CLINICAL EPIDEMIOLOGY OF SCHIZOPHRENIA

OUTLINE

- Introduction
- Prevalence
- Incidence
- Risk Factors
- Co-morbidity
- Conclusion

INTRODUCTION

Clinical epidemiology is the basic science of preventive medicine.

- predictions about the emergence (onset)
- persistence (prognosis) of disease
- evaluation of inherited and acquired characteristics
- attributes, behaviors, and exposures, known as risk factors (determinants)

INTRODUCTION

These risk factors increase an individual's likelihood of developing :-

1. a precursor of the clinical disorder (a condition or state preceding the recognized onset of a disease)
2. a clinical disease
3. a particular course and outcome trajectory for the disease process.

INTRODUCTION

- Clinical epidemiology attempts to harness the heterogeneity observed in risk factors, course, and outcome and uses this variation to generate hypotheses and develop empirically based conceptual frameworks (models) of disease.
- Heterogeneity is the hallmark of schizophrenia, with manifest variation in risk factors for onset, symptomatology, course, and outcome
- investigate how differences in genetic endowment moderate the effect of environmental risk factors

VARIATIONS IN INCIDENCE AND PREVALENCE

PREVALENCE

- In developed countries - the range 2.4 to 6.7 per 1,000 population at risk
- In developing countries - the range 1.4 to 6.8 per 1,000 population at risk
- A systematic review of 188 studies in 46 countries, published between 1965 and 2002, estimated the median value for point prevalence at 4.6 per 1,000 persons and for lifetime prevalence at 7.2 per 1,000.

Selected Prevalence Studies of Schizophrenia

Author	Country	Population	Method	Prevalence per 1,000 Population at Risk
Brugger (1931)	Germany	Area in Thuringia (*n* = 37,561); age 10+ years	Census; interview of sample	2.4
Strömgren (1938); Bøjholm and Strömgren (1989)	Denmark	Island population (*n* = 50,000)	Census interviews; repeat census	3.9 → 3.3
Böök (1953); Böök et al. (1978)	Sweden	Genetic isolate (*n* = 9,000); age 15–50 years	Census interviews; repeat census	9.5 → 17.0
Essen–Möller et al. (1956); Hagnell (1966)	Sweden	Community in southern Sweden	Census interviews; Repeat census	6.7 → 4.5
Rin and Lin (1962); Lin et al. (1989)	Taiwan	Population sample	Census interviews; repeat census	2.1 → 1.4
Crocetti et al. (1971)	Croatia	Sample of 9,201 households	Census based on hospital records and interviews	5.9
Dube and Kumar (1972)	India	4 areas in Agra (*n* = 29,468)	Census based on hospital and clinic records	2.6
Rotstein (1977)	Russia	Population sample (*n* = 35,590)	Census based on hospital and clinic records	3.8
Keith et al. (1991)	USA	Aggregated data across 5 ECA sites	Sample survey; interviews	7.0 (point) 15.0 (lifetime)
Jeffreys et al. (1997)	UK	London health district	Census; interview of	5.1

INCIDENCE

- Using a “broad” definition of scz (ICD-8, ICD-9, or unspecified) report approximately a threefold difference in the rates, for example, from 0.17 to 0.54 per 1,000 population per year for first admissions or first contacts.
- Studies using specified diagnostic criteria, such as the DSM-III, DSM-III-R, DSM-IV, or ICD-10, produce considerably lower incidence rates

Selected Incidence Studies of Schizophrenia

Author	Country	Population	Method	Rate per 1,000
Ödegaard (1946)	Norway	Total population	First admissions 1926–1935 (*n* = 14,231)	0.24 (hospital diagnoses)
Walsh (1969)	Ireland	City of Dublin (*n* = 720,000)	First admissions	0.57 (males, ICD-8) 0.46 (females, ICD-8)
Murphy and Raman (1971)	Mauritius	Total population (*n* = 257,000)	First admissions	0.24 (Africans) 0.14 (Indian Hindus) 0.09 (Indian Moslems)
Lieberman (1974)	Russia	Moscow district (*n* = 248,000)	Follow-back of prevalent cases	0.20 (males) 0.19 (females)
Helgason (1977)	Iceland	Total population	First admissions (case register)	0.27 (ICD-8)
Lin et al. (1989)	Taiwan	3 communities (*n* = 39,024)	Door-to-door survey	0.17 ("Bleulerian" criteria)
Castle et al. (1991)	UK	London (Camberwell)	First admissions (case register)	0.25 (ICD-9) 0.17 (RDC)

