Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

McMaster University

Hamilton Health Sciences

Bariatric surgery for the Reduction of Cardiovascular Events: Overview and Design

Jorge A. Wong, MD MPH FRCPC
Arrhythmia Service, Hamilton Health Sciences
Assistant Professor, McMaster University
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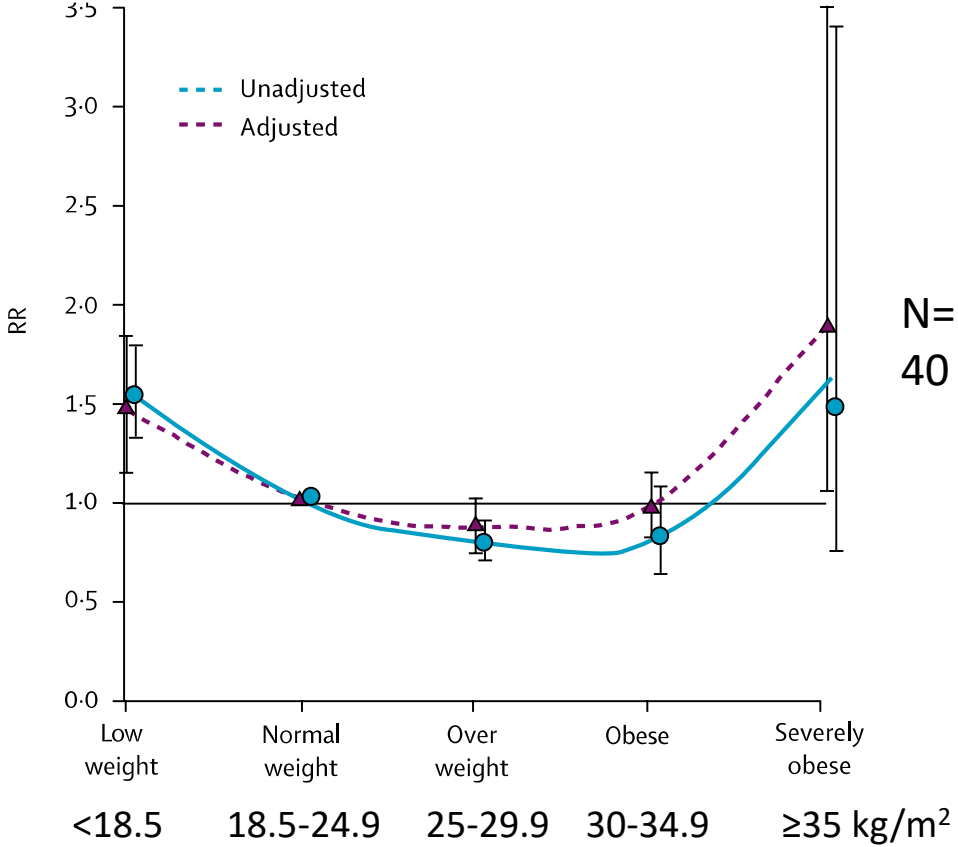
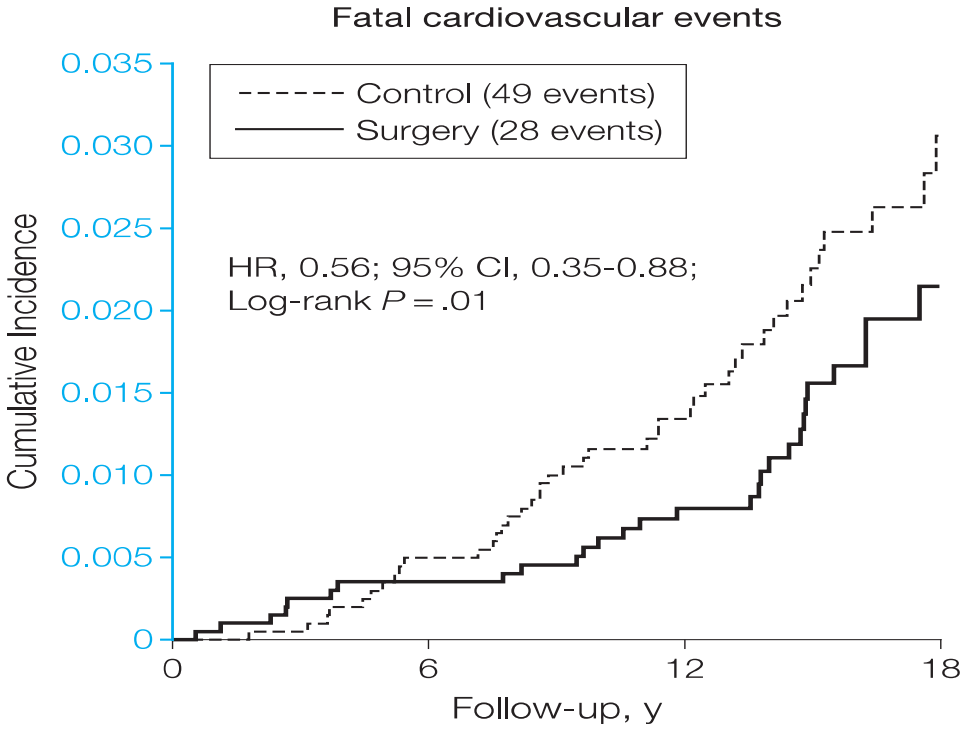
Obesity and CV Mortality in CAD Patients



