



Demographics and Initial Results of “POuND OUT” Study (Phentermine/topiramate to eND Obesity and Uric acid stones Trial)

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BACKGROUND

- Uric acid nephrolithiasis (UAN) is the second most common kidney stone type, affecting almost 3 million Americans lifelong and roughly 60,000 Americans annually¹
- UAN risk is six-fold higher in overweight and diabetic individuals due to increased insulin resistance/metabolic syndrome which leads to impaired renal ammonium production²
- Lack of ammonia buffer results in disproportionately acidic urine pH (the greatest contributing factor to UAN), making weak acids less soluble and leading to increased uric acid crystal formation
- Traditional UAN therapies include allopurinol (decreases uric acid production) and citrate salts (raises urine pH by alkaline load). These medications target downstream affects of obesity and DM but do not address the underlying biochemical causes³
- Carbonic anhydrase inhibitors (CAI) have been shown to raise urine pH through renal mechanisms of bicarbonate wasting
- Numerous RCTs have demonstrated the success of phentermine and topiramate (a CAI) in weight loss and reduction of diabetes, cardiovascular, and other factors seen with metabolic syndrome⁴
- Thus, we created an 18-month, open-label randomized trial to study the effect of these two weight loss drugs on this disease. Enrollment opened April 2021

METHODS

- Eligibility criteria include ages 18-75, BMI > 30 kg/m², diabetic or pre-diabetic, and established history of pure uric acid stones
- Patients are randomized (2:1) to either the treatment block (phentermine/topiramate) or control (continue standard of care) block and followed for 18 months to monitor for UAN recurrence
- During this study, patients will undergo:
 - Five in-person visits and three telephone visits
 - 2 sets of CT imaging (prior to enrollment, end of study)
 - 2 sets of DEXA-BC scans (prior to enrollment, end of study)
 - Multiple 24-hour urine collections + metabolic evaluation
 - Periodic blood draws
 - PHQ-9 questionnaire (mental health)

RESULTS

Figure 1: CONSORT Diagram
This flow-chart illustrates the 2:1 treatment-control allocation process

