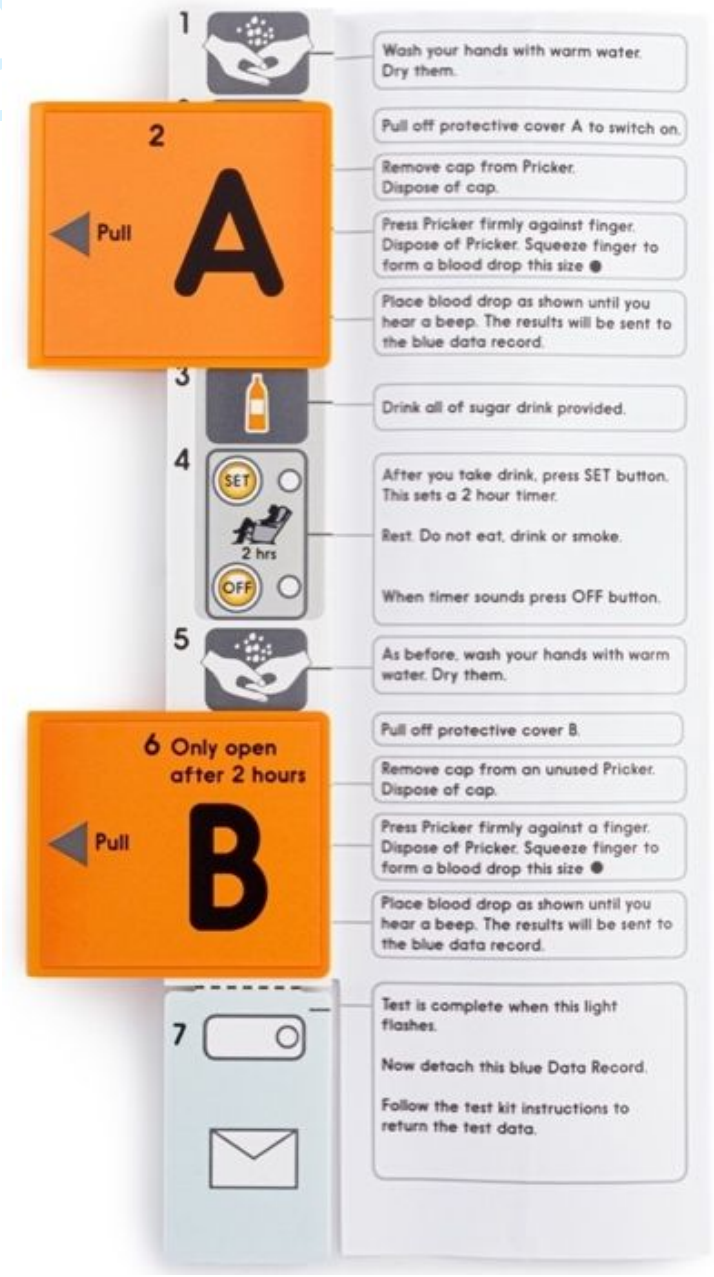
Supplementary Figure 10. A stacked bar chart indicating the responses to questions 2 to 6 of the acceptability questionnaire for participants in study 2. Percentages are grouped strongly disagree and disagree (left), neither agree nor disagree (middle), agree and strongly agree (right).

Supplementary Table 1. Sensitivity and specificity of the capillary OGTT device for the classification of glycemia status at pre-defined cut-offs, using reference plasma glucose at fasting, 60-min and 120-min time points.

For Peer Review Only/Not for Distribution

Threshold	N	Sensitivity (95% CI)	N	Specificity (95% CI)
0-min glucose time point				
5.6-6.9 mmol/L Dysglycemia	2/3	0.67 (0.09 – 0.99)	33/34	0.97 (0.85 – 1.00)
≥ 7.0 mmol/L Hyperglycemia	3/6	0.50 (0.12 – 0.88)	37/37	1.00 (0.91 – 1.00)
60-min glucose time point				
≥ 11.1 mmol/L Dysglycemia	6/7	0.86 (0.42 – 1.00)	12/13	0.92 (0.64 – 1.00)
120-min glucose time point				
7.8-11.0 mmol/L Dysglycemia	4/7	0.57 (0.18 – 0.90)	23/24	0.96 (0.79 – 1.00)
≥ 11.1 mmol/L Hyperglycemia	8/10	0.80 (0.44 – 0.98)	31/31	1.00 (0.89 – 1.00)

For Peer Review Only/Not for Distribution



Supplementary Figure 1. A picture of the GTT@home device.