N=250,152
40 Observational studies

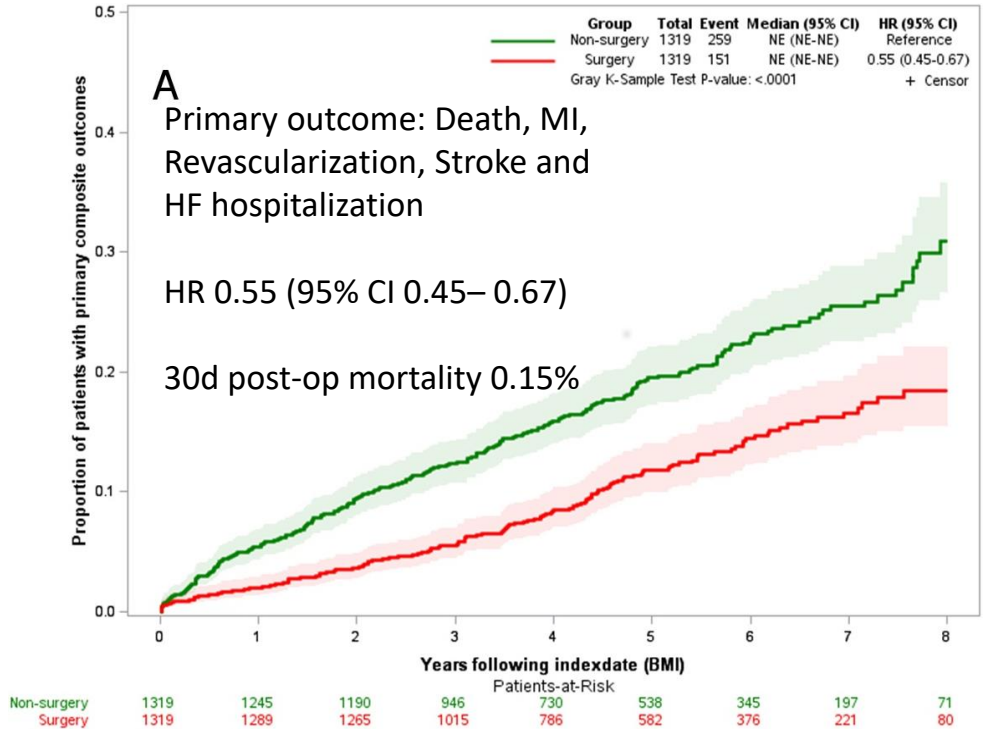
Romero-Corral et al. Lancet 2006

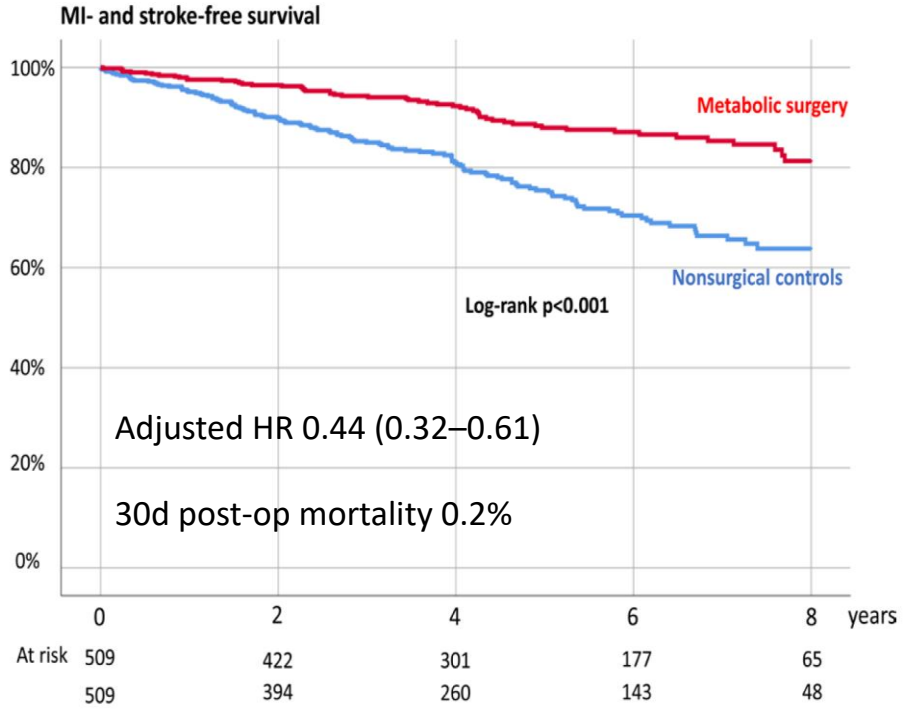
Bariatric Surgery and CV endpoints