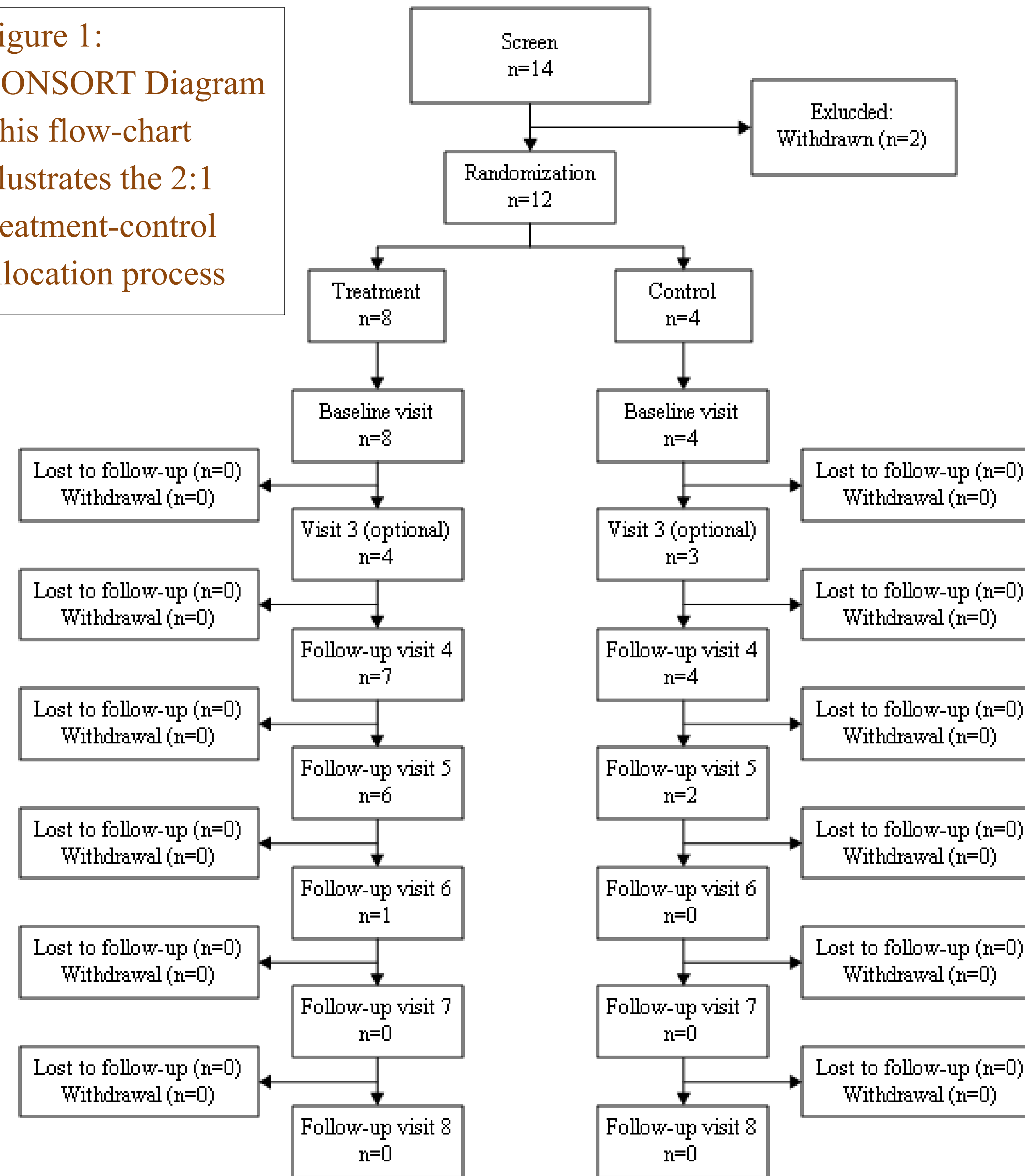


Figure 2: Cartoon image adjacent to DEXA-BC scans. In this study, 3 body masses (bone, fat, lean) are calculated by distinguishing adipose (visceral, subcutaneous, intramuscular) from skeletal muscle/organ and from bone. This helps determine the origin of body weight loss.