For Distribution

Study 1 - Method Comparison Acceptability Questionnaire: For participants aged 16 years and above

Participant number_____ Date

(DD/MM/YY)_____

Please rate the following:

1. How painful was the finger-prick blood test?

Please use the scale below to indicate how painful you found the finger-prick blood test:

Not painful at all			**Moderately painful**			**Very painful**		**I do not know/I am unable to comment**
1	2	3	4	5	6	7		
☐	☐	☐	☐	☐	☐	☐		☐

2. How painful was the blood test using a needle to take blood from the vein?

Please use the scale below to describe how painful you found the blood test using the needle:

Not painful at all			**Moderately painful**			**Very painful**		**I do not know/I am unable to comment**
1	2	3	4	5	6	7		

For Peer Review Only/Not for Distribution

☐	☐	☐	☐	☐	☐	☐		☐

3. The time it took to complete the oral glucose tolerance test (OGTT) did not bother me.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

4. The time taken to travel to and from the hospital for the test did not bother me.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

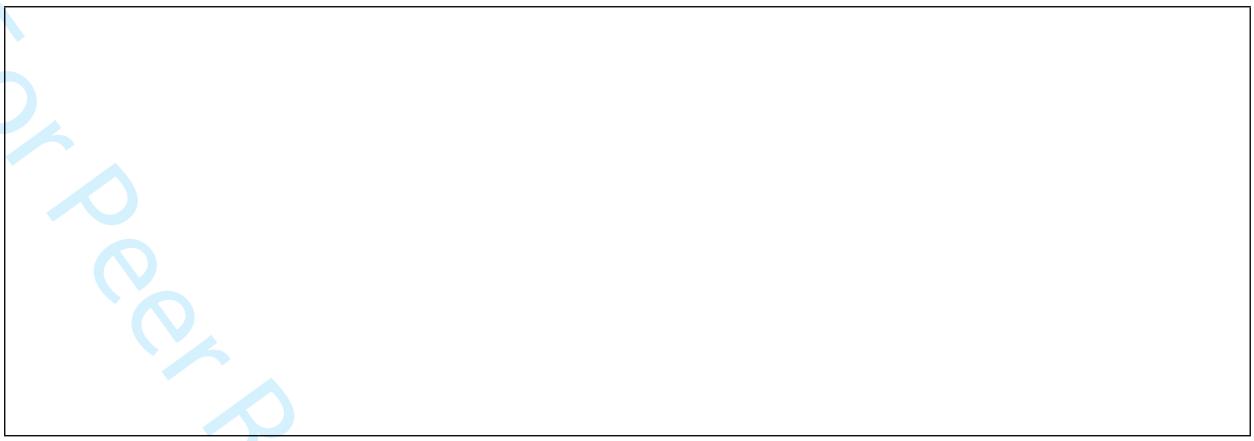
5. If I had another OGTT in the future, I would choose:

☐ The OGTT using a finger-prick blood test

☐ The OGTT using a needle to take blood from a vein in the arm

6. Is there any other information you would like to provide?

For Peer Review Only/Not for Distribution



Supplementary Figure 2. An example questionnaire used to assess acceptability in study 1.

For Peer Review Only/Not for Distribution

Study 2 - Home OGTT Acceptability Questionnaire: For participants aged below 16 years

Participant number_____ Date (DD/MM/YY)_____

Please tell us who completed this form

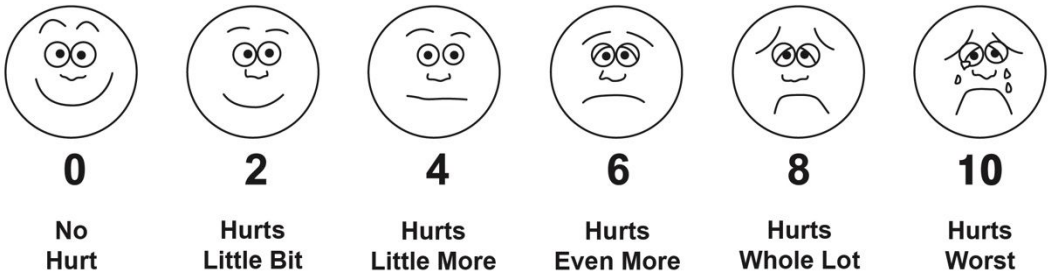
☐ Child or young person ☐ Adult looking after the participant

Please rate the following:

1. How painful was the finger-prick blood test?

Please use the scale below to indicate how painful you found the finger-prick blood test:

Wong-Baker FACES® Pain Rating Scale



©1983 Wong-Baker FACES Foundation. www.WongBakerFACES.org
Used with permission.

