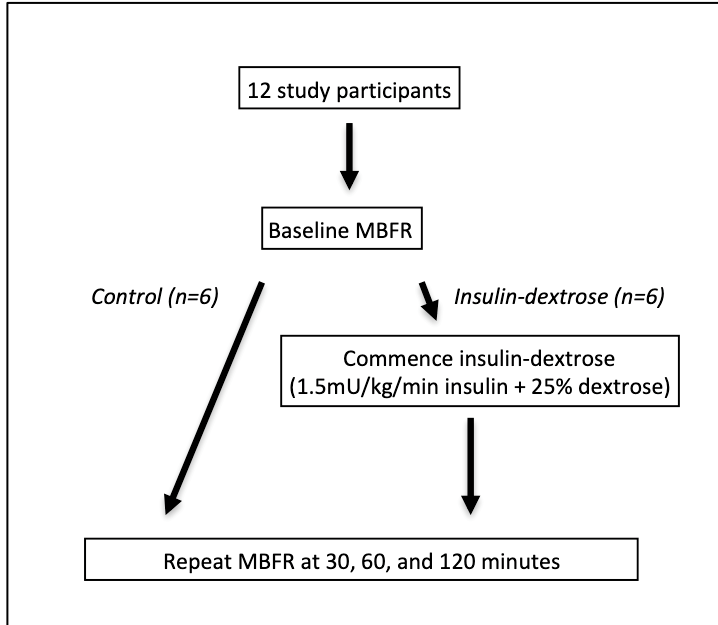# Supplementary Material

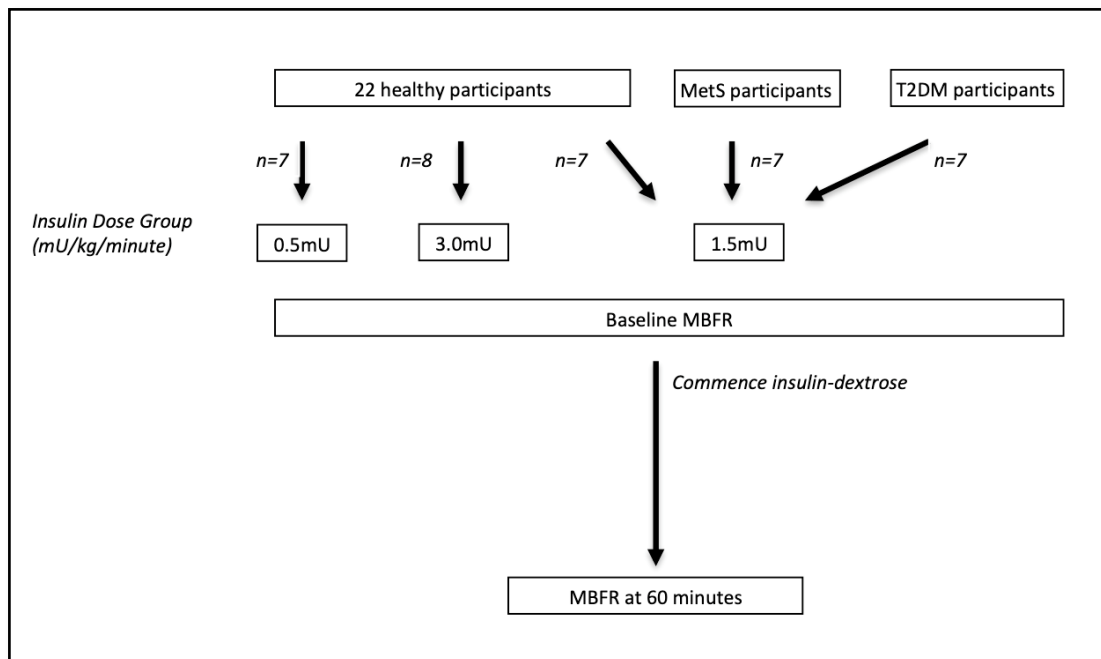## Supplementary Methods

<u>Experimental protocol schematics</u>
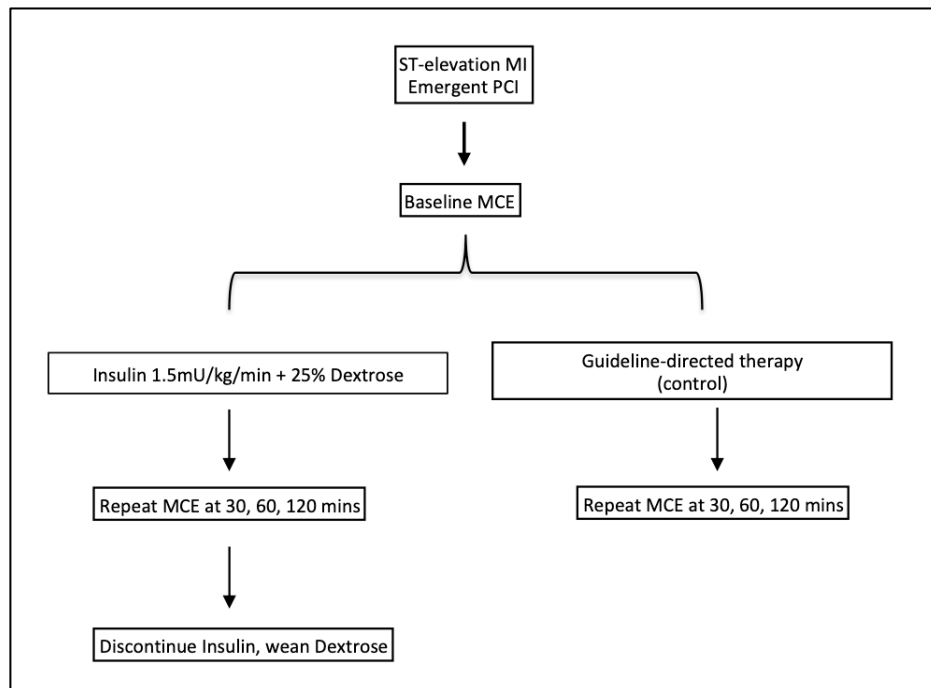
Experiment 1

