



Centre for
Heart Lung Innovation
UBC and St. Paul's Hospital



Obesity Paradox in Sepsis

Keith R. Walley, MD

St. Paul's Hospital

University of British Columbia

Vancouver, Canada

Disclosure / Conflict of Interest

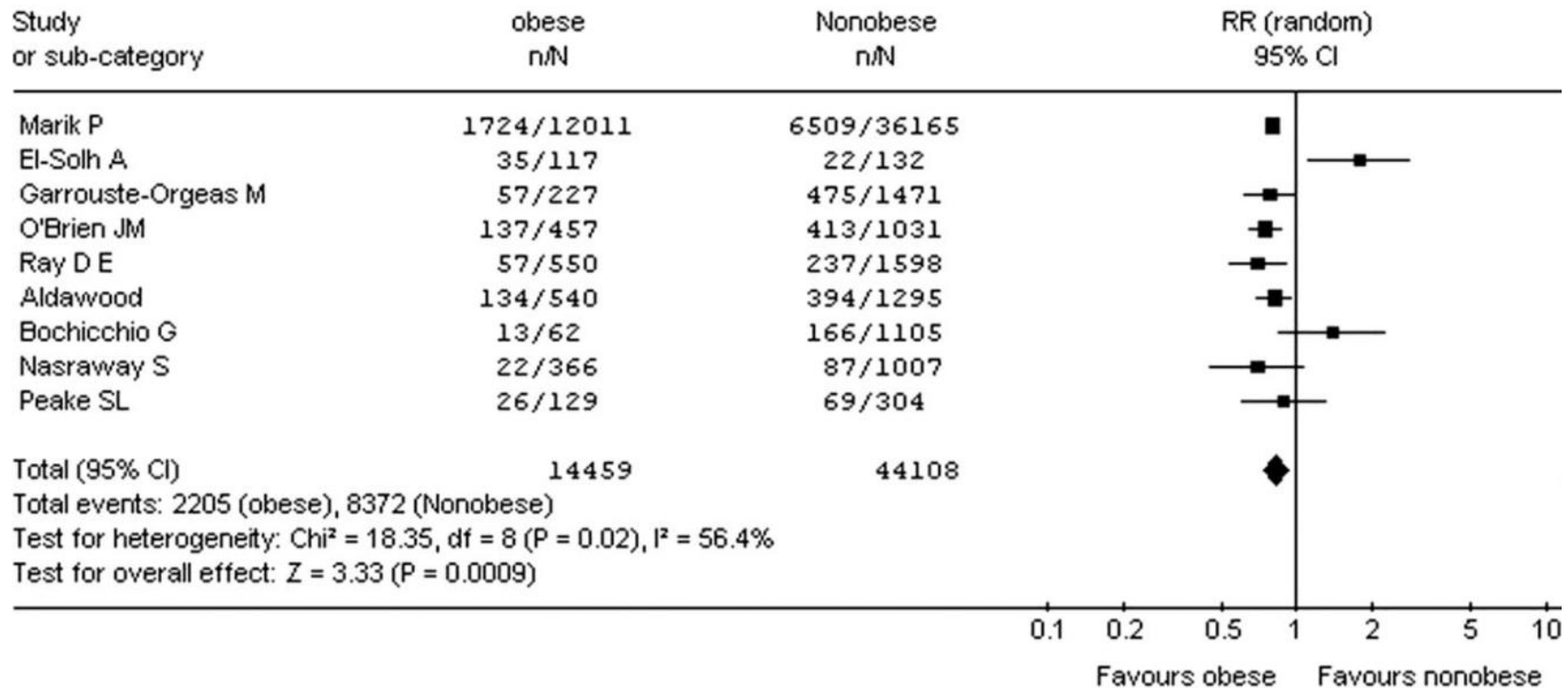
- No Conflict of Interest with respect to this presentation.

Obesity Paradox

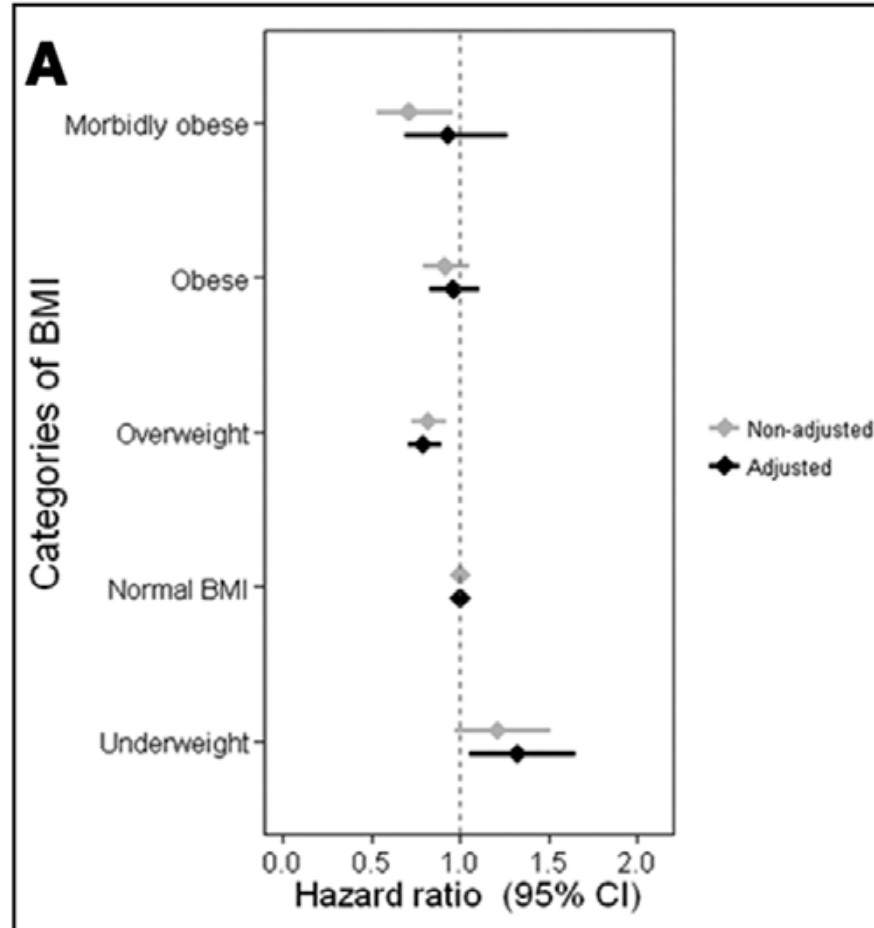
- Critically ill obese patients have better outcomes despite:
 - Diabetes
 - Respiratory dysfunction
 - Chronic inflammatory state
- Is this true in sepsis?
- Is the inflammatory response different?
- Relationship to cytokines, lipoprotein levels?