Sjostrom et al. JAMA 2012

Effect of Bariatric Surgery on CV outcomes: ICES





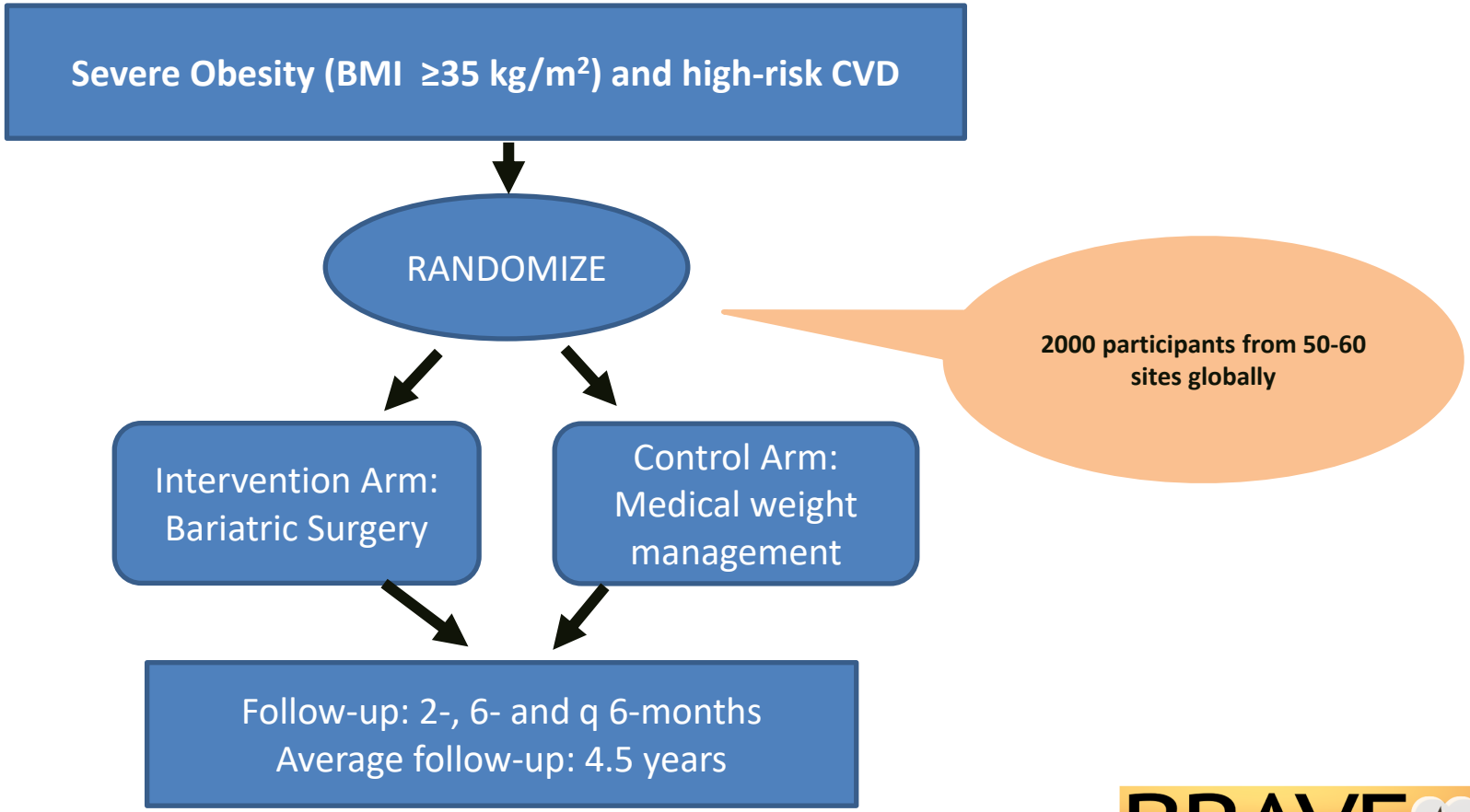
Doumouras A, Wong JA et al. Circulation 2021

