CASE VIGNETTE

- 39 year old female with first episode psychosis,
- No evidence of HT, DM, substance use, suicidal ideas.
- No f/h/o of mental illness.
- H/o DM in both parents.
- On examination → obese ++, rest NAD
- Routine investigations → WNL,

Question: drug of your choice:

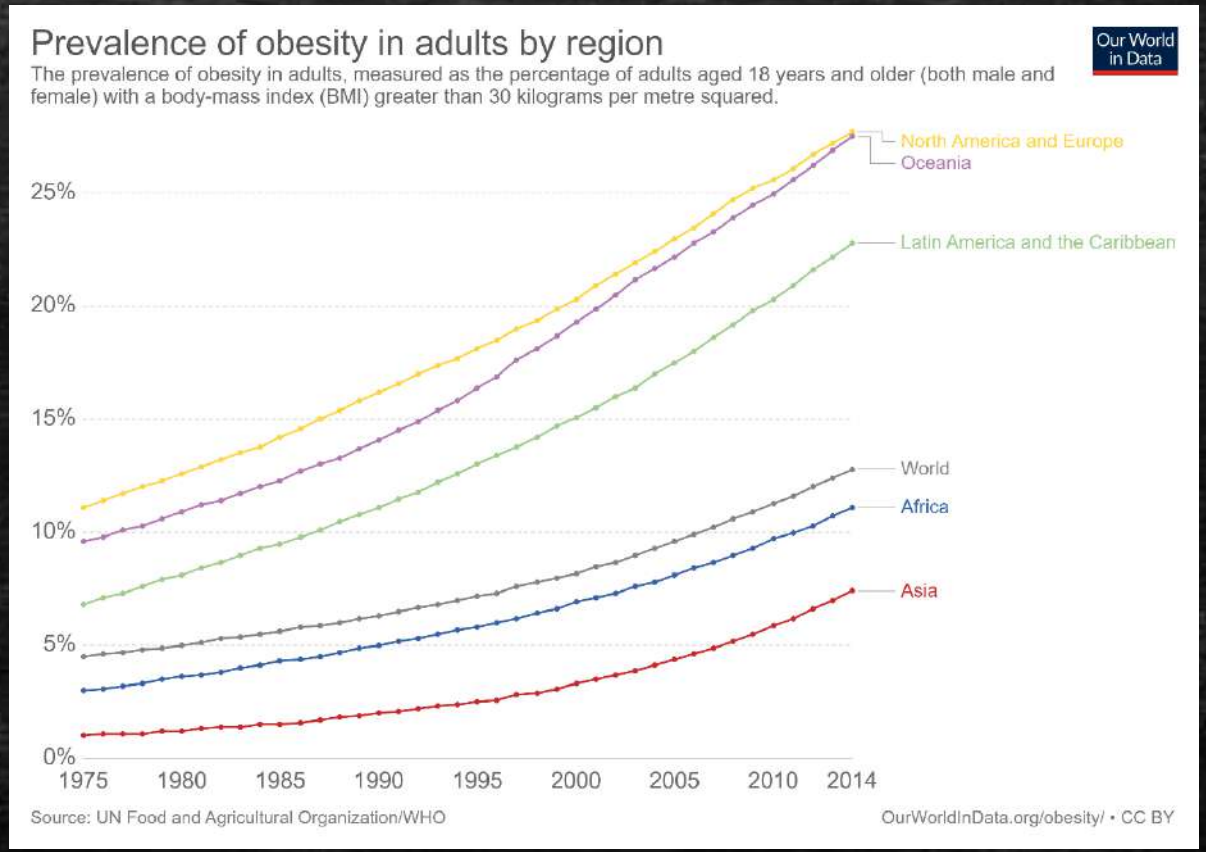
A) Aripiprazole

B) Olanzapine

C) Risperidone

D) Ziprasidone

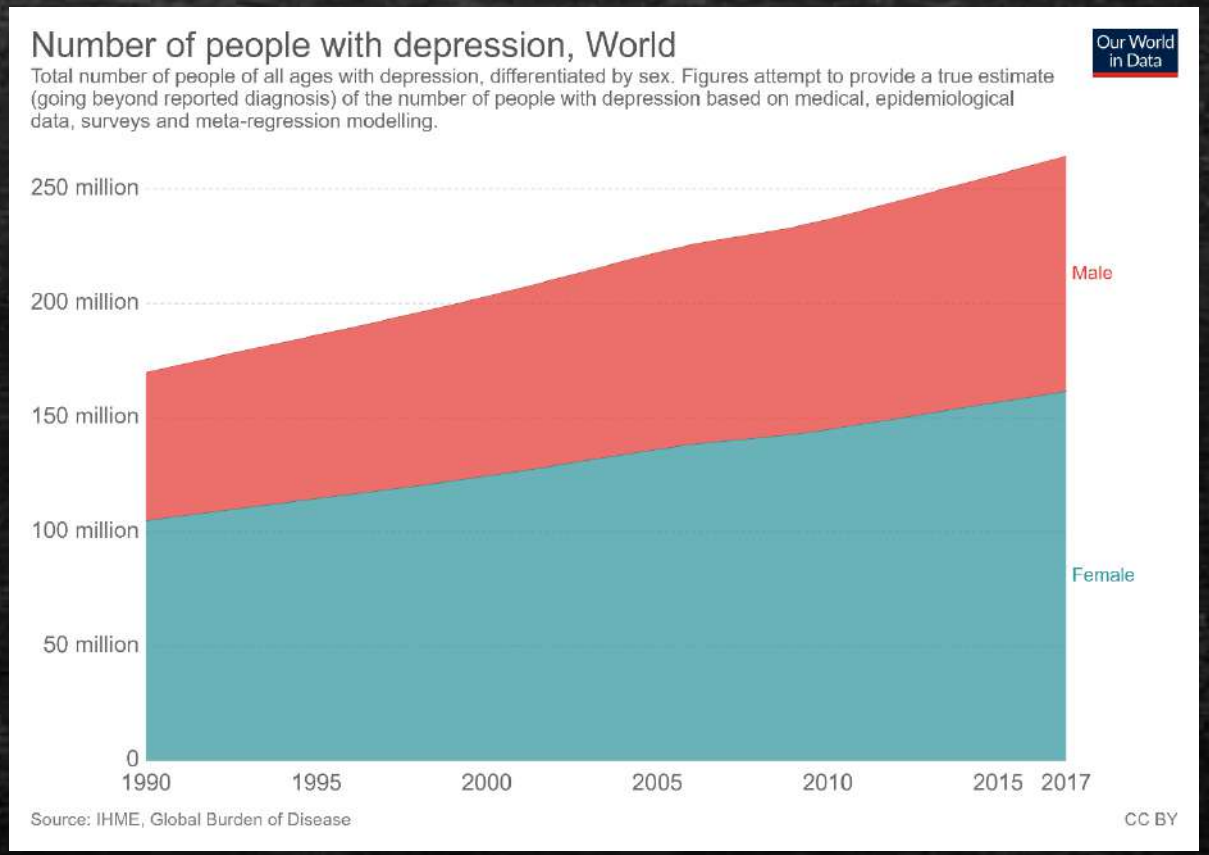
Prevalence of obesity: past 3 decades



Global prevalence of obesity has ↑ over past 3 decades.

