

# Metabolic Syndrome in Schizophrenia

Presented by  
Jane Dumontet, Pharm D  
Nov 25, 2009

# Outline

---

- Schizophrenia and physical illness
- Metabolic syndrome – what is it?
- The metabolic syndrome in schizophrenia
- Monitoring: Prevention: Treatment

# Physical Illness in Mental Illness

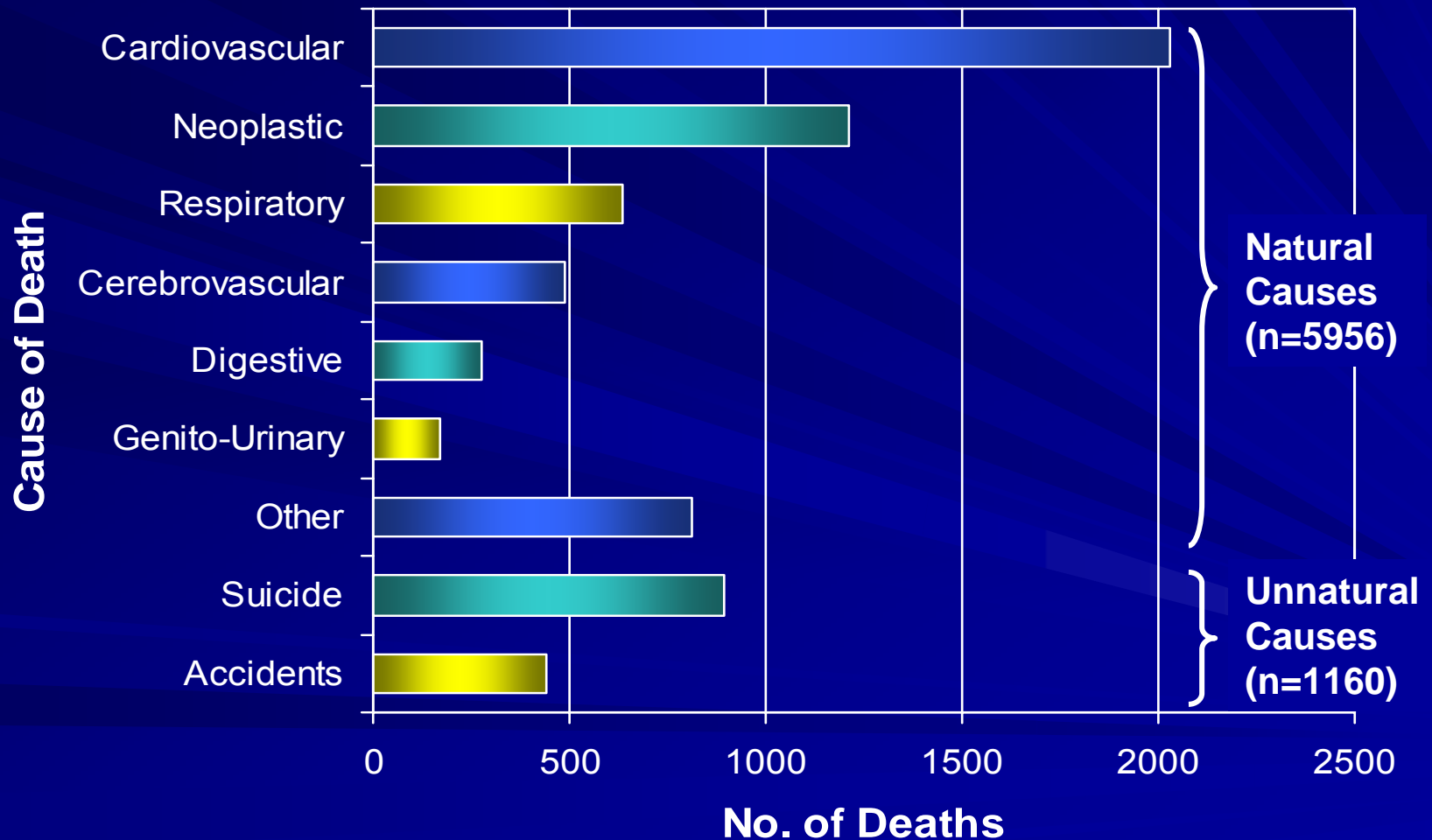
---

- Higher rates of physical illness
- Higher death rates from major diseases
- Physical illnesses less likely to be diagnosed
- Less likely to receive appropriate treatment

