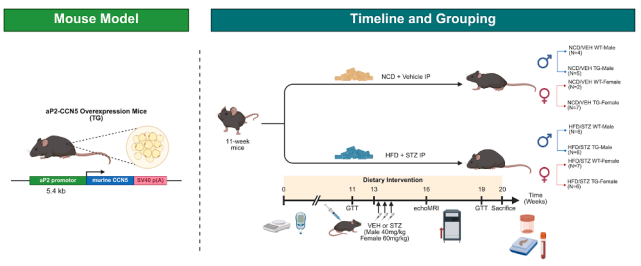
improve vascularization. Human pancreas-derived MSCs were coated onto electrospun polylactic-co-glycolic acid and gelatin (PLGA+G) scaffolds, followed by implantation into the SC space of non-diabetic immunodeficient mice (M/F), with PLGA+G alone as the control. Two weeks after implantation, grafts were excised and assessed for neovascularization. In separate cohorts, 3,000 neonatal porcine islets (NPIs) were transplanted into the PLGA+G+MSC-conditioned SC space (PGM) of diabetic mice (M/F), with PLGA+G alone and kidney capsule (KC) transplants as controls. Blood vessel number ($p=0.0003$), area ($p<0.0001$), and size ($p=0.0001$) were significantly increased at the PGM site compared to controls at 2 weeks. Metabolic follow-up revealed significantly faster diabetes reversal in the PGM group compared to PLGA+G recipients ($p=0.0193$). These data demonstrate that MSCs enhance vascularization in the SC space, which correlates to improved NPI engraftment and function. This approach is anticipated to improve engraftment, increase the success rate for single donor transplants and make islet transplantation more accessible to persons living with T1D.

DCO010

Adipocyte-Specific CCN5 Overexpression Confers Limited Metabolic Benefit and Uncouples Its Paracrine Mitogenic Effects on β-Cell Expansion

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Background: Restoring functional β-cell mass is a central therapeutic goal for type 2 diabetes mellitus (T2DM). While the matricellular protein CCN5/WISP2 promotes β-cell proliferation in vitro and ex vivo, its systemic role in metabolic homeostasis in vivo is poorly defined. Here, we investigated whether adipocyte-specific overexpression of CCN5 (aP2-CCN5) could protect against β-cell dysfunction and metabolic deterioration.
Methods: Eleven-week-old aP2-CCN5 transgenic mice and wild-type controls were subjected to a 13-week high-fat diet (HFD) to induce insulin resistance, followed by streptozotocin (STZ) intraperitoneal injections over three consecutive days (40 mg/kg in males, 60 mg/kg in females) to model late-stage T2DM. Key metabolic parameters, including body weight, glycemia, glucose tolerance, and body composition, were monitored throughout the 20-week study.
Results: The HFD-STZ protocol successfully induced obesity, increased adiposity, and severe glucose intolerance in both sexes. However, CCN5 overexpression did not mitigate hyperglycemia, prevent diet-induced weight gain, or alter body composition. While most metabolic parameters remained unchanged, a significant improvement in glucose tolerance was observed exclusively in HFD-STZ-treated male transgenic mice.
Conclusions: The combined HFD-STZ regimen effectively models late stage T2DM (severe metabolic stress combining insulin resistance and direct β-cell insult), yet increasing endocrine CCN5 from adipose tissues does not confer broad protection. This highlights a potential disconnect between the known local, paracrine actions of CCN5 in vitro/ex vivo and its limited efficacy as a circulating endocrine factor, suggesting its therapeutic utility may be highly context- and sex-dependent.



DCO011

Pancreatic Natural Killer Cells Mediate Surveillance of Stressed Beta Cells in Type 1 Diabetes