				0.08 (DSM-III)
Rajkumar et al. (1993)	India	Area in Madras (*n* = 43,097)	Door-to-door survey and key informants	0.41 (ICD-9)
Wig et al. (1993)	India	A rural area (*n* = 103,686) and an urban area (*n* = 348,609) in northern India	Case-to case finding and key informants	0.38 (urban, ICD-9) 0.09 (urban, Catego S+) 0.44 (rural, ICD-9) 0.12 (rural, Catego S+)
Brewin et al. (1997)	UK	Nottingham	2 cohorts of first contacts (1978–1980 and 1992–1994)	0.25 → 0.29 (all psychoses, ICD-10) 0.14 → 0.09 (ICD-10 schizophrenia)
Mahy et al. (1999)	Barbados	Total population (*n* = 262,000)	First contacts; PSE interviews; Catego	0.32 (ICD-9) 0.28 (Catego S+)
Bresnahan et al. (2000)	USA (California)	Birth cohort (*n* = 12,094)	Case register study; cumulative risk by age 38 years	0.93 (males, DSM-IV) 0.35 (females, DSM-IV)

INCIDENCE

A systematic review of incidence data from some 160 studies from 33 countries, published between 1965 and 2001,

- yielded a median value of 0.15
- mean value of 0.24 per 1,000
- a fivefold range of the rates and a tendency for recent studies to report lower rates.

CHHOTEN COUNTRY STUDY

WHO TEN COUNTRY STUDY

- The WHO Ten- Country Study remains to date the only investigation that has applied a uniform design and common research tools to generate directly comparable incidence data for different populations.
- Incidence counts in the study were based on first-in-lifetime contacts with any “helping agency”, which were monitored over a 2-year period

THE CHICHESTER COUNTRY STUDY

- In 86 percent of the 1,022 patients, the onset of diagnostic symptoms of schizophrenia was within the year preceding their first contact.
- Caseness was based on ICD-9 schizophrenia and paranoid psychoses, and a more restrictive definition of “nuclear” schizophrenia
- No differences were found between the “broad” and “nuclear” cases with regard to age at onset, or 2-year course and outcome.

Incidence Rates per 1,000 Population, Age 15–54 Years, for a "Broad" and a "Narrow" Case Definition of Schizophrenia (WHO Ten-Country Study, 1992)

		"Broad" Definition (ICD-9)			"Narrow" Definition (CATEGO S+)		
Country	Area	Male	Female	All	Male	Female	All
Denmark	Aarhus	0.18	0.13	0.16	0.09	0.05	0.07
India	Chandigarh (rural area)	0.37	0.48	0.42	0.13	0.09	0.11
	Chandigarh (urban area)	0.34	0.35	0.35	0.08	0.11	0.09
Ireland	Dublin	0.23	0.21	0.22	0.10	0.08	0.09
Japan	Nagasaki	0.23	0.18	0.20	0.11	0.09	0.10
Russia	Moscow	0.25	0.31	0.28	0.03	0.03	0.02
UK	Nottingham	0.28	0.15	0.22	0.17	0.12	0.14
USA	Honolulu	0.18	0.14	0.16	0.10	0.08	0.09

GENDER AND AGE

- Schizophrenia is equally prevalent in men and women.
- The two genders differ, however, in the onset and course of illness.
- Onset is earlier in men than in women.
- The peak ages of onset are :-
  - 10 to 25 years for men
  - 25 to 35 years for women.

RISK FACTORS FOR THE ONSET OF SCHIZOPHRENIA

GENETIC RISK

1. Family Studies:-
   - from a systematic review of the studies published during the period 1980 to 2003 found the 1st relatives of probands to have a higher morbidity risk for schizophrenia than the relatives of controls
   - Estimates ranged from 2 to 9% compared to a morbidity risk in the relatives of controls at about 0.5%