Experiments 2 and 3

Experiment 4

```
                          ┌─────────────────┐
                          │  ST-elevation MI │
                          │   Emergent PCI   │
                          └─────────────────┘
                                   │
                                   ▼
                          ┌─────────────────┐
                          │   Baseline MCE   │
                          └─────────────────┘

        ┌──────────────────────────────────────┐      ┌──────────────────────────────┐
        │ Insulin 1.5mU/kg/min + 25% Dextrose    │      │  Guideline-directed therapy   │
        │                                        │      │          (control)            │
        └──────────────────────────────────────┘      └──────────────────────────────┘
                          │                                           │
                          ▼                                           ▼
        ┌──────────────────────────────┐              ┌──────────────────────────────┐
        │ Repeat MCE at 30, 60, 120 mins│              │ Repeat MCE at 30, 60, 120 mins│
        └──────────────────────────────┘              └──────────────────────────────┘
                          │
                          ▼
        ┌──────────────────────────────────┐
        │ Discontinue Insulin, wean Dextrose │
        └──────────────────────────────────┘
```
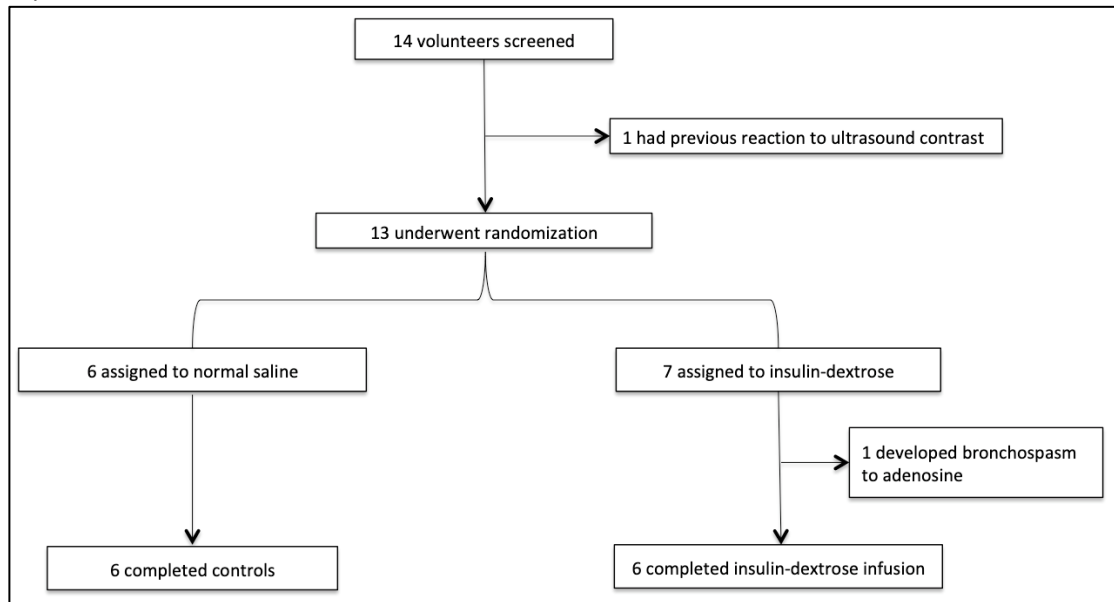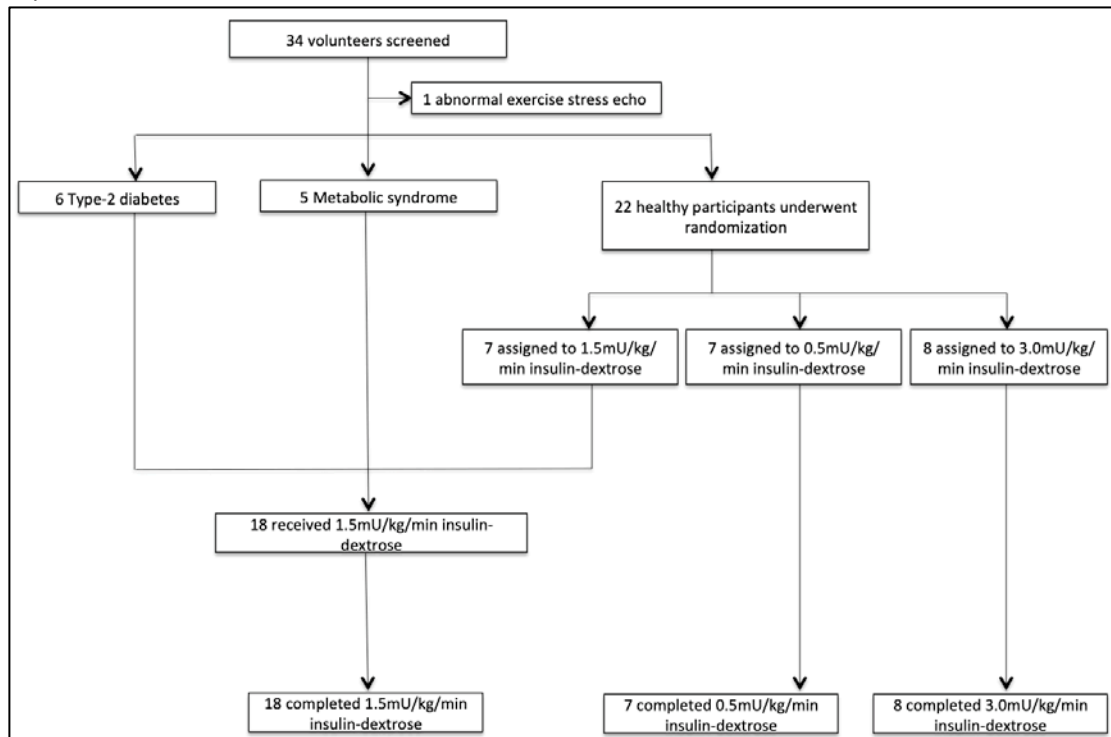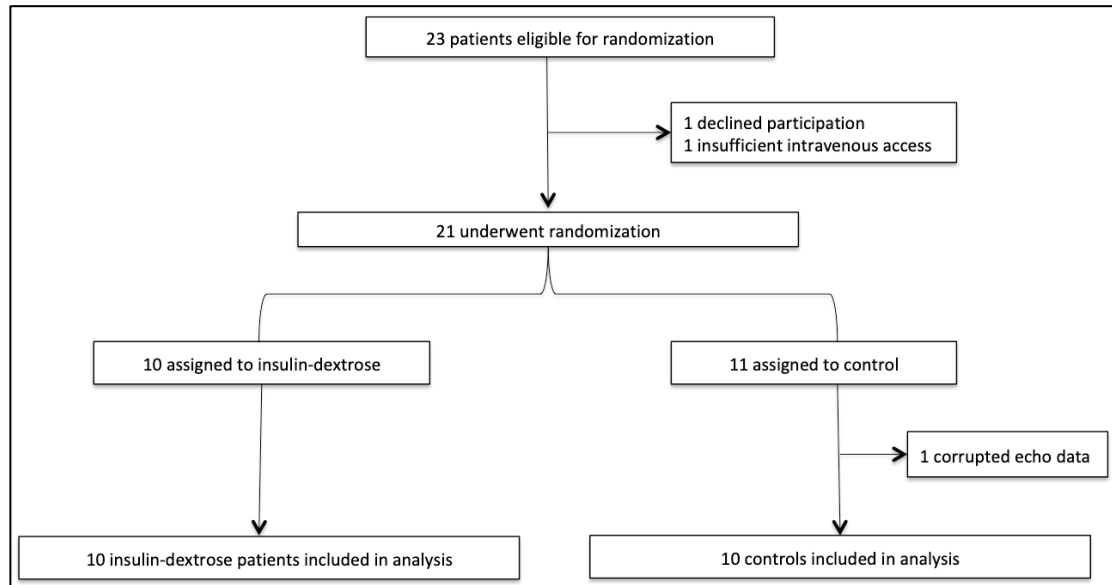
Recruitment flow diagrams