Source: ourworldindata.org accessed on 17/09/2019

Prevalence of depression: past 3 decades

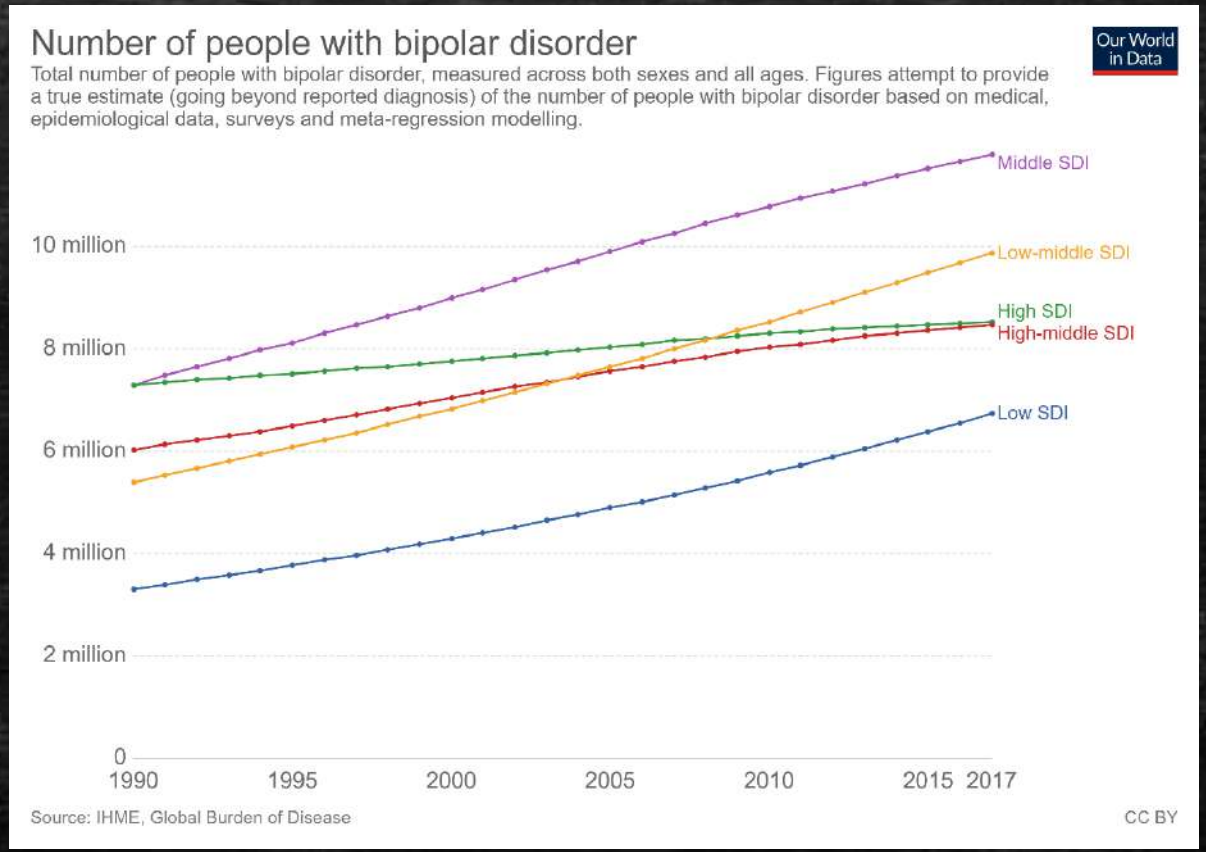


Global prevalence of depression has ↑ over past 3 decades.

Source: ourworldindata.org accessed on 17/09/2019

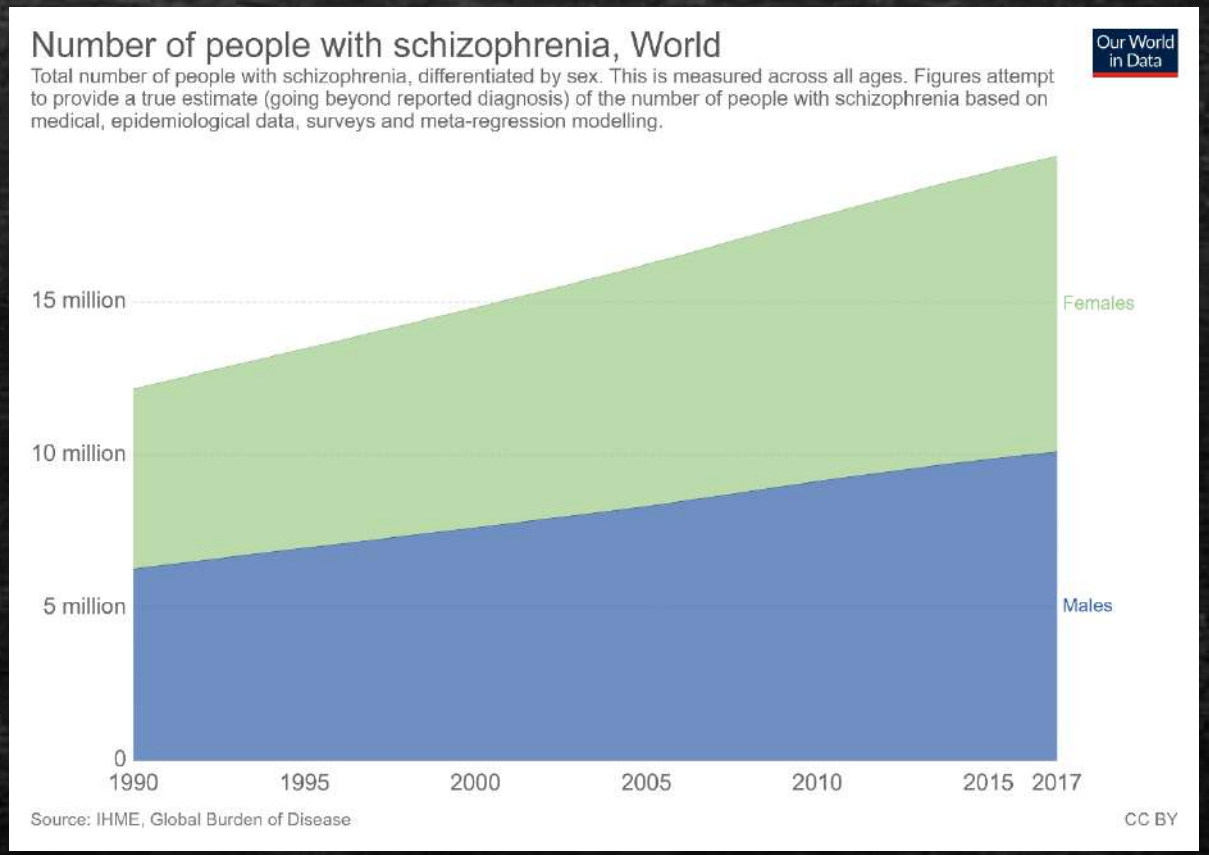
Prevalence of bipolar disorder: past 3 decades

Global prevalence of bipolar disorder has ↑ over past 3 decades.



Source: ourworldindata.org accessed on 17/09/2019

Prevalence of schizophrenia: past 3 decades

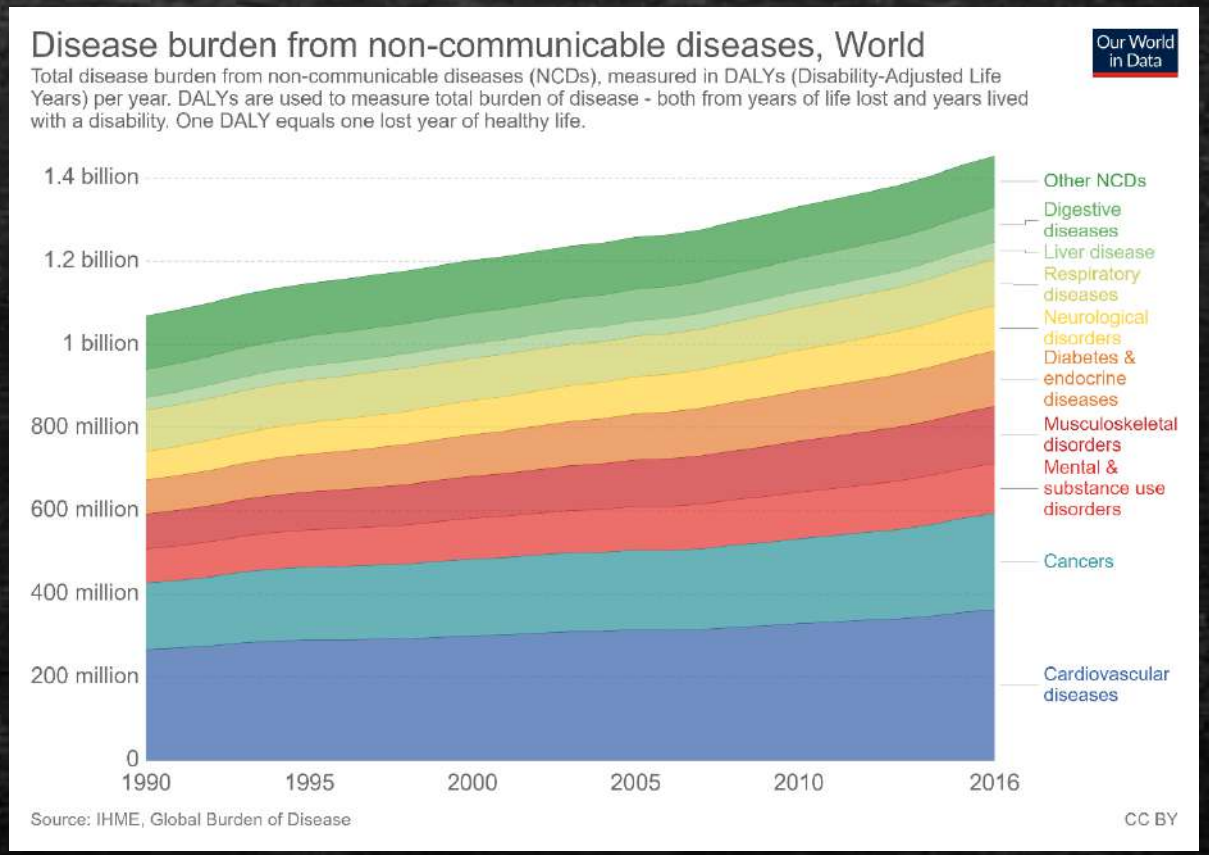


Global prevalence of schizophrenia has ↑ over past 3 decades.

