

# Challenging Traditional Cardiovascular Risk Assessment

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## The Ancestral Health Symposium



### Introduction

Cardiovascular risk has been traditionally assessed by measuring cholesterol (stored in lipoproteins) based on Framingham methodology. We present a modern-day approach that properly addresses the root causes, including metabolic disease and hormonal dysregulation. Tools including the insulin assay and cardiovascular imaging such as the calcium heart scan prove useful.

Pathologist Joseph R. Kraft, MD performed over 16,000 five hour insulin assays on patients and found glycemic measurement to be the inferior method. Based on autopsy data, Dr. Kraft supposed the following:

**"Those identified with cardiovascular disease, not identified with diabetes, are simply undiagnosed."**

Stanford University physician Gerald Reaven supported this supposition based on his work that described the insulin resistance syndrome or metabolic syndrome.

What are the best methods to assess CV risk?

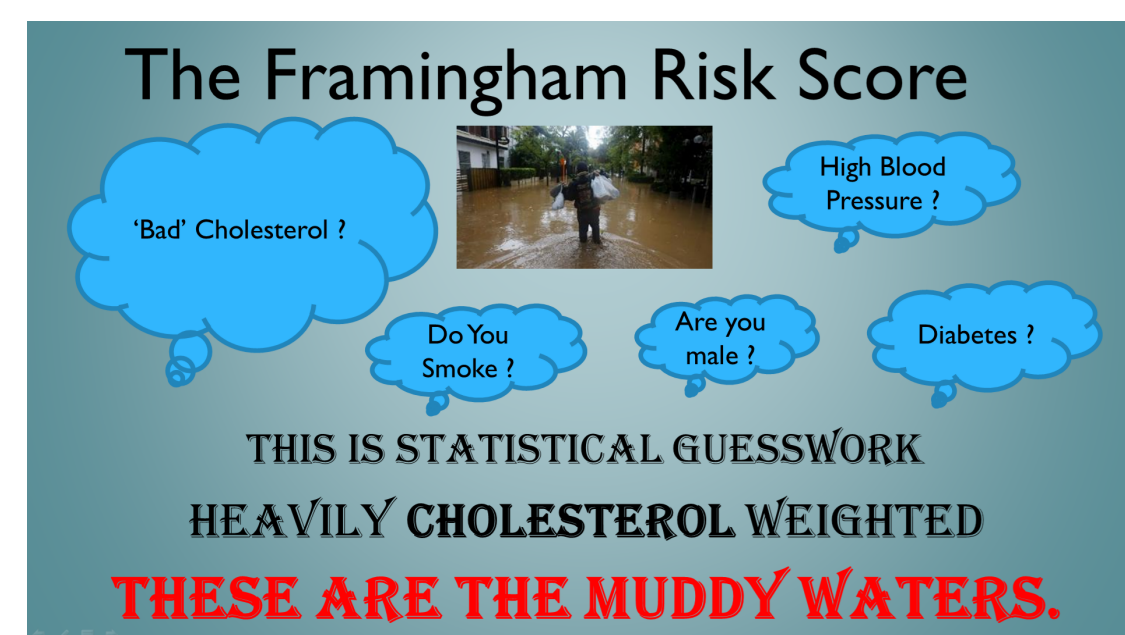
### Cholesterol & Cardiovascular Risk

#### The Muddy Waters of Framingham

In the late 1940s, in the small town of Framingham Massachusetts scientists began following the population to see who developed heart disease. They tracked many variables, noting the ones that appeared to be associated with bad outcomes and called them risk factors. We know them today as 'bad cholesterol', smoking, HTN, diabetes and so on. Since the original Framingham work there have been updates to these guidelines, various tools and risk calculators all based on a central theme, to lower 'bad cholesterol', including LDL-C, LDLp and ApoB. The question as suggested by Framingham remains. Is cholesterol innately toxic?

Framingham remains problematic. It is difficult to apply population risk to the individual. Although diabetes is a risk factor hyperglycemia is not properly measured, insulin isn't measured and diabetes as a contributing factor is underemphasized as a result. Atherosclerosis is now recognized as a complex metabolic disease and 'the muddy waters' of Framingham fails to address this.