2. The procedure of collecting blood from the finger did not bother me.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

For Peer Review Only - Not for Distribution

3. The time it took to complete the oral glucose tolerance test did not bother me.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

4. Completing the test at home without a healthcare professional present did not bother me.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

5. I was able to finish the sugary drink within 10 minutes with no issues.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

☐ Disagree

☐ Strongly disagree

For Peer Review Only/Not for Distribution

6. I was able to scan the OGTT device with my smartphone and upload the results easily.

☐ Strongly agree

☐ Agree

☐ Neither agree nor disagree

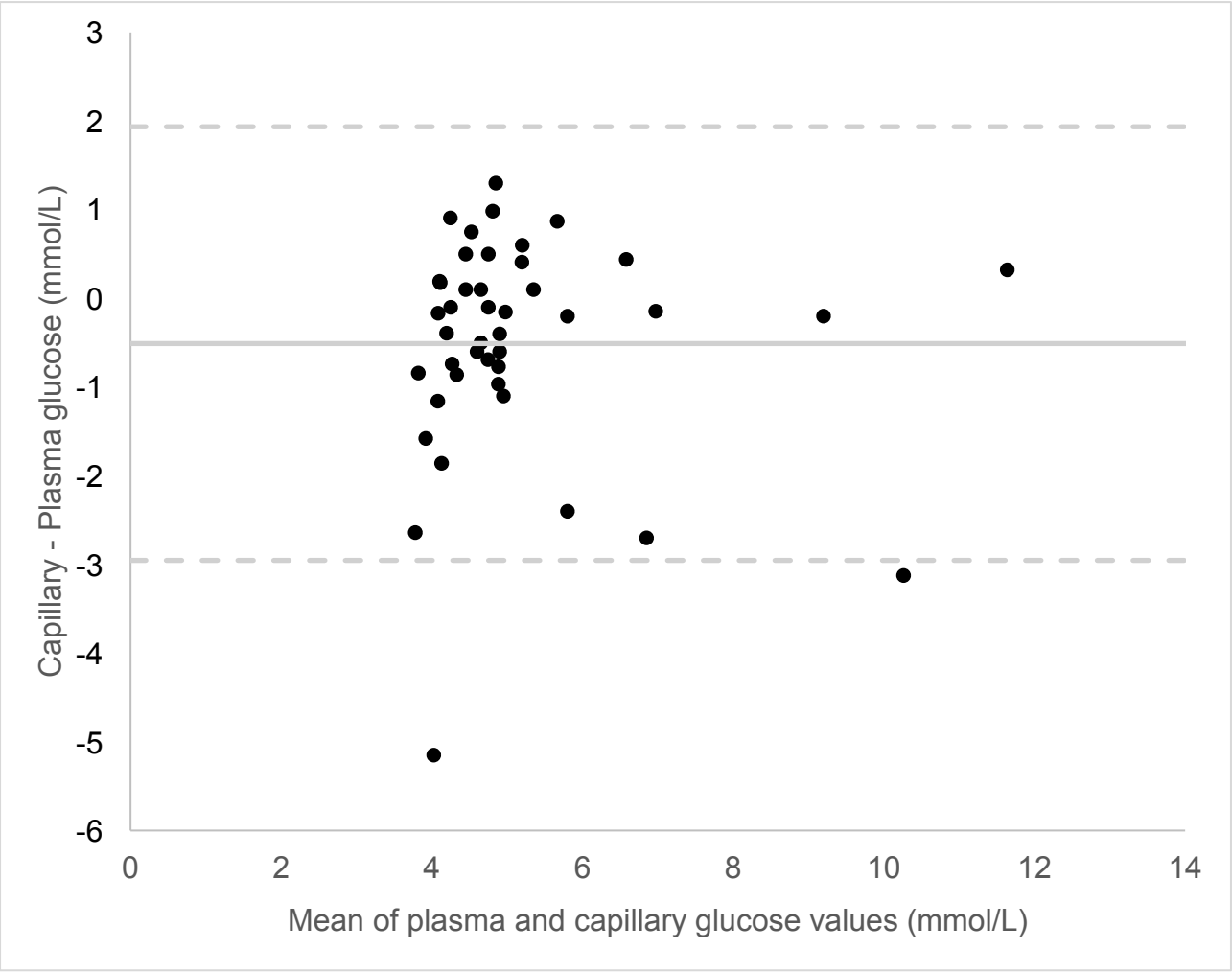
☐ Disagree

☐ Strongly disagree

7. Is there any other information you would like to provide?

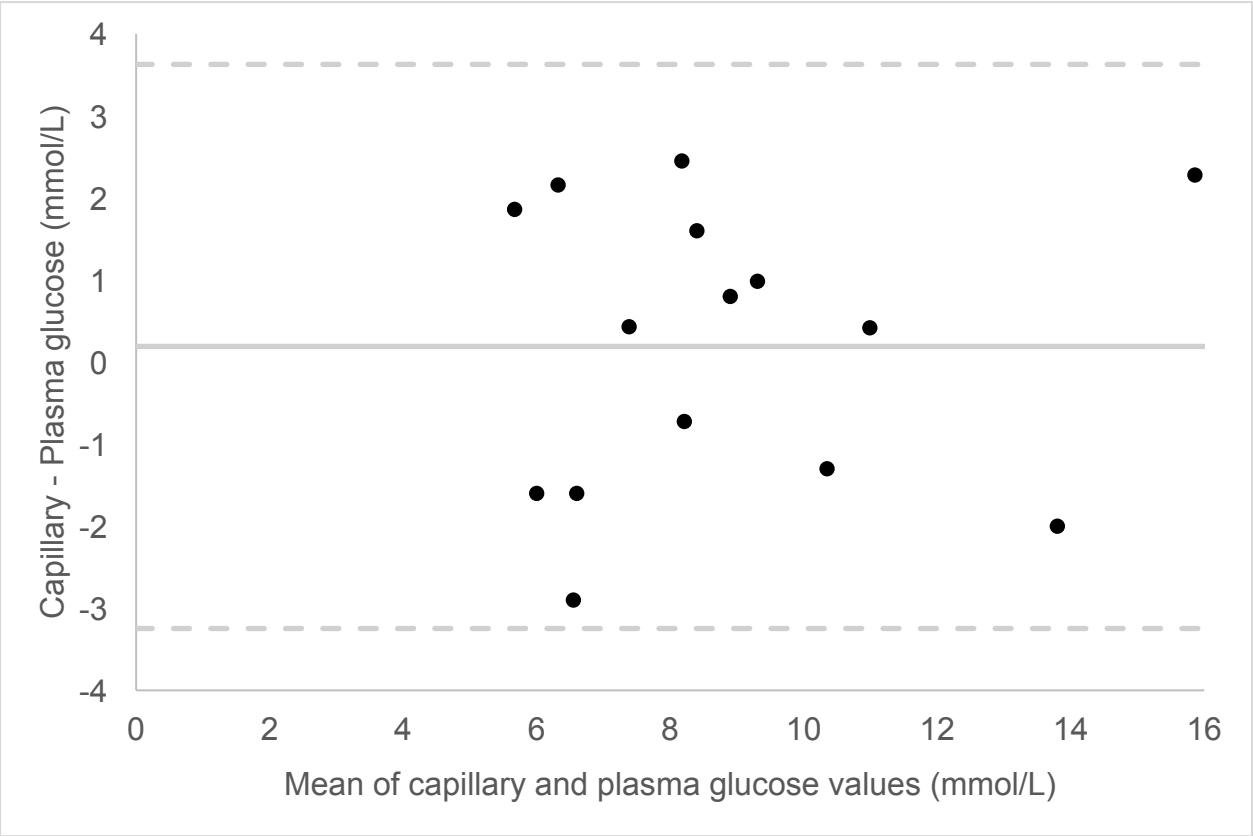
Supplementary Figure 3. An example questionnaire used to assess acceptability in study 2.