Source: ourworldindata.org accessed on 17/09/2019

Disease burden from NCDs: past 3 decades

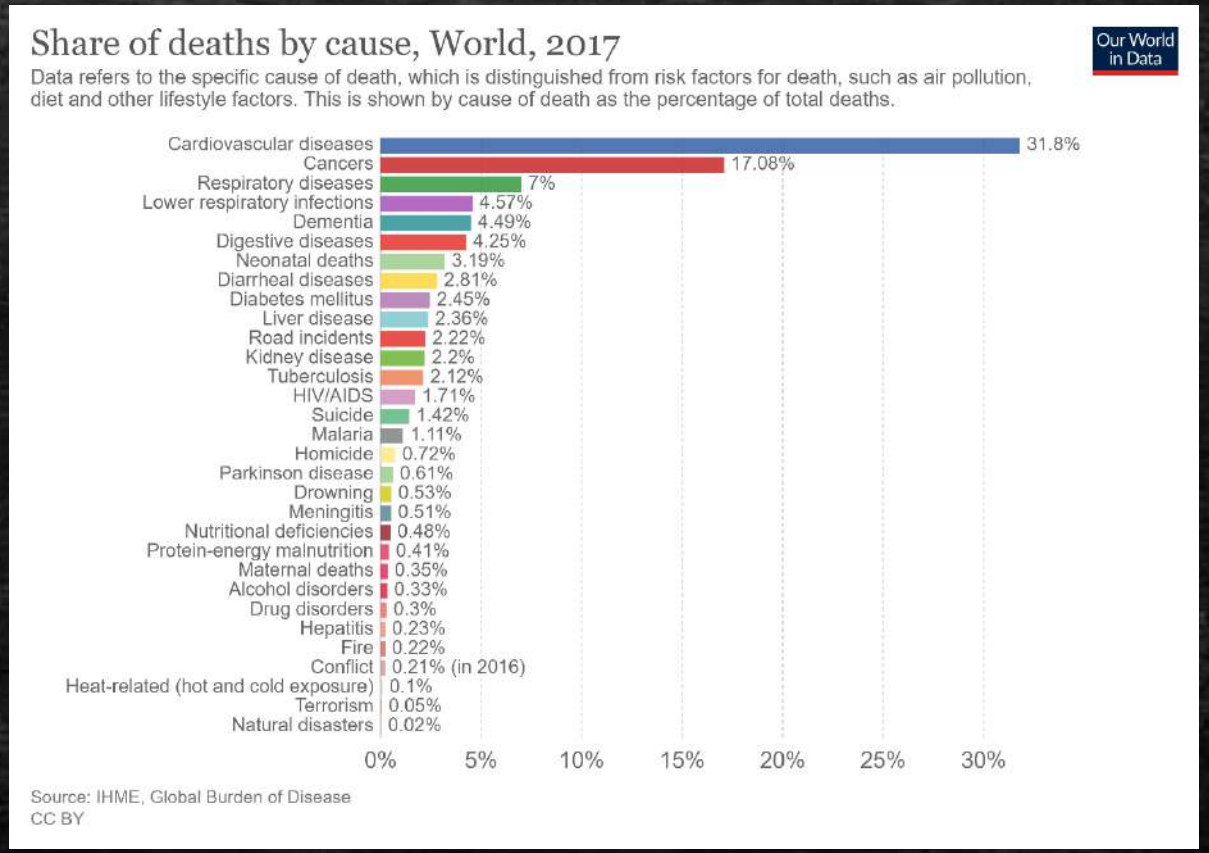
Non-communicable disease burden has increased over past 3 decades.



Source: ourworldindata.org accessed on 17/09/2019

Causes of death: past 3 decades

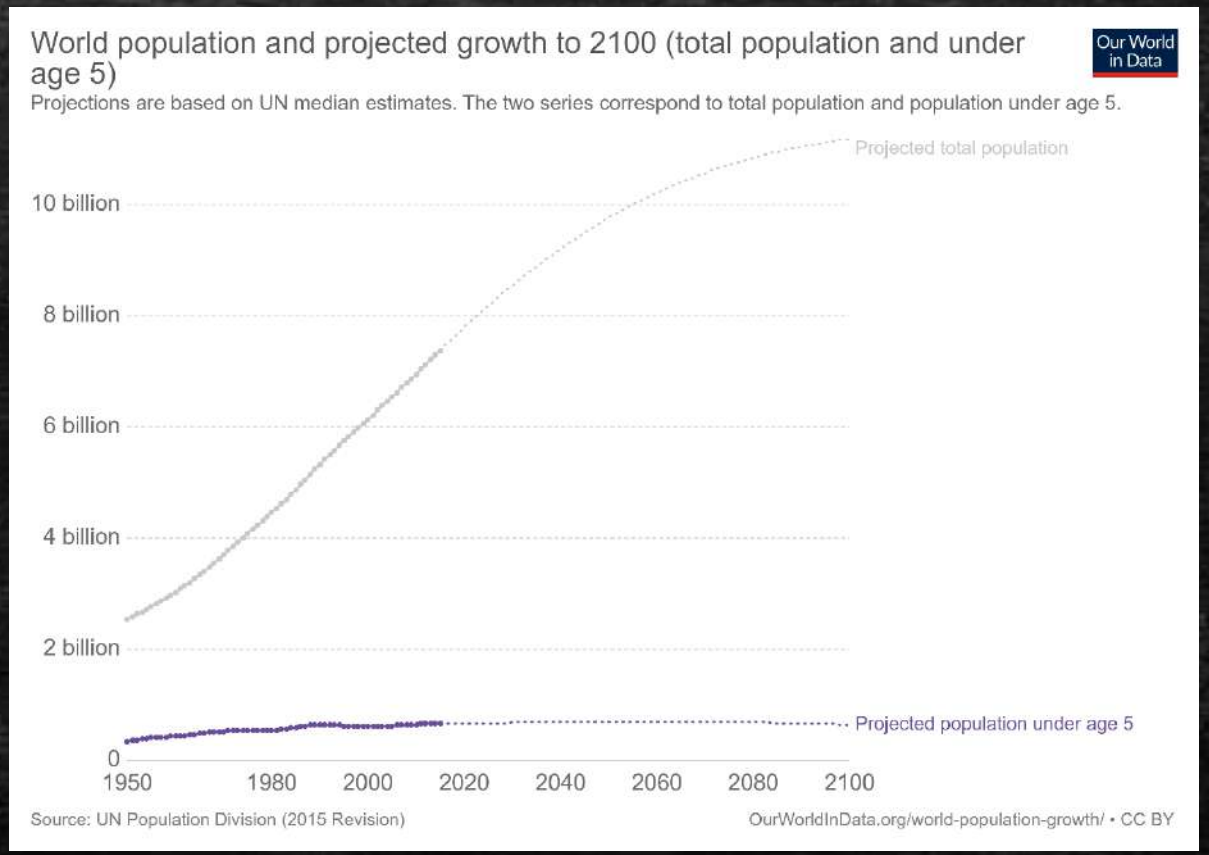
Death due to Cardiovascular diseases has increased over past 3 decades.