Experiment 1

Experiments 2 and 3

Experiment 4

List of regular medications taken by participants at time of enrolment

Experiment 1: None

Experiment 2:
0.5mU/kg/minute insulin group: 1 Aspirin, 2 Statin
1.5mU/kg/minute insulin group: 1 Aspirin, 1 Statin, 1 Angiotensin Receptor Blocker or ACE Inhibitor
3.0mU/kg/minute insulin group: 1 Statin.

Experiment 3:
Metabolic Syndrome group: 1 Aspirin, 1 Statin, 2 Angiotensin Receptor Blocker or ACE Inhibitor
Type-2 diabetes mellitus group: 2 Aspirin, 2 Statin, 2 Angiotensin Receptor Blocker or ACE Inhibitor, 4 Metformin, 1 Gliclazide, 3 Gliptin, 1 Empaglofloxin, 1 long acting insulin

Adenosine / dipyridamole protocols

Dipyridamole was infused at 0.56mg/kg over 4 minutes to achieve hyperemia. Peak hyperemia occurs between 6 minutes and 10 minutes after commencing infusion.[2]
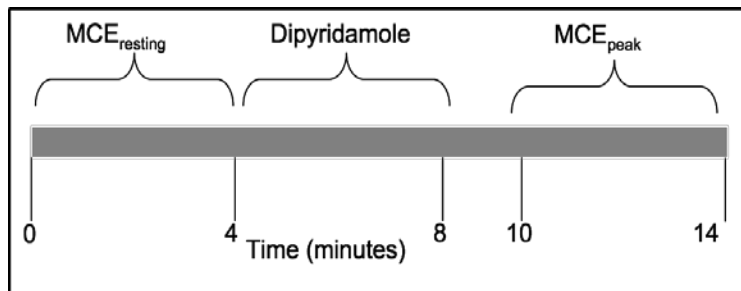
Adenosine was infused at 140mcg/kg/min over a total of 6 minutes. Peak hyperemia occurs from 3 minutes after commencing infusion.
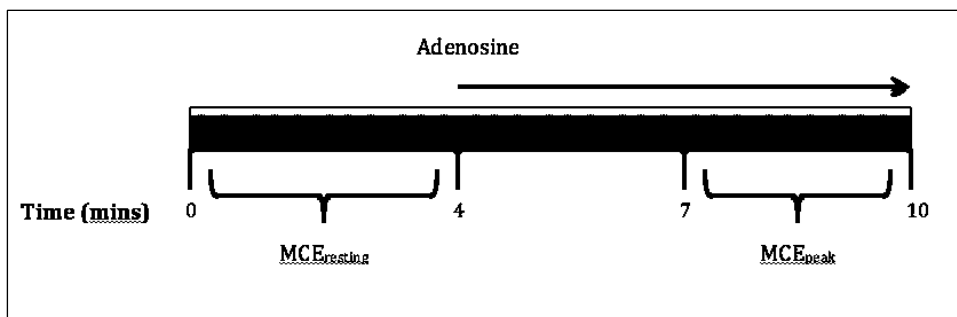
Metabolic Syndrome definition (International Diabetes Federation criteria 2005) [1]

