# NAMI NJ
# 2015
# Annual Conference

# Psychosis: Approaches to treatment, before and after the first episode

# Robert G. Stern, M.D.


**Attending Psychiatrist**

Staten Island University Hospital

Tel: 718-226-2351

email: rstern1@nshs.edu

**Clinical Associate Professor**

Department of Psychiatry

Rutgers – RWJ-Medical School

# Treating Schizophrenia Before and After the First Psychotic Episode

1. Preventive measures and early tx will greatly decrease the incidence and severity of schizophrenia as it happened with heart disease.
2. Defining the high risk population
3. Treating individuals likely to develop schizophrenia before the first psychotic episode.
4. Treating individuals likely to develop schizophrenia after their first psychotic episode.

# I

Preventive measures and early tx have greatly decreased the incidence and severity of heart disease.

# Coronary Artery Disease as Analogy

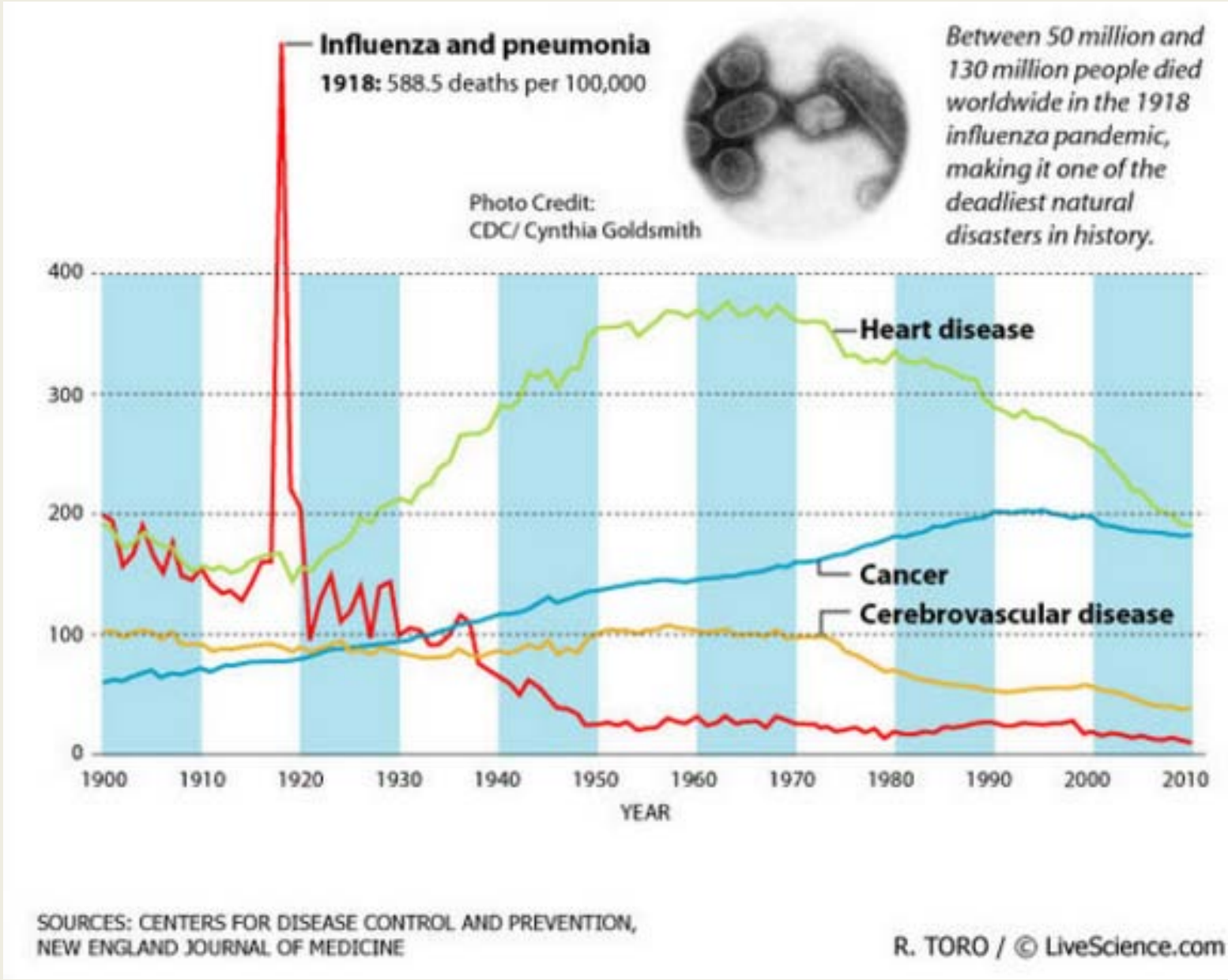
- Coronary artery disease develops when the coronary arteries — the major blood vessels that supply one's heart with blood, oxygen and nutrients — become damaged or diseased. Cholesterol-containing deposits (plaque) in your arteries and inflammation are usually to blame for coronary artery disease.