Source: ourworldindata.org accessed on 17/09/2019

Global population: past 3 decades and projection

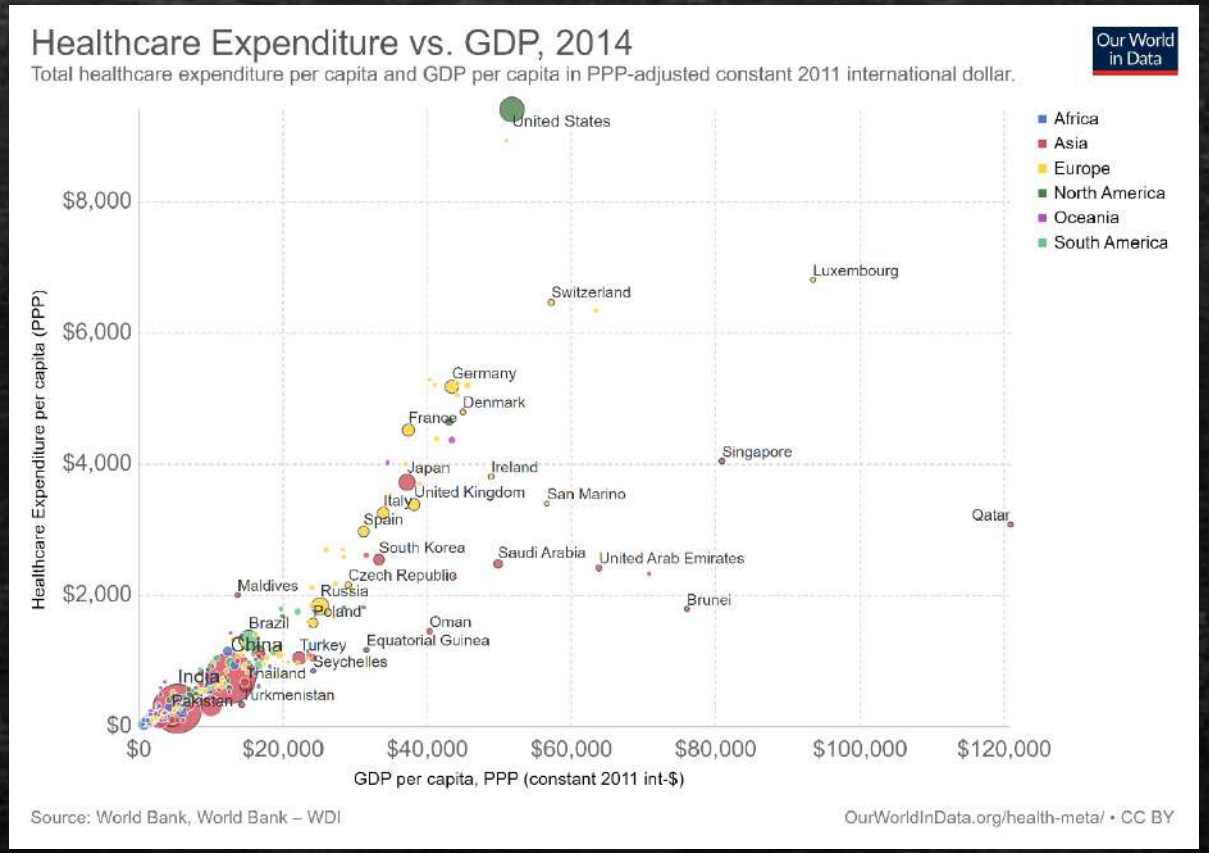
Global population has gone from ~ 5 Billion to ~7.5 Billion in past 3 decades.



Source: ourworldindata.org accessed on 17/09/2019

Health expenditure Vs GDP 2014

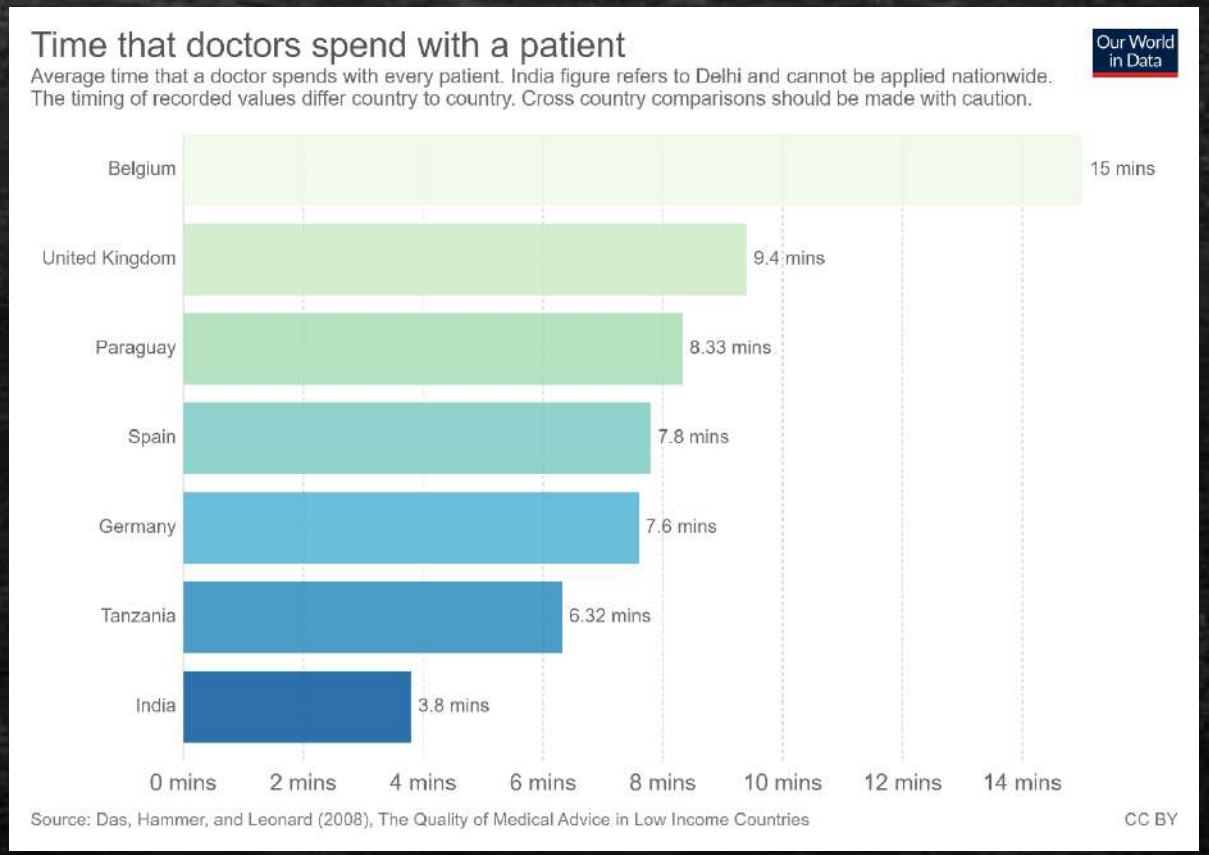
Developed nations have higher proportion of health expenditure Vs their GDP as compared with developing nations.



Source: ourworldindata.org accessed on 17/09/2019

Average time spent by doctors with a patient

In Delhi average time spent by doctors with a patient is under 4 minutes.



Source: ourworldindata.org accessed on 17/09/2019

Why were the previous slides shown?

A remarkable increase in absolute (? relative) number of NCDs, the disease burden and cause of death due to NCDs.

Financial and time resources are limited, so prevention of onset of NCDs is necessary.

As psychiatrists let's see what we can do to prevent NCDs.

Metabolic Syndrome in Psychiatric Disorders

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AGENDA

1. What is metabolic syndrome, and its prevalence : slides 14 to 24.
2. Prevalence of metabolic syndrome in various psychiatric disorders, underlying mechanism of causation and impact: slides 25 to 49.
3. How to screen psychiatry patients for metabolic syndrome, prevent onset and treatment for metabolic syndrome: slides 50-54.
4. Discussion: slide 55.

Psychiatric disorders and life expectancy

Life expectancy shortened by 0.7 to 2.4 decades.

Chesney E et al. *World Psychiatry*. 2014;13(2):153-160.

Mortality attributed 60% to cardiovascular diseases.

Cardiovascular diseases →role of metabolic factors.

Metabolic syndrome in psychiatric disorders 58% higher than general population.

Vancampfort D et al. *World Psychiatry*. 2015;14(3):339-347.

Metabolic syndrome predisposes to cardiovascular disease and diabetes.

Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72.

Metabolic syndrome: Introduction

Haller and Hanefeld in 1975 first coined the term metabolic syndrome.

S. O'Neill et al. Obesity reviews (2015) **16**, 1–12

A heterogeneous concept with a constellation of interconnected physiological, biochemical, clinical and metabolic risk factors.

Core components are:

1. insulin resistance,
2. central obesity,
3. dyslipidemia,
4. arterial hypertension.