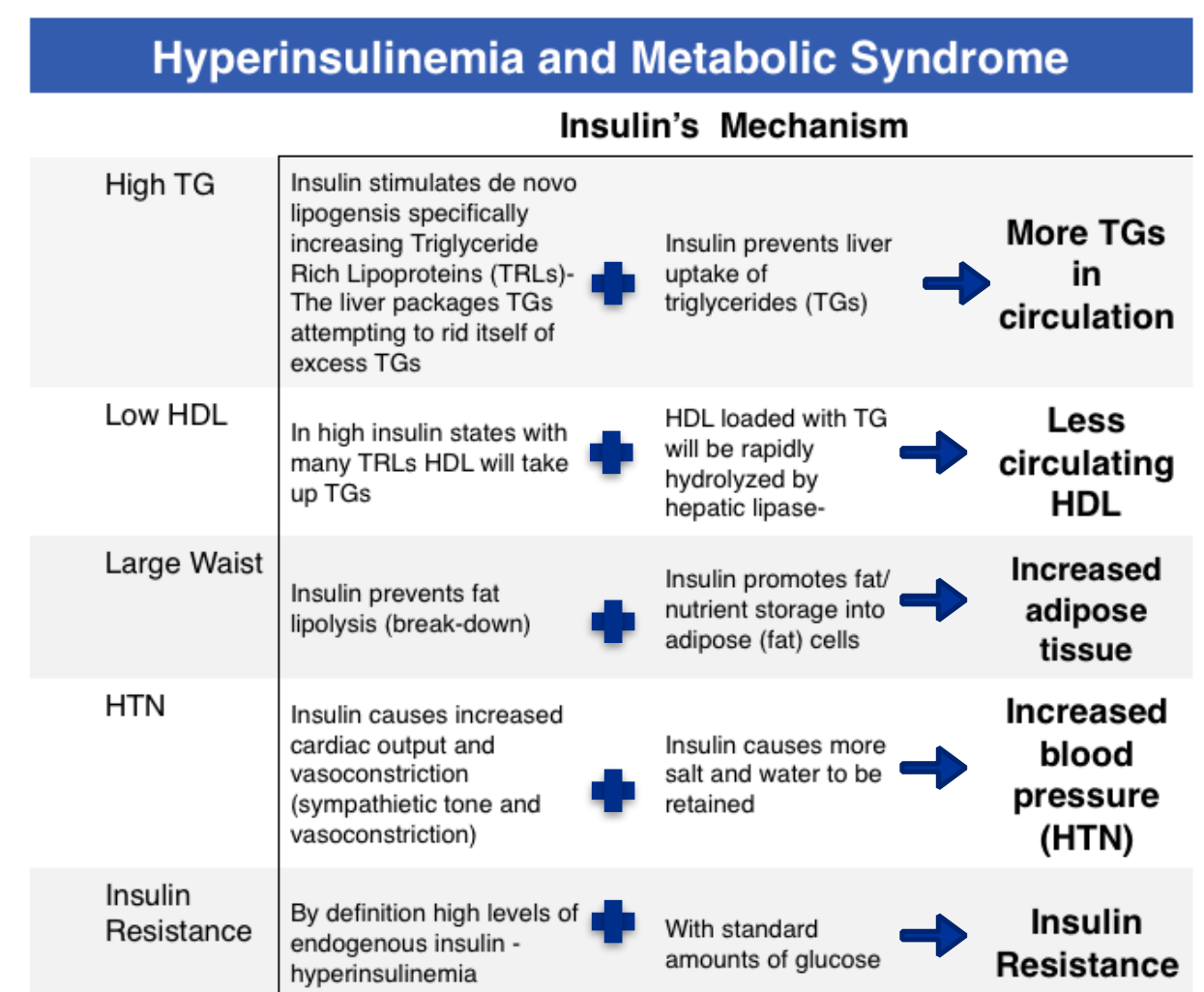
Consider that cholesterol is vitally important to cell function as it constitutes cell membranes and hormones. Lipoprotein containing cholesterol serves to transport fat soluble substances in a water based blood system. Cholesterol helps to repair damaged blood vessels that are exposed to the forces of inflammation, oxidative stress and advanced glycation and can become damaged itself. Perhaps cholesterol's presence is a consequence of metabolic disease rather than a cause. It's Metabolic Mayhem!