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Background: During type 1 diabetes (T1D), some β-cells activate stressed states, including unfolded protein response (UPR) and senescence, accelerating disease progression. In other tissues, senescent cells are removed through immune surveillance mechanisms involving natural killer (NK) cells but whether NK cells target stressed β-cells in T1D remains unknown. NK cells in human and mouse models of T1D exhibit impaired cytotoxicity, suggesting diminished immune surveillance. Notably, NK cell activation with double-stranded RNA mimic polyinosinic-polycytidylic acid (PolyI:C) prevents T1D in non-obese diabetic (NOD) mice, though the mechanism is unclear. This study investigated whether NK cells mediate β-cell surveillance and whether NK cell activation removes stressed β-cells during T1D.
Methods/results: Prediabetic female NOD mice received PolyI:C or phosphate buffered saline (PBS) twice weekly to activate NK cells and their pancreas/pancreatic islets and spleen were analyzed to examine disease progression and β-cell stress pathways. Activation of NK cells ($p< 0.0001$), and no changes in T cells or non-NK/T cells were observed in the PolyI:C mice. PolyI:C mice showed slowed disease progression, increased insulin+ area ($p<0.005$), and reduced insulitis ($p<0.0005$). Interestingly, PolyI:C mice had reduced senescent ($p<0.05$) and UPR ($p<0.005$) stressed β-cells, concomitant with an increase in β-cell proliferation ($p<0.005$). Cell surface proteomics identified upregulation of Calreticulin on senescent β-cells, potentially mediating interactions with NK cells.
Conclusions: Activating NK cells leads to a novel effect of limiting stressed β-cells while mitigating T1D progression. We propose that NK cells trigger immune surveillance that clears senescent and UPR-stressed β-cells in NOD mice.

DC SCIENCE STREAM (CLINICAL RESEARCH) — ORAL PRESENTATIONS

DCO012

A 4-Week Community-Implemented Diabetes Prevention Program Significantly Improves Metabolic Outcomes 12 Months After Participation

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Nearly six million people in Canada are living with prediabetes, of which 70% will progress to type 2 diabetes (T2D) if left untreated. Slowing this progression is essential to reduce the negative macro- and microvascular complications and healthcare costs associated with T2D. Small Steps for Big Changes (SSBC) is a 4-week evidence-based diabetes prevention program delivered by non-medical personnel in the community. This study assessed the effectiveness of SSBC at reducing clinical risk factors associated with T2D using a single-arm pragmatic trial with repeated measures at baseline, 6 months, and 12 months. A total of 389 individuals at risk of developing T2D were enrolled in SSBC (mean age=58.8±8.7 years; 84% white; 75% female), with a 97% program completion rate. Data were analyzed using linear mixed models. Twelve months after SSBC

completion, there were significant reductions in HbA1c (-0.19 [95% CI: -0.25, -0.13]%), weight (-3.03 [-4.15, -1.91]kg), waist circumference (-4.07 [-5.26, -2.89]cm), and improvements in distance walked on the six-minute walk test (38.54[30.90, 46.18]m). SSBC is a brief, low-cost diabetes prevention program that is effective at reducing clinically relevant risk factors associated with T2D 12-months post-program when delivered in a community setting, by non-professionals. The changes in clinical outcomes, including HbA1c, are comparable to more time-intensive and costly diabetes prevention programs that are currently being delivered around the world. These findings support broader implementation of SSBC in community settings across Canada, with the potential to significantly reduce the national burden of T2D.

DCO013

A Decision Support System for Automated Adjustment of Insulin Parameters in Type 1 Diabetes During Ramadan: A Randomized Controlled Trial

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[3] *Virginia, United States*

Introduction and objectives: Fasting during Ramadan can present unique challenges for individuals with type 1 diabetes (T1D). We aimed to evaluate the effectiveness of our iBolus decision support system (DSS) in supporting glycemic management during Ramadan fasting.
Methods: We conducted a randomized, controlled, crossover trial in adults with T1D who are practicing fasting during Ramadan. Participants underwent both the experimental (iBolus DSS app) and control phases, each for 2 weeks, in random order. The iBolus DSS automatically adjusted bolus and basal doses every 4–5 days while the control group maintained their current standard of care.
Results: A total of 37 participants completed both study arms, but 12 were excluded due to infrequent/incorrect use of the app. Therefore, 25 were included in the final analysis (48% females; HbA1c 7.7 (0.5); age 37 (10)). No differences were observed between the two arms in any glucose metrics when the total duration was used for analysis. However, in the last 5 days, after the DSS made 1–2 changes to insulin parameters, time in range (3.9 to 10.0 mmol/L) increased from 53.3% (control) to 58.9% (app) (difference: 5.6%, 95% CI [1.2, 10.0], p=0.02) and time above 10 mmol/L decreased by 5.6% (95% CI [−10.9, −0.4], p=0.04). No differences in times spent in hypoglycemia were observed between arms.
Conclusion: Our iBolus DSS has the potential to improve glucose control during Ramadan fasting. A longer, parallel-design study is warranted.

