SCHIZOPHRENIA & OTHER PSYCHOTIC DISORDERS

Pawan Kumar Gupta, Associate Professor,
Department of Psychiatry,
KGMU, UP, Lucknow
WELCOME MESSAGE

Hello everyone !
I welcome you to this online presentation during COVID-19 pandemic as we are all staying at our homes. I hope you will find this lecture engaging and helpful in your studies. Stay home, stay healthy and keep learning. Best wishes!

Pawan Kumar / Associate Professor

PRESENTATION MAP

My presentation will include following slides:

- What is psychosis?
- How do you classify and diagnose psychosis?
- Definition of schizophrenia.
- Symptoms and diagnosis of schizophrenia.
- Risk factors of schizophrenia
- Basic neurobiology of schizophrenia
- Course and prognosis of schizophrenia
- Management of schizophrenia
- My Contact details and study resources
- Self-assessment
WHAT IS PSYCHOSIS?
Psychosis is a common symptom of many psychiatric, neurodevelopmental, neurologic, and medical conditions and is an important target of evaluation and treatment in neurologic and psychiatric practice.

Psychosis is also identified as only one of several dimensions of neuropsychiatric disturbance in these disorders, with others encompassing abnormal psychomotor behaviors, negative symptoms, cognitive impairments, and emotional disturbances.

References:
WHAT IS PSYCHOSIS?
Concepts and definitions of Psychosis.

ICD-10 clinical description & diagnostic guidelines

"Psychotic" has been retained as a convenient descriptive term, particularly in F23, Acute and transient psychotic disorders. Its use does not involve assumptions about psychodynamic mechanisms, but simply indicates the presence of hallucinations, delusions, or a limited number of severe abnormalities of behaviour, such as gross excitement and overactivity, marked psychomotor retardation, and catatonic behaviour.

- Presence of hallucinations,
- Delusions,
- or a limited number of severe abnormalities of behaviour, such as:
  - gross excitement and overactivity,
  - marked psychomotor retardation, and
  - catatonic behaviour"
Schizophrenia spectrum and other psychotic disorders
comprises schizophrenia and related disorders, other major psychoses, and disorders with sub threshold psychoses.
All are unified by the presence of one or more of the following five domains of psychopathology:
“delusions, hallucinations, disorganised thinking, grossly disorganised or catatonic behaviour and negative symptoms.”
The first four domains are examples of psychosis,
negative symptoms are characterised by the absence of something that should be present, such as fluency and spontaneity of verbal expression.

In both of these current diagnostic classification systems, impaired reality testing remains central conceptually to psychosis.

In their current conceptualization of psychosis, both the APA and the World Health Organization define psychosis narrowly by requiring the presence of hallucinations (without insight into their pathologic nature), delusions, or both hallucinations without insight and delusions.

This dimensional approach regards hallucinations and delusions as arising from neural systems subserving perception and information processing, thereby aligning the neurobiological framework used to describe and study such symptoms in primary psychotic disorders with those used to study psychosis associated with other neurologic conditions.

References:
Diagnosis is done by clinical evaluation and it is either based on ICD-10 or DSM-5.
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ICD-10 CLASSIFICATION OF PSYCHOTIC DISORDERS
Coded from F20-F29.

Schizophrenias
20

Other acute and transient psychotic disorders
28

Schizotypal disorder
21

Persistent delusional disorders
22

Acute and transient psychotic disorders
23

Induced delusional disorders
24

Psychosis with Unknown etiology
Unspecified Or NOS

Other acute and transient psychotic
This diagnosis is made when the criteria of F20-25 are not met.

Schizotypal disorder
Schizotypal disorder possesses many of the characteristic features of schizophrenic disorders and is probably genetically related to them; however, the hallucinations, delusions, and gross behavioural disturbances of schizophrenia itself are absent and so this disorder does not always come to medical attention.

Persistent delusional disorders
Most of the delusional disorders are probably unrelated to schizophrenia, although they may be difficult to distinguish clinically, particularly in their early stages. They form a heterogeneous and poorly understood collection of disorders, which can conveniently be divided according to their typical duration into a group of persistent delusional disorders and a larger group of acute and transient psychotic disorders.

