

# Background - I

- Cardiovascular disease is increased in treated HIV+ patients<sup>1</sup>
- Common risk factors for CVD disease are frequently present in HIV+ patients<sup>2</sup>
- Identification of HIV+ patients with elevated CVD risk remains problematic
- Traditional CVD risk markers may not reliably identify a significant minority of at risk patients<sup>3</sup>

# Background - II

- Non-traditional CVD risk markers have been evaluated to determine their additional usefulness in identifying at risk non-HIV patients<sup>4</sup>
- A cluster of metabolic abnormalities including (1) small, dense LDL particles, (2) increased apolipoprotein-B, and (3) increased insulin levels, has been shown to reliably add useful CVD risk information to that provided by traditional markers<sup>5</sup>
- This “metabolic triad” is prevalent among abdominally obese individuals with increased visceral adipose tissue (VAT)

# Background - III

- Surrogate markers for components of the metabolic triad, waist circumference for Apo-B and increased insulin, and triglycerides for small dense LDL, have been shown to reliably identify patients at high risk for CVD<sup>6</sup>
- In HIV(-) patients the combination of distinct metabolic abnormalities plus body composition changes, referred to as the Metabolic Syndrome (MetS), occurs in over 30% of patients older than 50<sup>7</sup>
- The diagnosis of Metabolic Syndrome, using established criteria, confers an increased CVD risk on affected patients<sup>8,9</sup>
- HIV+ patients with features of the Met-S may be at particular risk for CVD

# Hypotheses

- The combination of an increased waist circumference (WC) with an increased fasting serum triglyceride (TG) may identify HIV+ patients at high risk of CVD
- HIV+ patients identified by the combination of increased WC plus increased TG may also have other abnormal metabolic and body composition parameters which are known CVD risk factors

# Methods - I

- Convenience sample of 94 regularly followed HIV infected males
- Patients underwent DXA scans (Lunar or Norland) for body composition analysis
- Chart review to obtain: CVD risk factors; antiretroviral history; anthropometrics; BP readings; lab data including fasting lipids, glucose, insulin, HOMA

# Methods - II

- The date of measurement of the waist circumference was taken as the reference date
- DXA derived body composition data includes:
  - BMI
  - Trunk Fat Mass (Trunk FM)
  - % Trunk FM/Total Trunk Tissue (%Trunk FM/Trunk Mass)
  - % Trunk FM/Total Body Fat Mass (%Trunk FM/TBFM)
  - Trunk FM/Peripheral Fat Mass (Trunk/PeriFM)
- Fasting metabolic parameters obtained from the routine testing date closest to the reference date were extracted and the time interval between these 2 dates calculated (WC-Lab diff)
- The time interval between the WC reference date and the DXA scan was calculated (WC-DXA diff)
- BP readings were the average of the reading at the time of the WC measurements and of BP readings before and after this reference date

# Methods - III

- Subjects were grouped into distinct categories for comparison of variables
  - Hypertriglyceridemic – Waist classification
    - I – WC > 90 cm + TG's > 2.0 mmol/L
    - II – WC > 90 cm + TG < 2.0
    - III – WC < 90 and TG > 2.0
    - IV – WC < 90 cm + TG < 2.0
  - Framingham derived scores were used to classify subjects as being in low, moderate, or high 10-year CVD risk
- The diagnosis of Metabolic Syndrome was made according to published NCEP criteria
- Comparison of means +/- S.D. or medians and 95% CI, with correction factors as needed, was done

# Hypertriglyceridemic – Waist Classification

- I – WC > 90 cm and TG > 2.0 mmol/L
- II – WC > 90 cm and TG < 2.0 mmol/L
- III – WC < 90 cm and TG > 2.0 mmol/L
- IV – WC < 90 cm and TG < 2.0 mmol/L

# Results – Clinical Characteristics - I

| Variable                         | Group 1<br>n = 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|----------------------------------|-------------------|-------------------|-------------------|-------------------|
| Age (yr)                         | 51 ± 11           | 49 ± 8            | 49 ± 7            | 47 ± 9            |
| Current Rx PI+ NRTI              | 13/27 (48%)       | 3/14 (21%)        | 13/29 (45%)       | 6/24 (25%)        |
| NNRTI+ NRTI                      | 6/27(22%)         | 8/14 (57%)        | 5/29 (17%)        | 7/24 (29%)        |
| NRTI only                        | 3/27(11%)         | 2/14 (14%)        | 5/29 (17%)        | 5/24 (21%)        |
| Other                            | 4/27(15%)         | 4/14 (7%)         | 3/29 (10%)        | 4/24 (17%)        |
| CD4's                            | 470 ± 340         | 560 ± 275         | 465 ± 265         | 420 ± 220         |
| Log <sub>10</sub> V <sub>L</sub> | 2.4 ± 0.9         | 1.7 ± 0.4         | 2.4 ± 1.1         | 2.4 ± 1.1         |
| % V <sub>L</sub> <50             | 15/27 (56%)       | 12/14 (86%)       | 17/29 (59%)       | 14/24 (59%)       |