# Schizophrenia compared to the general population

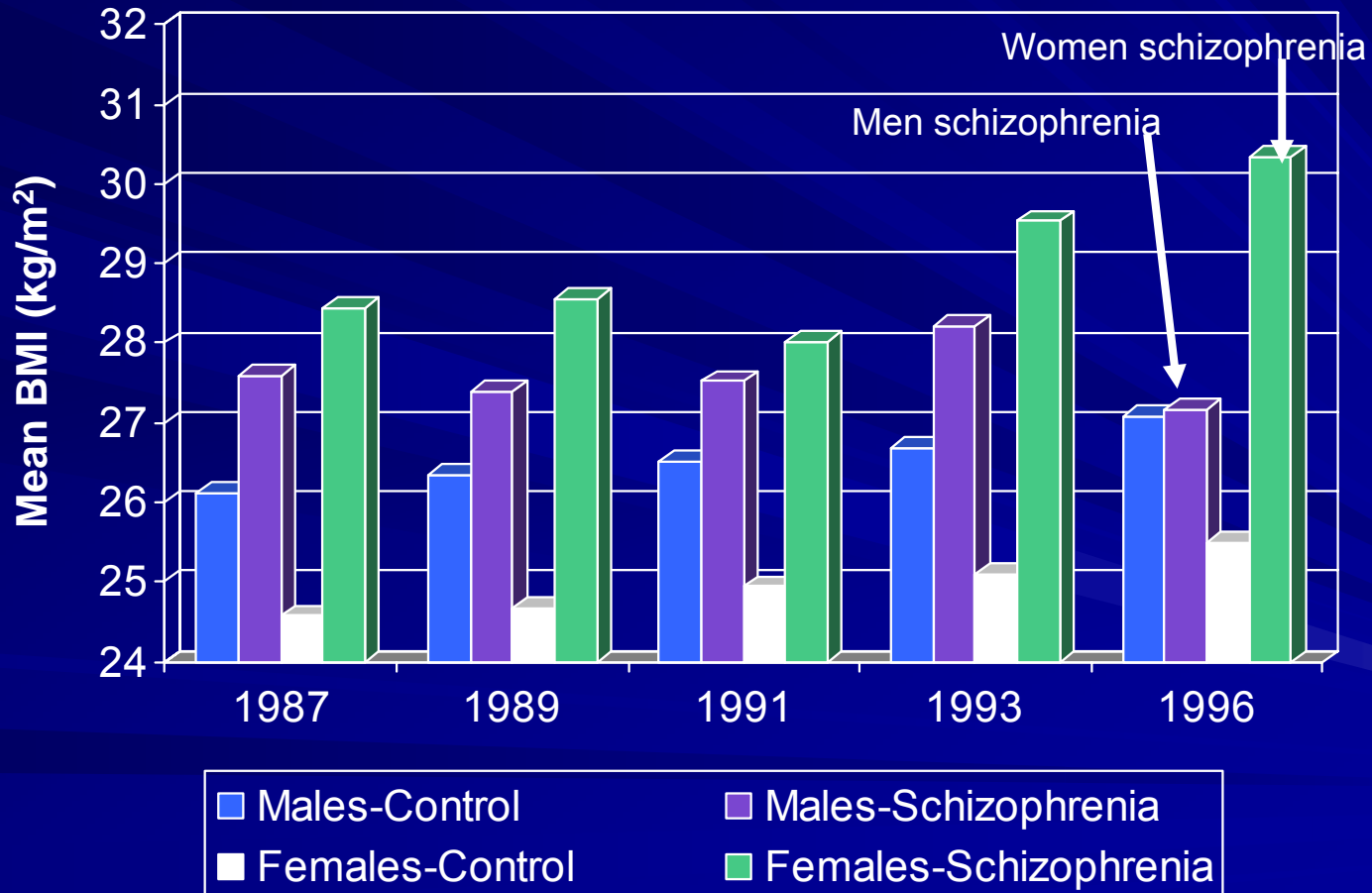
- 1.5-2 fold higher incidence of obesity
  - Risk factor for diabetes, hypertension, lipid disorders, heart disease, stroke, sleep apnea, osteoarthritis, gallstones, depression, certain types of cancer
- 2 fold increased incidence of diabetes
- 5 fold increase in lipid disorders
  - 2 fold increase in death from heart disease