Acute and Transient psychotic disorders
This category is very common in developing countries.

Schizoaffective Disorders
The subdivisions listed here should be regarded as provisional. Schizoaffective disorders have been retained in this section in spite of their controversial nature.

Schizophrenia, schizotypal And Delusional disorders

This diagnosis is made when the criteria of F20-25 are not met.

Other acute and transient psychotic

Schizotypal disorder possesses many of the characteristic features of schizophrenic disorders and is probably genetically related to them; however, the hallucinations, delusions, and gross behavioural disturbances of schizophrenia itself are absent and so this disorder does not always come to medical attention.

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DSM-5 CLASSIFICATION OF PSYCHOTIC DISORDERS

1. SCHIZOTYPAL DISORDERS

2. SCHIZOPHRENIA

3. SCHIZOPHRENIFORM DISORDERS

4. DELUSIONAL DISORDERS

5. SCHIZOAFFECTIVE DISORDER SUBSTANCE / MEDICATION INDUCED DUE TO OTHER MEDICAL CONDITION
CATATONIA ASSOCIATED WITH ANOTHER MENTAL DISORDERS

CATATONIA DUE TO ANOTHER MENTAL DISORDERS

OTHER

UNSPECIFIED CATATONIA

UNSPECIFIED
WHAT IS SCHIZOPHRENIA?

Heterogenous group of symptoms diagnosed based on ICD-10 or DSM-5.
WHAT IS SCHIZOPHRENIA?
Symptoms dimensions of schizophrenia

DELUSIONS
- Themes: persecutory, referential, somatic, religious, grandiose, erotomanic and nihilistic delusions
- Bizarre delusions are clearly implausible and not understandable to same culture peers and do not derive from ordinary life experiences
- Thought insertion, thought withdrawal, delusions of control are considered bizarre delusions

HALLUCINATIONS
- Vivid and clear, with the full force and impact of normal perceptions, and not under voluntary control
- Occur in clear sensorium
- Auditory hallucinations are experienced as voices heard distinct from one’s thoughts

DISORGANISED THINKING AND SPEECH
- Formal thought disorder includes
  - Derailment or loose associations,
  - Tangentiality,
  - Incoherence or word salad

DISORGANISED BEHAVIOUR
- Grossly disorganized or abnormal motor behavior (including catatonia)
  - Problems in goal directed behavior
  - Catatonia

THINKING

PERCEPTION

CONTACT US
### WHAT IS SCHIZOPHRENIA?

**Symptoms dimensions of schizophrenia**

#### NEGATIVE SYMPTOMS
- **Affective blunting**: inability to understand and express emotions
- **Alogia**: decrease in verbal communication e.g. poverty of speech, blocking
- **Anhedonia**: loss of ability to find pleasure from relationships and/or activities
- **Avolition**: loss of will or drive e.g. hygiene, school
- **Asociality**: social withdrawal

#### COGNITIVE SYMPTOMS
- Attention
- Episodic memory
- Executive functions (including language function)
- Working memory
- Processing speed
- Inappropriate Affect
- Inhibitory capacity

#### AFFECTIVE SYMPTOMS
- Depression
- Anxiety
- Anger
- Hostility
- Aggression

#### CATATONIC BEHAVIOUR
- Motor abnormalities
- Repetitive
- Complex gestures
  - Usually of the fingers or hands
- Excitable
- Wild flailing of limbs.

#### THINKING
- **THINKING AND SPEECH**

#### PSYCHOMETRIC
IMPORTANT PERSONALITIES
WHO CONTRIBUTED IN EVOLUTION OF THE CONCEPT.
EMIL KRAEPELIN (1856-1926)
Dementia Praecox

IMAGE EUGENE BLEULAR (1857-1939)
4 A's

KURT SCHNEIDER (1887-1967)
First Rank Symptoms

IMPORTANT PERSONALITIES
WHO CONTRIBUTED IN EVOLUTION OF THE CONCEPT.
The positive symptoms of schizophrenia are thought to be caused by an excess of dopamine in the mesolimbic pathway, although the reasons for this increase are not known.

