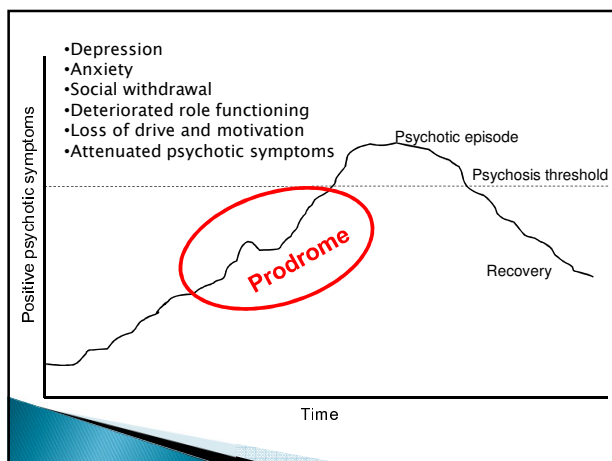




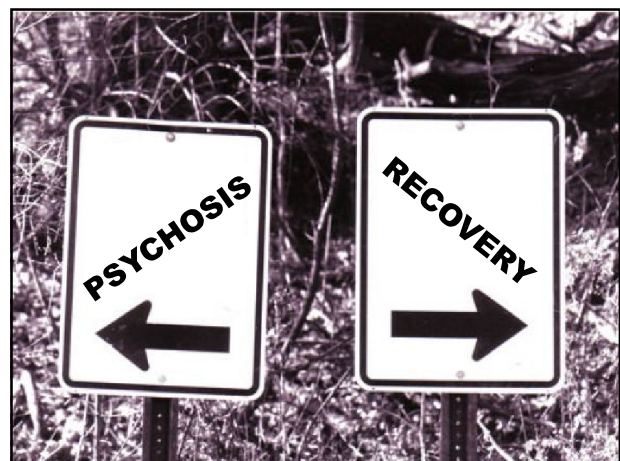
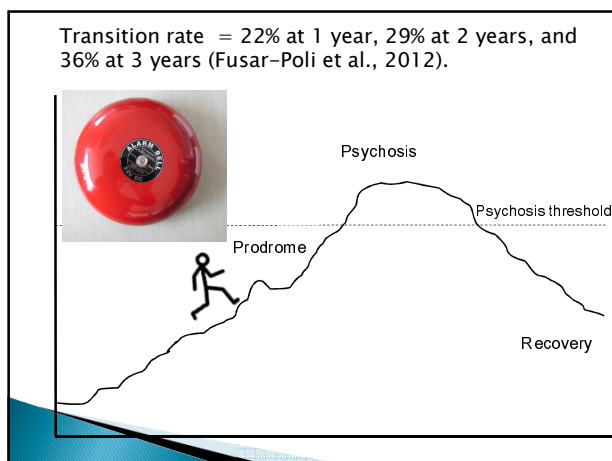
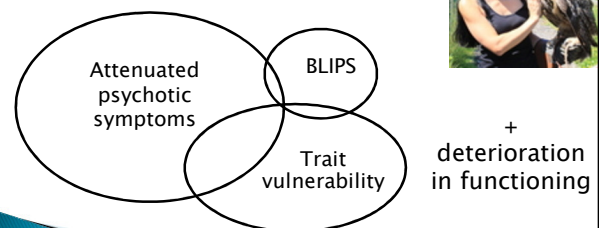
Outline

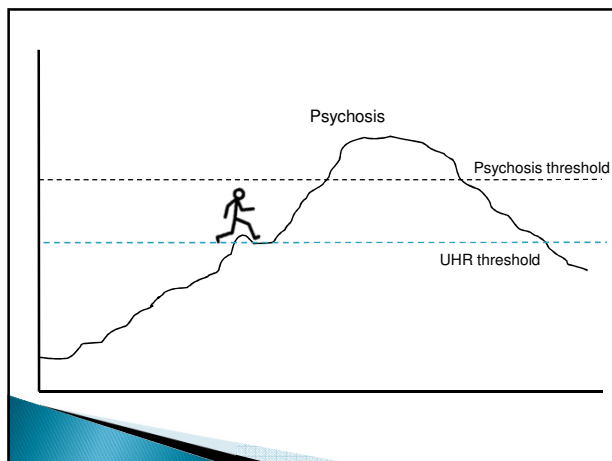
- ▶ What is the ultra-high risk for psychosis (UHR) paradigm?
- ▶ What are the problems with the way we use it?
- ▶ Why is a clinical staging framework needed?
- ▶ What is a clinical staging model of mental illness?
- ▶ How can it be useful?
- ▶ Aims and challenges for the future