# Mortality of Schizophrenia



# BMI Trend from 1987-1996

## Schizophrenics vs. Non-Schizophrenics



# Body Mass Index (BMI)

- Weight in kg divided by height in m<sup>2</sup>
- 160 lb woman 5 ft 4 inches = 27.5
- 200 lb male 5 ft 10 inches = 28.7
- “BMI calculator”

# Body Weight Classification and Risk of Health Problems by BMI

BMI (kg/m <sup>2</sup> )	Weight Classification	Risk of Health Problems
< 18.5	Underweight	Increased
18.5 - 24.9	Normal weight	Least
25.0 - 29.9	Overweight	Increased
≥ 30.0	Obese	
30.0 - 34.9	Class I	High
35.0 - 39.9	Class II	Very high
≥ 40.0	Class III	Extremely high

# Metabolic Syndrome

---

- AKA (also known as)
  - Syndrome X
  - Insulin resistance syndrome
  - The deadly quartet
  - Hypertriglyceridemic waist
- 1998 World Health Organization (WHO)
- Joint definition in 2009 – specific criteria
  - International Diabetes Federation (IDF)
  - National Heart, Lung and Blood Institute (NHLBI)
  - World Heart Federation
  - International Atherosclerosis Society
  - American Heart Association

# What is it?


It is a cluster of risk factors that appear to directly

- promote heart disease
  - People with metabolic syndrome are 2-3 x more likely to have a heart attack or stroke
- promote diabetes
  - 5 x more likely to develop type 2 diabetes
- Fatty liver, polycystic ovary syndrome, cholesterol gallstones, sleep apnea, lipodystrophies

# Criteria for Clinical Diagnosis of Metabolic Syndrome

Diagnosis established when  $\geq 3$  of 5 risk factors present:

Risk Factor	Defining Level
1) Elevated Waist circumference Men Women	Population and country specific $\geq 102$ cm (~40 inches) $\geq 88$ cm (34.6 inches)
2) Elevated Triglycerides**	$\geq 1.7$ mmol/L
3) Reduced HDL-C** Men Women	$< 1.03$ mmol/L $< 1.29$ mmol/L
4) Elevated Blood pressure**	$>130$ or $\geq 85$ mmHg
5) Elevated Fasting glucose**	$\geq 5.6$ mmol/L



\*\*Or on drug treatment for risk factor

# Waist Circumference

- Correlates strongly with insulin resistance
- Better predictor than BMI of future diabetes
- The best technique –
  - video on the Heart and Stroke Foundation of Canada website ([heartandstroke.bc.ca](http://heartandstroke.bc.ca))
  - finding the upper hip bones (iliac crests), located on your sides just above your belt line
  - Then, in a standing position and with your stomach muscles relaxed, tie the tape measure around your waist at this level.