Central Obesity (defined as waist circumference >94cm in males, >80cm in females)

plus any two of the following four:
Raised triglycerides (>150mg/dL)
Reduced HDL cholesterol (<40mg/dL in males, <50mg/dL in females)
Raised blood pressure (systolic BP > 130 or diastolic BP >85 mmHg or treatment of previously diagnosed hypertension)
Raised fasting plasma glucose (Fasting plasma glucose > 100mg/dL or 5.6mmol/L)

Supplementary Tables and Figures

Tables showing absolute MBF values in experiments 1 to 3

Experiment 1

Group		Time (mins)			
		0	30	60	120
Control	Rest	5.51±2.05	3.23±1.85	2.98±0.86	3.49±0.94
	Hyperemia	11.34±5.77	7.94±3.89	6.76±1.25	7.19±1.66
ID	Rest	4.36±3.08	3.89±1.63	3.52±1.40	4.07±1.28
	Hyperemia	10.96±7.95	10.22±4.62	12.18±4.38	12.76±5.37

Values are mean±SD MBF (dB^2/s)

Experiment 2

		Time (mins)	
Insulin Dose		0	60
0.5	Rest	2.62±1.84	3.65±1.63
	Hyperemia	4.83±2.42	6.70±2.24
1.5	Rest	1.78±0.86	2.18±1.04
	Hyperemia	4.18±1.93	5.75±2.34
3.0	Rest	2.34±1.79	3.39±1.82
	Hyperemia	4.40±3.84	5.96±2.84

Values are mean±SD MBF (dB^2/s)

Experiment 3

		Time (mins)	
Diabetic State		0	60
Healthy*	Rest	1.78±0.86	2.18±1.04
	Hyperemia	4.18±1.93	5.75±2.34
MetS	Rest	2.47±0.39	3.08±1.27
	Hyperemia	4.74±1.14	8.07±2.71
T2DM	Rest	4.03±1.78	3.61±3.41
	Hyperemia	6.13±2.91	5.52±4.47

*same data set as 1.5 dose group in Experiment 2
Values are mean±SD MBF (dB^2/s)

Table showing blood glucose and blood insulin levels in experiment 4 STEMI study patients who received insulin-dextrose infusion

Time (mins)	0	30	60	120	p-value
Glucose (mmol)	7.9±2.6	7.9±0.7	7.9±0.9	8.4±1.2	NS
Insulin (pmol/L)	62±53	340±276	361±285	493±361	0.006

Values are mean±SD

Experiment 4 Regional and Global MBF's (dB^2/s)

Group		Time (mins)				p value*
		0	30	60	120	
Control	Global MBF	6.64±5.20	3.89±1.92	4.24±3.95	4.27±3.86	NS
	Remote MBF	7.00±5.70	3.80±1.80	3.83±3.90	4.13±4.07	NS
	Ischemic MBF	7.71±9.42	7.14±9.54	5.44±9.39	5.59±7.06	0.03
ID	Global MBF	5.18±4.11	4.30±3.07	4.34±2.25	4.65±2.86	NS
	Remote MBF	4.59±3.49	4.19±3.23	3.18±2.26	4.10±2.35	NS
	Ischemic MBF	7.87±13.9	3.19±3.75	6.73±5.73	6.85±9.15	NS

*Mixed linear model longitudinal time series.
Numerical values are mean±SD.

References

1.   Alberti KG, Zimmet P and Shaw J. The metabolic syndrome--a new worldwide definition. *Lancet (London, England)*. 2005;366:1059-62.

2.   Chan SY, Brunken RC, Czernin J, Porenta G, Kuhle W, Krivokapich J, Phelps ME and Schelbert HR. Comparison of maximal myocardial blood flow during adenosine infusion with that of intravenous dipyridamole in normal men. *Journal of the American College of Cardiology*. 1992;20:979-85.