- Positive symptoms include hallucinations and delusions.
- Theoretically, decreasing dopamine in this pathway would be therapeutic.

The negative and cognitive symptoms of schizophrenia are thought to be caused by a shortage of dopamine in the mesocortical pathway. Theoretically, increasing dopamine in this pathway would be therapeutic.

THE TUBEROINFUNDIBULAR PATHWAY

Mesocortical pathway

Mesolimbic pathway

Tuberoinfundibular pathway
Regulation of prolactin secretion

THE NIGROSTRIATAL PATHWAY CAUSING EPS

DOPAMINE HYPOTHESIS FOR SYMPTOMS & SIDE EFFECTS


**Tuberoinfundibular pathway**
Regulation of prolactin secretion

**Mesocortical pathway**
Cognition and executive function

Negative symptoms *(hypodopaminergic)*:
- Alogia
- Affective flattening
- Avolition

**Nigrostriatal pathway**
D₂ receptor antagonism by antipsychotic drugs can result in EPS

**Mesolimbic pathway**
Regulation of emotional behaviour

Positive symptoms *(hyperdopaminergic)*:
- Delusions
- Hallucinations
- Disorganised thought, speech, & behaviour

**Mesocortical pathway**
Cognition and executive function

**Mesolimbic pathway**
Regulation of emotional behaviour

**Mesolimbic pathway**
Regulation of emotional behaviour

**Negative symptoms** *(hypodopaminergic)*:
- Alogia
- Affective flattening
- Avolition

**Positive symptoms** *(hyperdopaminergic)*:
- Delusions
- Hallucinations
- Disorganised thought, speech, & behaviour

ANTIPSYCHOTIC DRUGS AND THE DOPAMINE PATHWAYS OF THE BRAIN

- The therapeutic actions of typical antipsychotic drugs are due to antagonism of D₂ receptors, specifically in the mesolimbic dopamine pathway.

- This has the effect of reducing the excess release of dopamine in this pathway that is thought to cause the positive symptoms of psychosis.

- However, typical antipsychotics block D₂ receptors throughout the brain and not just those in the mesolimbic dopamine pathway;

- this extensive blockade of D₂ receptors is responsible for many undesirable adverse effects. Atypical antipsychotics are more discriminating.

D₂ receptor antagonism by typical antipsychotics can cause or worsen negative and cognitive symptoms.

D₂ receptor antagonism by antipsychotic drugs can result in EPS.

D₂ receptor antagonism by antipsychotic drugs reduces positive symptoms.
In the ‘normal’ brain

- Dopamine levels within both the mesolimbic and the mesocortical dopamine pathways are at normal levels, therefore no symptoms of schizophrenia are experienced.
In the schizophrenia brain

- Dopamine levels in the mesolimbic pathway are increased, causing the positive symptoms of schizophrenia.
- Simultaneously, the dopamine levels in the mesocortical pathway are decreased, leading to negative and cognitive symptoms.
Schizophrenia treated with D₂ antagonist (TYPICAL) antipsychotic

- Treating a patient with schizophrenia with a dopamine antagonist can successfully treat their positive symptoms by reducing dopamine signalling in the mesolimbic pathway.
- However, the dopamine antagonist also reduces signalling in the mesocortical pathway, meaning that the negative and cognitive symptoms are not addressed, and in some cases can be worsened.
Schizophrenia treated with an atypical, D₂ partial agonist antipsychotic

- A dopamine partial agonist works to reduce the excess dopamine in the mesolimbic pathway, treating the positive symptoms of schizophrenia
- Simultaneously, within the mesocortical pathway a dopamine partial agonist will act to enhance dopamine signalling, meaning that the negative and cognitive symptoms of schizophrenia could be improved as well
The role of glutamate in the pathology of schizophrenia

It seems clear that changes in dopamine signalling in the brains of patients with schizophrenia underlie the symptoms of psychosis, but what causes these changes?