For Peer Review Only/Not for Distribution



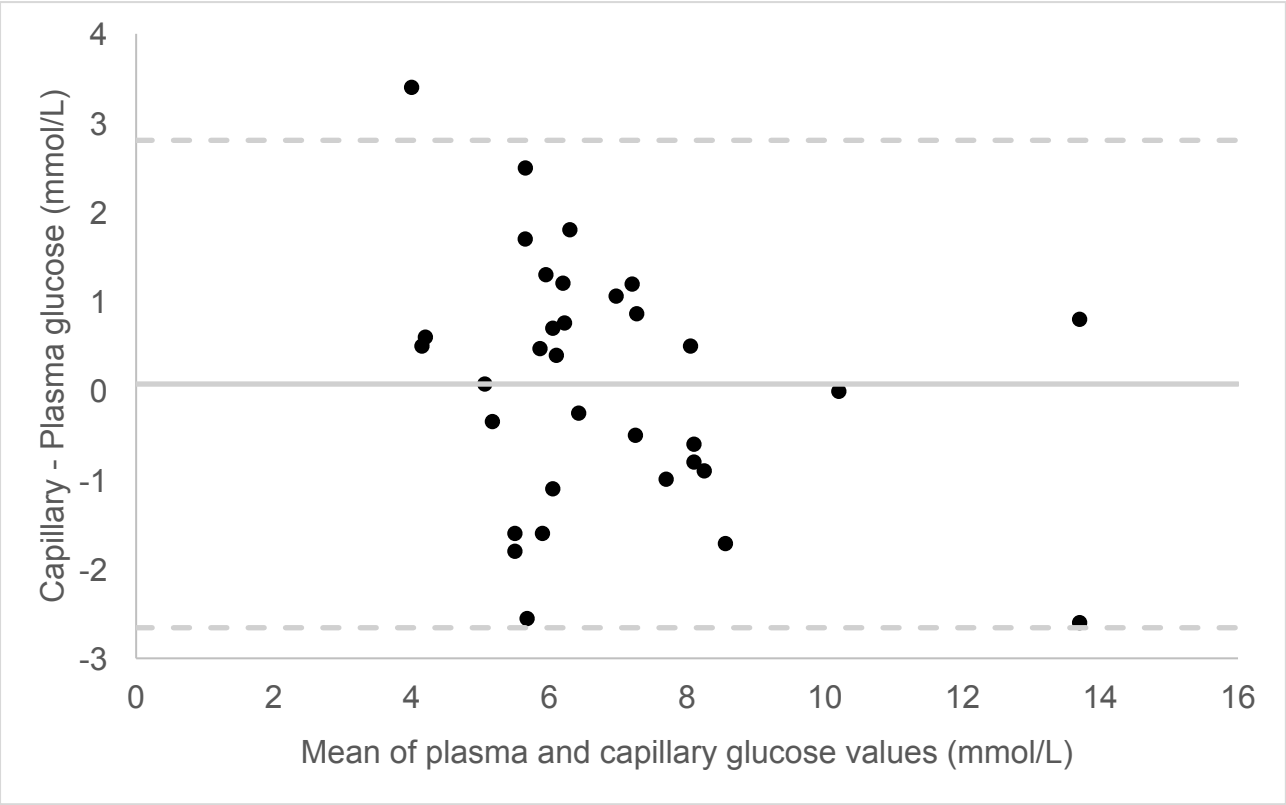
Supplementary Figure 4. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 0-min OGTT time point in 43 paired samples. The solid line indicates the bias (-0.51 mmol/L). The dashed lines represent the 95% limits of agreement (2.95 to 1.94 mmol/L).

For Peer Review Distribution



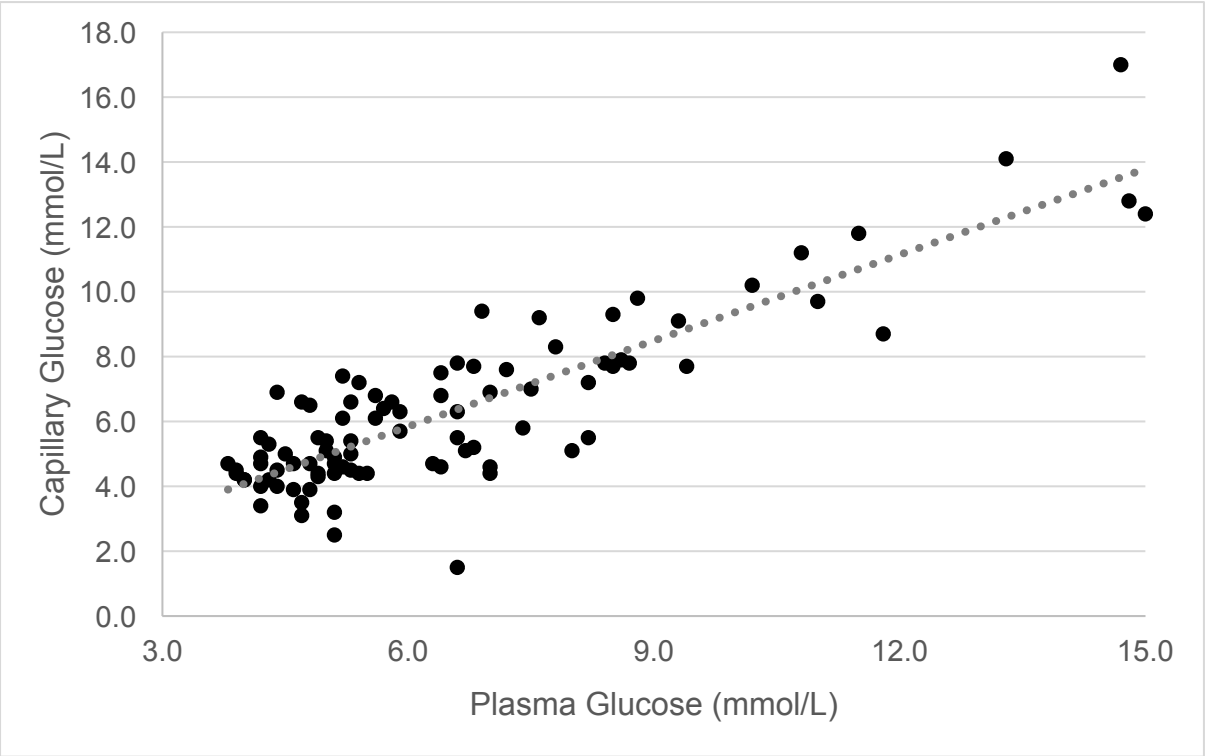
Supplementary Figure 5. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 60-min OGTT time point in 15 paired samples. The solid line indicates the bias (0.19 mmol/L). The dashed lines represent the 95% limits of agreement (-3.25 to 3.63 mmol/L).