Critically ill obese patients: meta-analysis

Review: Influence of obesity on mortality in intensive care units
 Comparison: 01 RCT
 Outcome: 01 In-hospital Mortality

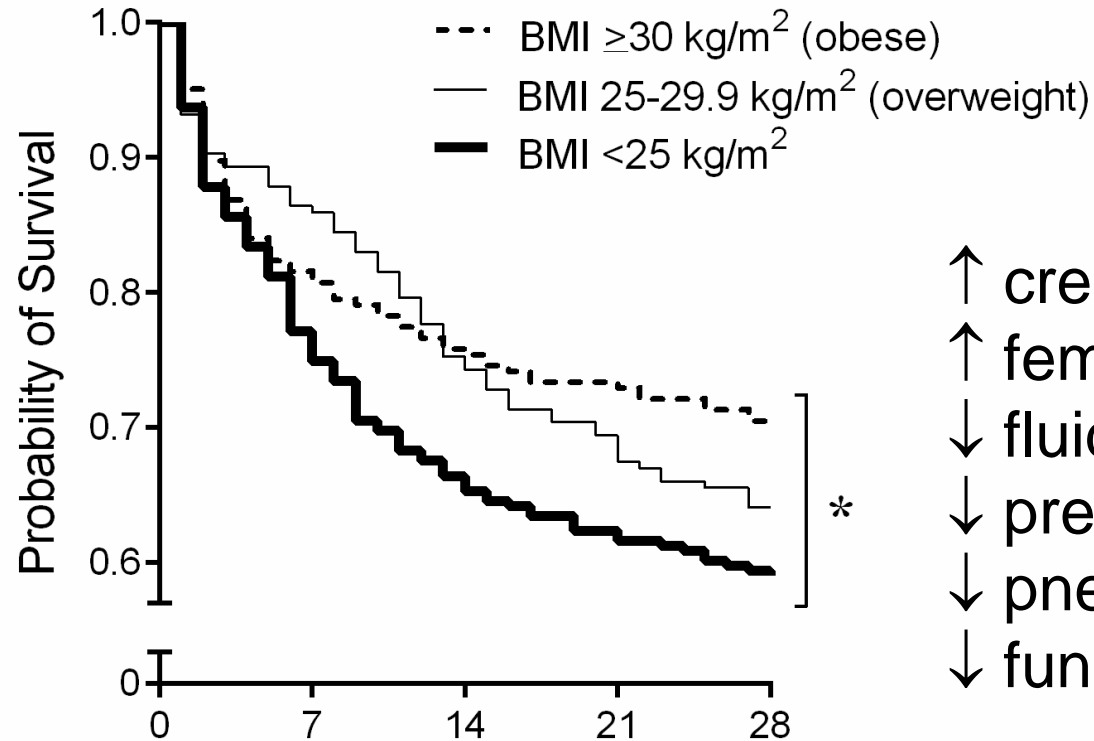


60-Day In-Hospital Mortality (ICON ICU patients n=8829)



p = 0.018

Septic shock: VASST



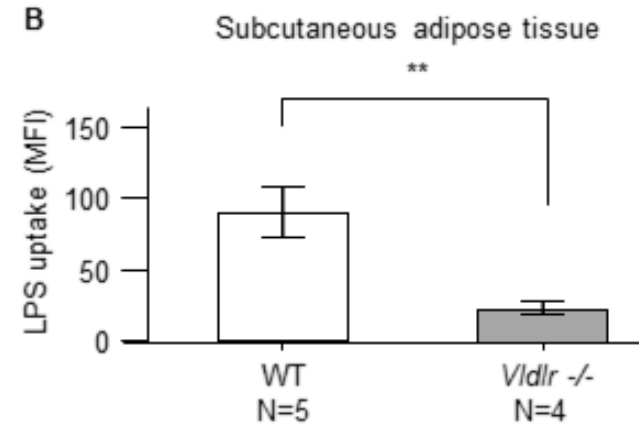
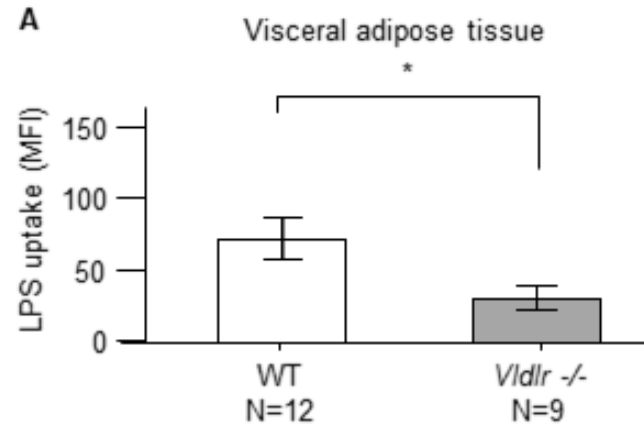
- ↑ creatinine 191 vs 130 μ mol/L
- ↑ female 45 vs 38%
- ↓ fluid/kg 130 vs 180 mL/kg
- ↓ pressor/kg NE 0.13 vs 0.26
- ↓ pneumonia 35 vs 50%
- ↓ fungal 8.2 vs 15.6%

Number at Risk

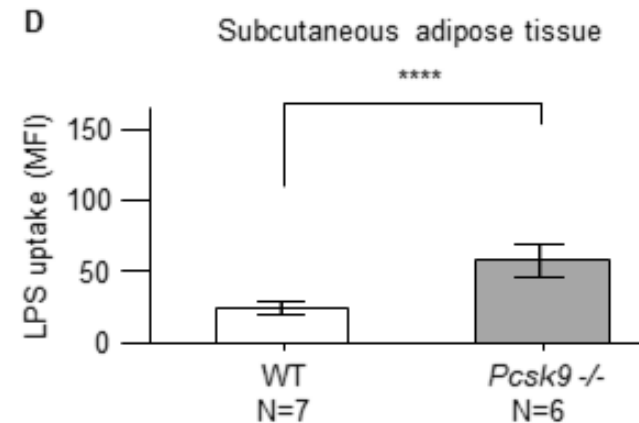
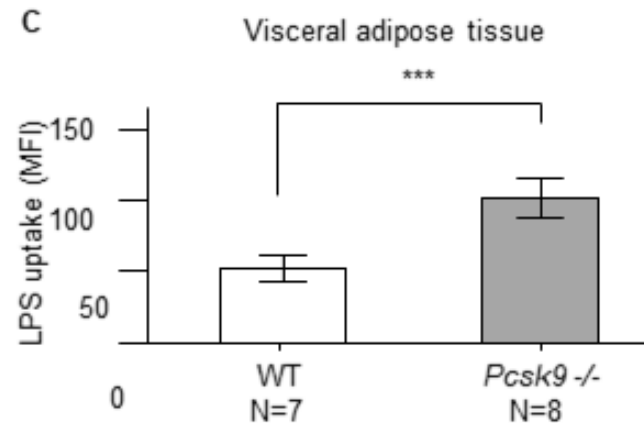
	0	7	14	21	28
BMI ≥ 30 kg/m ²	245	201	187	179	174
BMI 25-29.9 kg/m ²	209	181	160	143	135
BMI <25 kg/m ²	276	220	183	169	162