Naslund JA. et al. Circulation 2021

Overall Question

- In patients with severe obesity (BMI ≥35 kg/m^2) and CVD does bariatric surgery compared to medical weight management decrease the risk of future cardiovascular events

BRAVE RCT Study Design



BRAVE

Inclusion / Exclusion Criteria

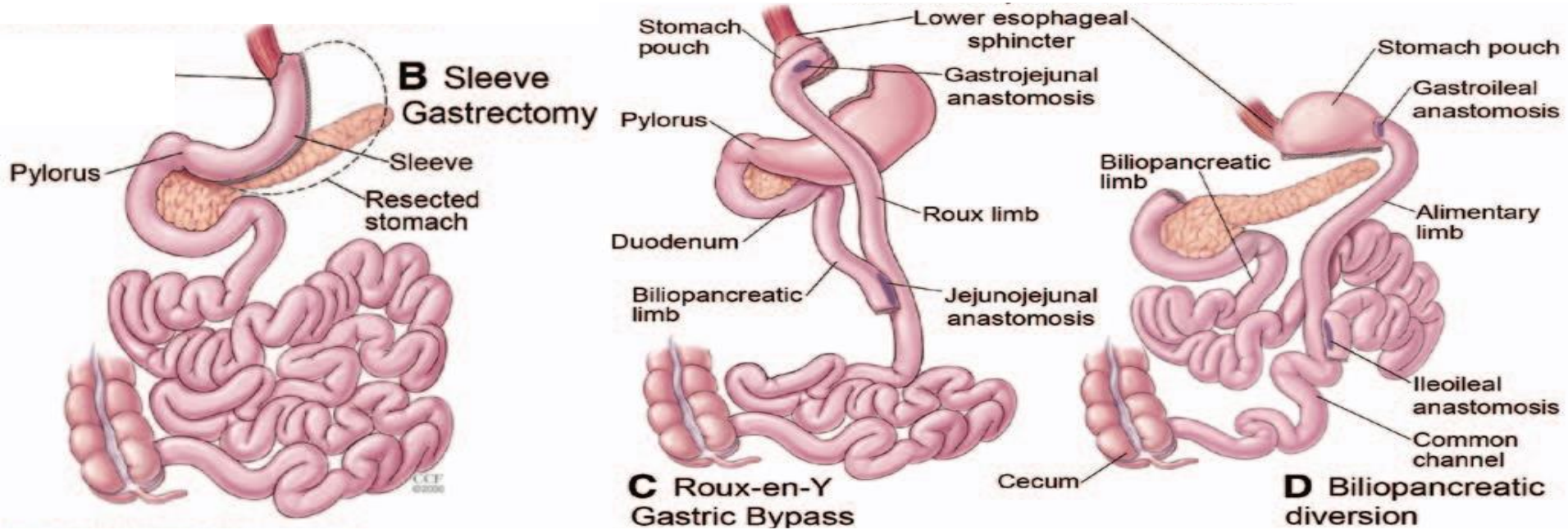
- Body mass index ≥35 kg/m^2
- Age ≥18 years
- Cardiovascular disease, defined as any 1 of:
  - Prior MI or revascularization
  - HFrEF (LVEF ≤ 40%) or HFpEF (LVEF > 40%)
  - AF with CHA_2DS_2-VASc score ≥2
  - History of stroke
  - Peripheral artery disease
- Patient eligible for bariatric surgery according to local practice guidelines
- Key exclusions: Contraindications to surgery and prior bariatric surgery