International Diabetes Federation (2006) The IDF Consensus Worldwide Definition of the Metabolic Syndrome

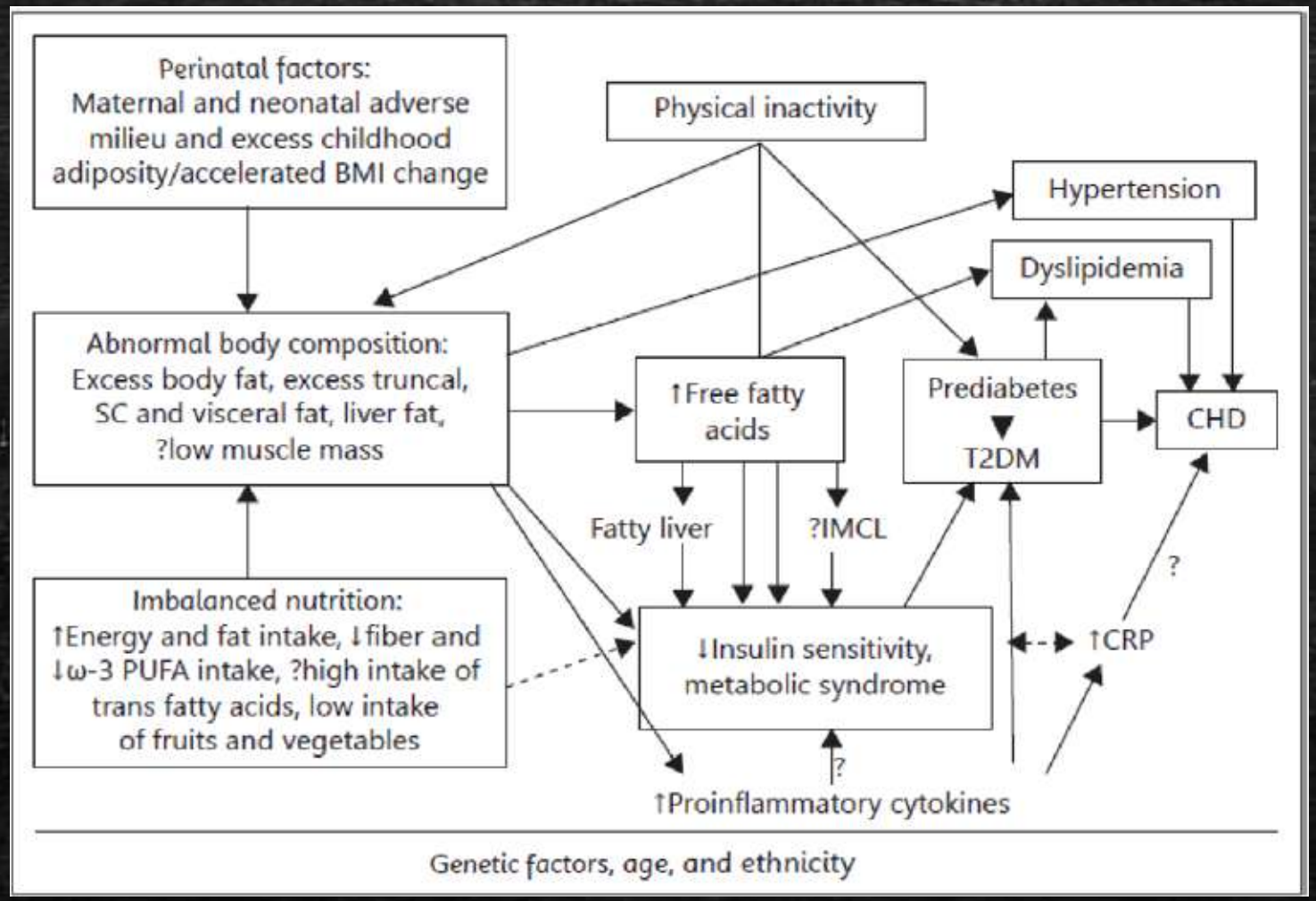
Factors in insulin resistance, T2DM and CHD

CRP =
C reactive protein

IMCL =
Intramyocellular lipids

T2DM = Type 2 diabetes mellitus

CHD = Coronary heart disease



Summary:
Several factors including intrauterine, individually
or
interlinked
determine vulnerability to T2DM, CHD and IR .

Source: Mohanan PP. Hypertens J 2016, 2(1):1-6

Metabolic syndrome: diagnostic criteria

- Many expert groups have developed clinical criteria for metabolic syndrome.
- Most widely accepted criteria were produced by:
  1. World Health Organization (WHO),
  2. European Group for the Study of Insulin Resistance (EGIR), and
  3. National Cholesterol Education Program - Third Adult Treatment Panel (NCEP ATP III).
  4. International Diabetes Federation (IDF).

Source: International Diabetes Federation (2006) The IDF Consensus Worldwide Definition of the Metabolic Syndrome

Metabolic syndrome: diagnostic criteria

Criteria	WHO	IDF	EGIR	NCEP-ATP III
	Diabetes plus at least two of the following:	Central obesity plus at least two of the following:	Insulin resistance plus at least two of the following:	At least three of the following:
Central obesity/waist circumference	Waist/hip ratio >0.90 (men), >0.85 (women); or BMI >30 kg/m^2	Waist circumference, based on ethnicity-specific values. If BMI >30 kg/m^2, waist circumference does not need to be measured	Waist circumference: ≥94 cm (men), ≥80 cm (women)	Waist circumference: >102 cm (men), >88 cm (women)
Triglycerides	≥1.7 mmol/l	>1.7 mmol/l, or specific treatment for lipid abnormality	≥2.0 mmol/l, or treatment for lipid abnormality	>1.7 mmol/l
High-density lipoprotein (HDL) cholesterol	<0.9 mmol/l (men), <1.0 mmol/l (women)	<1.04 mmol/l (men), <1.29 mmol/l (women); or specific treatment for lipid abnormality	<1.0 mmol/l	<1.04 mmol/l (men), <1.29 mmol/l (women)
Blood pressure (systolic/diastolic)	≥140/90 mmHg	Systolic blood pressure >130 or diastolic blood pressure >85 mmHg, or antihypertensive treatment	≥140/90 mmHg, or antihypertensive medication	>130/85 mmHg
Fasting plasma glucose	Impaired	>5.6 mmol/l, or previously diagnosed type 2 diabetes	≥6.1 mmol/l	>6.1 mmol/l
Urinary albumin	Excretion rate ≥20 µg/min, or albumin/creatinine ratio ≥30 mg/g	Not included	Not included	Not included

WHO, World Health Organization (1999); IDF, International Diabetes Federation (2006); EGIR, European Group for the Study of Insulin Resistance (Balkau 1999); NCEP-ATP III, US National Cholesterol Education Program Adult Treatment Panel III (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001); BMI, body mass index.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome: diagnostic criteria difference

- Most definitions → presence of at least three abnormal parameters for diagnosing metabolic syndrome.
- Criteria by IDF (international diabetic federation) and NCEP ATP-III (National Cholesterol Education Program - Third Adult Treatment Panel) → easy to measure, no lab tests.
- NCEP ATP-III is the most commonly used criteria-set for defining metabolic syndrome.
- NCEP ATP-III criteria require presence of any of the three out of five criteria for diagnosing metabolic syndrome.
- IDF criteria - waist circumference a mandatory criterion plus any two other criteria for diagnosing metabolic syndrome.

Source: Grover et al. Indian Journal of Psychological Medicine; Apr - Jun 2012 ,Vol 34, Issue 2

Metabolic syndrome: diagnostic criteria in Indians

Presence of any 3 out of the 5 = Metabolic syndrome

Risk Factor	Harmonization criteria for Asian Indians
1. Abdominal obesity	
Waist circumference Male / Female	>90 cm / >80 cm
Body mass index	>23 Kg/m^2
Waist hip ratio Male / Female	>0.9 / >0.8
2. Fasting plasma glucose	≥ 100 mg/dl
3. Blood pressure	≥130 / ≥85 mm Hg
Dyslipidemia	
4. Triglycerides	≥ 150 mg/dl
5. HDL cholesterol Male / Female	<40 mg/dl / <50 mg/dl

Source: Misra A et al. JAPI Feb 2009, 57; 163-170.

All five individual components should be deemed important in risk prediction.

These components are independent risk factors for coronary heart disease, cerebrovascular disease and diabetes.

Source: Kassi E et al (2011) Metabolic syndrome: definition and controversies. *BMC Medicine,* 9: 48.