LPS is sequestered in adipose tissue via VLDLR

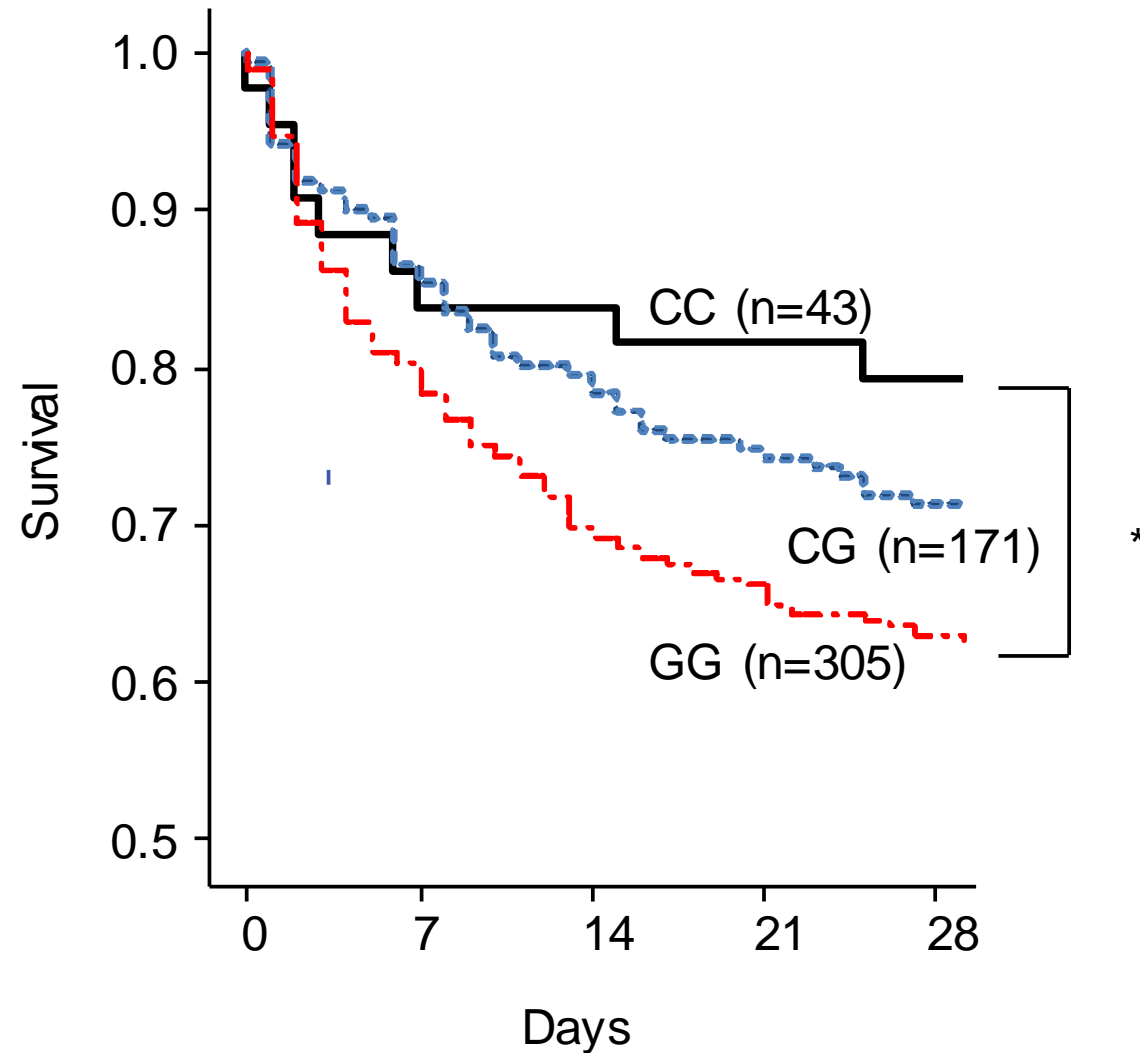
Decreased VLDLR expression using *Vldlr* knockout



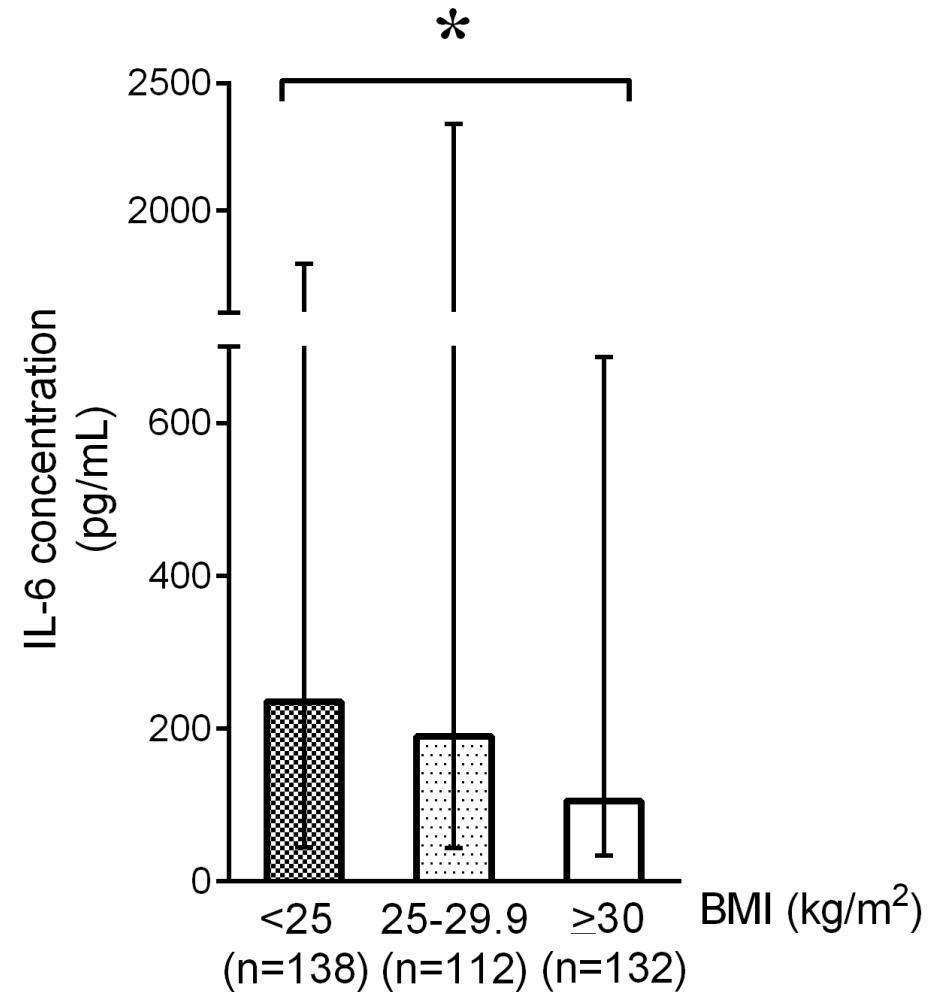
Increased VLDLR expression using *Pcsk9* knockout