# Results – Clinical Characteristics - II

| Variable                        | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|---------------------------------|------------------|-------------------|-------------------|-------------------|
| WC (cm)                         | 98 ± 5           | 95 ± 6            | 83 ± 6            | 82 ± 6            |
| TG (mmol/L)                     | 4.2 ± 3.3        | 1.7 ± 0.5         | 4.3 ± 2.2         | 1.3 ± 0.4         |
| WC-Lab interval<br>(month)      | 0.2 ± 2.4        | 0.4 – 1.7         | 0.7 ± 1.9         | -0.4 ± 1.5        |
| WC-DXA interval<br>(month)      | -1.5 ± 7.3       | 1.6 ± 7.4         | -0.9 ± 7.6        | 0.2 ± 8.5         |
| Current/recent<br>cigarette use | 11/23 (48%)      | 6/13 (40%)        | 16/26 (62%)       | 17/22 (77%)       |

# Results – Lipid Parameters (median [95% CI])

| Variable                  | Group 1<br>n = 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|---------------------------|-------------------|-------------------|-------------------|-------------------|
| TC (mmol/L) <sup>1</sup>  | 5.8 (5.2-6.4)     | 4.7 (3.9-5.1)     | 5.5 (5.0-5.9)     | 4.5 (4.0-5.0)     |
| LDL (mmol/L) <sup>2</sup> | 3.2 (2.5-3.8)     | 2.8 (2.1-3.2)     | 2.8 (2.6-3.6)     | 2.5 (2.3-3.2)     |
| TG (mmol/L) <sup>3</sup>  | 3.1 (2.5-3.8)     | 1.8 (1.3-2.0)     | 3.3 (2.7-4.6)     | 1.3 (1.0-1.5)     |
| HDL (mmol/L) <sup>4</sup> | 1.2 (1.0-1.3)     | 1.1 (0.8-1.5)     | 1.1 (0.9-1.2)     | 1.2 (1.0-1.3)     |
| TC/HDL                    | 5.1 (4.4-5.5)     |                   |                   | 4.0 (3.1-4.3)     |

1 – Normal range = <5.19

2 – Normal range = <3.37

3 – Normal range = 0.40-2.29 mmol/L

4 – Normal range = >1.1

Kruskal-Wallis Multiple Comparison Z Value

T1 > T4 for: TC, LDL, TG, TC/HDL

# Results – Glucose Homeostasis (median [95% CI])

| Variable                      | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|-------------------------------|------------------|-------------------|-------------------|-------------------|
| FBG (mmol/L) <sup>1</sup>     | 5.2 (4.7-5.7)    | 5.0 (4.6-5.7)     | 4.8 (4.2-5.0)     | 4.3 (3.9-4.7)     |
| Insulin (pmol/L) <sup>2</sup> | 103 (63-123)     | 88 (55-95)        | 83 (60-109)       | 48 (34-65)        |
| HOMA <sup>3</sup>             | 3.5 (2.0-3.9)    | 2.4 (1.7-3.1)     | 2.1 (1.7-2.9)     | 1.4 (0.9-1.7)     |