### Metabolic Syndrome

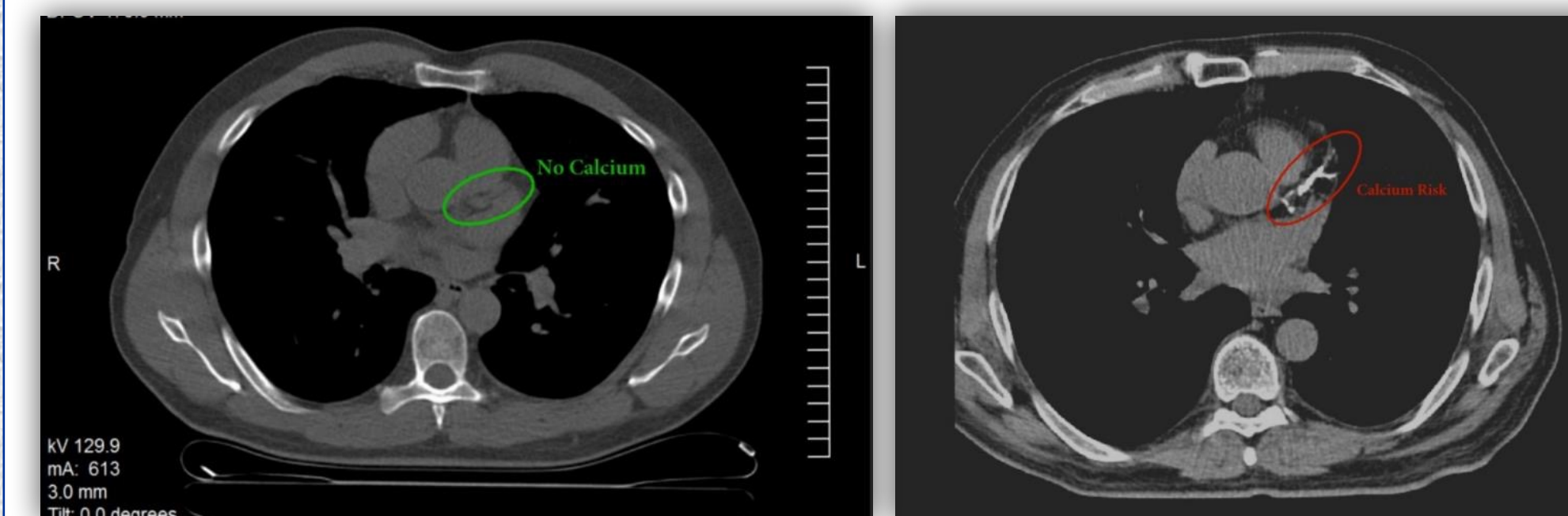
#### Insulin Resistance Syndrome

3 of 5 Criteria for Diagnosis



### The Calcium Heart Scan

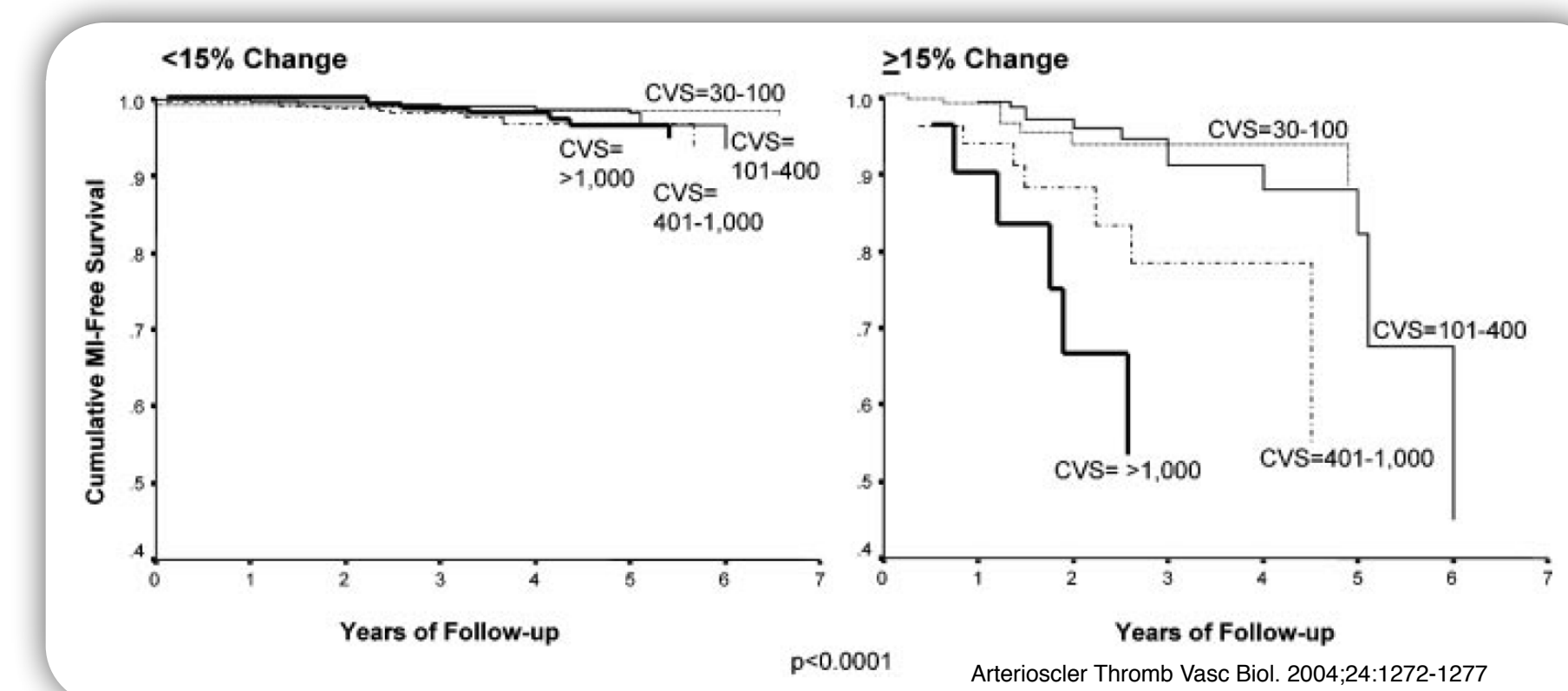
#### Calcium sees the Disease - Framingham Guesses



| Calcium Score | Risk Equivalent | 10-Year Event Rate, % |
|---------------|-----------------|-----------------------|
| 0             | Very low        | 1.1-1.7               |
| 1-100         | Low             | 2.3-5.9               |
| 101-400       | Intermediate    | 12.8-16.4             |
| >400          | High            | 22.5-28.6             |
| >1000         | Very high       | 37                    |

| Muddy Waters: Framingham Risk Score | 0   | 1-80 | 81-400 | 401-600 | >600 |
|-------------------------------------|-----|------|--------|---------|------|
|                                     | 10% | 2.4% | 5.4%   | 16%     | 25%  |
|                                     |     |      |        |         | 36%  |

#### Goal is to Stabilize Calcium Progression



### Conclusions

- Insulin is an important biomarker for predicting cardiovascular risk
- The current recommended approach to assess cardiovascular disease is a cholesterol panel with secondary questioning for risk factors.
- Insulin assays and calcium scores are far more sensitive tools for the early assessment of cardiovascular risk.
- Insulin resistance and hyperinsulinemia are important predictors of risk compared to LDL-C.
- Further research is needed to show that lifestyle changes including LCHF diet address hormonal dysregulation and improve cardiovascular outcomes.