↑ VLDLR increases septic shock survival (VLDLR rs7852409 C allele is gain-of-function)

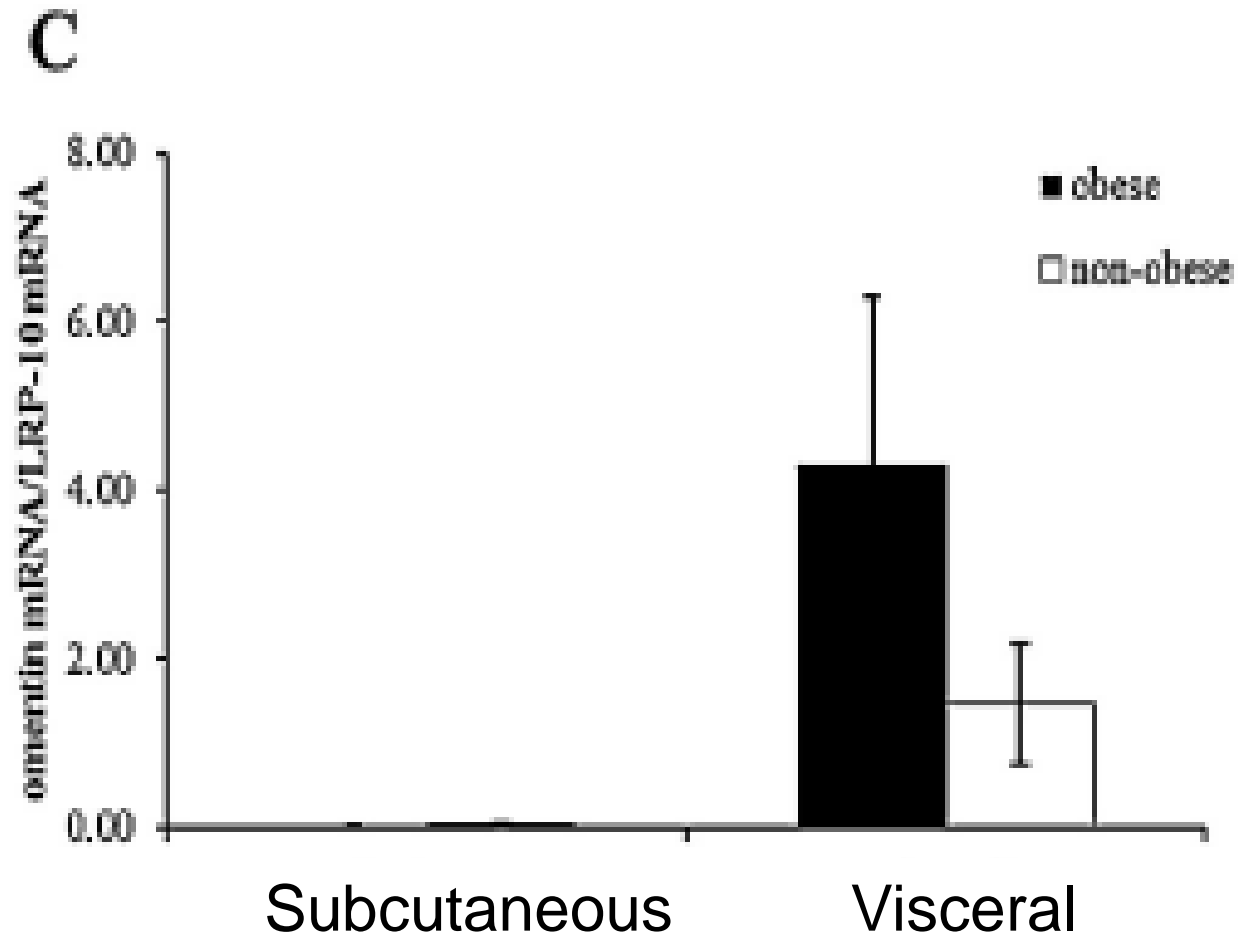


Cytokine inflammatory response



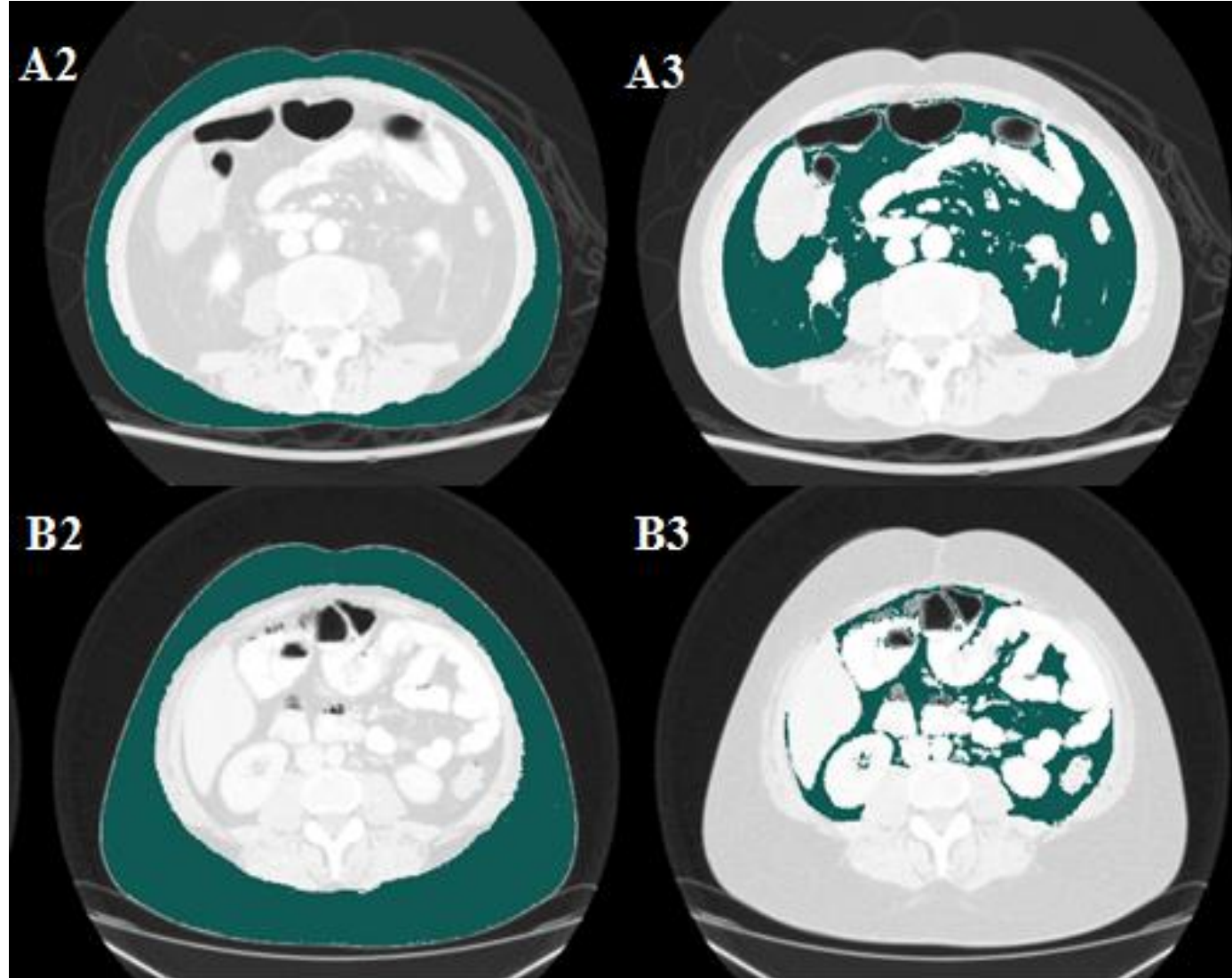
Subcutaneous adipose tissue may be “good” fat