For Peer Review Only/Not for Distribution



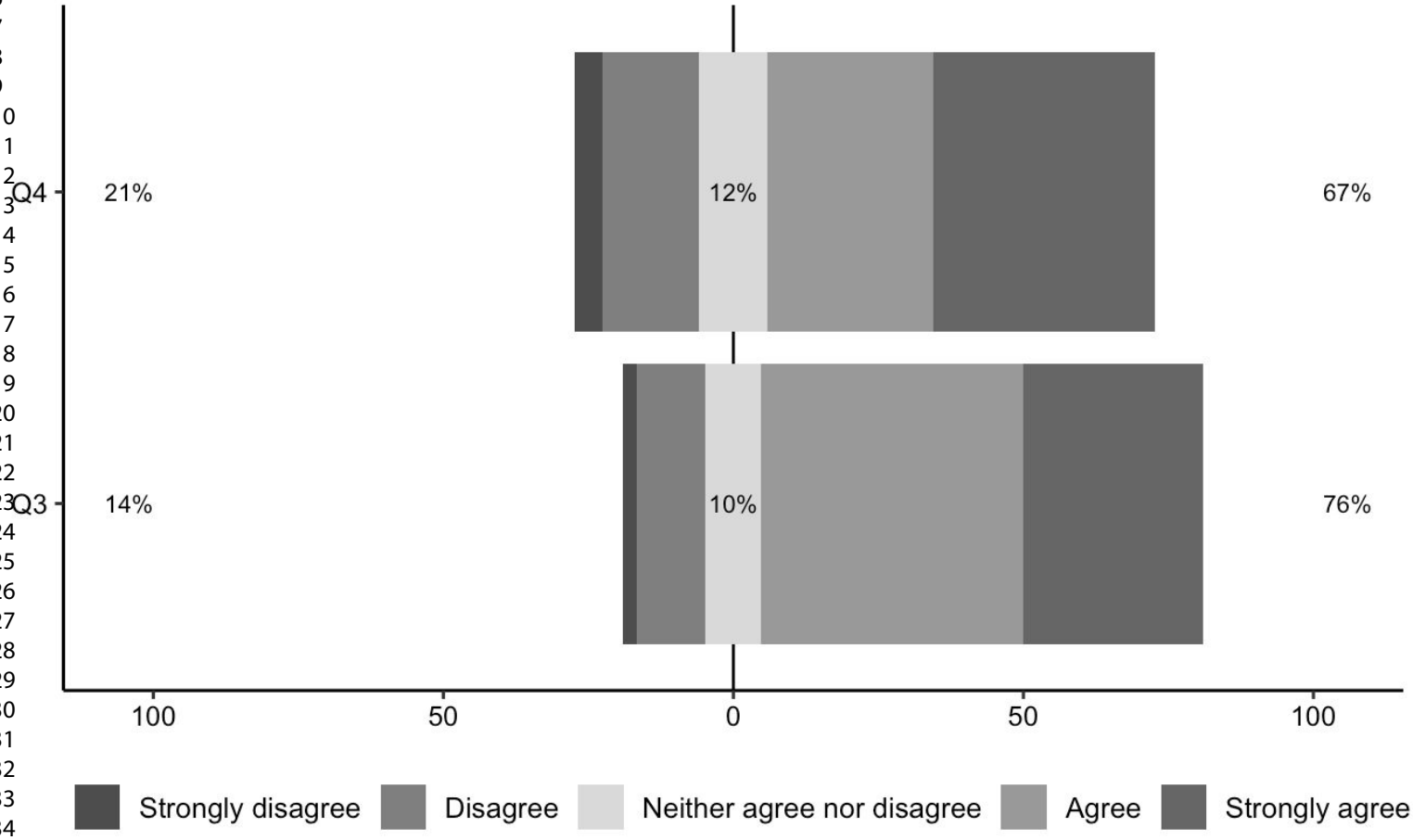
Supplementary Figure 6. A Bland Altman plot comparing capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) at the 120-min OGTT time point in 33 paired samples. The solid line indicates the bias (0.07 mmol/L). The dashed lines represent the 95% limits of agreement (-2.66 to 2.81 mmol/L).