DCO014

Diagnostic Accuracy of One Physical Examination Test (The Diabetes Canada Approach) Versus Three (The American Diabetes Association Approach) For Diabetic Peripheral Neuropathy Screening

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Aim: ADA guidelines recommend a three-test strategy (temperature or pinprick for small-fiber function, vibration for large-fiber function, and monofilament) for annual screening of diabetic peripheral neuropathy (DPN). Other organizations, including Diabetes Canada, suggest single-test approaches. We aimed to compare the diagnostic accuracy of these approaches.
Methods: In updated analysis of baseline data from the Toronto Diabetic Neuropathy longitudinal cohort (N=474), we defined 5 index tests: 1. Monofilament; 2. Pain (by pinprick); 3. Vibration (by the on-off method); 4. clinical Sum of Three Abnormal Tests (using published thresholds favouring specificity, defined by ≤3 sensate responses out of 8 for each); and 5. a theoretical Model-based probability from multiple logistic regression including the quantitative scores for each test. Reference standard for DPN was defined by nerve conduction studies. Primary analysis was the comparison (by Delong's Test) of the Area Under Curve (AUC) from Receiver Operating Characteristic analysis of the individual tests vs Sum of Abnormal Tests, while exploratory analysis compared them with the AUC for Model-Based Probabilities.
Results: The AUC for the Sum of Three Abnormal Tests did not differ from the AUC for monofilament (0.80 vs. 0.79, p=0.55) but was greater than the other two tests (p≤0.05 for both comparisons, Figure 1). However, the AUC for the Model-Based Probability was greater than all other index tests (p≤0.0004 for all comparisons).
Conclusion: A single-test approach (monofilament) provides similar diagnostic accuracy to the three-test approach. However, in theory three quantitative scores entered into a risk calculation equation could marginally improve accuracy.

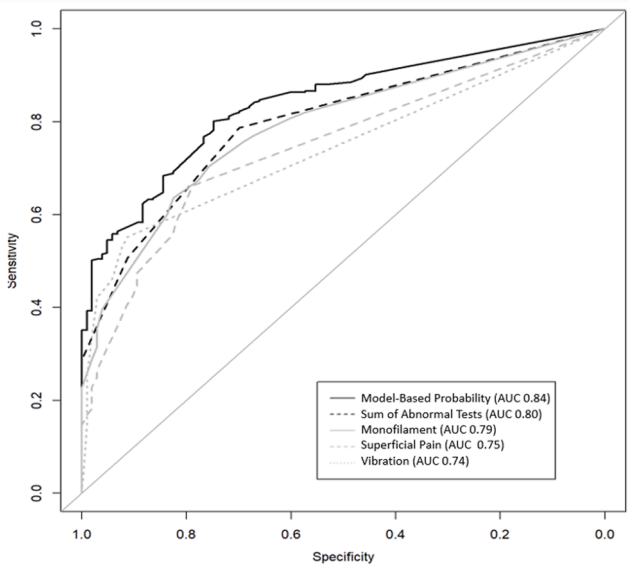


FIGURE 1. ROC Curves for Each of the Three Single Tests, For the Sum of Abnormal Tests, and for a Multivariable Logistic Regression Model-Based Probability Score

DCO015

Economic Analysis and Return On Investment (ROI) for Diabetic Retinopathy (DR) Screening and Treatment Through Diabetes Eye Screening Program (DESP) Among Uninsured Patient Populations Living With Diabetes and Seeking Care

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[1] *Toronto, Ontario*

Background: DESP is less costly and more effective in diagnosing DR than standard screening among vulnerable populations. Canadian DR screening practice falls behind recommended guidelines. Individuals seeking services at Ontario CHCs do not require health insurance to receive care.
Objective: To determine ROI associated with implementation of screening and treatment in comparison with no screening and no treatment option for DR for uninsured populations.