The glutamate hypothesis

- The predominant ‘go’ neurotransmitter in the brain is glutamate\(^1,2\)
- There are many lines of evidence implicating glutamate NMDA receptors in schizophrenia:\(^1\)
  - Post mortem changes in NMDA receptors in the brains of patients with schizophrenia
  - NMDA-receptor antagonists can cause psychotic symptoms in humans
  - Some glutamatergic drugs have shown promise in treating schizophrenia

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GABA=gamma-aminobutyric acid; NMDA=N-methyl-D-aspartic acid

HYPOTHESES FOR THE UNDERLYING CAUSES OF SCHIZOPHRENIA
THE NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA

- Normal cortical development involves proliferation, migration of cells, dendritic arborisation (circuit formation), and myelination, with the first two processes occurring mostly during prenatal life and the latter two continuing through the first two post-natal decades. ¹
- A progressive reduction of grey-matter volume with age is observed with longitudinal neuro-imaging. ¹,² The combined effects of pruning of the neuronal arbor and myelin deposition are thought to account for this. ¹
- Psychosis nearly always emerges in late adolescence or early adulthood, with a peak between the ages of 18 and 25, when the prefrontal cortex is still developing. ¹
- The neurodevelopmental trajectory in children developing schizophrenia could include reduced elaboration of inhibitory pathways, and excessive pruning of excitatory pathways, leading to altered excitatory–inhibitory balance in the prefrontal cortex. ¹

There have been attempts to explain schizophrenia using cognitive models\textsuperscript{1,2}

Cognitive models of schizophrenia suggest that the interpretation of social adversity (e.g., child abuse) through biased cognitive schema and appraisal processes, results in the individual judging the adversities as being externally driven, giving rise to paranoid delusions\textsuperscript{1,2}

Attempts have been made to integrate these cognitive models with the known patho-physiology of schizophrenia, postulating that genetic predisposition and neurodevelopmental insults disrupt the dopamine system, alongside social adversity leading to biased cognitive schema – these forces act in concert to hardwire the individual in favour of the psychotic interpretation of the world around them\textsuperscript{1}

## Evidence for involvement in the pathophysiology of schizophrenia

<table>
<thead>
<tr>
<th>Neuronal Transmitter</th>
<th>Evidence</th>
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| **Dopamine**         | Drugs that prevent the activity of dopamine in the brain, by blocking D<sub>2</sub> receptors, can reduce positive symptoms<sup>1</sup>  
|                      | Amphetamines, which increase the levels of dopamine in the brain, can increase psychotic symptoms<sup>1</sup>  |
| **Glutamate**        | NMDA receptor antagonists, such as phencyclidine and ketamine, produce psychosis-like features indistinct from schizophrenia<sup>1</sup>  |
| **GABA**             | Reduced synthesis and reuptake of GABA has been demonstrated in the prefrontal cortex in patients with schizophrenia<sup>1</sup>  |
| **Acetylcholine**    | Decreased levels of cholinergic receptors are observed in the hippocampus, thalamus, and striatum in patients with schizophrenia<sup>1</sup>  |
| **Serotonin**        | Prefrontal 5-HT<sub>2A</sub> receptors have been linked to the pathogenesis of schizophrenia<sup>2,3</sup>  
|                      | Activation of 5-HT<sub>2A</sub> receptors induces a schizophrenia-like psychosis in humans<sup>2,3</sup>  |
INFLAMMATION AND SCHIZOPHRENIA

- The immune system is linked to the pathology of schizophrenia, with evidence including elevated cytokines and microglial activation\(^1,2\)
- PET imaging has been used to examine immune system activity in patients with schizophrenia\(^1\)
- One study found elevated microglial activity in unmedicated patients with sub-clinical symptoms who were at ultra high risk of psychosis, and found a significant positive correlation with symptom severity\(^1\)
- These data indicate that neuroinflammation is linked to the risk of psychosis and related disorders, and the expression of sub-clinical symptoms\(^1\)

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**Table:**

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<thead>
<tr>
<th></th>
<th>Healthy controls (n=14)</th>
<th>Patients with schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total grey matter</td>
<td><img src="chart.png" alt="Chart" /></td>
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<tr>
<td>Frontal lobe</td>
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<tr>
<td>Temporal lobe</td>
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</tbody>
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**References:**

**Note:**
PET = positron emission tomography; SD = standard deviation.
The makeup and function of the gut microbiota is increasingly being linked to the pathology of neurological disorders, including schizophrenia, depression, and bipolar disorder\(^1\)\(^-\)\(^3\).