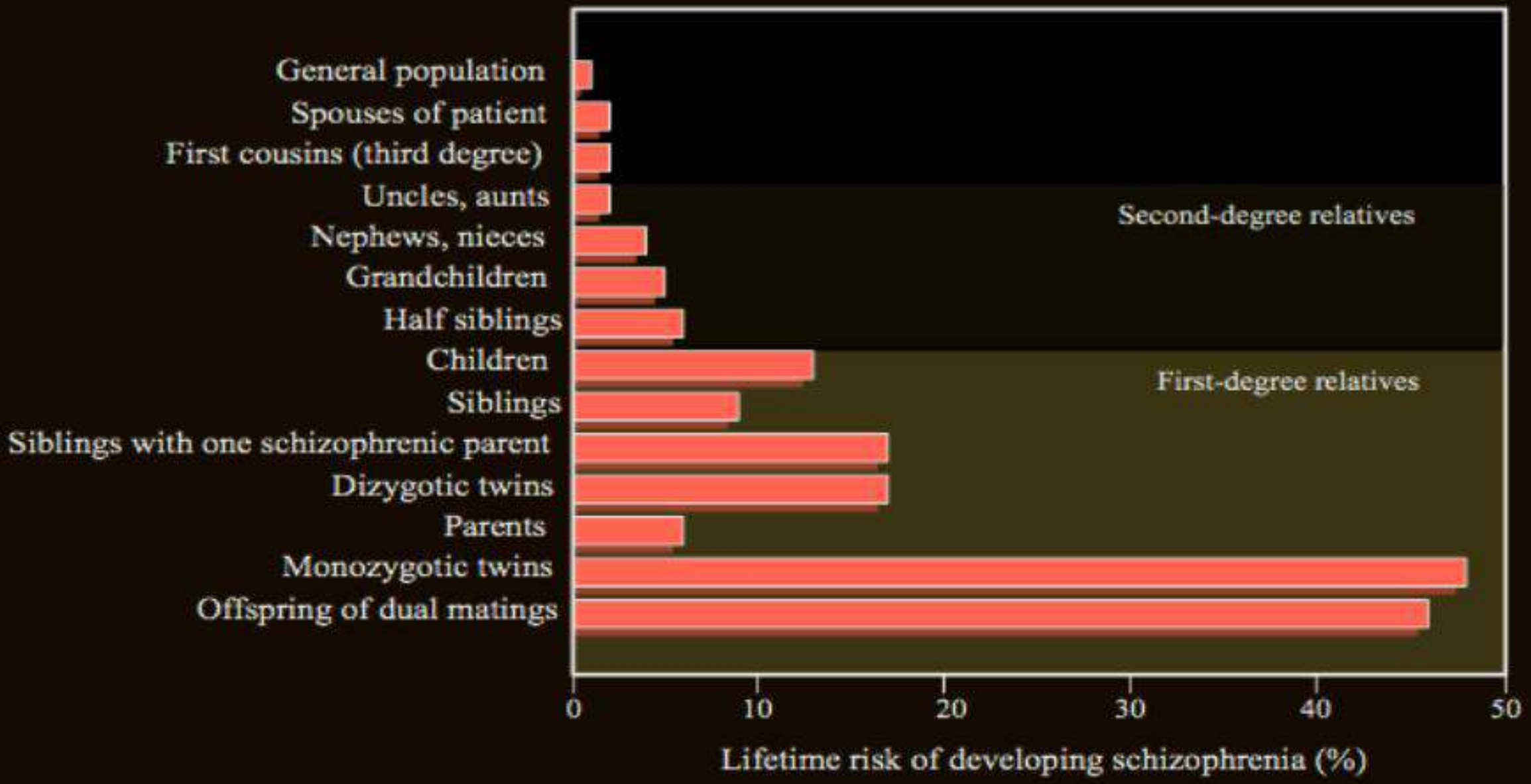
GENETIC RISK

2. Adoption Studies:-
   - Studies, showed the biological relatives to be at a higher risk of schizophrenia than the adoptive relative.
   - Demonstrated higher rates of schizophrenia in the adopted offspring of affected mothers, compared to the rates in the offspring of the unaffected controls

GENETIC RISK

3. Twin Studies:-
   - Twin pairs are equally exposed to environmental risk factors for schizophrenia
   - The concordance rate for monozygotic twins was higher in twins with an early rather than a late onset of schizophrenia.
   - Shows higher monozygotic concordance rates for the hebephrenic subtype compared to the paranoid type

