Patients were followed for at least one year from the date of surgery. Participants were randomized in a 3:2 ratio to either four days of outpatient preoperative dietary restriction (PCR) or their regular ad libitum diet. We performed an open label randomized controlled trial in patients scheduled for any elective open vascular procedure. We showed in mice that short-term protein-calorie restriction (PCR) is a novel method to upregulate endogenous production of H2S and induce stress resistance and longevity. In preclinical studies, pre-operative restriction of proteins and/or calories (PCR) has been shown to limit ischemia-reperfusion damage, slow intimal hyperplasia, and improve metabolic fitness. We have now done two short-term PCR studies performed on inpatients undergoing elective vascular surgery which proved feasible and had no adverse effects in our enrolled patients. Whether these dietary regimens are feasible and safe in the vascular surgery outpatient population remains unknown. For this study, we enrolled patients undergoing vascular surgery and randomized them to PCR or control diet to be implemented in an outpatient setting.

**INTRODUCTION**
- Vascular surgery patients suffer from high failure rates and frequent complications. With rising health care expenditures and an aging population, there is a serious need for feasible strategies to enhance clinical outcomes after invasive major operations.
- Pre-operative dietary restrictions an emerging research field with the potential to address these problems.
- Recently we showed that a novel method to increase endogenous H2S production is via short-term dietary restriction. We showed in mice that short-term protein-calorie restriction (PCR) is a novel method to upregulate endogenous production of H2S and induce stress resistance and longevity.
- In pre-clinical studies, pre-operative restriction of proteins and/or calories (PCR) has been shown to limit ischemia-reperfusion damage, slow intimal hyperplasia, and improve metabolic fitness.
- We have now done two short-term PCR studies performed on inpatients undergoing elective vascular surgery which proved feasible and had no adverse effects in our enrolled patients.
- Whether these dietary regimens are feasible and safe in the vascular surgery outpatient population remains unknown.
- For this study, we enrolled patients undergoing vascular surgery and randomized them to PCR or control diet to be implemented in an outpatient setting.

**METHODS**
- We performed an open label randomized controlled trial in patients scheduled for any elective open vascular procedure.
- Participants were randomized in a 3:2 ratio to either four days of outpatient pre-operative protein-calorie restriction (30% calorie, 70% protein restriction) or their regular ad libitum diet.
- Blood was drawn at baseline, pre-operative, and post-operative day 1 time points. An extensive leukocyte subset flow cytometry panel was also performed at these time-points.
- Peri-procedural subcutaneous and perivascular adipose tissue was sampled and analysed for adipokine, cytokine, hematology, and chemical blood parameters.
- Patients were followed for at least one year from the date of surgery.

**RESULTS**
- Data collected via the Meallogger application allowed us to calculate that patients in the PCR group achieved a 29.4% calorie and 84.4% protein restriction on average compared to their pre-study intake.
- Compared to their weight at baseline, patients allocated to the PCR group appeared to have lost weight at the preoperative visit (Figure 3A). The same trend was noted when comparing BMI at baseline with their pre-operative BMI (Figure 3B), in the PCR group. In terms of diet compliance, both the Meallogger data and weight parameters are indicative of adherence to the PCR diet.
- To test whether our PCR diet would result in malnutrition, we measured baseline and pre-op levels of pre-albumin, a short half life protein. (35) Figure 3C shows no difference in pre-albumin levels between groups and before/after the diet, suggestive of weight loss in the PCR group without malnutrition. In our study, we were not able to detect a difference in baseline and pre-op glucose levels (Figure 3D). However, we did see a trend towards increased insulin sensitivity as a result of the PCR diet (Figure 3E).

**CONCLUSIONS**
- Four days of pre-operative outpatient protein-calorie restriction (PCR) in vascular surgery patients resulted in weight loss and BMI decrease, without inducing malnutrition. Insulin sensitivity was improved, while leukocyte populations were maintained.
- Pre-operative outpatient PCR appears safe and feasible in patients scheduled for vascular surgery.
- 19 patients were enrolled, of whom 11 completed the study. No diet-related reasons for non-completion were reported, and there was no intervention group crossover. The PCR diet induced weight loss and BMI decrease, without malnutrition (similar pre-albumin levels between time-points). Insulin sensitivity was improved after 4 days of PCR. Between diet groups, there were similar rates of re-intervention, wound infection and cardiovascular complications. Leukocyte populations were maintained after four days of PCR.

**FUTURE DIRECTIONS**
- A future, larger scale trial should be able to delineate whether short-term PCR improves glucose metabolism, and whether this can be linked to improved clinical outcomes and wound healing.
- The present study adds to a growing body of evidence that highlights the safety and feasibility of short-term pre-operative dietary restriction in patients scheduled for elective surgery. Scheduling and logistical issues can make dietary intervention before elective surgery challenging, but PCR is not untenable.
- Although the present study and our previous pilot study are the only studies to date attempted in vascular surgery patients, several other studies have shown feasibility and safety in transplant patients, coronary bypass surgery and patients scheduled for liver resection. Future studies should delineate whether PCR confers any improvement in clinical outcomes in vascular surgery patients.