Visceral adipose tissue may be “bad” fat



VAT/SAT

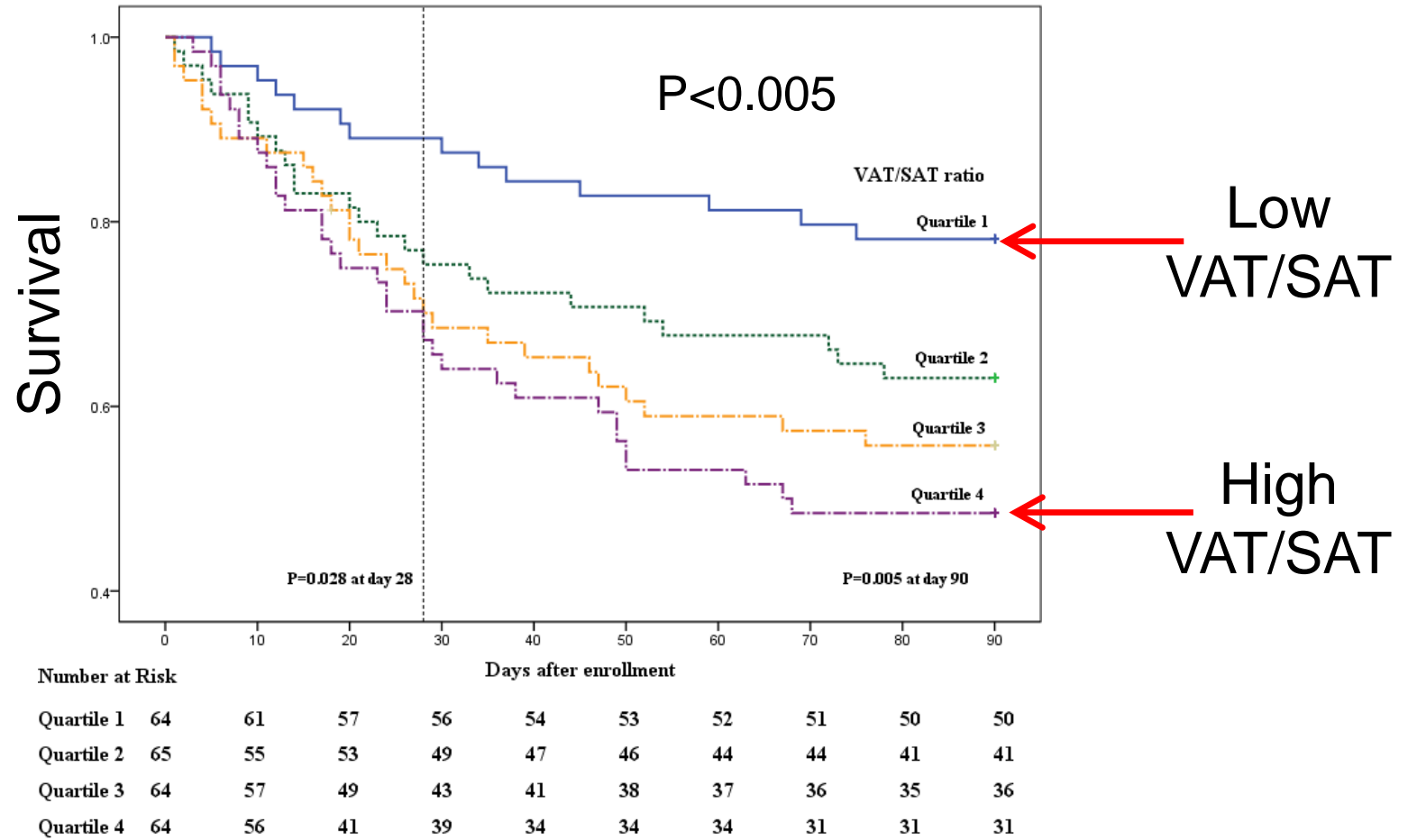
Visceral Adipose Tissue / Subcutaneous Adipose Tissue