LIFETIME RISK OF DEVELOPING SCHIZOPHRENIA



RELATIONSHIP TO SUBCLINICAL PSYCHOSES PHENOTYPES

- Some close relatives of patients with schizophrenia, although never frankly psychotic, display symptoms.
- Exhibits positive + Negative Symptoms
- The DSM combined these quasi-psychotic (schizotypic) features under the diagnostic category of schizotypal personality disorder.
- lifetime prevalence of 2.8 to 8.2 percent

RELATIONSHIP TO OTHER PSYCHOTIC DISORDERS AND BIPOLER DISORDER

- Can be schizophreniform, schizoaffective, delusional, and atypical delusional disorders in biological relatives.
- SczA. disorder occurs at similarly increased rates in the families of probands with scz and bipolar disorder
- family studies of schizoaffective disorder demonstrate increased risk for both scz and bipolar disorder
- The population attributable risk associated with psychiatric family history in general was nearly 30 %, whereas family histories including schizophrenia accounted for only 6 %.

GENE ENVIRONMENT INTERACTION

- Linear association of environmental exposures to risk for onset and persistence of schizophrenia.
- Gene－env. correlation occurs when a genotype could increase the likelihood of a person becoming exposed to an environmental risk factor
- Gene－environment interaction (synergism) (G × E) posits that instead of inheriting a disease state per se, a person actually inherits a set of genetic susceptibility factors that act to moderate the effects of (causal) environmental exposures.

RISK FACTORS OPERATING DURING EARLY DEVELOPMENT

PATERNAL AGE

- Advanced paternal age, the risk of schizophrenia in offspring.
- The association is strong and independent and the findings are consistent.
- Fathers age >50y, increases risk 3-4times.
- Advancing paternal age
  - accumulation of de novo mutations in the germ cells
  - interferes with the DNA methylation process of gene expression

SEASON OF BIRTH

- In the Northern Hemisphere, including the United States, persons with schizophrenia are more often born in the months from January to April.
- In the Southern Hemisphere, persons with schizophrenia are more often born in the months from July to September.
- Persons who develop schizophrenia are more likely to have been born in the winter and early spring and less likely to have been born in late spring and summer.

PREGNANCY AND BIRTH COMPLICATIONS

- increasing risk with decreasing birth weight, length at birth, placental weight and maternal starvation during pregnancy
- risk increased when multiple hypoxia-associated complications were present.
- Exposure to influenza epidemics
- The risk is greater for mothers with schizophrenia but is not confined to mothers with onset prior to delivery or to the births of the children who develop schizophrenia themselves later in life

RISK FACTORS OPERATING DURING CHILDHOOD AND ADOLESCENCE

URBAN BIRTH AND UPBRINGING

- Twofold increase in risk of schizophrenia in urban as compared to rural settings.
- Risk not due to social drift during the prodrome (reverse causation) but prior to the onset of the disorder.

