RID – DIAGNOSI
LA PREVENZIONE DEI DISTURBI PSICOTICI E APPLICAZIONI DELLA NETWORK ANALYSIS

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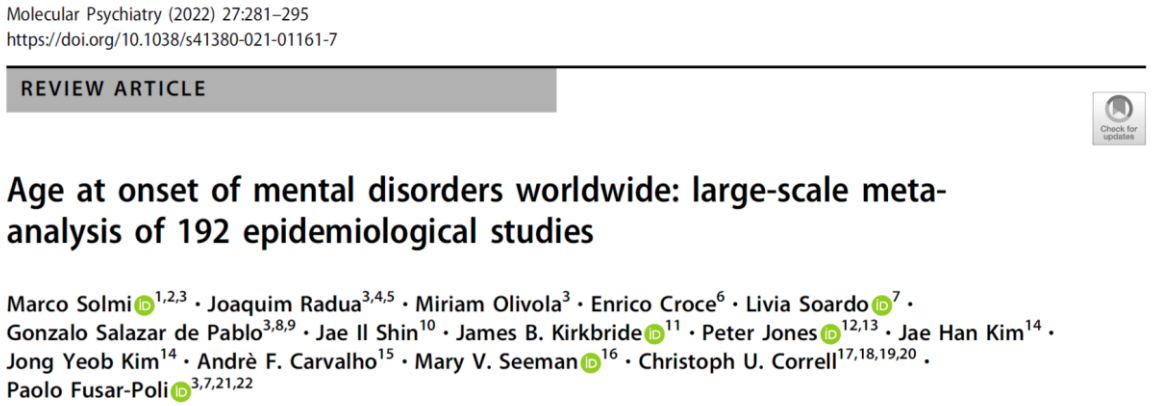
Prevenire i disturbi psicotici: Rationale

- Aspettativa di vita ridotta di 10-20 anni. Prevalenza: 0.3% → una delle cause principali di disabilità tra i giovani (WHO, 2022).
- Durata della psicosi non trattata → sintomi psicotici e non psicotici più severi, ridotta risposta al trattamento, maggiori deficit nel funzionamento sociale e di ruolo (Penttilä et al., 2014);
- Oltre 90 miliardi di Euro nel 2010 solo in Europa associati ai dist. psicotici (Gustavsson et al., 2011);
- Quando? 47.8% esordi entro i 25 anni, picco a 20.5 anni (Solmi et al., 2022).



World Health Organization. World Mental Health Report: Transforming Mental Health for All. WHO, 2022