For Distribution



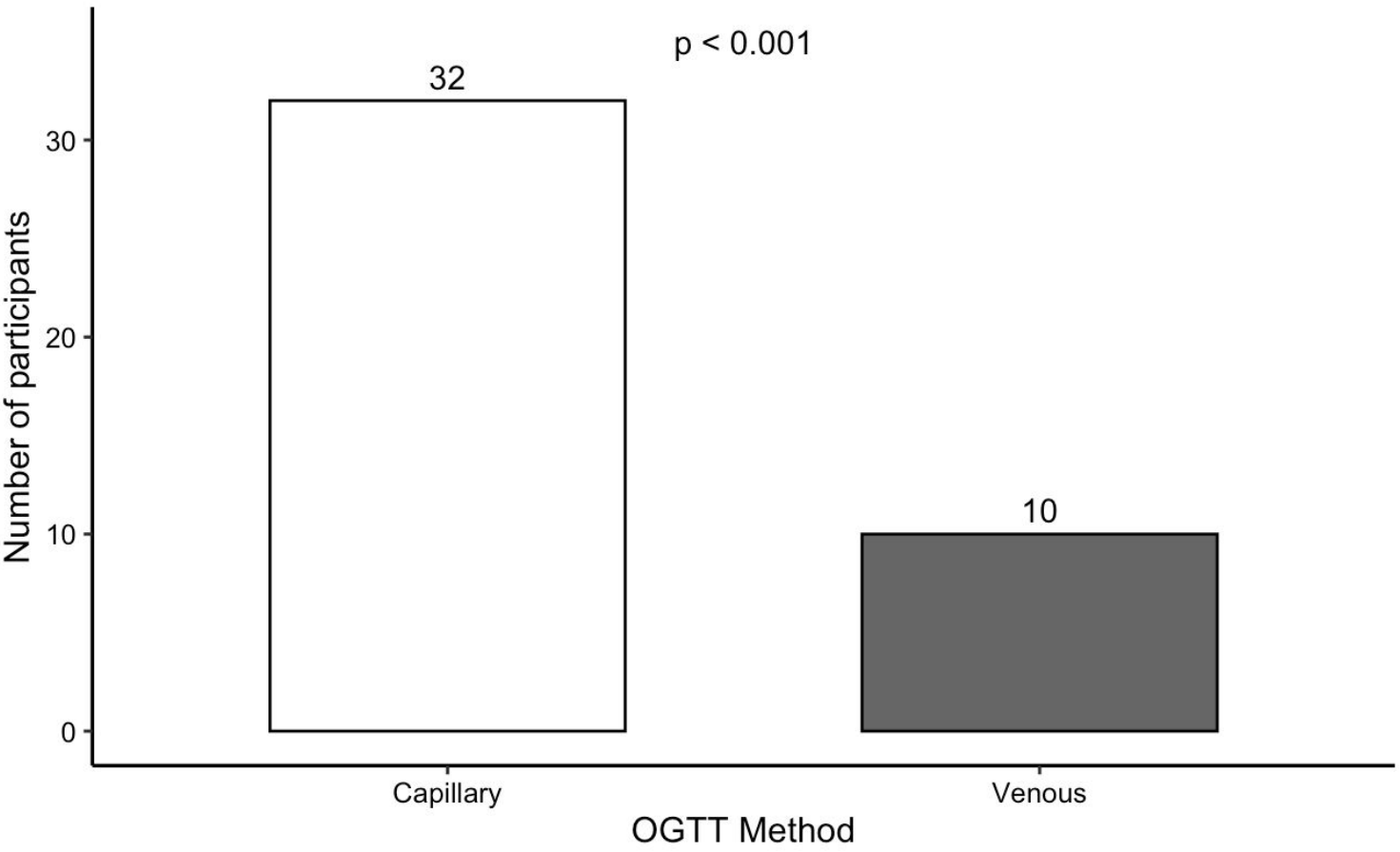
Supplementary Figure 7. A scatter plot showing the relationship between capillary and plasma glucose measurements within the diagnostic range (3.5-15 mmol/L) in 90 paired samples (Spearman's Rho = 0.74, p <0.001). Dotted line presents line of best fit.