Additional metabolic criteria for research

Criteria	Tests
Abnormal body fat distribution	General body fat distribution (DEXA) Central fat distribution (CT/MRI) Adipose tissue biomarkers: leptin, adiponectin Liver fat content (MRS)
Atherogenic dyslipidemia (beyond elevated triglyceride and low HDL)	ApoB (or non-HDL-C) Small LDL particles
Dysglycemia	OGTT
Insulin resistance	Fasting insulin / pro-insulin levels HOMA-IR Insulin resistance by Bergman Minimal Model Elevated free fatty acids (fasting and during OGTT) M value from clamp
Vascular dysregulation	Measurement of endothelial dysfunction Microalbuminuria
Proinflammatory state	Elevated HsCRP Elevated inflammatory cytokines (TNF-α, IL-6) Decrease in adiponectin plasma levels
Prothrombotic state	Fibrinolytic factors (PAI-1, etc) Clotting factors (fibrinogen, etc)
Hormonal factors	Pituitary adrenal axis

Source: International Diabetes Federation (2006) The IDF Consensus Worldwide Definition of the Metabolic Syndrome

Metabolic syndrome: prevalence worldwide

- ~ 20–25% population worldwide has metabolic syndrome.
- Metabolic syndrome (MetS) is associated with:
  - two fold increase in the likelihood of death
  - three fold increase in the risk of heart attack or stroke
  - five fold risk to develop type 2 diabetes mellitus.
- A big impact on financial, emotional & psychosocial well-being.
- ↑ risk of psychiatric disorders e.g. depression, ↓ reduced QOL.
- MetS prevalence ↑ 2–3 times in severe psychiatric disorders.

International Diabetes Federation (2006) The IDF Consensus Worldwide Definition of the Metabolic Syndrome.

Holt R, et al (2010). *Journal of Psychopharmacology,* 24: 867–73

Metabolic syndrome: prevalence in India

- Nationally representative studies generally not available in any south Asian country.
- ~ 33% population in Indian cities have metabolic syndrome.
- Significant differences exists within different urban socioeconomic groups.
- Equally prevalent in both genders; beyond age 70 years increased prevalence in female gender.
- Males and females age group 40-59 years were 3 times more likely to have metabolic syndrome compared with age group 20-39 years.

Source: Mohanan PP. Hypertens J 2016, 2(1):1-6

Metabolic syndrome in psychiatric disorders overview

Schizophrenia

- estimated prevalence varies from 8.9% to 68%.

Bipolar disorder

- prevalence varies from 16% to 67%.

Major Depressive Disorder

- prevalence ranges from 36% to 50%.

Common risk factors for metabolic syndrome in chronic psychiatric illness

1. Inactive lifestyle.
2. Poor dietary choices.
3. Genetic vulnerabilities.
4. Hormonal imbalance involving cortisol and leptin.
5. Increased alcohol consumption.
6. Gut microbiome alterations.
7. SGAs and their related side-effects.

Sources: Grover et al. Indian Journal of Psychological Medicine; Apr - Jun 2012 ,Vol 34, Issue 2; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in psychiatric disorders overview

Cognitive decline & dementia

- Metabolic syndrome associated with cognitive decline, Alzheimer's disease and vascular dementia

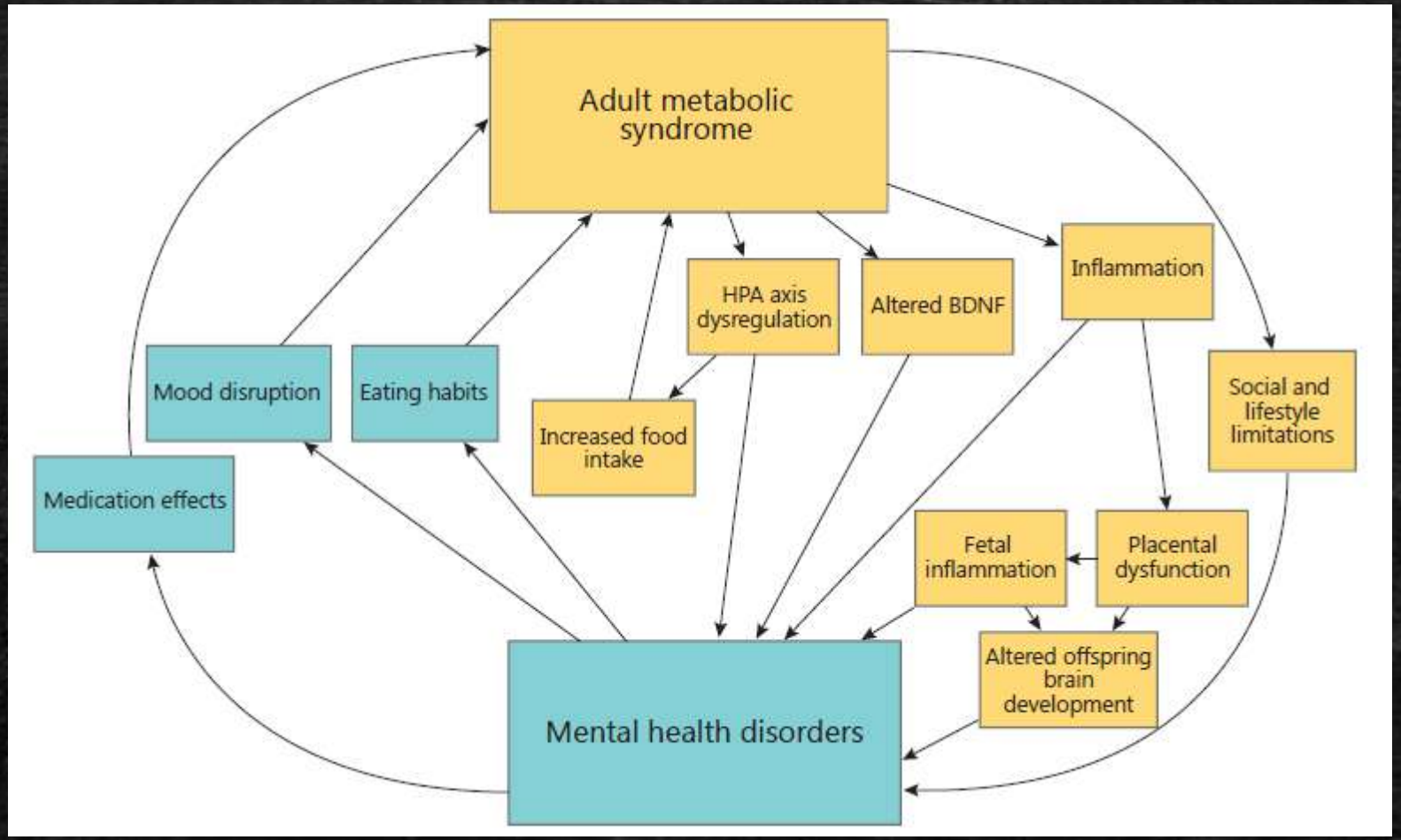
Post-Traumatic Stress Disorder

- Chronic severe PTSD - higher risk of metabolic syndrome

Others

- Binge eating disorder
- Borderline Personality disorder
- Alcohol use disorder
- Autism spectrum disorders

Metabolic syndrome and psychiatric disorders mechanisms



Elizabeth Nousen et al. Neuroendocrinology 2013;98:254–266

Metabolic syndrome in schizophrenia

- Mortality is two to threefold higher than general population, and cardiovascular diseases are the leading cause of death.
- Individuals with schizophrenia are at significantly higher risk of:
    1. abdominal obesity (OR=4.43),
    2. hypertriglyceridemia (OR=2.73),
    3. low HDL-C (OR=2.35),
    4. metabolic syndrome (OR=2.35),
    5. hypertension (OR=1.36).
- MetS prevalence ~ 5 times higher than general population.
- Schizoaffective have slightly higher risk of MetS Vs schizophrenia.
- Increased risk of MetS in women Vs men.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

- 2-3 fold higher prevalence of T2DM than general population.
- Increased prevalence of T2DM independent of APD use.
- APD naïve schizophrenia patients had higher insulin resistance, impaired glucose tolerance and increased intra-abdominal fat deposition compared with normal controls.
- Siblings of individuals with schizophrenia were found to have increased glucose intolerance, while parents of those with non-affective psychosis had increased prevalence of T2DM.
- Metabolic abnormality may probably be an intrinsic component of schizophrenia, with biological & genetic predisposing factors.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

A. Genetic factors:

An at-risk allele of T2DM, rs7903146[T], has been found in the transcription factor 7-like 2 (TCF7L2) gene and this genotype is also associated with an increased risk of schizophrenia.

Associations between weight gain in patients with schizophrenia and various genetic polymorphisms have also been identified. E.g. presence of the Arg347 allele of alpha-1A adrenergic receptor (ADRA1A).