Ultra-high risk – Identifying people in the prodrome

- ▶ Age = greatest risk factor – late teens/early adulthood





Efficacy of Using Cognitive Status in Predicting Psychosis: A 7-Year Follow-Up

Neurocognitive indicators for a conversion to psychosis: Comparison of patients in a potentially initial prodromal state who did or did not convert to a psychosis

Prospective study of cannabis use in adolescents at clinical high risk for psychosis: impact on conversion to psychosis and functional outcome

Memory Impairments Identified in People at Ultra-High Risk for Psychosis Who Later Develop First-Episode Psychosis

Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features

Sexual Trauma Increases the Risk of Developing Psychosis in an Ultra High-Risk "Prodromal" Population

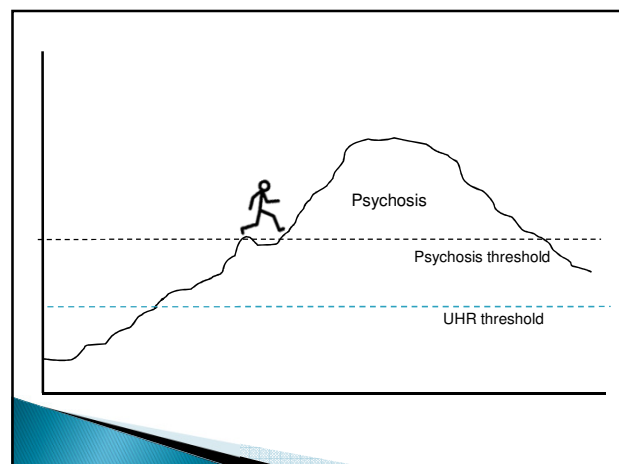
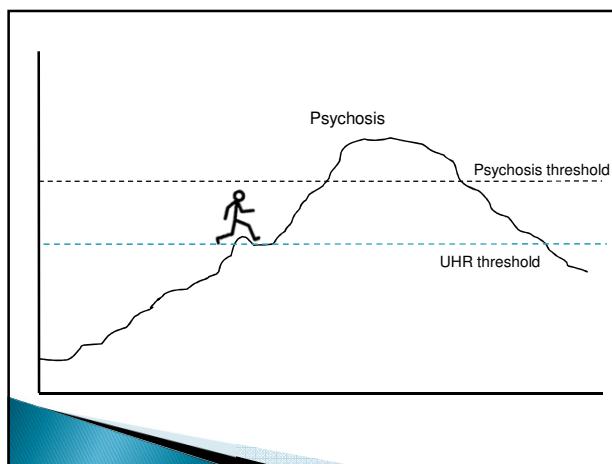
Baseline differences in clinical symptomatology between ultra high subjects with and without a transition to psychosis

Experience of trauma and conversion to psychosis in an ultra-high-risk (prodromal) group

Neuropsychology of the Prodrome to Psychosis in the NAPLS Consortium

Relationship to Family History and Conversion to Psychosis

Sustained attention in young people at high risk of psychosis does not predict transition to psychosis



CAARMS

Psychosis:

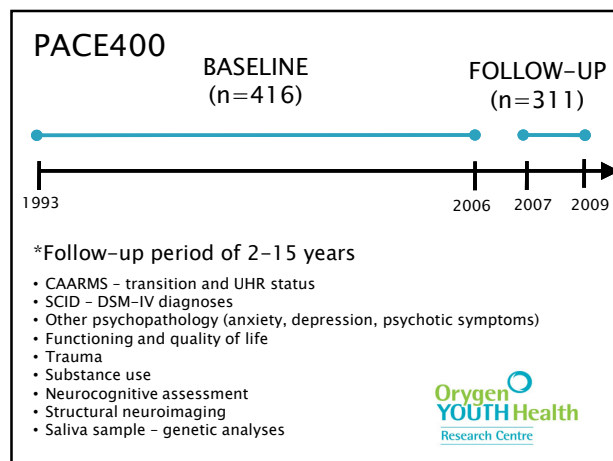
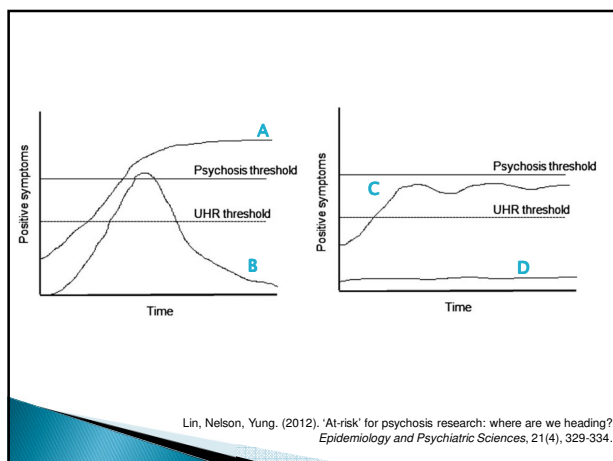
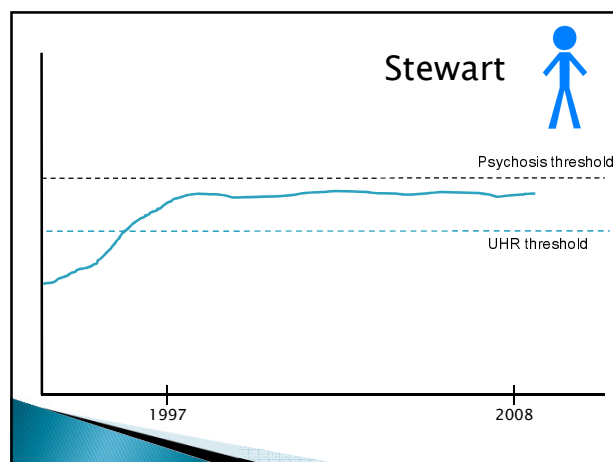
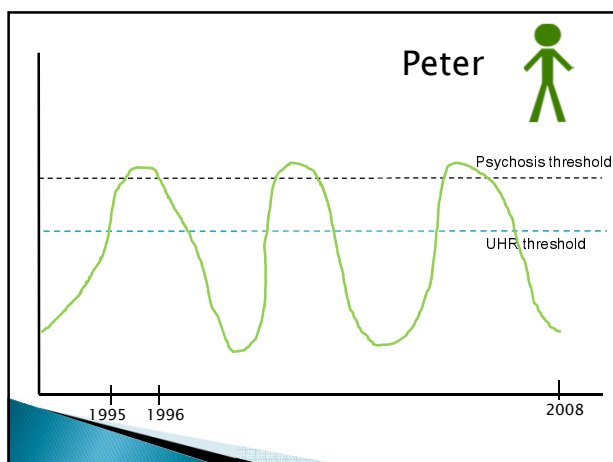
- At least fully psychotic and severe symptom
- For 3–6 times a week for more than an hour OR daily for less than an hour
- For at least 1 week

SIPS/SOPS

Schizophrenic psychosis:

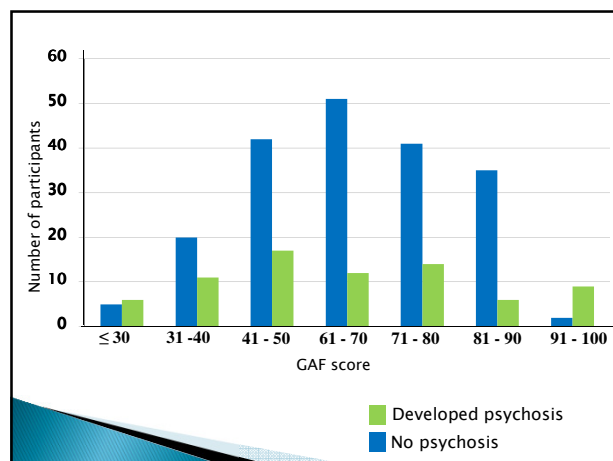
- At least one fully psychotic and severe symptom
- For 4 days a week
- For at least 1 month OR at least one day if symptom is seriously disorganising or dangerous
- Began within the last 3 months