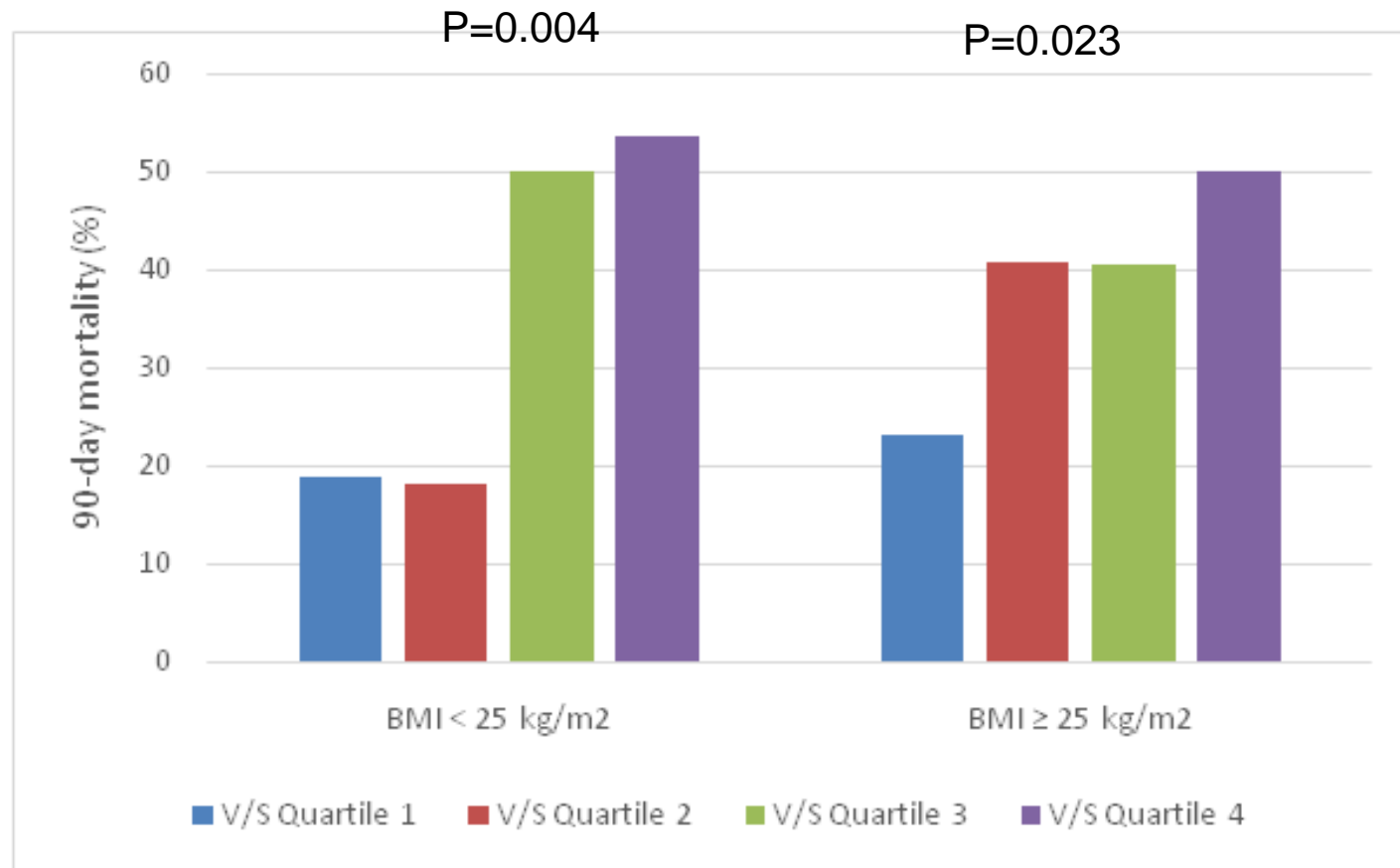
High
VAT/SAT
(Bad?)

Low
VAT/SAT
(Good?)