1 – Normal range = 3.3-6.4 mmol/L

2 – Normal range = 0-160 pmol/L

3 – >4.0 is suggestive of the presence of insulin resistance

Kruskal-Wallis Multiple Comparison Z Value

T1 > T4 for: FBG, Insulin, HOMA

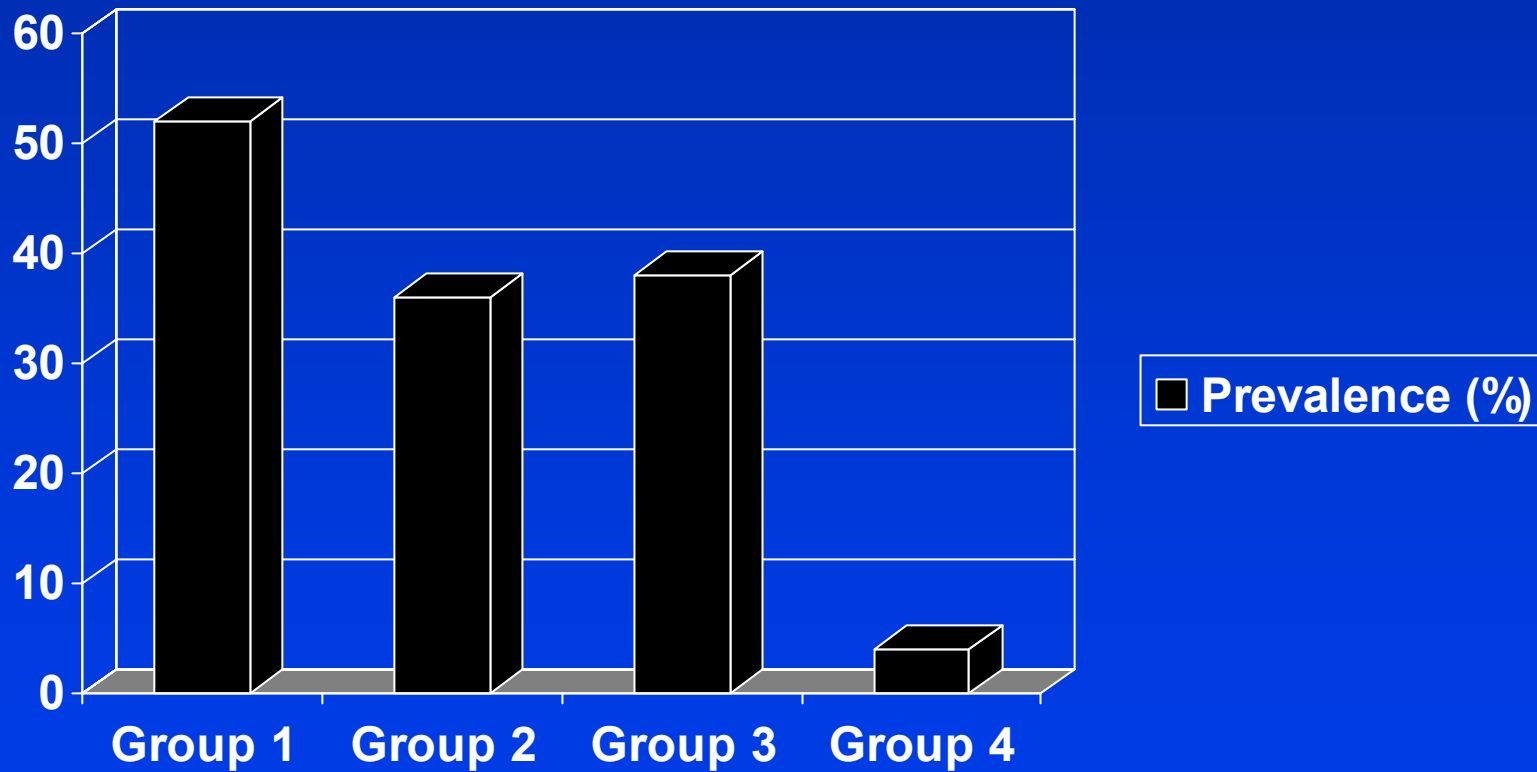
# Results – Body Composition (median [95% CI])

| Variable              | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|-----------------------|------------------|-------------------|-------------------|-------------------|
| BMI                   | 26 (25-28)       | 26 (24-27)        | 22 (21-25)        | 23 (22-24)        |
| Trunk FM (kg)         | 9.5 (8.2-11.7)   | 8.9 (6.5-11.6)    | 4.7 (3.9-5.6)     | 6.2 (4.8-7.0)     |
| % Trunk FM/Trunk Mass | 25 (21-29)       | 23 (20-28)        | 16 (13-17)        | 19 (15-21)        |
| % Trunk FM/TBFM       | 61 (56-63)       | 57 (52-59)        | 57 (52-61)        | 54 (49-58)        |
| Trunk/Peripheral FM   | 1.8 (1.5-2.0)    | 1.5 (1.3-1.7)     | 1.7 (1.5-2.0)     | 1.4 (1.1-1.2)     |

Kruskal-Wallis Multiple Comparison Z Value

T1 > T4 for: BMI, trunk FM, % trunk fat/trunk mass, % trunk FM/TBFM

# Prevalence of Metabolic Syndrome



# Results – Prevalence of Metabolic Syndrome\*

| Variable   | TG-WC<br>Group 1<br>n= 27 | TG-WC<br>Group 2<br>n = 14 | TG-WC<br>Group 3<br>n = 29 | TG-WC<br>Group 4<br>n = 24 |
|------------|---------------------------|----------------------------|----------------------------|----------------------------|
| NCEP Met-S | 14/27 (52%)               | 5/14 (36%)                 | 11/29 (38%)                | 1/24 (4%)                  |

|                  |              |             |              |             |
|------------------|--------------|-------------|--------------|-------------|
| WC >102cm        | 7/27 (26%)   | 2/14 (14%)  | 0/29 (0%)    | 0/24 (0%)   |
| TG ≥1.7 mmol/L   | 27/27 (100%) | 7/14 (50%)  | 29/29 (100%) | 4/24 (17%)  |
| HDL ≤1.04 mmol/L | 10/27 (37%)  | 5/14 (36%)  | 15/29 (52%)  | 5/14 (36%)  |
| BP>130/85        | 20/27 (74%)  | 11/14 (79%) | 17/29 (59%)  | 13/24 (54%) |
| FBG ≥6.1 mmol/L  | 4/27 (15%)   | 3/14 (21%)  | 2/29 (7%)    | 0/24 (0%)   |