The normal flora of the gut is made up of several species of bacteria, and also of viruses and fungi, which colonise the gut at birth\(^4\).

In a comparison of 16 patients with schizophrenia and 16 controls, differences in oropharynx flora were:\(^5\)

- Patients with schizophrenia were dominated by a greater number of microbiome species.
- Patients with schizophrenia had greater abundance of lactic acid bacteria.
- There were differences in the metabolic pathways controlling glutamate and B12 transport (increased in schizophrenia) and carbohydrate and lipid metabolism (decreased in schizophrenia).

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ENIRONMENTAL FACTORS
THE ENVIRONMENT AND SCHIZOPHRENIA

- Factors pre- and post-natal have been linked to an increased risk of schizophrenia\(^1,2\)
- Epidemiological studies and twin studies have identified many environmental factors that are linked to the development of schizophrenia, for example:\(^1,2\)
  - Prenatal exposure to viral infections
  - Poor pre-natal nutrition
  - Adverse obstetric events
  - Cannabis smoking during adolescence

GENETIC FACTORS
Numerous studies have shown that the risk of developing schizophrenia is greater in the relatives of patients with schizophrenia\(^1\)–\(^3\)

Data from twin studies and adoption studies support the significant role of genetic factors in schizophrenia\(^1\)

Research conducted more recently has identified susceptibility genes that may result in an increased risk of developing schizophrenia\(^2,4,5\)

It was found that early age of schizophrenia onset in the first twin was a risk factor for the second twin developing schizophrenia – this suggests that early-onset schizophrenia may have a stronger genetic component of risk than other subtypes of schizophrenia\(^6\)

These results demonstrate that there is a high genetic component to the risk of developing schizophrenia, however, vulnerability to the illness is not solely genetic\(^6,7\)

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THE GENETIC HERITABILITY OF SCHIZOPHRENIA

47% MONOZYGOTIC TWINS

40% DIZYGOTIC TWINS

12% BOTH PARENTS

8% ONE PARENT/ SIBLING

1% GENERAL POPULATION

79%

• An ambitious genome-wide association study (GWAS) was conducted by the Schizophrenia Working Group of the Psychiatric Genomics Consortium, analysing genetic data from >35,000 individuals with schizophrenia and >110,000 controls

• This GWAS analysis identified 108 distinct loci – 83 of which had not been previously implicated in schizophrenia

• Noteworthy gene locations included:
  • **The dopamine receptor D₂ gene** – highlighting the known importance of dopamine neurotransmission in the pathology of schizophrenia
  • Several **genes encoding proteins involved in glutamatergic neurotransmission**, and several **voltage-gated calcium channel component proteins** – providing an aetiologically relevant foundation for treatment development
  • **Genes expressed in tissues with important roles in immunity** – supporting the hypothesised link between schizophrenia and the immune system
  • In an analysis of data from several different GWAS studies, attempting to integrate the data, six crucial genes have been identified as being linked to an increased risk of developing schizophrenia – five of which are related to neurodevelopment

GWAS=genome-wide association study
COURSE AND PROGNOSIS
Schizophrenia progression may lead to functional decline.
GOOD PROGNOSTIC FACTORS

LATE ONSET

PRESENCE OF PRECIPITATING FACTOR

ACUTE ONSET

01. POSITIVE AND AFFECTIVE

02. + A

03. GOOD FAMILY SUPPORT

04. PF

05. GOOD COMPLIANCE/TOLERANCE

06. Acute

07. FEMALE GENDER

CATIE=Clinical Antipsychotic Trials of Intervention Effectiveness.
APPROACH TOWARDS MANAGEMENT

IN NEXT FEW SLIDES YOU WILL UNDERSTAND HOW TO INCORPORATE ALL THE PREVIOUS INFORMATION IN YOUR CLINICAL ASSESSMENT
ASSESSMENT OF A CASE WITH PSYCHOTIC SYMPTOMS

HISTORY TAKING

CHIEF COMPLAINTS
EXAMPLES: HEARING VOICES, ODD BEHAVIOUR, DECREASED SLEEP

HISTORY OF PRESENT ILLNESS
EXPLORE IN DETAIL ABOUT EACH COMPLAINTS, ASSOCIATED SYMPTOMS
ONSET
COURSE
DURATION
EPISODES
PRECIPITATING FACTORS
TREATMENT TAKEN
HISTORY TAKING

NEGATIVE HISTORY
TO RULE OF DIFFERENTIAL DIAGNOSIS
SUICIDE, HOMICIDE,
SUBSTANCE USE
MEDICAL HX.