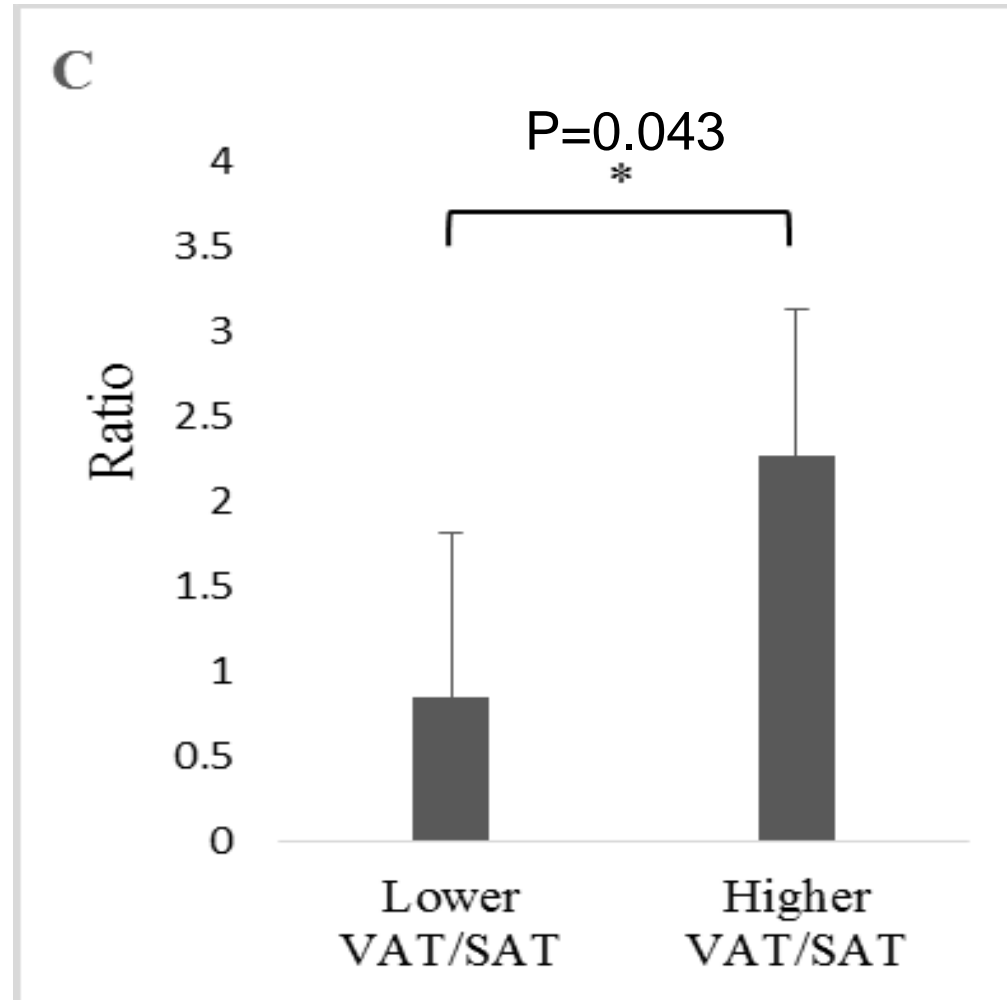
High VAT/SAT is bad



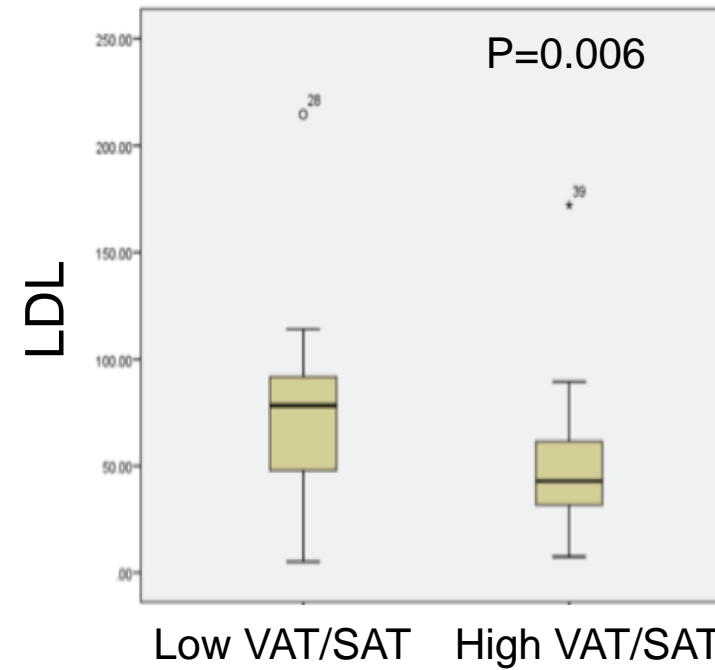
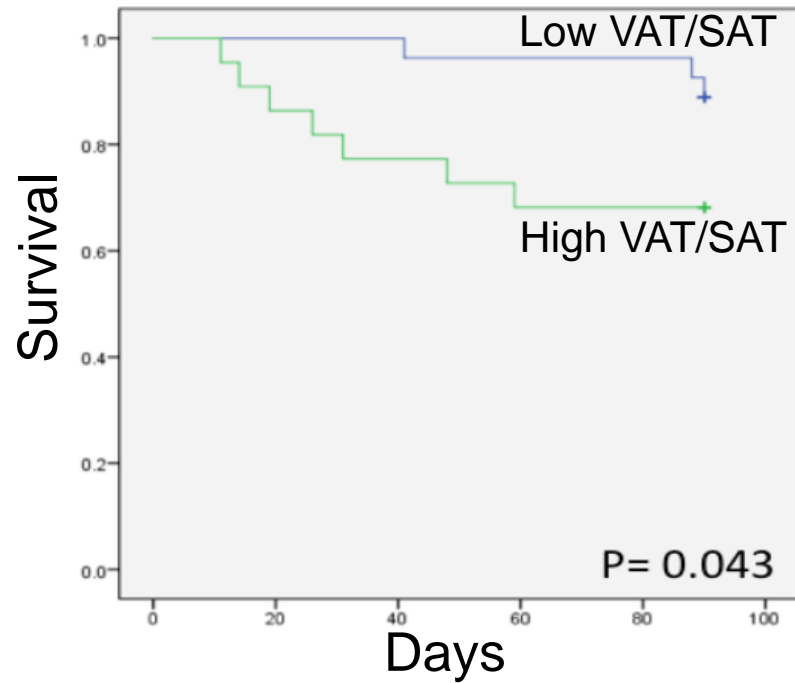
90-day mortality by VAT/SAT