# Body Weight Classification and Risk of Health Problems by BMI

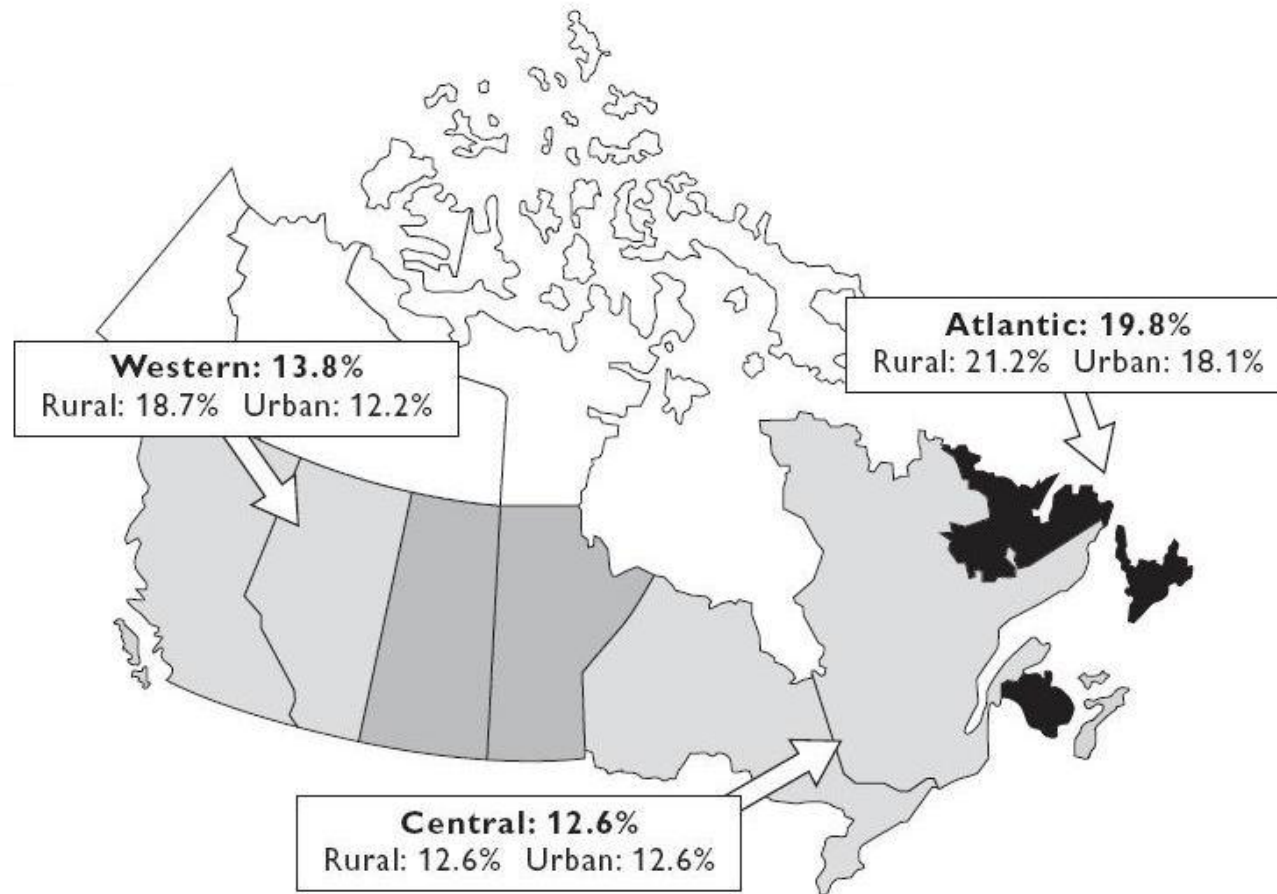
Waist circumference	Normal 18.5- 24.9	Overweight 25-29.9	Obese Class I 30-34.9
<102 cm men <88 women	Least risk	Increased risk	High risk
>102 cm men. >88 women	Increas ed risk	High risk	Very high risk