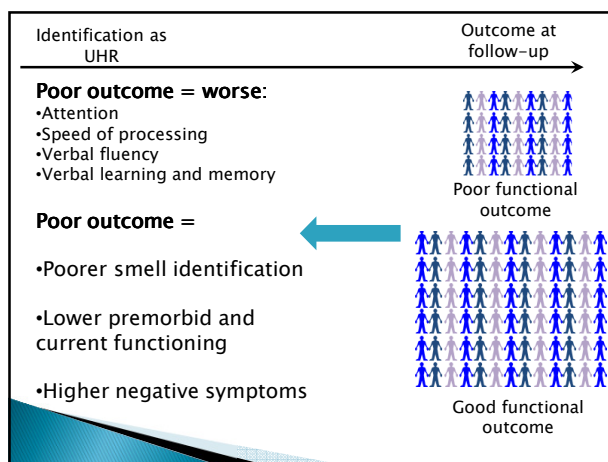
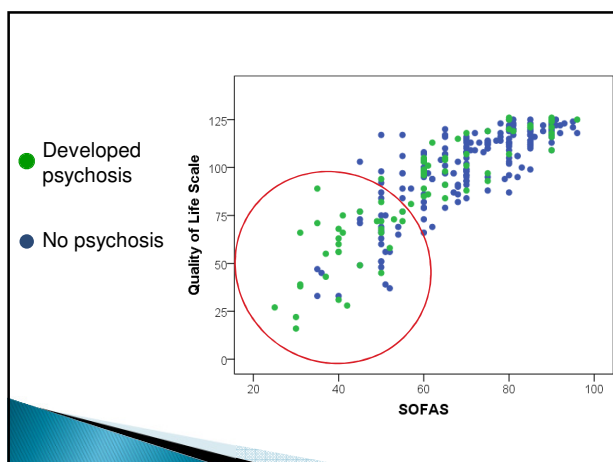




What happens to “non-transitioners”?

- ▶ There is VERY little data on this!
- ▶ **Poor functional (psychosocial) outcome**



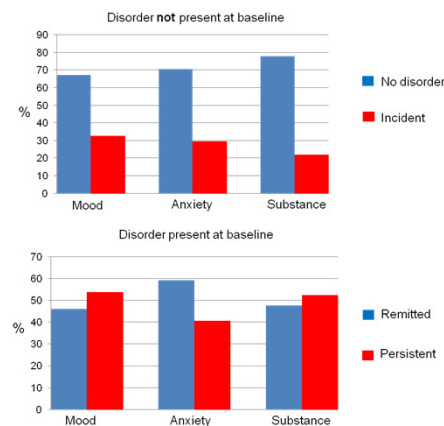


What happens to “non-transitioners”?

- There is VERY little data on this!
- Poor functional (psychosocial) outcome
- Other psychiatric (non-psychotic) disorders

	N	%
Any mood disorder	110	48.7
Major depressive disorder	92	40.7
Dysthymic disorder	8	3.5
Bipolar I disorder	6	2.7
Bipolar II disorder	3	1.3
Any anxiety disorder	78	34.5
Panic disorder with agoraphobia	11	4.9
Panic disorder without agoraphobia	16	7.1
Agoraphobia without panic	6	2.7
Social phobia	25	11.1
Specific phobia	8	3.5
GAD	14	6.2
OCD	7	3.1
PTSD	10	4.4

	N	%
Any substance use disorder	66	29.2
Alcohol abuse	23	10.5
Alcohol dependence	20	8.8
Cannabis abuse	7	3.1
Cannabis dependence	33	14.6
Amphetamine/stimulant abuse	15	6.6
Amphetamine/stimulant dependence	10	4.4
Other drug abuse	14	6.2
Other drug dependence	7	3.1
Any somatoform disorder	6	2.7
Any eating disorder	11	4.9



What happens to “non-transitioners”?

- ▶ There is VERY little data on this!
- ▶ Poor functional (psychosocial) outcome
- ▶ Other psychiatric (non-psychotic) disorders
- ▶ **Continued attenuated positive psychotic symptoms**

Need large cohort studies with wider outcomes of interest

→ Clinical staging

Clinical staging:
A new way
forward



What's wrong with diagnostic systems (DSM and ICD)?