BRAVE

Intervention Arm

- Either laparoscopic sleeve gastrectomy, gastric bypass or duodenal switch performed at the surgeon's discretion

Intervention Arm: The bariatric surgery procedures



Vest et al. Circulation 2013

Control arm

- Medical weight management:
  - Reflects best medical therapy locally available
  - May consist of the following:
    - Lifestyle / behavioral modification
    - Low-calorie meal replacement (i.e., Optifast)
    - Locally approved anti-obesity medications (i.e., semaglutide)
- Guideline-based management of CVD risk factors and underlying cardiac conditions strongly recommended

Primary Endpoint

Composite of all-cause death, MI, stroke, and HF hospitalization

Secondary & Other Endpoints

- CV mortality
- New / remission of diabetes
- Atrial fibrillation
- Obesity-related cancers
- Integrated cardiovascular risk factor score
- Cognition
- Weight
- Cost effectiveness

Safety

- Perioperative complications
- Long-term procedure morbidity

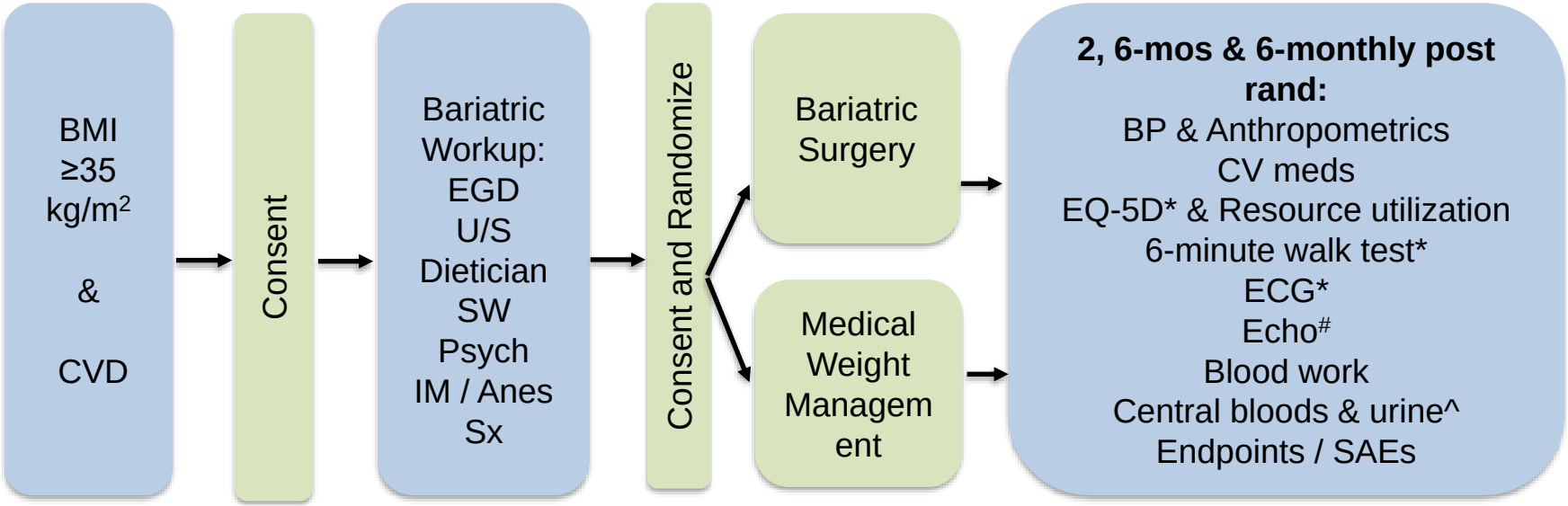
BRAVE

Sample Size

- 2000 patients will give 90% power to detect 29% RRR, and 80% power to detect 25% RRR at alpha of 5%
- Average follow up 4.5 years
- Power will be increased if follow up extended

BRAVE

BRAVE Study Schedule



Complete in 2-3 months

1 mo. to deliver intervention

ECG, echo and bloodwork collected if performed clinically
* baseline, 1-, 3-, 5-years, and study end
# baseline, 1- and 3-years
^ baseline, 2-mo and 12 mo.