# Death Rates in the US

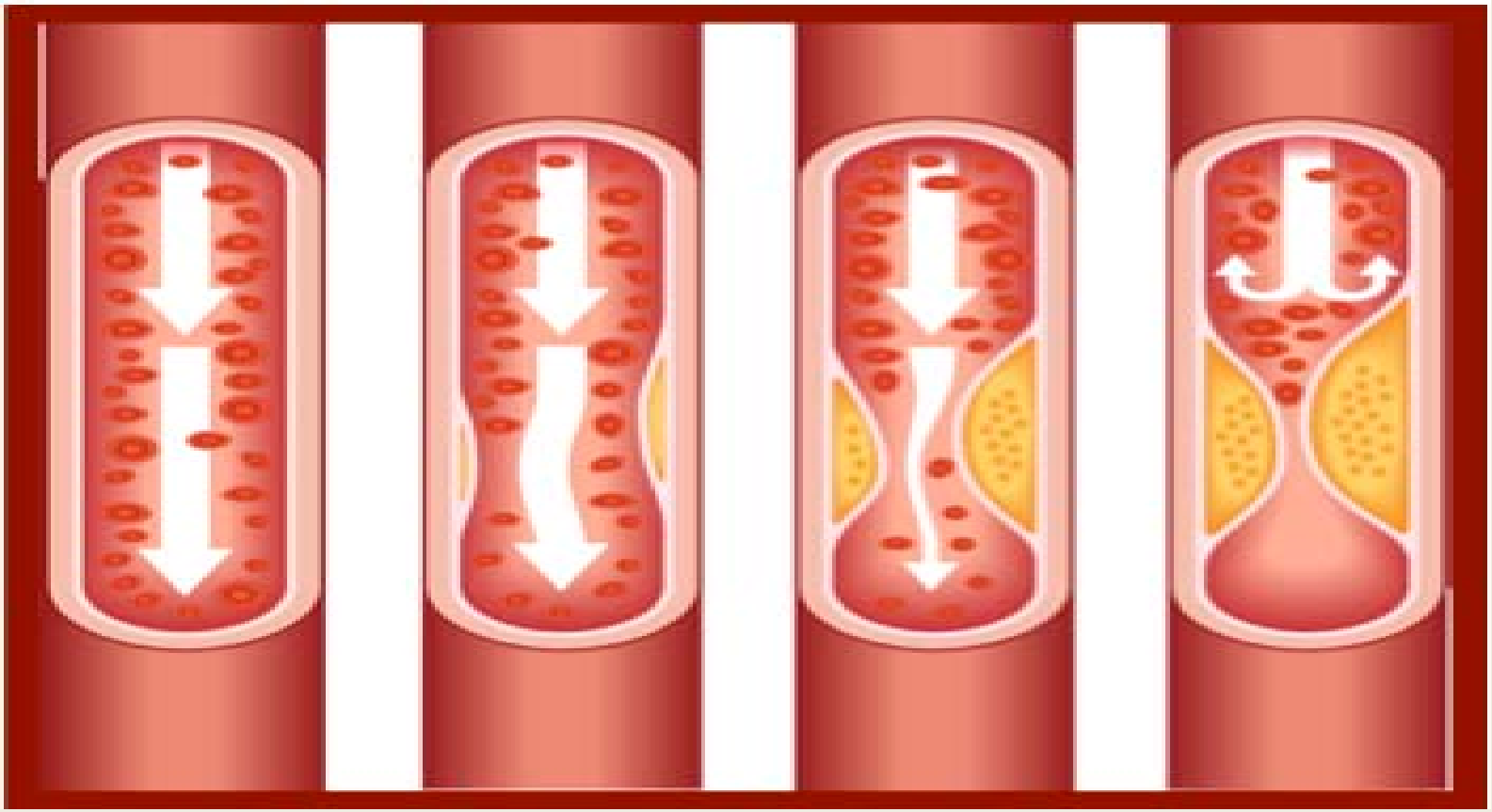
# Leading causes of deaths in the U.S. since 1900

Number of deaths per 100,000

| 1900 | | 1950 | | 2010 | |
|---|---|---|---|---|---|
| **1.** Influenza and pneumonia | **202.2** | **1.** Heart disease | **355.5** | **1.** Heart disease | **192.9** |
| **2.** Tuberculosis | **194.4** | **2.** Cancer | **139.8** | **2.** Cancer | **185.9** |
| **3.** Gastrointestinal infections | **142.7** | **3.** Cerebrovascular disease | **104.0** | **3.** Chronic airways disease | **44.6** |
| **4.** Heart disease | **137.4** | **4.** Diseases of early infancy | **40.5** | **4.** Cerebrovascular disease | **41.8** |
| **5.** Cerebrovascular disease | **106.9** | **5.** Non-motor-vehicle accidents | **37.5** | **5.** All accidents | **38.2** |


Influenza and pneumonia
1918: 588.5 deaths per 100,000
Photo Credit:
CDC/ Cynthia Goldsmith
Between 50 million and 130 million people died worldwide in the 1918 influenza pandemic, making it one of the deadliest natural disasters in history.
Heart disease
Cancer
Cerebrovascular disease
400
300
200
100
0
1900
1910
1920
1930
1940
1950
1960
1970
1980
1990
2000
2010
YEAR
SOURCES: CENTERS FOR DISEASE CONTROL AND PREVENTION,
NEW ENGLAND JOURNAL OF MEDICINE
R. TORO / © LiveScience.com

# Progressive Arterial Narrowing Means Decreasing Blood and Oxygen Supply



# Diminished Oxygen Supply to the Heart Muscle

- When plaques build up, they narrow the coronary arteries, decreasing blood flow and oxygen supply to the heart. Eventually, the decreased blood flow may cause chest pain (angina), shortness of breath, or other coronary artery disease signs and symptoms. A complete blockage can cause a heart attack.