For Peer Review Only - Not for Distribution



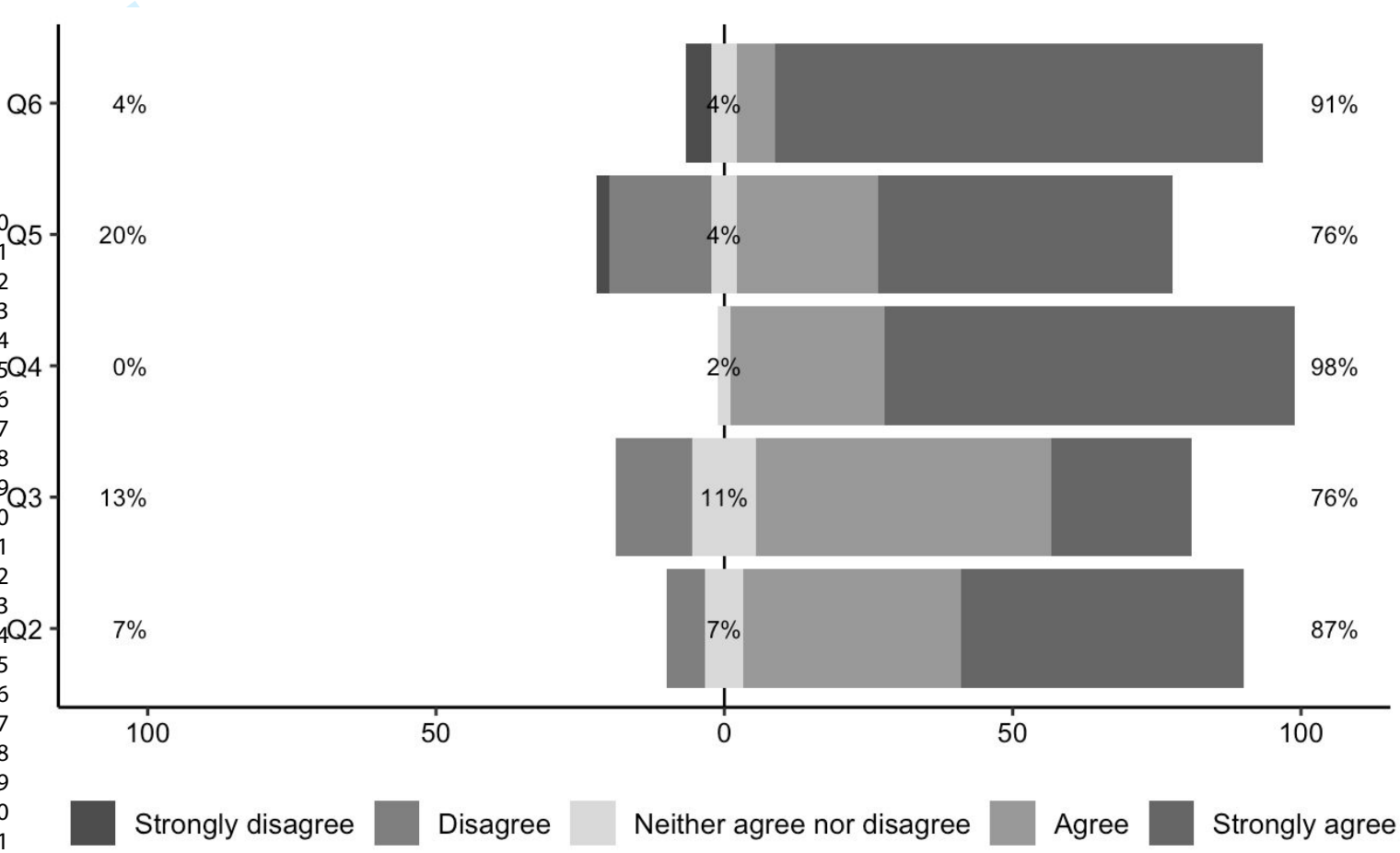
Supplementary Figure 8. A stacked bar chart indicating the responses to questions 3 and 4 of the acceptability questionnaire for participants in study 1. Percentages are grouped strongly disagree and disagree (left), neither agree nor disagree (middle), agree and strongly agree (right).

For Peer Review Not for Distribution



Supplementary Figure 9. A bar chart showing participant preference for future glycemic assessment, comparing capillary with venous OGTT.

For Distribution



Supplementary Figure 10. A stacked bar chart indicating the responses to questions 2 to 6 of the acceptability questionnaire for participants in study 2. Percentages are grouped strongly disagree and disagree (left), neither agree nor disagree (middle), agree and strongly agree (right).

Not for Distribution

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-12
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-12
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6-12
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-12
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	10

Continued on next page

Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801

For Peer Review Only/Not for Distribution

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6-12
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12-16
		(b) Give reasons for non-participation at each stage	12-16, Figure 1A/1B
		(c) Consider use of a flow diagram	Figure 1A/1B
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-16, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	12-16, Figure 1A/1B
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*n/a*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*n/a*
		Cross-sectional study—Report numbers of outcome events or summary measures	*12-16*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-16
		(*b*) Report category boundaries when continuous variables were categorized	Table 2

For Peer Review Only/Not for Distribution

Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-16 and suppl materials
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-24
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-24
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	26

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For Peer Review Only/Not for Distribution

Mary Ann Liebert, Inc., 140 Huguenot Street, New Rochelle, NY 10801