### References

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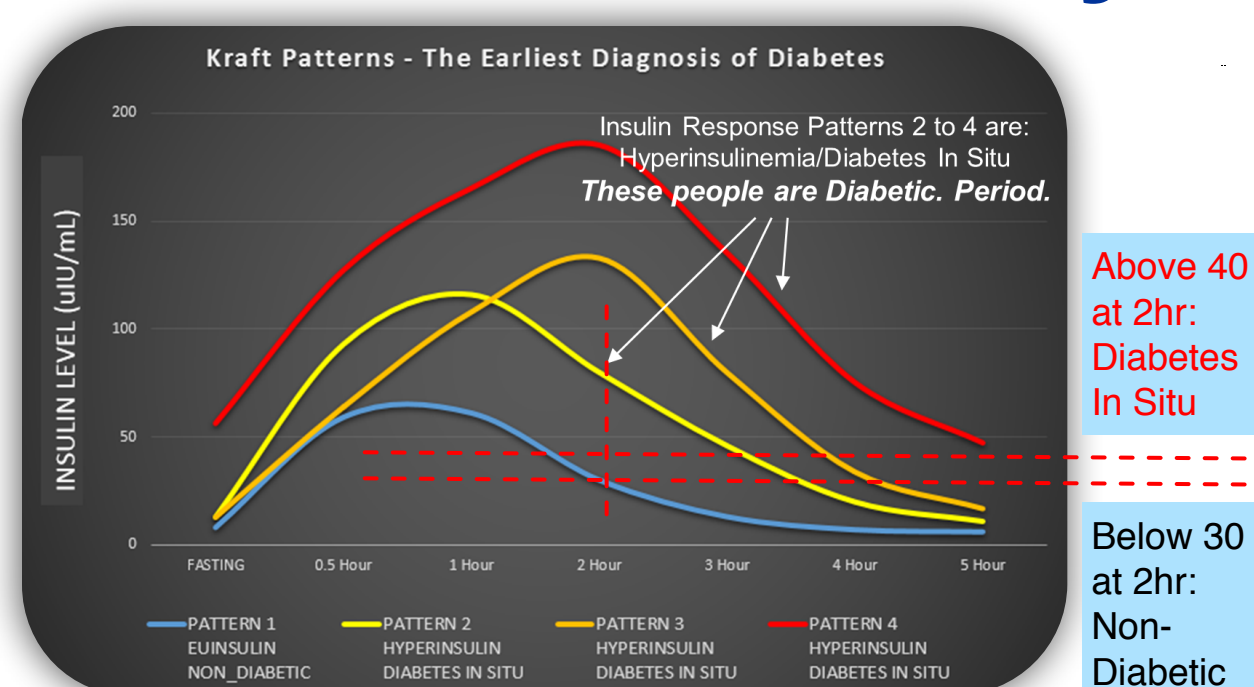
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### The Insulin Assay



| Hyperglycemia | Hyperinsulinemia       |                        |  | Totals | PPV 97% | NPV 28% |
|---------------|------------------------|------------------------|--|--------|---------|---------|
|               | Disease                | No Disease             |  |        |         |         |
| Positive      | True Positives 6180    | False Positives 186    |  | 6366   |         |         |
| Negative      | False Negatives 5764   | True Negatives 2254    |  | 8018   |         |         |
| Totals        | 11944                  | 2440                   |  | 14384  |         |         |
|               | <b>Sensitivity 52%</b> | <b>Specificity 92%</b> |  |        |         |         |

Recompiled from Kraft, Diabetes Epidemic & You. 2011

### Insulin & Cardiovascular Risk

Although the mechanisms are vastly complex, insulin signaling and hormonal dysregulation best describe atherosclerosis as a metabolic disease. Hyperinsulinemia, hyperglycemia and insulin resistance are intimately related, but it has been proposed that hyperinsulinemia is the first insult.

Hyperinsulinemia alters lipid metabolism unfavorably. Excess energy converted to fat (de novo lipogenesis) leads to the overproduction of triglyceride rich lipoproteins including VLDL, IDL and LDL and circulating free fatty acids. In the hyperinsulinemic state lipoprotein uptake is diminished, resulting in increased circulating time and concentration of lipoprotein that promotes inflammation and oxidative stress.