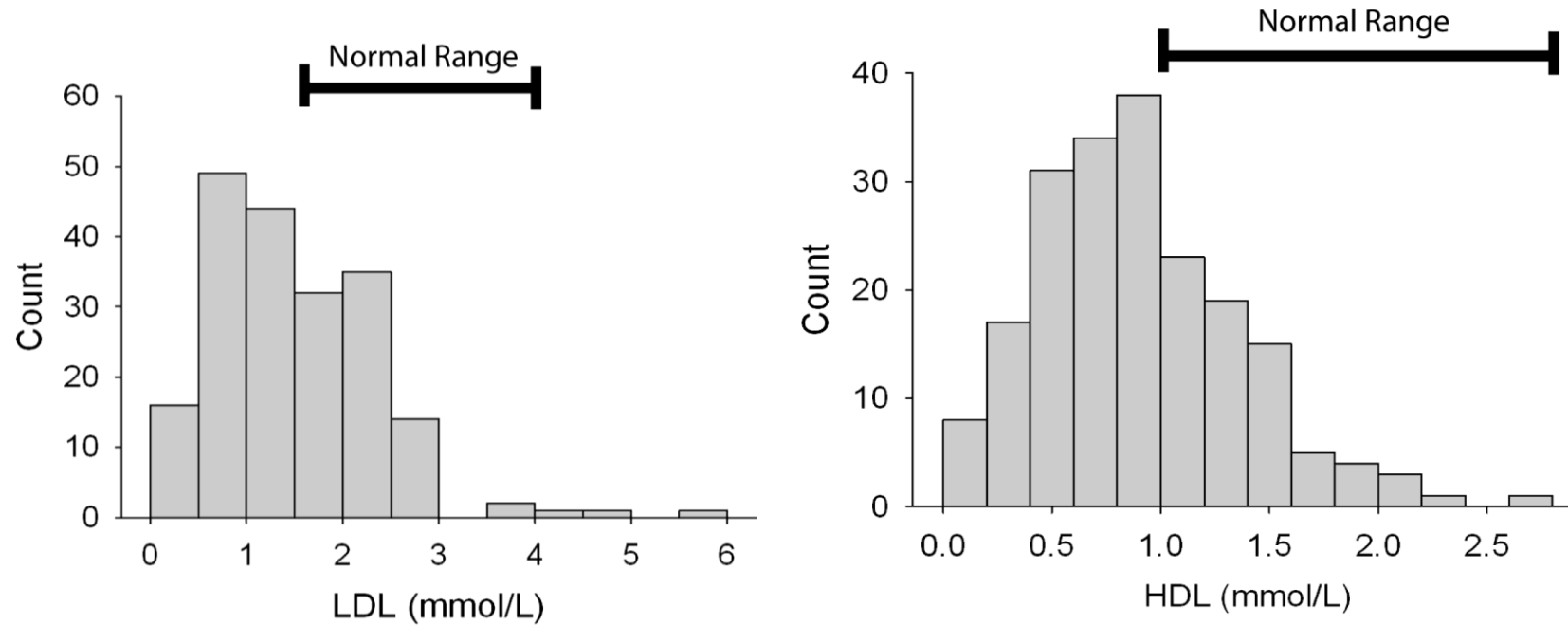
Pro/anti-inflammatory ratio: IL8 / IL10



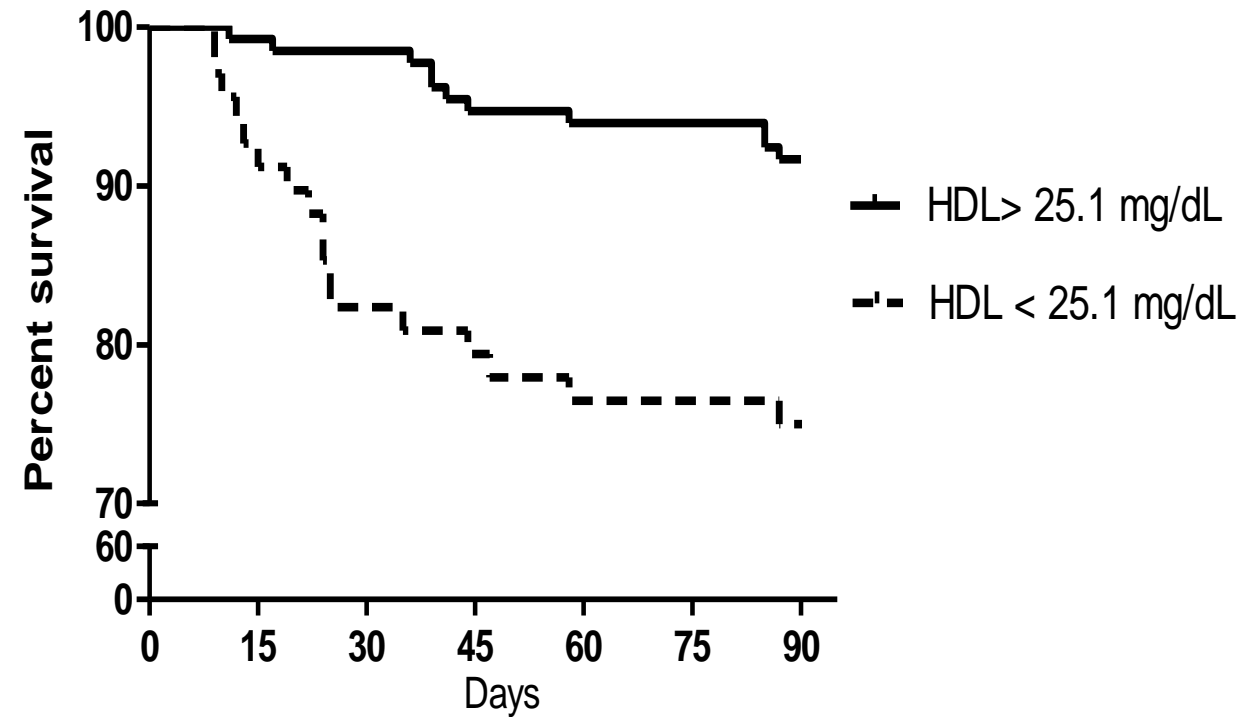
VAT/SAT related to LDL, HDL?



Low LDL, HDL levels in sepsis



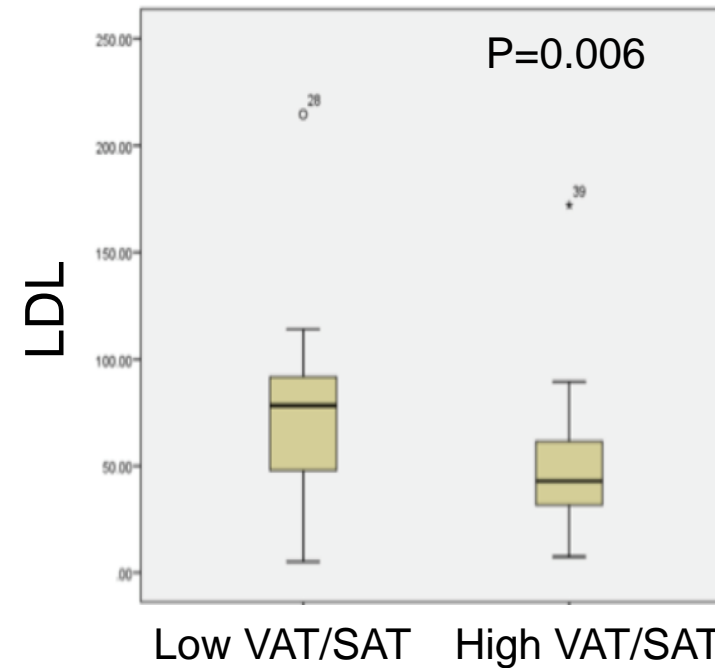
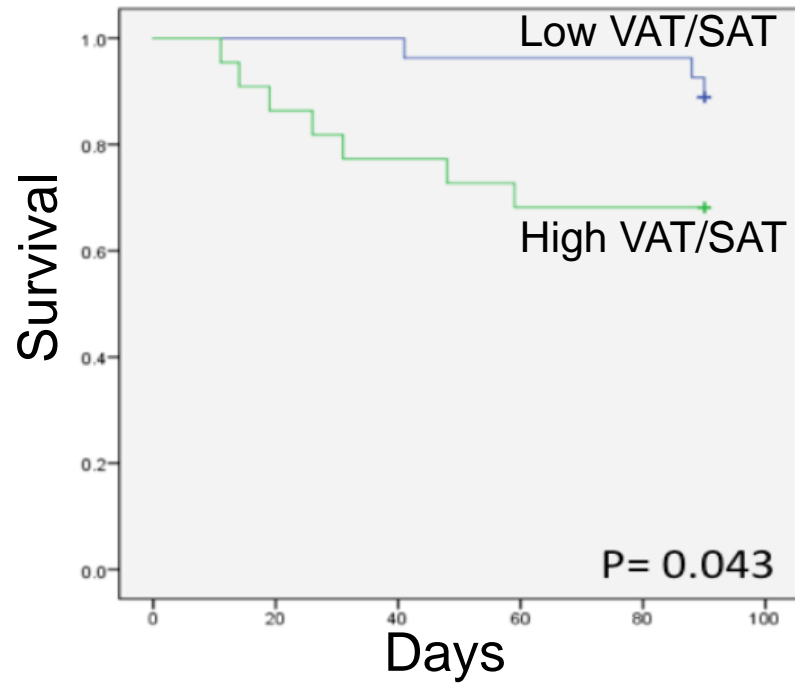
Low LDL, HDL are bad



At-risk patients:

HDL > 25.1mg/dL	132	131	130	125	124	123	121
HDL < 25.1mg/dL	68	62	57	54	52	52	51

VAT/SAT related to LDL, HDL?



Conclusions

- Obesity paradox is particularly strong in sepsis
 - High BMI protects against mortality
 - Better nutritional state?
 - Sequesters pathogen lipids?
- Low VAT/SAT is beneficial at any BMI
- Subcutaneous Adipose Tissue (SAT) is good
 - Not as pro-inflammatory as VAT
 - Protects against lipoprotein drop

Clinical Implications

- Another reason nutrition is important?
- Novel strategies to increase LPS sequestration in adipose tissue (PCSK9 inhibitors)?
- Do anti-inflammatory therapies work better in patients with high VAT/SAT?
- Important to understand why low LDL, HDL are low in sepsis and associated with adverse outcome (supplement HDL?)



John Boyd
Jim Russell
Harvey Coxson
Mihai Cirstea
Chawika Pisitsak
Bandarn Suetrong
Kelly Genga
Joseph Lee

VASST Investigators

Keith.Walley@hli.ubc.ca



Centre for
Heart Lung Innovation
UBC and St. Paul's Hospital



Size of the problem

Severe Sepsis
All hospitalized
Half ICU

Iwashyna. J Am Ger Soc. 60:1070-1077, 2012
Angus. Crit Care Med. 29:1303-1310, 2001
Gaeski. Crit Care Med 41(5):1167-1174, 2013