# Slow Progression Over Decades

- Because coronary artery disease often develops over decades, it can go unnoticed until a heart attack occurs. But there's plenty one can do to prevent and treat coronary artery disease.

# *Stages of development of blockage in heart arteries (coronary plaque).*

- *The left-most artery is a healthy normal artery. As atherosclerosis develops, the artery gradually narrows, as shown from left to right in this diagram. Over time, extensive plaque can build up but still allow blood to pass through as in the blood vessels. Finally, the blockage becomes so severe that it restricts blood from passing through, as shown in the far right illustration.*

Research suggests that preventive measures and early tx will greatly decrease the incidence and severity of schizophrenia in the near future.

# II

# Identifying Those at Risk of Developing Schizophrenia

# Concepts for Identifying Those in Pre-Psychosis & Pre-Schizophrenia States

Early initial prodrome sate:

A. “Basic Symptoms”

Late initial prodrome state AKA “Ultra-high-risk of psychosis” (UHR-P):

B. Prodromal Symptoms

C. At-risk-mental-state “(ARMS)

# A. Basic Symptoms

- Bonn Scale for the Assessment of Basic Symptoms (BSABS)
- Long questionnaire, over 100 items
- 1987
- Bonn, Germany

# BSABS

- More than a hundred detailed descriptions and questions on subjective impairments in cognitive, emotional, motor and autonomic functioning, bodily sensation, energy, external perception and tolerance to normal stress, and represents the immediate experience of a special vulnerability to schizophrenia

# Conversion Rates for Individuals Identified as Being at Risk for Schizophrenia based on BSABS

- Within 10 years 70% of BSABS + individuals developed schizophrenia
- Conversion rate ca 10% per year
- In contrast only 4% of individuals who based on the BSABS were identified as not at risk for schizophrenia developed the disorder.

# B. Prodromal Symptoms

- Scale of Prodromal Symptoms [SOPS]
- A combination of symptoms (5 positive, 6 negative, and  4 general) + GAF score + schizoypal PD rating+ Family Hx.
- 2001
- USA

# Conversion Rates based on The Scale of Prodromal Symptoms

- Conversion rate to psychosis in the first study:
  - 46% at 6 months, and
  - 54% at 12 months
- In another study
  - 45.7%  at 12 months

# C. At-risk-mental-state (ARMS)

- Comprehensive Assessment of At-Risk Mental States or CAARMS
- Three methods for identifying risk
- 1996
- Australia

# Comprehensive Assessment of At Risk Mental States (CAARMS)

- Defines three groups at risk for schizophrenia

1. Attenuated positive psychotic symptoms
2. Brief limited intermittent psychotic symptoms [BLIPS]
3. Trait and state risk factors [TASRF]

# Group1: Attenuated positive psychotic symptoms [APPP]

Group1 (APPP) : Presence of more than one of the following symptoms:

1. Ideas of reference,
2. Odd beliefs or magical thinking, perceptual disturbance,
3. Paranoid ideation, odd thinking and speech,
4. Odd behavior, and appearance

# Group1 (APPP) - cont.

- Frequency of symptoms: at least several times a week
- Recency of symptoms: present within the past year
- Duration of symptoms: present for ≥1 wk and ≤5 y

# Group 2:

## Brief limited intermittent psychotic symptoms [BLIPS]

# Group 2 (BLIPS)-Transient psychotic symptoms: presence of one or more of the following:

1. Ideas of reference, magical thinking, perceptual
2. Disturbance, paranoid ideation, and
3. Odd thinking or speech

# Group 2 (BLIPS) - cont.

- Duration of episode: <1 wk
- Frequency of symptoms: at least several times per week
- Symptoms resolve spontaneously
- Recency of symptoms: must have occurred within the past yea

# Group 3:

# Trait and state risk factors [TASRF]

# Group 3 (TASRF)

1. Schizotypal personality disorder in the identified individual or a first-degree relative with a psychotic disorder
2. Significant decline in mental state or functioning (30% drop in GAF score), maintained for at least ≥1 mo and ≤5 y
3. This decline in functioning must have occurred within the past year

# Conversion Rates based on CAARMS

- In a follow-up study in Australia a 40% annual rate of conversion to psychosis was observed.