- ▶ Developed from observations of tertiary and chronic groups
- ▶ Not necessarily representative of nature – e.g. psychosis in different forms
- ▶ Don't differentiate between symptoms present early and later in illness
- ▶ Low reliability earlier in the course of illness – implications for treatment
- ▶ Can actually be thought of as outcomes or end states

What is clinical staging?

Clinical staging is a practical tool that defines the extent of progression of disease at a particular point in time, and where a person's condition currently lies along a continuum of the course of illness in terms of:

- Biological progression
- Symptom progression
- Psychosocial progression

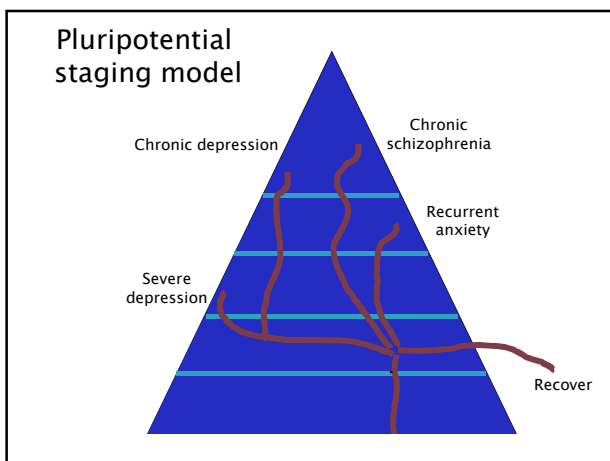
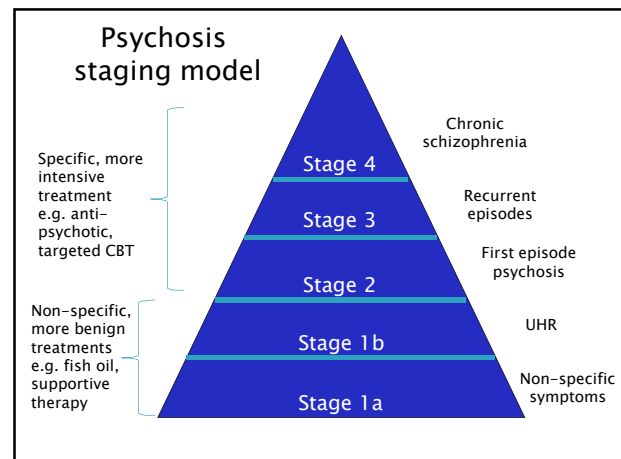
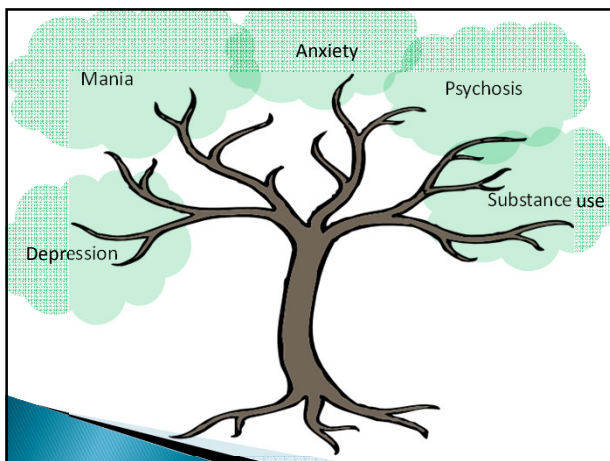
Clinical staging– a useful model

- ▶ Prognosis and treatment
 - Understanding the development of the illness
 - More precisely match treatment to illness progression
 - Intervention in earlier phase related to better response
 - More benign/acceptable treatments can be used earlier
 - Avoids overtreatment
- ▶ Important research applications

Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions

Patrick D. McGorry, Ian B. Hickie, Alison R. Yung, Christos Pantelis, Henry J. Jackson

Australian & New Zealand
Journal of Psychiatry, 2006, 40:
616–22



Clinical staging – the future

THERE ARE MORE QUESTIONS THAN ANSWERS!