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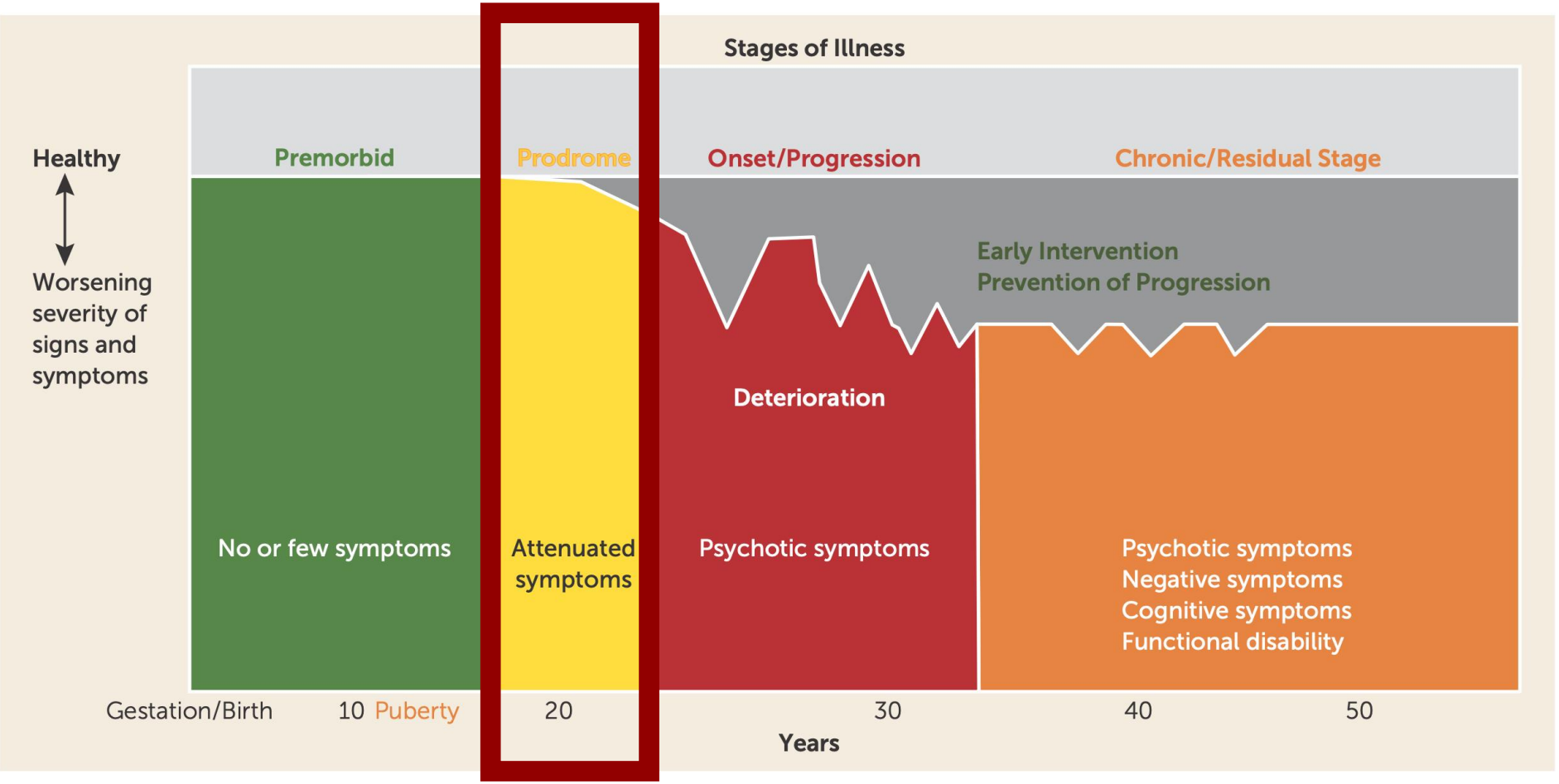
Modificare la traiettoria clinica (prevenzione primaria)→ prevenire o ritardare l'insorgenza del disturbo e ridurre la durata della psicosi non trattata