# Ultra High Risk Criteria for Schizophrenia

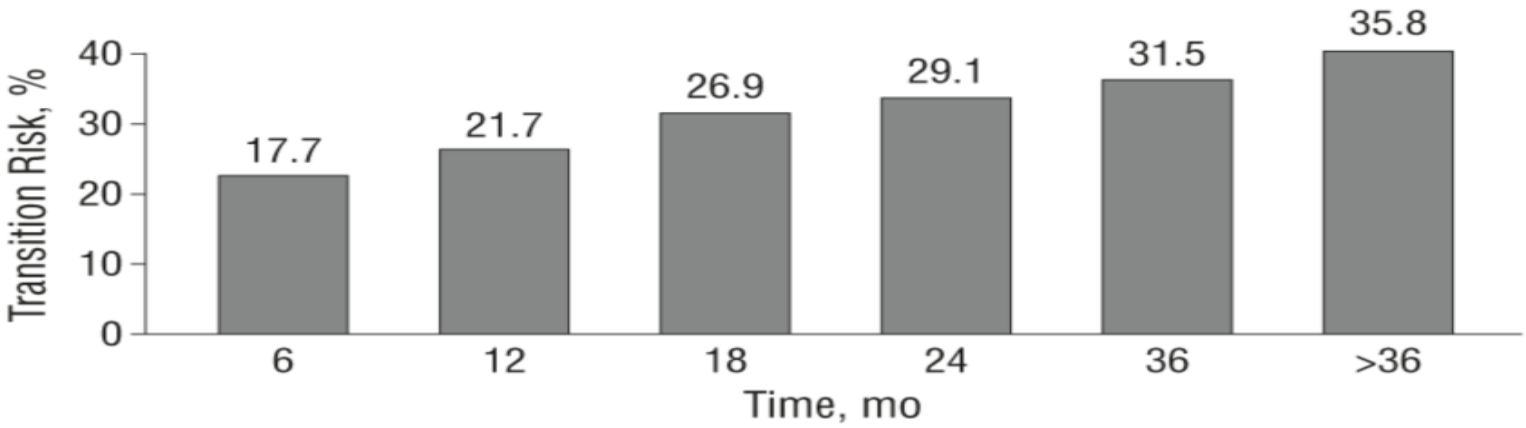
- Must be aged between 15 and 30 years,
- Have been referred to a specialized service for help, and
- Meet the criteria for 1 or more of the 3 groups.

# Conversion Rate for “Ultra-high-risk”

- The average conversion rate for “ultra-high-risk” patients during 12 months is 38.2%.

- Schulze-Lutter (List of studies concerning conversion of ultra-high-risk patients to psychosis; personal communication, 2005) has calculated from nine studies [50], [139], [143–149] that

# Meta-analyses of transition risks from clinical high risk to full psychosis at different time points of follow up.




| No. of Studies | Follow-up, mo | Transition Risks, 95% CI |
|---|---|---|
| 9 | 6 | 17.7 (12.3-24.9) |
| 13 | 12 | 21.7 (16.6-27.8) |
| 4 | 18 | 26.9 (19.5-35.9) |
| 12 | 24 | 29.1 (23.2-35.7) |
| 6 | 36 | 31.5 (23.8-35.0) |
| 4 | >36 | 35.8 (29.6-42.5) |

*P*<.001 for all.

Figure Legend:

From: **Predicting Psychosis: Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk**

Arch Gen Psychiatry. 2012;69(3):220-229. doi:10.1001/archgenpsychiatry.2011.1472

# III Approaches to Treatment Before the First Episode

- Goal: delaying or preventing the first psychotic episode.

# Tested Interventions

- CBT
- Antipsychotics
- Omega-3 fatty acids

# Comparing Risk of Transition to Psychosis by Treatment Intervention

- Psychological interventions (e.g CBT) 25%

vs NonSpecific Supportive Tx 33%

- Antipsychotics  23% vs no AP 37%

# CBT and Risk of Transition to Psychosis

- Cognitive behavioral therapy Five studies used CBT as an intervention. Now it appears that CBT intervention is effective, but the NNT of 13 is somewhat higher than seen in the prevention trials that did not rely on CBT — perhaps owing to the lower transition rates observed in recent studies.

# Antipsychotics and Risk of Transition to Psychosis

- The risk of onset of disorder is reduced by 54% to 52% (1 study excluded) after 12 months, and by 37% to 35% (1 study excluded) in the longer-term (between 2 and 4 years). This suggest that preventive effects are slightly diminished over 2–4 years, but still successful in reducing the risk of  developing a first psychosis.

- Antipsychotic medication is effective in reducing the rate of transition to psychosis by 45%, but antipsychotics are associated with high attrition rates, e.g. 54.8% in the McGlashan et al. (2006) and McGorry et al. (2002) studies, and 37.2% in the McGorry et al. (2013) study. In addition, McGlashan and colleagues reported an 8.8 kg weight gain.

- The conclusion of the recent study by McGorry and colleagues was that antipsychotic medication should not be offered as a first line treatment in CHR patients. After all, the data on antipsychotic medication in CHR patients are based on small trials and more evidence is needed to demonstrate efficacy and safety.

# Omega-3 and Risk of Transition to Psychosis

- Omega-3 was promising in preventing a first episode of psychosis in CHR patients, but this impression is based on a small study and requires replication. A replication study is now being conducted in two large trials: the NEURAPRO-E trial (Australian and the NAPLS-2 trial that is now running in the United States and Canada.

# IV Approaches to Treatment After the First Episode

- Preventing deterioration and improving outcomes after the first psychotic episode.