Baseline characteristics

	Randomized (N=49)
Age (years)	62.3 ± 6.5
Sex (N, % female)	20 (40.8%)
BMI (kg/m^2)	43.2 ± 6
Waist circumference (cm)	135.2 ± 15
Systolic BP (mmHg)	123 ± 19
Diabetes (N)	23 (46.9%)
Hypertension (N)	40 (81.6%)
Prior MI PCI (%) CABG (%)	16 (32.7%) 11 (22.4%) 5 (10.2%)
Prior Stroke / TIA (N)	5 (10.2%)
Heart failure (N)	17 (34.7%)
Atrial fibrillation (N)	38 (77.6%)
History of CKD (%)	6 (12.2%)

BRAVE

Baseline Investigations

Randomized	N=49
Creatinine (ULN 150 umol/L)	98.2 ±46 umol/L
Triglycerides (ULN 1.7 mmol/L)	1.64 ±0.94 mmol/L
LDL (ULN 2.0 mmol/L)	1.86 ±0.87 mmol/L
HDL (LLN 1.0 mmol/L)	1.18 ±0.34 mmol/L
Total Cholesterol (ULN 5.2 mmol/L)	3.74 ±1.05 mmol/L
LVEF	47.4 ±11 %
IVSd (0.6-1.1 cm)	1.04 ±0.18 cm
LVPWd (0.6-1.1 cm)	1.02 ±0.14 cm
LV Mass (men: <224 gm; women: <162 gm)	213 ±63 grams
LVEDV index (men: <74 mL/m^2 ; women: <61)	49.2 ±19 mL/m^2
LA diameter (< 4.0 cm)	4.6 ±0.6 cm
LAESV indexed (mL/m^2)	35.0 ±11 mL/m^2

BRAVE

Medications

	Baseline (N = 49)	6 months (N = 28)
Beta blocker	33 (67.3%)	15 (53.6%)
ACE inhibitor or ARB	32 (65.3%)	14 (50%)
Sacubitril/Valsartan	6 (12.2%)	0 (0%)
MRA	9 (18.4%)	3 (10.7%)
Aspirin	10 (20.4%)	2 (7.1%)
Warfarin	3 (6.1%)	2 (7.1%)
Direct Oral Anticoagulant	34 (69.4%)	24 (85.7%)
Diuretic	25 (51%)	9 (32.1%)
Statin	36 (73.4%)	19 (67.9%)
Ezetimibe	4 (8.2%)	2 (7.1%)
Insulin	8 (16.3%)	3 (10.7%)
Metformin	17 (34.7%)	7 (25%)
SGLT2 inhibitors	17 (34.7%)	3 (10.7%)
DPP4 inhibitors	8 (16.3%)	3 (10.7%)
GLP-1 receptor agonists	13 (25.6%)	7 (25%)

Outcomes

	Baseline	6-months
Sleeve gastrectomy	100%	n/a
Optifast	94%	42.8%
Systolic Blood pressure (mmHg)	123.3 ±18	124.8 ±12
Diastolic Blood pressure (mmHg)	74.4 ±13	73.8 ±8
Weight (kg) Surgery Medical	133.6 ±29 138.1 ±31 127.2 ±28	121.0 ±36 117.7 ±36 120.1 ±22
BMI (kg/m^2) Surgery Medical	44.6 ±7 46.0 ±6 42.9 ±7	39.9 ±9 40.0 ±8 39.5 ±7

Median time from rand to surgery = 33 (IQR 2 5, 42) days

Conclusions

- Obesity potent risk factor for CVD and may worsen prognosis in CVD
- Efficacy of weight loss in reducing adverse clinical outcomes in CVD patients not well understood
- Non-randomized studies suggest large benefit in reducing CVD outcomes in patients with obesity
- BRAVE will examine the efficacy of bariatric surgery compared to medical weight management on patients with obesity and CVD