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

B. Immune, metabolic and endocrine factors:

1. Chronic subclinical inflammation occurs in metabolic syndrome (MetS). Inflammatory markers are currently not part of MetS diagnostic criteria.
2. CRP, TNF-α, IL-6, adiponectin, leptin levels are altered in MetS.
3. Adiponectin & leptin control energy homeostasis, glucose & lipid metabolism: Adiponectin level ↓ with ↑ adiposity.
4. Adiponectin +vely associated with insulin sensitivity and is anti-atherogenic. Leptin impairs insulin action and promotes inflammation by ↑ synthesis of TNF-α & IL-6.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

B. Immune, metabolic and endocrine factors:

5. Increasing evidence that inflammation contributes to the development of MetS in schizophrenia.

6. Schizophrenia & obesity: ↓ adiponectin & ↑ leptin, ↑ TNF-α & IL-6 →higher risk of atherosclerosis and coronary artery disease.

7. Blood serum levels of CRP, TNF-α and homocysteine ↑ in schizophrenia.

8. CRP has +ve association with waist circumference and DBP.

9. Homocysteine has +ve association with waist circumference, SBP+DBP, triglycerides and glucose.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

B. Immune, metabolic and endocrine factors:

10. Abnormal baseline levels of IL-6 predict significantly greater elevations in both total cholesterol and LDL following a 12-week treatment with olanzapine.

11. Total WBC count, a surrogate parameter of inflammation, is a risk factor for MetS, its values +vely correlate with ↑ in waist circumference & glucose during a 24-week treatment with paliperidone.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

C. Lifestyle factors:

Inactive lifestyle, poor dietary choices, poor sleep hygiene, excessive alcohol consumption and smoking contribute to development of MetS in schizophrenia.

Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

These lifestyle factors are partly due to negative symptoms of schizophrenia, poor insight and sedation due to APD.

Reduced likelihood of psychiatric patients receiving standard (optimal) levels of medical care likely contributes to an unhealthier metabolic profile among psychiatric patients.

Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72.

Metabolic syndrome in schizophrenia

Mechanisms:

D. Antipsychotics and APD induced weight gain:

Robust evidence that APD reduce morbidity, suicide & hospital admissions.

FGA Vs SGA: EPS, weight gain, cognition and affective symptom control.

Ranking SGAs on basis of relative risk for development of metabolic syndrome:

1 Clozapine (highest risk)

2 Olanzapine

3 Quetiapine

4 Risperidone

5 Aripiprazole

6 Ziprasidone (lowest risk)

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

D. Antipsychotics and APD induced weight gain:

Prevalence of MetS in first-episode schizophrenia who are treated with APDs is estimated at ~ 10% using NCEP-ATP III criteria and 18% using IDF criteria.

5-HT2C receptor antagonism → ↑ insulin resistance and ↓ glucose uptake by skeletal muscles → ↑ risk of diabetes.

H1 and H3 receptors mediators of energy intake and expenditure. Histamine agonists attenuate weight gain. APDs that have anti-histaminergic properties, lead to sedation and reduction in metabolism.

Twin studies suggest genetic variability in APD induced weight gain (HTR2C gene, which encodes for 5-HT2C receptors.)

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in schizophrenia

Mechanisms:

D. Antipsychotics and APD induced weight gain:

Genetic variations involving the satiety pathways have also been implicated.

The **leptin system** regulates appetite and energy metabolism via the melanocortin system (alpha-melanocyte stimulating hormone and agouti-related peptide) and neuropeptide Y.

Polymorphisms in the leptin gene LEP and leptin receptor gene LEPR are associated with increased risk of developing metabolic syndrome.

Increasing trend of combining different APDs in treating patients with treatment-resistant schizophrenia. Multiple APDs incidence of MetS =50% Vs APD monotherapy =34%. Combination of clozapine and aripiprazole is beneficial.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in bipolar disorder

- Metabolic syndrome in bipolar disorder estimated between 25% and 27%.
- In different studies the rates varied from 16.7% to 67%.
- Multiple factors across both phases of bipolar disorders are implicated:
  1. HPA axis dysregulation (glucocorticoid resistance),
  2. impaired glucose tolerance and insulin resistance,
  3. sympathetic nervous system dysregulation,
  4. increased pro-inflammatory cytokine production and
  5. unhealthy lifestyle.

Sources: Grover et al. Indian Journal of Psychological Medicine; Apr - Jun 2012 ,Vol 34, Issue 2; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in bipolar disorder

- Following are clinical risk factors for developing MetS :
  - longer duration of illness,
  - bipolar disorder- I,
  - greater number of lifetime depressive and manic episodes,
  - more severe and difficult-to-treat index affective episode,
  - depression at onset and during acute episodes,
  - later age of onset at first manic episode,
  - later age at first treatment for the first treatment for both phases,
  - less healthy diet as rated by patients themselves,
  - absence of physical activity and
  - family history of diabetes mellitus.

Sources: Grover et al. Indian Journal of Psychological Medicine; Apr - Jun 2012 ,Vol 34, Issue 2; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in bipolar disorder

- Metabolic syndrome affects the course of bipolar disorder.
  1. Bipolar disorder with T2DM are more likely to experience rapid cycling, lower level of functioning and more psychiatric hospital admissions than those without T2DM.
  2. High rates of lifetime suicide attempts in patients with bipolar disorder and metabolic syndrome have also been reported.
- Mood stabilisers, particularly lithium and sodium valproate, have been associated with metabolic syndrome.
- Simultaneous treatment with mood stabilisers and APDs or concurrent use of 2 to 3 mood stabilisers is associated with significantly higher metabolic disturbances.

Sources: Grover et al. Indian Journal of Psychological Medicine; Apr - Jun 2012 ,Vol 34, Issue 2; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in depression

- Prevalence of MetS in patients with depression = 36% to 50%.
- A systematic review (n= 1,55,333), found depression and MetS were modestly associated (adjusted OR=1.34).
- A Netherlands study (n= 3000) showed evidence for a dose-response association between depression and MetS.
- Scarce prospective evidence for a bidirectional relationship, yet depression appears to predicts onset of MetS, and MetS appears to predict the onset of depression over time.

Sources: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in depression

- Consistent evidence exists between depression and abdominal obesity, low HDL-C & hypertriglyceridemia. Associations with hyperglycemia and hypertension are confirmed less frequently.
- Comorbid depression and MetS contribute to patient remaining in a depressed state.
- Depressive symptoms in patients with MetS predominantly neurovegetative features (fatigue, anhedonia & loss of energy) and less likely to have affective & cognitive features.

Sources: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in depression

- Factors involved in development of MetS in depression:
  1. Physical inactivity.
  2. Activation of HPA axis.
  3. Chronic increase of insulin and leptin.
  4. Increase of pro-inflammatory cytokines and leptin resistance.
  5. Vascular endothelial dysfunction resulting from ↓ VEGF.

- Short-term weight gain greater risk with amitriptyline, mirtazapine, and paroxetine.

- TCAs & SNRIs : elevate systolic and diastolic blood pressure.

Sources: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome & cognitive decline & dementia

- Elderly people with metabolic syndrome are more likely to develop cognitive impairment than those without the syndrome.
- Cognitive deficits that are linked to metabolic syndrome involve memory, visuospatial abilities, executive functioning, processing speed and overall intellectual functioning.
- MetS effect on brain includes neuroinflammation, oxidative stress, impaired glucose metabolism and impairment of vascular reactivity.
- ↑ production of pro-inflammatory cytokines like IL-1β, IL-6 and TNF-α. IL-1β and IL-6 stimulate over-expression of AβPP and deposition of amyloid-β in brain → ↑ cytokines →vicious circle.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome & cognitive decline & dementia

- ↑ production of cytokines →accelerate atherosclerosis → AD.
- ↑ carotid stiffness & intima-media thickness reported in MetS → ↓ cerebral blood flow, nutrient supply & metabolic waste removal → disruptions of neuronal activity → possible progression to cognitive decline.
- Adiponectin related to cognitive function in several studies. Plasma adiponectin ↑ in MCI or Alzheimer's disease, cerebrospinal fluid adiponectin was significantly ↑ in MCI.
- Renal clearance of adiponectin in the elderly is lower than in younger adults. Thus, plasma adiponectin levels in elderly people should be interpreted with caution.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in PTSD

- Meta-analysis (n 9673 PTSD with n 6852 controls), MetS prevalence in PTSD patients was 38.7%.
- Patients with PTSD had a 1.82-times higher risk for MetS. Risk was consistent across geographical regions and populations (war veterans or not).
- PTSD associated with CVS risk factors like hypertension, T2DM and obesity.
- Chronic and severe PTSD associated with ↑ risk of MetS.
- Stress-related dysregulation of glucose and lipid metabolism in PTSD can also lead to the development of MetS.