# The Core Components of a Specialized Early Psychosis Service

# I Early detection 1-3

- Component 1: Community education to improve awareness of young people's mental health issues among the general public and those who work closely with young people.
- Component 2: Easy access to the service through one clear entry point with a “no wrong door” policy and guaranteed referral for those who do not meet entry criteria.

- Component 3: Home-based assessment and care available via a mobile multidisciplinary team able to provide triage, assessment, crisis intervention, and home-based acute treatment 24 hrs a day, 7 days a week

# II Acute care 4-5

- Component 4: Acute phase care delivered in the community by the mobile team, or when necessary, in a dedicated youth-friendly inpatient unit.
- Component 5: Access to subacute care for additional support after an acute episode.

# III Continuing care 6-16

- Component 6: Case management with an individual case manager who provides an individually tailored treatment approach as well as support with practical issues
- Component 7: Medical interventions, primarily low-dose pharmacotherapy
- Component 8: Psychological interventions, including psychoeducation, individual psychotherapy, and cognitive behavioural therapy

- Component 9: A functional recovery program with an emphasis on returning to full social, educational, and vocational functioning
- Component 10: Group programs to enhance psychosocial and functional recovery. The focus should be on topics of interest to young people, ranging from health-related issues, such as stress management, coping with anxiety and reducing drug use, to study, school, and work issues, as well as social and leisure activities such as music, art, and outdoor adventure

- Component 11: Family programs and family peer support for the families and friends of young people with early psychosis
- Component 12: Youth participation and peer support is crucial for maintaining youth-friendliness and accountability to young people in these services

- Component 13: Mobile outreach for those young people with complex issues who have difficulty engaging with services
- Component 14: Partnerships with other organizations that can enhance the support for young people with mental health issues

- Component 15: Workforce development to create highly skilled and clinically expert mental health professionals specializing in youth mental health
- Component 16: Ultra-high risk young people should be treated within a specialized service with the aim of minimizing symptoms and distress and maintaining a normal functional trajectory to prevent further deterioration in functioning to prevent a first episode of psychosis

# Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program

- Kane et al. 2015

# Objectives

- The primary aim of this study was to compare the impact of NAVIGATE, a comprehensive, multidisciplinary, team-based treatment approach for first-episode psychosis designed for implementation in the U.S. health care system, with community care on quality of life.

# Interventions

The experimental treatment, NAVIGATE (19), includes four core interventions:

1. Personalized medication management
2. Family psychoeducation;
3. Resilience-focused individual therapy;
4. Supported employment and education (SEE). SEE services (5 hours/week).

# Methods

- Thirty-four clinics in 21 states were randomly assigned to NAVIGATE or community care. Diagnosis, duration of untreated psychosis, and clinical outcomes were assessed via live, two-way video by remote, centralized raters masked to study design and treatment.

# Participants

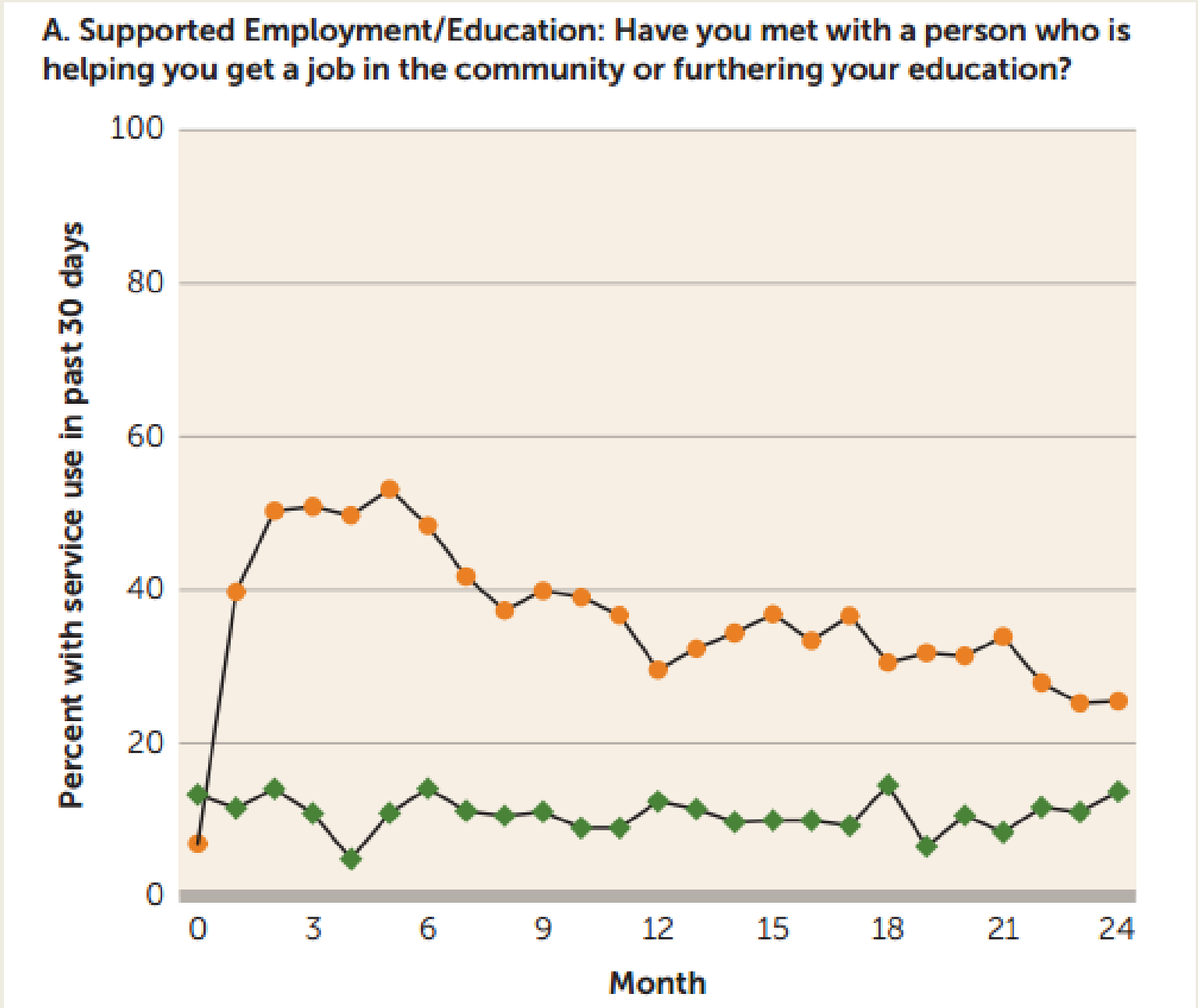
- Participants (mean age, 23) with schizophrenia and related disorders and ≤6 months of antipsychotic treatment (N=404) were enrolled and followed for ≥2 years.
- The primary outcome was the total score of the Heinrichs-Carpenter Quality of Life Scale, a measure that includes sense of purpose, motivation, emotional and social interactions, role functioning, and engagement in regular activities.