\* NCEP Diagnostic Criteria for MetS = ≥ 3/5\*\*

# Results – Prevalence of Metabolic Syndrome

| Variable   | Hyper TG-Waist<br>Group 1<br>n= 27 | Framingham<br>High Risk<br>n = 12 |
|------------|------------------------------------|-----------------------------------|
| NCEP Met-S | 14/27 (52%)                        | 5/12 (42%)                        |

|                        |              |             |
|------------------------|--------------|-------------|
| WC >102cm              | 7/27 (26%)   | 2/12 (17%)  |
| TG $\geq$ 1.7 mmol/L   | 27/27 (100%) | 10/12 (83%) |
| HDL $\leq$ 1.04 mmol/L | 10/27 (37%)  | 4/12 (33%)  |
| BP>130/85              | 20/27 (74%)  | 9/12 (75%)  |
| FBG $\geq$ 6.1 mmol/L  | 4/27 (15%)   | 4/12 (33%)  |

# Summary

- Easily obtained Hypertriglyceridemic-Waist Syndrome criteria identify a significant minority (29%) of treated HIV+ patients with metabolic and body composition indices characteristic of increased CVD risk
- A majority of these patients with Hypertriglyceridemic-Waist Syndrome meet NCEP criteria for the Metabolic Syndrome
- The use of Hypertriglyceridemic-Waist Syndrome criteria may identify a larger number of patients with increased CVD risk than does the traditional Framingham model

# References

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8. Grundy SM et al. Definition of Metabolic Syndrome – Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues related to definition. In *NHLBI/AHA Conference Proceedings*. January 2004;433-438.
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# Results – Lipid Parameters

| Variable                  | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|---------------------------|------------------|-------------------|-------------------|-------------------|
| TC (mmol/L) <sup>1</sup>  | 5.9± 1.2         | 4.7 ± 1.0         | 5.8 ± 1.2         | 4.4 ± 0.8         |
| LDL (mmol/L) <sup>2</sup> | 3.1 ± 0.9        | 2.7 ± 0.8         | 3.0 ± 1.0         | 2.6 ± 0.7         |
| TG (mmol/L) <sup>3</sup>  | 4.2 ± 3.3        | 1.7 ± 0.5         | 4.3 ± 2.2         | 1.3 ± 0.4         |
| HDL (mmol/L) <sup>4</sup> | 1.2 ± 0.3        | 1.2 ± 0.4         | 1.1 ± 0.3         | 1.2 ± 0.3         |
| TC/HDL                    | 5.1 ± 1.1        | 4.1 ± 0.9         | 5.5 ± 1.3         | 3.8 ± 0.9         |

1 – Normal range = <5.19

2 – Normal range = <3.37

3 – Normal range = 0.40-2.29 mmol/L

4 – Normal range = >1.1

# Results – Glucose Homeostasis

| Variable                      | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|-------------------------------|------------------|-------------------|-------------------|-------------------|
| FBG (mmol/L) <sup>1</sup>     | 5.7 ± 1.9        | 5.3 ± 1.0         | 4.7 ± 1.2         | 4.5 ± 0.6         |
| Insulin (pmol/L) <sup>2</sup> | 112 ± 107        | 92 ± 50           | 96 ± 59           | 49.2 ± 23         |
| HOMA <sup>3</sup>             | 3.9 ± 3.6        | 3.1 ± 2.2         | 2.9 ± 2.3         | 1.4 ± 0.3         |

1 – Normal range = 3.3-6.4 mmol/L

2 – Normal range = 0-160 pmol/L

3 – >4.0 is suggestive of the presence of insulin resistance

# Results – Body Composition

| Variable              | Group 1<br>n= 27 | Group 2<br>n = 14 | Group 3<br>n = 29 | Group 4<br>n = 24 |
|-----------------------|------------------|-------------------|-------------------|-------------------|
| BMI                   | 26 ± 3           | 26 ± 4            | 23 ± 3            | 23 ± 2            |
| Trunk FM (kg)         | 10 ± 3           | 10 ± 4            | 5 ± 2             | 6 ± 2             |
| % Trunk FM/Trunk Mass | 25 ± 6           | 24 ± 7            | 16 ± 6            | 18 ± 6            |
| % Trunk FM/TBFM       | 60 ± 6           | 56 ± 5            | 56 ± 7            | 54 ± 10           |
| Trunk/Peripheral FM   | 1.8 ± 0.5        | 1.5 ± 0.4         | 1.7 ± 0.5         | 1.6 ± 0.7         |