Contextual Precision Diagnosis:
A Complementary Diagnostic System?

Bunnik, 8-3-2013, Prof. dr. J. van Os
Disclosure
Jim van Os
INFO: www.vanosinterest.homestead.com

- **Speaker fees received from:**
  Universiteit Maastricht heeft in 2012 vacatiegelden ontvangen van: Lilly, Janssen, Lundbeck, Roche, Astra-Zeneca

- **Positions held on Advisory Boards:**
  None

- **Grants and sponsoring:**
  Research grants: Janssen
Problems Current Diagnosis

Patients in same category do not resemble each other

Do not map to treatment needs

Do not map to prognosis
Media Stereotypes of Psychiatry
Three Areas for Innovation

- Biological vs. Mental Mechanisms
- Genes vs. Environment
- Timing vs. Specificity
Redeeming diagnosis in psychiatry: timing versus specificity

Patrick McGorry, Jim van Os

In general medicine, diagnosis is a crucial step in the choice of appropriate treatment, prediction of the future course of an illness, education of patients and families, and helping patients to realise that they are not alone. By contrast, in psychiatry, attitudes to diagnosis remain mixed and polarised, and the value of diagnosis is continuously questioned. With revisions to the clarified. Little more than incremental and desultory change is expected in the forthcoming new versions of the DSM and international classification of diseases (ICD), which are increasingly buffeted by the forces of public opinion, politics, and ideology.\textsuperscript{8-11} A transformation is needed, but is it feasible?

Mental ill health has to start somewhere. Eaton and

McGorry and Van Os, Lancet, 2013
Mechanism-based or Symptom-based?

Diagnosis Mental Disorder

Biological Mechanisms

Schiz Res, 2011
Mechanism-based or Symptom-based?

Diagnosis Mental Disorder

Mental Mechanisms

Schiz Res, 2011
Simple but Underappreciated: Mental Mechanisms

Biological Cause

Affect ↔ Salience ↔ Fear ↔ Cognition ↔ Drive

DSM5 “schizophrenia”
Genes or Environment?

Adaptation

Plasticity

Environment
Context and Illness

Macro-level

Stress-reactive

Micro-level

Preserved nocturnal dip

24-hrs BP monitoring

DMS-IV™

Diagnostic Criteria

American Psychiatric Association
Transition from Health to Psychotic Disorder: GROUP

n=810 siblings  1.1%  RR=2.2
n=462 controls  0.4%

3-year transition rate
Van Nierop, Janssens & GROUP, submitted
### Transition from Health to Psychotic Disorder

<table>
<thead>
<tr>
<th>Environmental Exposure</th>
<th>Transitions (n=11)</th>
<th>Non-Transitions (n=1261)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>65%</td>
<td></td>
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</tbody>
</table>

Cannabis use, Minority status, Urban birth, Trauma

Van Nierop, Janssens & GROUP, submitted

OR=∞, p=0.014
Transition from Health to Psychotic Disorder

E=Cannabis use, Minority status, Urban birth, Trauma
G=high-risk sibling status

<table>
<thead>
<tr>
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<th>Exposed to both G &amp; E</th>
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<tr>
<td>Transitions (n=11)</td>
<td>82%</td>
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<tr>
<td>Non-Transitions (n=1261)</td>
<td>43%</td>
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p=0.03

Van Nierop, Janssens & GROUP, submitted
<table>
<thead>
<tr>
<th>Trauma Exposure</th>
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<tbody>
<tr>
<td>Transitions (n=11)</td>
<td>89%</td>
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<tr>
<td>Non-Transitions (n=1261)</td>
<td>21%</td>
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</tbody>
</table>

OR=34.4, p<0.001

PAF=86%

Van Nierop, Janssens & GROUP, submitted
Timing versus Specificity

Early non-specific psychopathology

\[ \text{Staging} \]

Specific syndromes
Lessons learned from the psychosis high-risk state: towards a general staging model of prodromal intervention

P. Fusar-Poli\textsuperscript{1,}\textsuperscript{*}, A. R. Yung\textsuperscript{2,3}, P. McGorry\textsuperscript{3} and J. van Os\textsuperscript{1,4,5}

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\textsuperscript{5} Department of Psychosis Studies, Institute of Psychiatry, King’s College London, UK
Precision Diagnosis: Staging and Mental Causation

Stage of non-specific mental distress

Psychosis HR state

Schizophrenia

McGorry & Van Os, Lancet, 2013

Fusar-Poli & Van Os, Acta Psych Scan, 2012
PsyMate®
(Mobile Precision Diagnostics)

www.PsyMate.eu
Experience Sampling Method (ESM)

Mental state 1
Mental state 2
Context 1
Context 2

DAY 1
DAY 2
DAY 3
DAY 4
DAY 5
DAY 6
DAY X

(day 4 in detail)
Precision Diagnosis

Van Os, Psychological Medicine, in press
Symptoms represent complex mental state dynamics