# Results

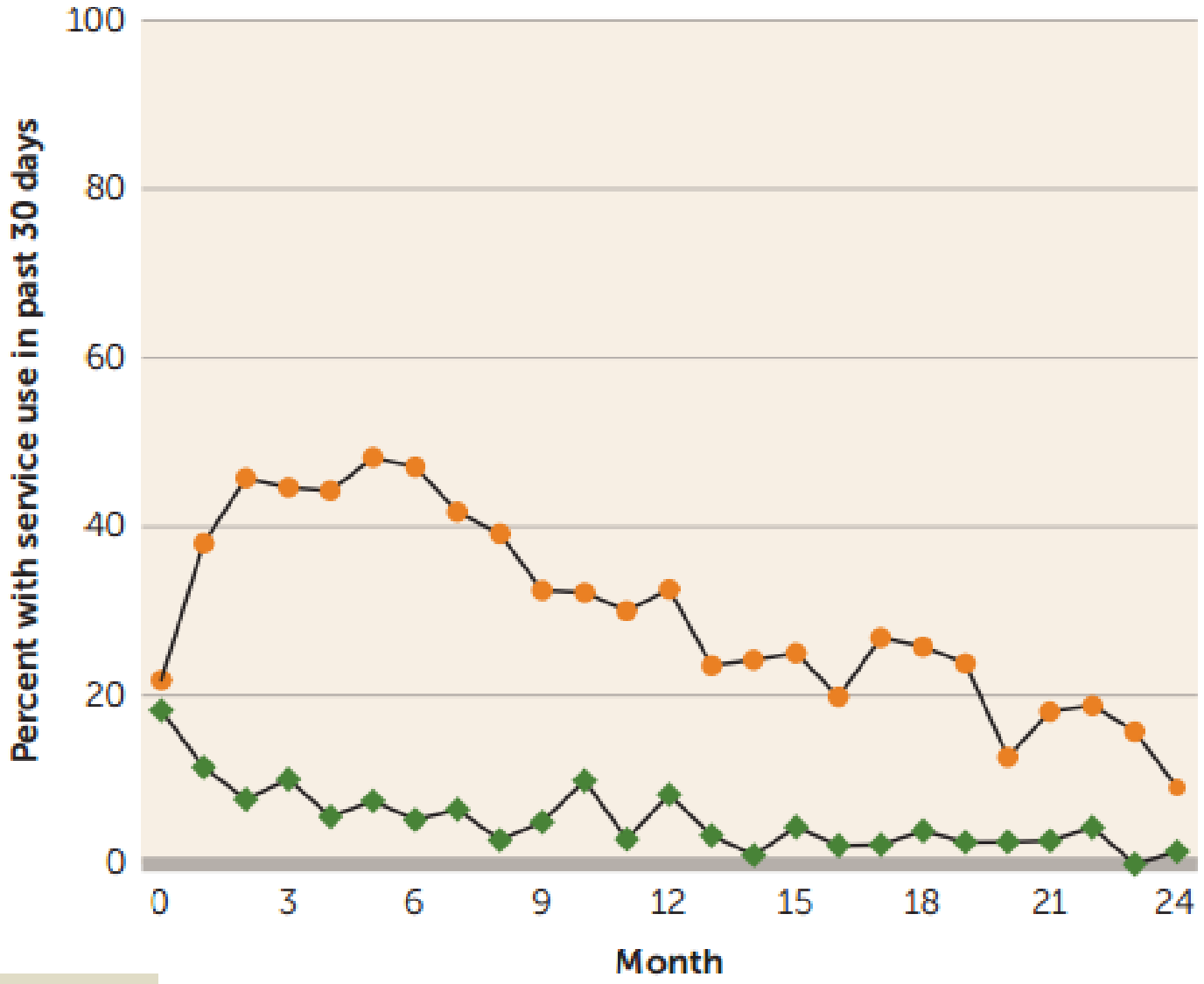
- The 223 recipients of NAVIGATE remained in treatment longer, experienced greater improvement in quality of life and psychopathology, and experienced greater involvement in work and school compared with 181 participants in community care.