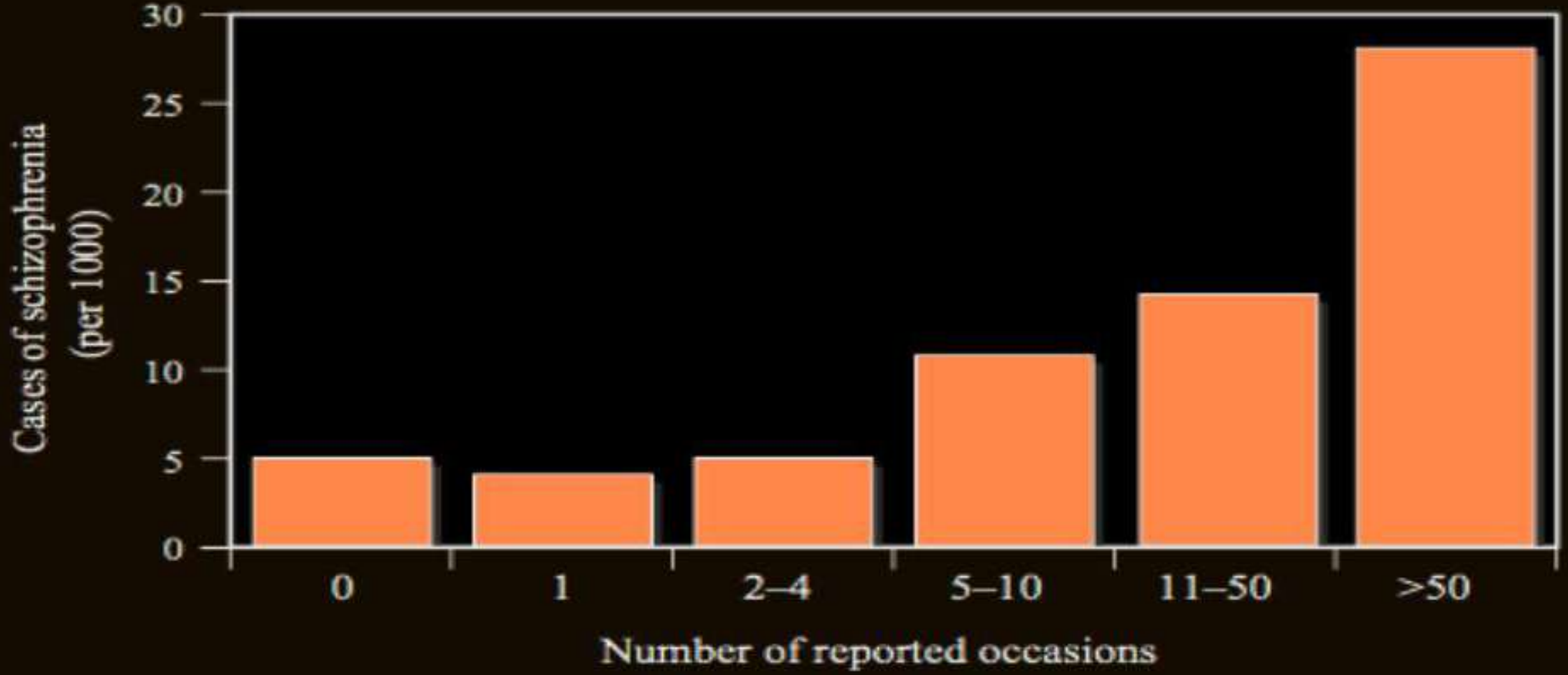
MIGRATION

- Many studies have reported increased rates of schizophrenia in migrants, especially among the second generation born in the new homeland.
- A special case is the exceptionally high incidence rate of schizophrenia (about 6.0 per 1,000) that has been found in the African-Caribbean population in the United Kingdom
- Migrant status is a binary exposure; one is either a migrant or one is not.

CANNABIS USE

- There is little doubt that cannabis intoxication is associated with transient psychotic symptoms in some individuals.
- Those reporting high levels of cannabis use (more than 50 occasions) were at six fold increased risk of schizophrenia compared with nonusers.
- The evidence to date may suggest some specificity of effect for schizophrenia and non affective psychosis
- controversy remains about whether cannabis is a risk factor for the development of schizophrenia or other psychotic disorders.

CANNABIS CONSUMPTION AT AGE 18 AND LATER RISK OF SCHIZOPHRENIA



THE BURDEN OF COMORBIDITY

Physical Disease

- Physical disease in patients with schizophrenia tends to be seriously undetected and underdiagnosed.
- it is the chronic non communicable diseases that in the past decades are taking an increasingly heavy toll on people with schizophrenia.
- CVD and the associated premature mortality are significantly increased in schizophrenia.

THE BURDEN OF COMORBIDITY

- Obesity and the concomitant metabolic syndrome involving insulin resistance and type II diabetes are at present common problems in patients with schizophrenia.

Substance Use

- The addictive use of cannabis, stimulants, and nicotine is disproportionately high among patients with schizophrenia and may be related to the underlying neurobiology of the disorder.

THE BURDEN OF COMORBIDITY

Variations in mortality

- In both developing and developed countries, schizophrenia is associated with excess mortality.
- A meta-analysis of 18 studies estimated a crude mortality rate of 189 deaths per 10,000 population peryear and a 10-year survival rate of 81 %.
- Mortality was significantly higher in males than in females, and the difference was primarily due to a male excess in suicides and accidents.

CONCLUSION

- There is no single cause for schizophrenia, rather a number of risk factors interact to propel the individual over a threshold for expression of the disease.

REFERENCES

- Kaplan & Saddock’s comprehensive textbook of psychiatry, 10th edition
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- Jeffrey Lieberman, Textbook of Schizophrenia, The American Psychiatric Publishing

THE END