PAST HISTORY
OF SIMILAR EPISODES
OTHER EPISODES
MEDICAL
SUBSTANCE USE
FAMILY HISTORY
- Remember about the familial risk factors
- Attitude of family
- Housing condition
- HX of psychiatric illness

PERSONAL HISTORY
- Perinatal, childhood, adolescents, education, occupation, marital
- Substance use
- Premorbid personality

HISTORY TAKING
NEVER FORGET TO PERFORM COMPLETE PHYSICAL EXAMINATION

FINDINGS OF PHYSICAL EXAMINATION CAN AFFECT THE WHOLE DIAGNOSIS AND MANAGEMENT
GENERAL APPEARANCE AND BEHAVIOUR
DISORGANISATION, ODDITY OF BEHAVIOUR, SPEECH, RAPPORT, THERAPEUTIC ALLIANCE

AFFECT
INAPPROPRIATE AFFECT, IRRITABILITY, PERPLEXITY

MENTAL STATUS EXAMINATION

THINKING.
FLOW (IRRELEVANCE, INCOHERENCE)
FORM-FORMAL THOUGHT DISORDERS
CONTENT: IDEAS OR DELUSIONS,

PERCEPTION
HALLUCINATIONS
AUDITORY (2 OR 3 PERSON)
MEMORY
Impairment in memory is not usual finding but may occur.

JUDGEMENT & INSIGHT
Usually impaired in psychosis indicates lost touch with reality.

HIGHER FUNCTIONS & INTELLIGENCE
Impairments not apparent on MSE but may present.

SUMMARIZE
CONSIDER IN BIO-PSYCHO-SOCIAL PERSPECTIVE

EXPLAINING THE DIAGNOSIS AND MANAGEMENT OPTIONS AND GOALS

DIAGNOSTIC FORMULATIONS

MANAGEMENT
MANAGEMENT OF SCHIZOPHRENIA

1. DECIDE TREATMENT SETTING
   INPATIENT OR OUTPATIENT.

2. LIAISON WITH OTHER SPECIALITIES
   PSYCHOLOGIST, SOCIAL WORKER, OCCUPATIONAL THERAPIST

3. PHARMACOLOGICAL MANAGEMENT
   CONSIDER PAST TREATMENT RESPONSE
   HISTORY OF SIDE-EFFECTS
   COST OF TREATMENT
   PATIENT’S FAMILY CHOICE
   ROUTE OF ADMINISTRATION
   HISTORY OF TREATMENT NONCOMPLIANCE
   TREATMENT RESISTANCE

4. ELECTROCONVULSIVE THERAPY
   SUICIDALITY
   CATATONIA
   AFFECTIVE SYMPTOMS
   PAST RESPONSE
   RAPID MANAGEMENT
   AUGMENTATION
5. **Non-pharmacological treatment**
   - Psychoeducation
   - Psychosocial intervention

6. **Evaluate treatment response**
   - Effect of medication decrease in symptoms
   - Side effects

7. **Non-response to treatment**
   - Re-evaluate diagnosis
   - Optimize treatment
   - Compliance
   - Treatment resistance

8. **Functioning**
   - Improve patient's functioning
     - Interpersonal
     - Social
     - Occupational

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e-mail me @

gpawan2008@gmail.com

Thank you!!
Improvement begins with “I”

Click here

Self-assessment
EPIDEMIOLOGY
THIS MEANS ABOUT 1 PERSON IN 100 WILL DEVELOP SCHIZOPHRENIA DURING THEIR LIFE TIME
GENDER & AGE

10-25 YEARS

25-35 YEARS

3-10% WOMEN

15-55 Yrs