# Patient Self-Reported Use of NAVIGATE Model Targeted Services During Study Period at NAVIGATE and Community Care Sites

- There was a tendency for the ratings to converge over the two year period.

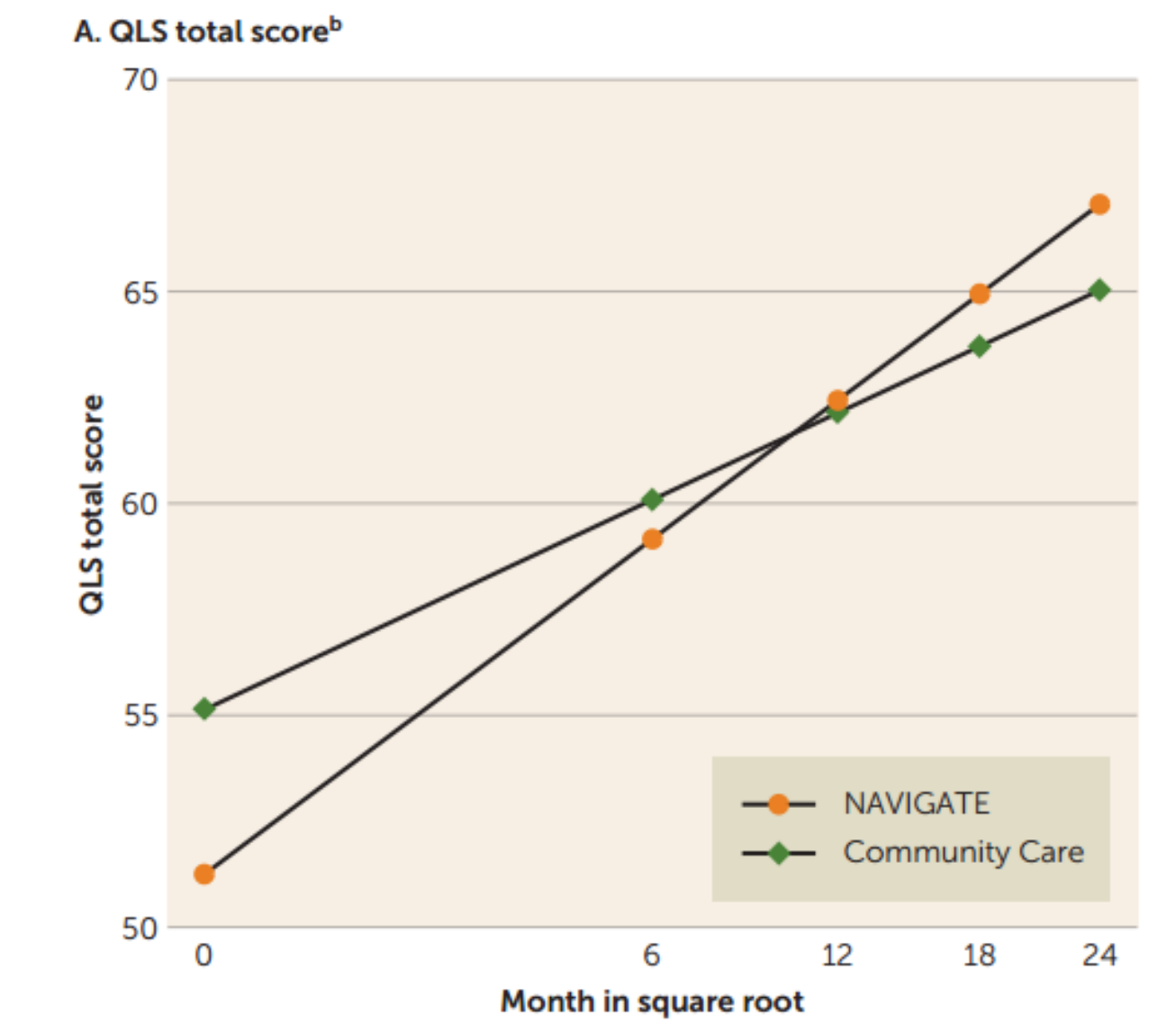

A. Supported Employment/Education: Have you met with a person who is helping you get a job in the community or furthering your education?
Percent with service use in past 30 days
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
Month