# Lipid Panel

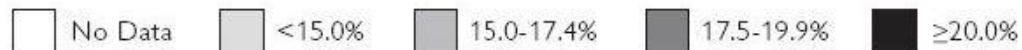
---

- Total cholesterol
- LDL – bad cholesterol - target for treatment for cardiovascular disease
- HDL – good cholesterol
- Triglycerides
  - Associated with insulin resistance
  - Atypical antipsychotic treatment
    - TG/HDL ratio -  $> 3.0$  predictor of insulin resistance

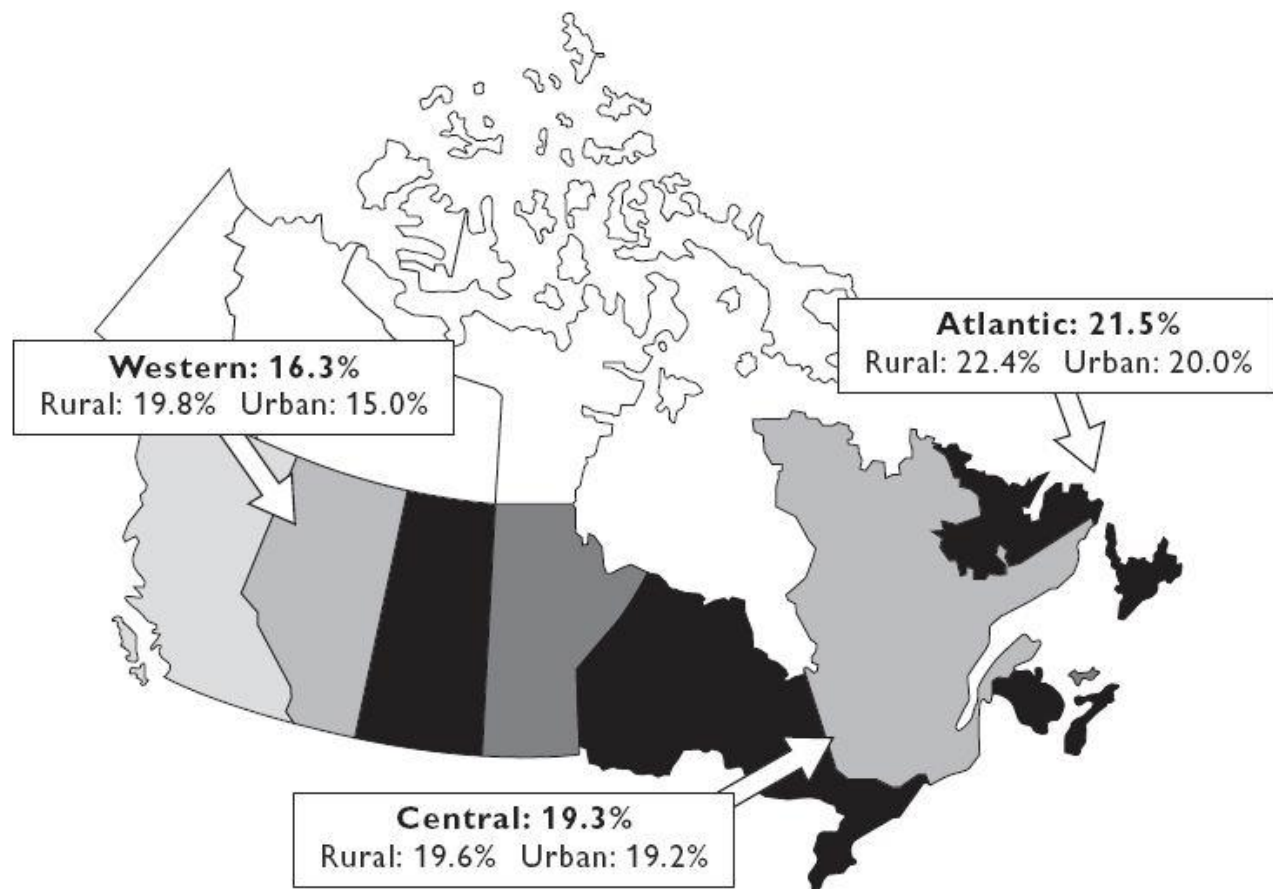
# Prevalence of Metabolic Syndrome in Canadian Women