PATIENT A

Level of paranoia

lack of sleep  anxiety  social stress  sad  work stress  anxiety  activity stress

PATIENT B

Level of paranoia

voices  voices

Oorschot et al, Schiz Bull, 2012
Altered Transfer of Momentary Mental States (ATOMS) as the Basic Unit of Psychosis Liability in Interaction with Environment and Emotions

Johanna T. W. Wigman¹,², Dina Collip¹,², Marieke Wichers¹, Philippe Delespaul¹, Catherine Derom³, Evert Thiery⁴, Wilma A. M. Vollebergh², Tineke Lataster¹, Nele Jacobs¹,⁵, Inez Myin-Germeys¹, Jim van Os¹,⁶

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Macro-level Symptoms and Micro-level Momentary Persistence

Non-Persistence phenotype: NO SYMPTOM

Persistence phenotype: SYMPTOM

Dynamics underlying Psychotic Symptoms


**A**
Paranoid state
\[ \text{negative context} \]
\[ \downarrow \]
\[ \text{negative affect} \]
\[ \downarrow \]
\[ \text{genes} \]
\[ \downarrow \]
Paranoid state
\[ \text{momentary transfer +} \]

**B**
Paranoid state
\[ \text{positive context} \]
\[ \downarrow \]
\[ \text{positive affect} \]
\[ \downarrow \]
Non-paranoid state
\[ \text{momentary transfer –} \]
Precision Diagnosis: Circuit Characteristics

Connection strength (within-person)

Connection variability (between person)
Stages of Severity & Specificity

Stage 1

Stage 2

Stage 3

Wigman et al, PLoS One, in press
The Plasticity Argument

Early Intervention

% Response after each relapse

15-year follow-up
Focus on Illness or Resilience?

Positive

Ability to use natural rewards

Negative

Stress sensitivity
MindMaastricht RCT

Sample: 130 patients diagnosed with severe mental illness, suffering from current subthreshold symptoms of depression

6 days Experience Sampling → Mindfulness Training → Control → 6 days Experience Sampling

FU 6 months
FU 12 months

Geschwind et al., J. Consulting & Clinical Psychology, 2011
MBCT impacts on PA-related momentary outcomes: RCT

Mindfulness Training Increases Momentary Positive Emotions and Reward Experience in Adults Vulnerable to Depression: A Randomized Controlled Trial

Nicole Geschwind, Frenk Peeters, and Marjan Drukker
Maastricht University Medical Centre
Jim van Os
Maastricht University Medical Centre and King’s College London
Marieke Wichers
Maastricht University Medical Centre

Daily-Life Reward Intervention

Flow of Daily Life

Positive Emotions
PA Persistence over Time

Positive Emotions

Flow of Daily Life
The Psychosis Circuit
Are Categories/Dimensions Flawed?

Latent Construct

Affect ↔ Salience ↔ Fear ↔ Cognition ↔ Drive
Auto-reinforcement – how it persists over time

Strong positive predictive effect

Strong negative predictive effect

Positive feedback loop; mutually reinforcing mental states

Negative feedback loop; mutually antagonistic mental states

1 – context 1 (stress)
2 – context 1 (company)
3 – mental state 1 (voice)
4 – mental state 2 (paranoia)
5 – mental state 3 (worry)
6 – mental state 4 (sad)
Networks and Treatment

Illness → Treatment

Resilience → Promotion
Psychosis

Trauma-related

Mania

Depression

Non-situational Anxiety

Situational anxiety

Trauma-related

Sleep-related

OCD

Eating-related

Somatic symptom-related

High NA
Low PA

“Inner” domain: Generic psychopathology

“Outer” domain: Specific psychopathology

Interpersonal-related

Sexual function-related

Substance-related
Increasing resolution:

- Micro-level

- Positive affect
- Negative affect
- Anomalous experience

Van Os et al, Nature, 2010
Context and Illness

Macro-level

Stress-reactive

Micro-level

Preserved nocturnal dip

24-hrs BP monitoring
Mindless or Brainless?

Brain activity

Correlated

Mind activity

?
Categories or Dimensions?

CAT1  CAT2  CAT3  CAT4  POP

Cognition

Affective dysregulation

Psychosis

Van Os & Kapur, Lancet, 2009
representation of the social world

Learned Environment: Top-down cortical processing

“Expectation”

Affectively meaningful

“Facts”

Actual Environment: bottom-up sensory input

Learning

Motivation

Interaction

Van Os et al, Nature, 2010
Psychopathology is conceptualized as resulting from dynamic interactions between symptoms over time.

Mental disorders represent sets of symptoms, connected through systems of causal relations.

Circuit or Network approach

Borsboom et al., 2011; Kendler et al, 2010; Linscott & Van Os, 2011