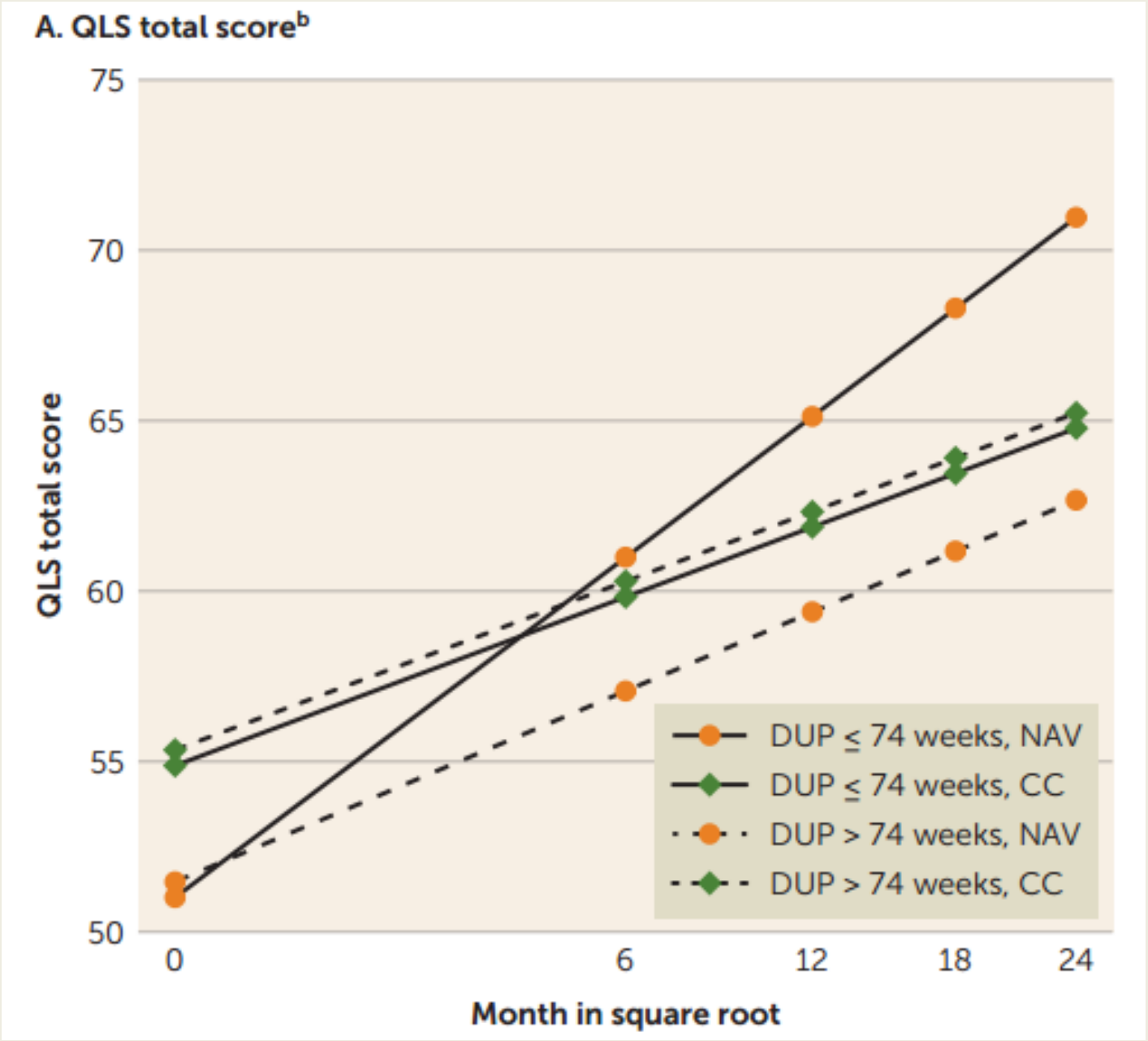
D. Family Psychoeducation: Has your family met with a mental health care provider to help them understand and address your situation?



# Rater Assessments of Quality of Life

- It is possible that untreated psychosis has long lasting detrimental impact on the outcome of the illness. Research suggests that patients with shorter DUP have much better response to early tx and have better outcomes.


A. QLS total score[b]
70
65
60
55
50
QLS total score
0
6
12
18
24
Month in square root
NAVIGATE
Community Care


A. QLS total score[b]
75
70
65
60
55
50
QLS total score
0
6
12
18
24
Month in square root
DUP ≤ 74 weeks, NAV
DUP ≤ 74 weeks, CC
DUP > 74 weeks, NAV
DUP > 74 weeks, CC

- NAVIGATE includes four core interventions: Personalized medication management; Family psychoeducation; Resilience-focused individual therapy; Supported employment and education (SEE) SEE services (5 hours/week).
- There is an urgent need to clarify how much each of the four interventions have contributed to the outcome.

# CONCLUSIONS

- The RAISE-ETP study demonstrates that diverse U.S. community clinics can implement a team-based model of first-episode psychosis care, producing greater improvement in clinical and functional outcomes as compared with standard care.

- Patients with with shorter duration of untreated psychosis derived substantially more benefit from NAVIGATE.
- Prolonged duration of untreated psychosis is an issue of national importance; reducing duration of untreated psychosis from current levels of >1 year to the recommended standard of <3 months (11) should be a major focus of applied research efforts.