Sources: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72; Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in other psychiatric disorders

- 50%-60% prevalence in **obese binge eating disorder** patients.
- ↑ insulin secretion, impaired fasting glucose and glucose tolerance, and elevated serum lipid levels likely factors.

- Prevalence of MetS in **borderline PD** is twice that of patients in primary care.
- Older age, higher BMI, SGAs, BDZ dependence, dysregulation of HPA system and binge eating behaviour likely factors.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in other psychiatric disorders

- Moderate consumption of red wine & ↓ incidence of metabolic syndrome: polyphenols→ ↑ activity of endothelial nitric oxide synthase (eNOS).
- Misuse of **alcohol** → disturbed of carbohydrate & lipid metabolism → ↑ risk of hypertension, impaired fasting glucose, high triglyceridaemia and abdominal obesity.
- Alcohol causes malnutrition and damage to almost every organ system in the body.
- Psychiatric disorders comorbid with alcoholism - major depression, bipolar disorder, schizophrenia, anxiety disorders and personality disorders.

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Metabolic syndrome in other psychiatric disorders

- A medical record study in children with **ASD** revealed an ↑ risk of obesity and obesity-related disorders (OR=1.85).
- ASD patients at risk partly because they are commonly using APDs, ADDs, or AEDs for extended periods of time.

- Hardly any research has been done in children with **ADHD**.
- Few reports in adults indicate that ADHD may involve an ↑ BMI and alterations in lipid profiles - findings seem inconsistent and well-powered studies are lacking.

Source: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72.

History = HT/DM/smoking/diet/physical activity/family history.
Physical exam = height & weight (BMI), BP, waist circumference.
Lab exam = FBS, GGT, ALT, total cholesterol, LDL, HDL, triglycerides.
Psychoeducation = advice on smoking cessation, diet and physical activity.
Choosing psychotropic = based on cardiometabolic profile of the drug.
Review choice if > 7% baseline weight gain occurs.
Referral = if one abnormal physical exam finding or three abnormal lab findings.

Timeline →	Baseline	1.5 months	3 months	12 months	Annually
History	♥				
Physical exam	♥	♥	♥	♥	♥
Lab exam	♥	♥	♥	♥	♥
Psychoeducation	♥	♥	♥	♥	♥
Choosing psychotropic	♥	♥			
Referral	♥	♥	♥	♥	♥

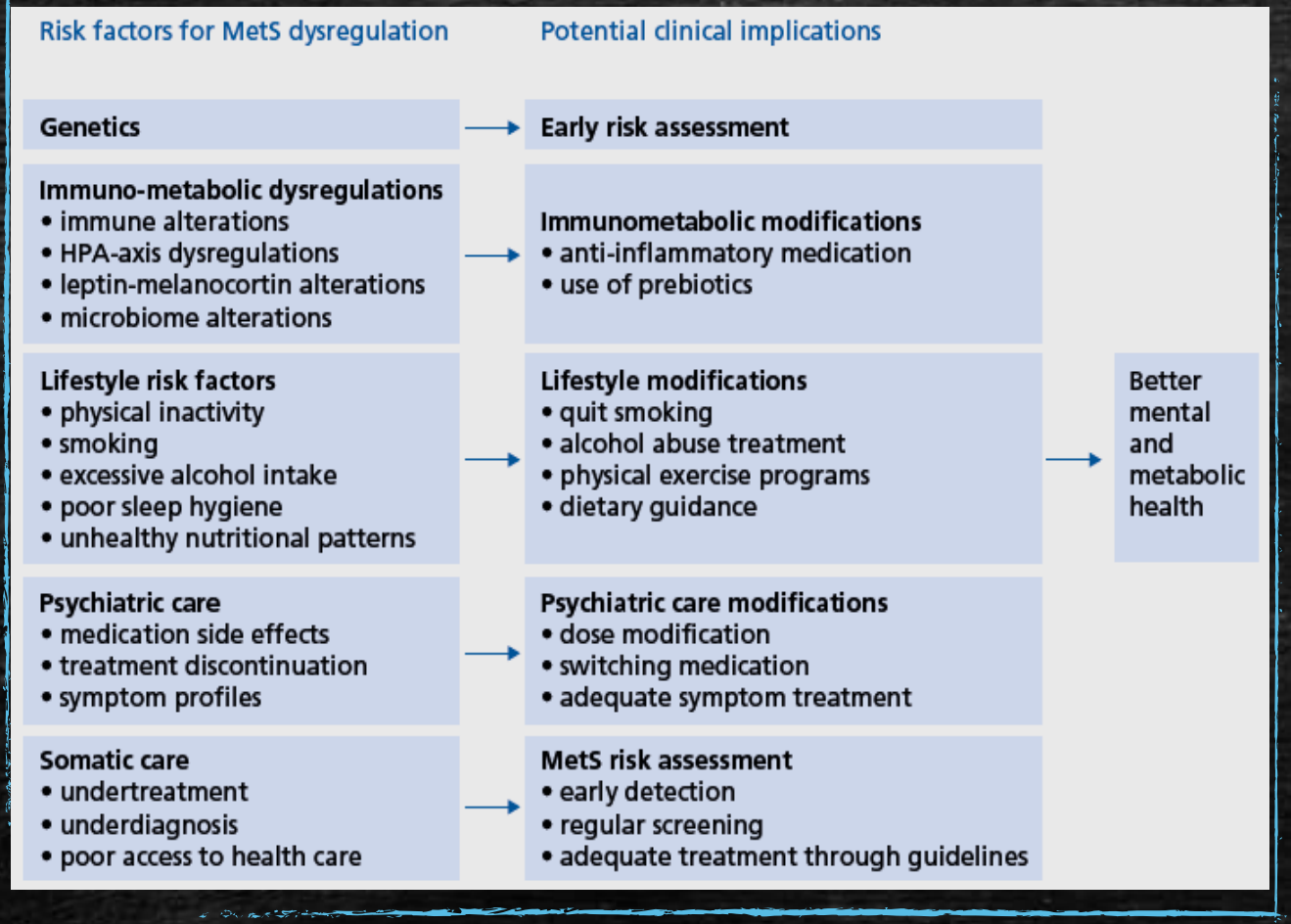
Screening for metabolic syndrome in psychiatric disorders

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

Survey of Indian psychiatrist

- What clinical parameters are measured at baseline ?
- Which are the main systemic side effects that they are vigilant about in short term and long term ?
- Self report about the level of awareness of metabolic syndrome in psychiatric disorders on a Likert scale.
- Unfortunately cannot demonstrate the results as no preceding EC approval was sought for this survey.

Preventing and treating MetS in psychiatry



1. Preventing MetS
2. Lifestyle interventions
3. Screening for MetS
4. Choosing a psychotropic
5. Treatment resistance
6. Pharmacological R_x MetS
7. Gut-brain axis interventions

Source: Brenda W. J. H. Penninx et al. Dialogues in Clinical Neuroscience. Mar 2018,Vol 20, pages 63-72.

Preventing and treating MetS in psychiatry

Treatment for:
- Hypertension, Dyslipidemia, T2DM

Weight loss:
- Meta-analysis of 32 RCTs in APD induced weight gain revealed the following descending order of efficacy for weight loss:

metformin, d-fenfluramine, sibutramine, topiramate, reboxetine, amantadine, nizatidine, orlistat, metformin plus sibutramine, famotidine, dextroamphetamine, fluoxetine, rosiglitazone.

- Bariatric surgery

Novel treatments:
- GLP-1 agonist – e.g. liraglutide

1. Preventing MetS
2. Lifestyle interventions
3. Screening for MetS
4. Choosing a psychotropic
5. Treatment resistance
6. Pharmacological R_X:MetS
7. Gut-brain axis interventions

Source: Cyrus Ho et al. Advances in psychiatric treatment (2014), vol. 20, 101–112

CONCLUSION

1. Psychiatric patients - high risk of premature mortality mainly CVS cause.

2. Many psychiatric disorders put the patient at an increased risk of MetS.

3. An association exists between severity and duration of psychiatric symptoms and a bidirectional longitudinal impact with MetS.

4. Unhealthy lifestyle, genetic polymorphisms, inflammation, endocrine abnormalities and psychotropic drugs play a contributory role for developing MetS.

5. Increased risk of metabolic syndrome in psychiatric disorders justifies a high vigilance for prevention, close monitoring, and treatment of at risk patient.

QUESTIONS?

THANK YOU FOR YOUR ATTENTION !