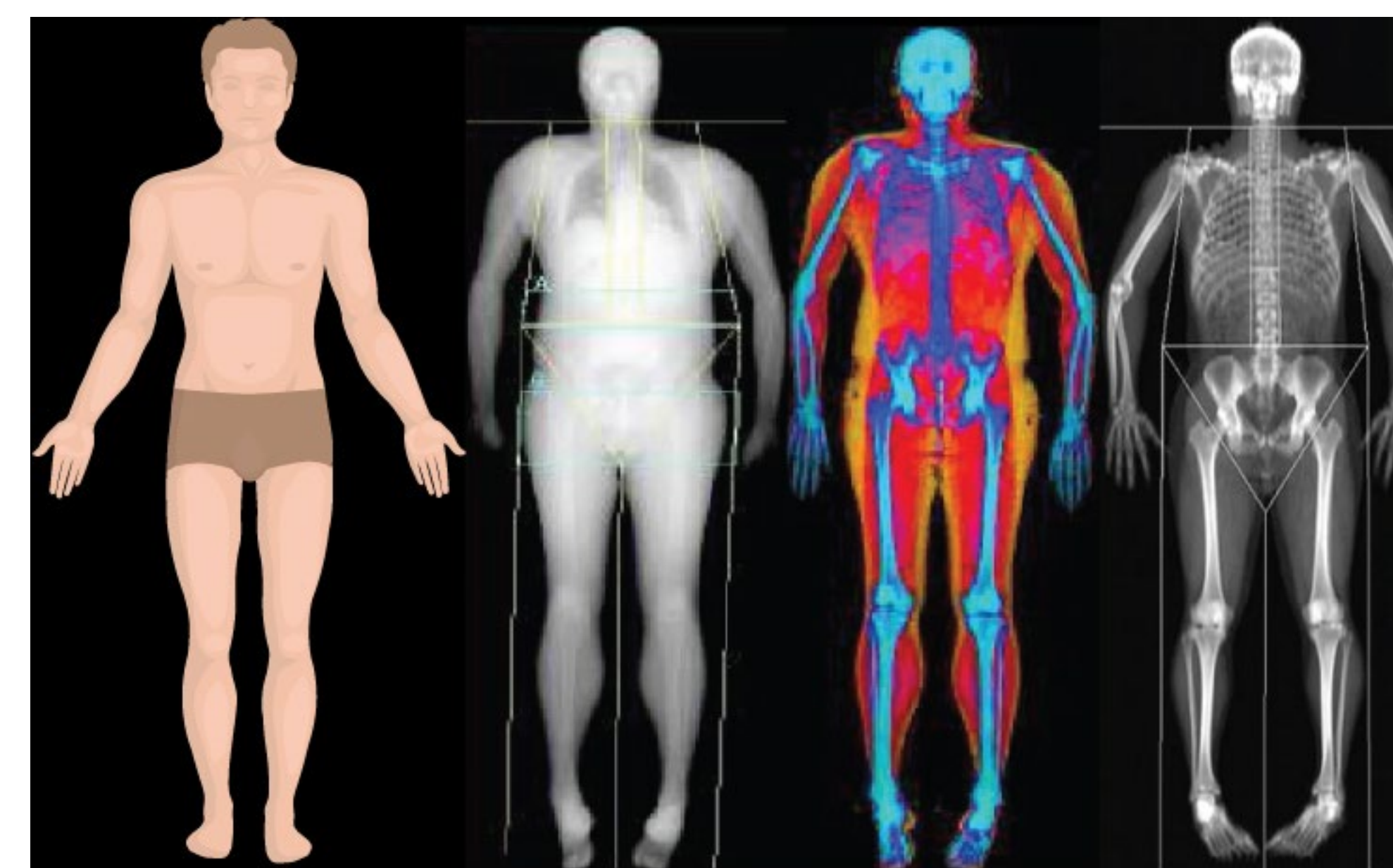


Figure 3: Demographics, medical history, and baseline body composition of study participants

Variable	Overall (n=12)	Treatment (n=8)	Control (n=4)	p-Value
Demographics				
Mean Age	60.7 ± 10.8	55.5 ± 9.1	71.0 ± 4.1	0.0098
Percentage of male patients	7 (58.3%)	5 (62.5%)	2 (50.0%)	0.6788
Medical History				
Mean age of first kidney stone	40.7 ± 16.8	35.3 ± 14.8	51.5 ± 16.9	0.1170
Percentage of patients stone free at start of study	4 (36.4%)	4 (57.1%)	0 (0.0%)	0.0581
Mean total lifetime stones	3.1 ± 4.4	4.2 ± 5.8	1.8 ± 1.5	0.4121
Percentage of patients with only 1 kidney	2 (18.2%)	2 (28.6%)	0 (0.0%)	0.2373
Percentage of patients with 2 kidneys	9 (81.8%)	5 (71.4%)	4 (100.0%)	
Body Composition				
Mean BMD (Bone Mineral Density)	1.2 ± 0.2	1.2 ± 0.2	1.1 ± 0.1	0.4487
Mean fat mass percentage	42.3 ± 7.2	43.0 ± 6.4	40.8 ± 9.5	0.6376
Mean bone mass percentage	2.4 ± 0.5	2.2 ± 0.4	2.8 ± 0.5	0.0658
Mean lean mass percentage (100% - body fat%)	57.7 ± 7.2	57.0 ± 6.4	59.2 ± 9.5	0.6376
Mean BMI at baseline	37.5 ± 6.8	40.5 ± 6.4	31.6 ± 1.7	0.0229

Figure 4: Baseline mean urine pH and additional labs of study participants

Variable	Overall (n=12)	Treatment (n=8)	Control (n=4)	p-Value
Baseline Labs				
Mean hemoglobin A1c at baseline	6.9 ± 1.4	7.1 ± 1.6	6.6 ± 0.9	0.5397
Mean pH of urine (RI: 5.8 – 6.2) at baseline	5.3 ± 0.2	5.3 ± 0.2	5.3 ± 0.2	0.8154
Mean protein catabolic rate (RI: 0.8-1.4 g/kg/d) at baseline	0.9 ± 0.3	0.9 ± 0.4	0.8 ± 0.3	0.8062
Mean PHQ-9 score at baseline	4.1 ± 3.3	4.5 ± 2.9	3.3 ± 4.3	0.5568

Full analysis comparing groups will be performed after completion of all follow-up visits

FUTURE DIRECTIONS

- Enrollment for the POuND OUT study only recently began in April 2021 and has a target enrollment of thirty participants
- The “POuND OUT” study will provide important, novel data regarding the effect of this weight-loss combination therapy on uric acid kidney stone growth and urinary pH outcomes

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