Need large cohort studies with 2 main aims:

1. Understanding the trajectories of symptoms, and corresponding psychosocial and biological trajectories
2. Identifying predictors of progression between stages

Predictions of a staging model

- ▶ Transition between stages should be associated with progressive changes in neurobiology
- ▶ Later stages should be associated with more pathology
- ▶ Example from neuropsychology:
UHR–non–psychotic > UHR–psychotic
> first episode > chronic schizophrenia

Clinical staging in severe mental disorder: evidence from neurocognition and neuroimaging

Ashleigh Lin,[†] Renate L. E. P. Reniers[†] and Stephen J. Wood

Summary

A new approach to understanding severe mental illnesses such as schizophrenia and affective disorders is to adopt a clinical staging model. Such a model defines the extent of the illness such that earlier and milder phenomena are distinguished from later, more impairing features. Part of the appeal of such a model is that it should have cross-diagnostic applications, but to date there has been no attempt to examine imaging or neurocognitive evidence for staging in this way. We review these two domains of study with particular focus on major depression and

bipolar affective disorder. Although there is some support for the staging model in affective disorders, conclusions are limited by the large variability in the clinical samples studied, especially with regard to the presence of psychotic symptoms. We suggest that future research needs to take a transdiagnostic and longitudinal approach.

Declaration of interest
None.

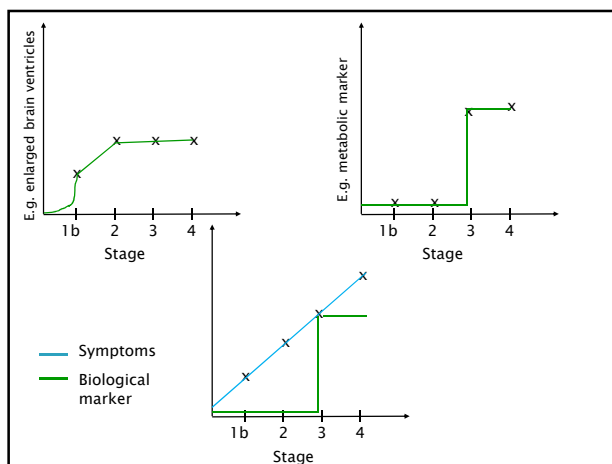
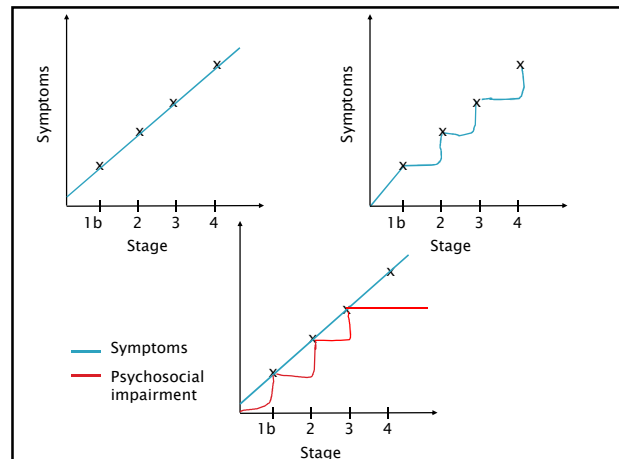
Lin, Reniers, Wood, *British Journal of Psychiatry* 2013, 202:s11–s17.

Aim 1: Understanding trajectories

- Understanding trajectories
 - biological
 - symptom
 - psychosocial

AND

- Understanding the association between symptom, functioning and biological trajectories – how do they correspond to each other?



Aim 2: Predicting progression between stages

Early on (i.e. Stage 1), we would like to determine:

- Who will progress to a later stage?
- Which specific illness will a person will progress to?
- Who will develop chronic illness?
- Who will recover with minimal intervention?
- Who will recover with intensive intervention?

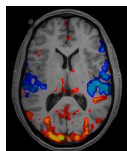
Once symptoms are clear cut and you know the diagnosis, then it is too late for early intervention...

...But we don't know where someone is going before they get there!

Possibilities

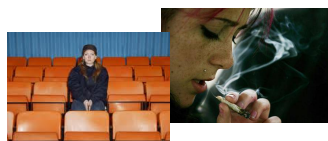
PREDICTABLE

Disorder is "pre-destined"



UNPREDICTABLE

Disorder is dependent on early stages –
e.g. substance use, social isolation, longer to seek treatment



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