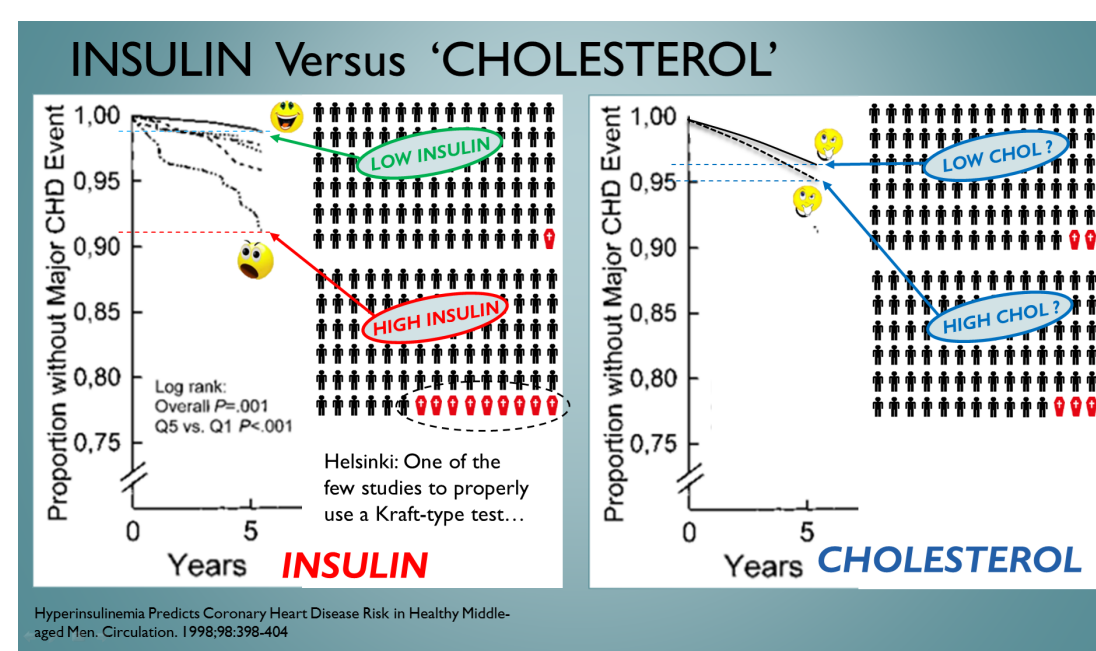
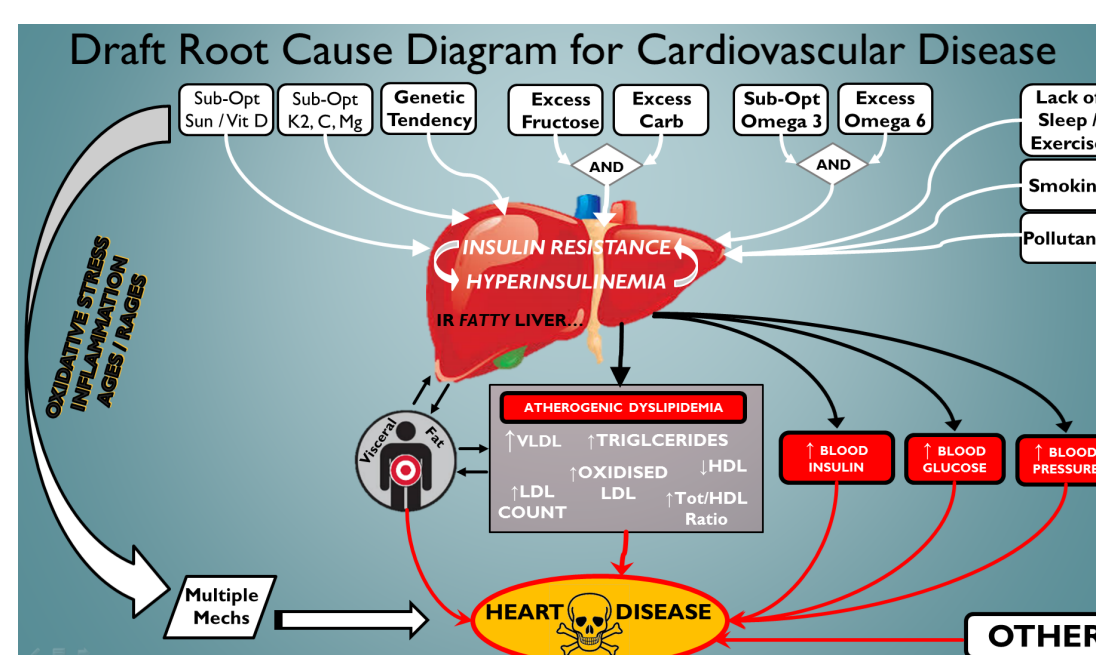
Hyperinsulinemia raises blood pressure by increasing sympathetic tone, decreasing sodium and water excretion in the kidneys, and directly vasoconstricting blood vessels.

Hyperinsulinemia precedes insulin resistance syndrome (arguably a dominant precursor for heart disease) through many mechanisms including atherogenic dyslipidemia, fatty liver, hyperglycemia, visceral fat accumulation and adiposity.

Hyperinsulinemia may play a direct role in atherogenesis through the interaction of receptors on the blood vessel wall.

Here we describe hyperinsulinemia as a root cause and yet it is not properly measured. The literature confirms that with more diabetes we see more heart disease. Recent estimates show that over half or the US population are diabetic and pre-diabetic, an estimate lacking insulin data. Fewer studies do properly measure insulin and blood sugar - but when compared to cholesterol, insulin predicts CV risk more precisely. Helsinki policeman study is one example.

### Metabolic Mayhem



Recompiled from Kraft, Diabetes Epidemic & You. 2011