Atlantic (PEI, NF, NB; N=2961); Central (ON, QC; N=1847); Western (MB, SK, AB, BC; N=3815)



# Prevalence of Metabolic Syndrome in Canadian Men



Atlantic (PEI, NF, NB; N=2797); Central (ON, QC; N=1782); Western (MB, SK, AB, BC; N=3728)

□ No Data    □ <15.0%    □ 15.0-17.4%    □ 17.5-19.9%    □ ≥20.0%

# Metabolic Syndrome

- Prevalence increases with age

	18-34 yrs	35-49 yrs	50-64 yrs
Men	8.7%	21.7%	27.1%
Women	4.6 %	12.2%	23.9%

Canadian data

- Highest prevalence worldwide
  - Native Americans
    - 60% women ages 45-49
    - 45% men ages 45-49

# Prevalence of Metabolic Syndrome in Patients with Mental Illness

Study	Study Characteristics	N	Mean Age (yrs)	Prevalence (%)
Cohn 2004	Prevalence study in Canada; n=240 Schizophrenia or schizoaffective disorder	84 ♀ 156 ♂	43.3	44.7
McEvoy 2005	Prevalence study of CATIE pts; n=689 Schizophrenia	180 ♀ 509 ♂	40.4	51.6% 36%
Correll 2006	Prevalence study in US; n=367 Schizophrenia/schizoaffective disorder (48%), bipolar disorder (20.7%), depressive disorder (20.7%), substance use disorder (4.6%), dementia (2.4%)	169 ♀ 198 ♂	42.9	36.7% 37.9% (Schizophrenia/ schizoaffective disorder cohort)

1. Cohn *et al.* Can J Psychiatry 2004;49:753-60.
2. McEvoy *et al.* Schizophr Res 2005;80:19-32.
3. Correll *et al.* J Clin Psychiatry 2006;67:575-83.

# Why is there an increased incidence?

## Environment versus Illness

### ■ Environment

- Inactivity
- Smoking
- Dietary habits
- stress

### ■ Schizophrenia

- in neuroleptic naïve individuals some studies show higher incidence of insulin resistance
- Certain genes that add risk of serious mental illness might also add risk of cardiometabolic disorders

# Contribution of medications

Antipsychotic	Weight Gain	Diabetes Risk	Dyslipidemia
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	?	?
Quetiapine	++	?	?
Aripiprazole	+/--	--	--
Ziprasidone	+/--	--	--

# Atypical antipsychotic medications

---

- Increased appetite
  - obesity → diabetes → heart disease
- Elevate triglyceride levels and lower HDL even in the absence of weight gain and obesity → insulin resistance and diabetes (particularly in patients with genetic risk for diabetes) (olanzapine and clozapine)

# Diabetic Ketoacidosis

- Potentially life-threatening complication resulting from an absolute shortage of insulin
- Patients with undiagnosed insulin resistance, prediabetes or diabetes
- Atypical antipsychotic
  - Sudden diabetic ketoacidosis from insulin deficiency

# Symptoms of Diabetes and diabetic ketoacidosis

## Diabetes

- Frequent urination
- Excessive thirst
- Extreme hunger
- Unusual weight loss
- Increased fatigue
- Irritability
- Blurry vision

## Diabetic ketoacidosis

- Thirst or very dry mouth
- Constantly feeling tired
- Dry or flushed skin
- Nausea, vomiting or abdominal pain
- Fruity odour on breath
- Difficulty paying attention or confusion

# Metabolic syndrome and cardiac risk

- Middle aged people and metabolic syndrome are at increased risk for heart disease
- 10 year risk (Framingham risk)
  - High risk (>20%)
  - Moderately high (10-20%)
  - Low to moderate (< 10%)
- Takes into account age, sex, smoking, total cholesterol

# Other Impacts

---

- Body image/self esteem
- Compliance
- Recovery

---

# Monitoring Prevention and Treatment

# Medical Illness in Schizophrenia

---

- Tends to be underdiagnosed, undertreated in a group of individuals who are at increased risk

# Monitoring

---

- Numerous guidelines
  - Baseline screening and monitoring
  - Ongoing monitoring
  - More intensive monitoring when starting a new medication
  - Appropriate treatment
- Challenges.....

# Monitoring of Antipsychotic Therapy

Antipsychotic therapy should be tailored for each individual

Recommended monitoring:

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 Years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

# Choice of antipsychotic therapy

---

- Consideration given to selecting metabolically neutral antipsychotics where risk factors exist
- Give consideration to reevaluating therapy if weight and metabolic parameters worsen
- More pro-active approach to preventing weight gain

# Cardiovascular Risk Factors

## Non-modifiable:

- Increasing age
- Sex
- Family history of obesity, diabetes, dyslipidemia, hypertension and coronary heart disease
- Ethnicity (increased rates in individuals of Asian, Hispanic, aboriginal and Native American ancestry)

# Cardiovascular risk factors

---

## Modifiable:

- Sedentary lifestyle
- Smoking
- Obesity, abdominal obesity
- Poor dietary habits
  - high in simple carbohydrates and fat

# AHA/NHLBI Recommendations for Clinical Management of Metabolic Syndrome

## Lifestyle Risk Factors:

1. Abdominal obesity:
  - reduce body weight by 7-10% during year 1 of therapy
  - continue weight loss thereafter with goal to ultimately achieve desirable weight (BMI <25 kg/m<sup>2</sup>)

# AHA/NHLBI Recommendations for Clinical Management of Metabolic Syndrome

## 2. Physical inactivity:

- regular moderate-intensity physical activity ( $\geq 30$  min, preferably  $\geq 60$  min, of continuous or intermittent activity  $\geq 5$  days/week, but preferably daily

## Sedentary lifestyle

- Predictor of cardiovascular events and mortality
  - Increased central adipose tissue
  - Reduced HDL cholesterol
  - Trend to increased triglyceride, blood pressure and glucose
- TV watching, computer etc:  $>4$  hours/day had twice the risk of metabolic syndrome compared to those using  $< 1$  hour/day

# Prevalence of Metabolic Syndrome and Physical Activity (Canada)

	Inactive	Active
Men	22.1%	9.4%
Women	13%	7.4%

# AHA/NHLBI Recommendations for Clinical Management of Metabolic Syndrome

---

3. Atherogenic diet:
  - reduce intake of saturated fat, trans fat, cholesterol

# AHA/NHLBI Recommendations for Clinical Management of Metabolic Syndrome

## Metabolic Risk Factors:

1. Atherogenic dyslipidemia: add lipid-lowering agent when...
  - Low-risk: LDL-C  $\geq$  5.0 mmol/L or TC/HDL-C  $\geq$  6.0
  - Moderate-risk: LDL-C  $\geq$  3.5 mmol/L or TC/HDL-C  $\geq$  5.0
  - High-risk: LDL-C  $\geq$  2.0 mmol/L or TC-HDL-C  $\geq$  4.0
2. Elevated BP:
  - BP  $\geq$  120/80 mmHg: **lifestyle modification**
  - BP  $\geq$  140/90 mmHg ( $\geq$  130/80 mmHg CKD or DM): add BP medication as needed to achieve BP goal
3. Elevated glucose:
  - IFG (6.1-6.9 mmol/L): **lifestyle modification**
  - DMII: lifestyle modification and pharmacotherapy

# In Summary

- Medical illness tends to be underdiagnosed, undertreated in a group of individuals who are at increased risk
- Improvement in screening, monitoring and treatment for metabolic risk factors must be consistently implemented and emphasis placed on a healthy lifestyle