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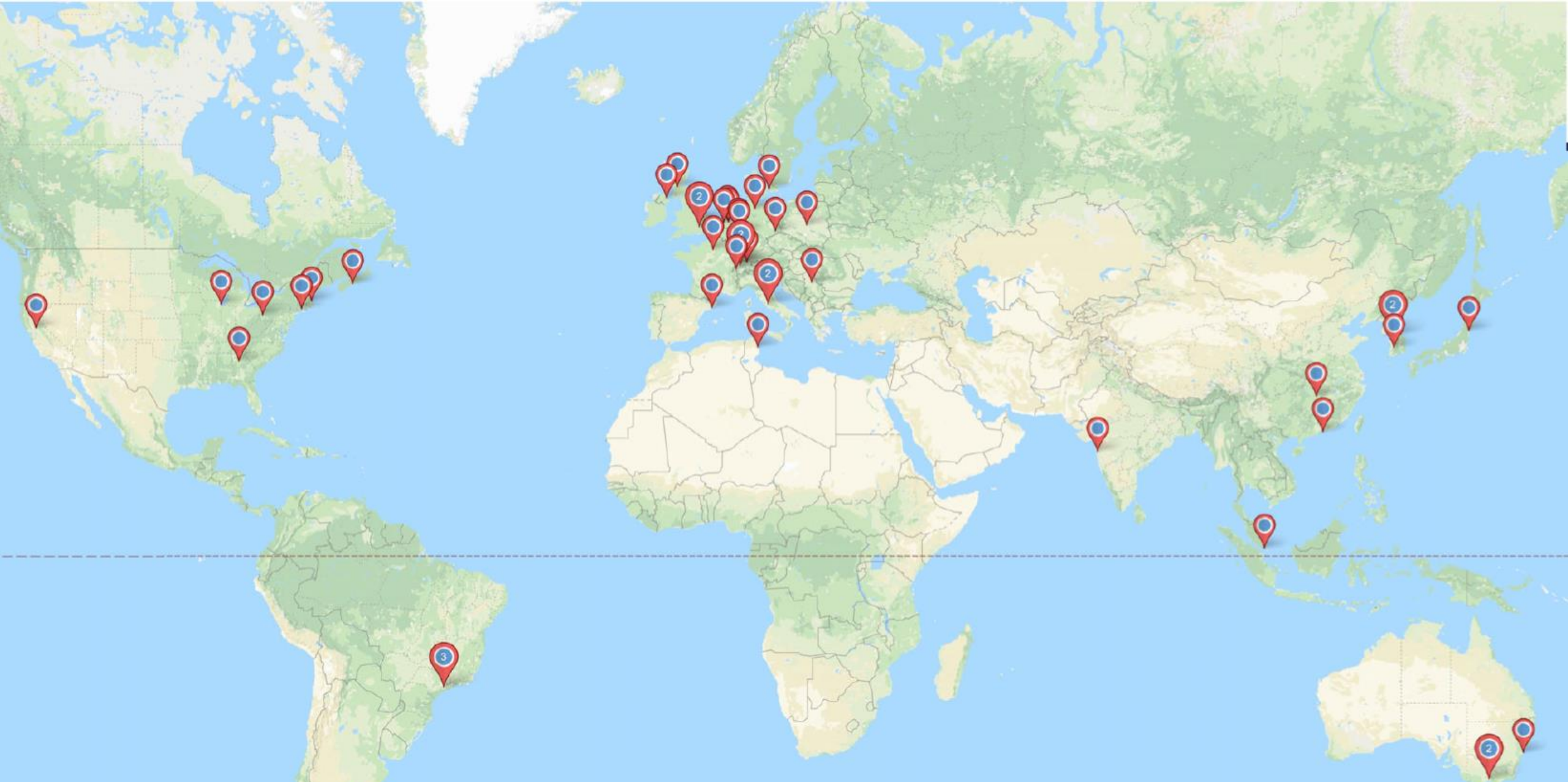

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Ultra high risk for psychosis (UHR)

- **Diagnosi:** Adolescenti e giovani adulti (12-25 anni) che richiedono aiuto (help-seekers) presso un servizio clinico specializzato, presentano sintomi psicotici positivi (es. deliri e allucinazioni) attenuati (per intensità, frequenza e durata), declino del funzionamento generale e ridotta qualità della vita (Fusar-Poli et al., 2020)
- **Prognosi**: 27% sviluppa un disturbo psicotico conclamato entro 36 mesi dalla presentazione presso il servizio (Salazar de Pablo et al., 2021). 22%-82% dei non-transitioners presenta almeno un disturbo mentale non psicotico al Follow Up (2-7.5 anni; Beck et al., 2019).


Clinical Review & Education

JAMA Psychiatry | Review

Prevention of Psychosis
Advances in Detection, Prognosis, and Intervention

Paolo Fusar-Poli, MD, PhD; Gonzalo Salazar de Pablo, MD; Christoph U. Correll, MD; Andreas Meyer-Lindenberg, MD, PhD; Mark J. Millan, PhD; Stefan Borgwardt, MD, PhD; Silvana Galderisi, MD, PhD; Andreas Bechdolf, MD, PhD; Andrea Pfennig, MD, PhD; Lars Vedel Kessing, MD, DMSc; Therese van Amelsvoort, MD, PhD; Dorien H. Nieman, PhD; Katharina Domschke, MD, PhD; Marie-Odile Krebs, MD, PhD; Nikolaos Koutsouleris, MD; Philip McGuire, MD, PhD; Kim Q. Do, PhD; Celso Arango, MD, PhD

Fusar-Poli, P., Salazar de Pablo, G., Correll, C. U., Meyer-Lindenberg, A., Millan, M. J., Borgwardt, S., Galderisi, S., Bechdolf, A., Pfennig, A., Kessing, L. V., van Amelsvoort, T., Nieman, D. H., Domschke, K., Krebs, M. O., Koutsouleris, N., McGuire, P., Do, K. Q., & Arango, C. (2020). Prevention of Psychosis: Advances in Detection, Prognosis, and Intervention. *JAMA psychiatry*, *77*(7), 755–765. https://doi.org/10.1001/jamapsychiatry.2019.4779


Schizophrenia Research 210 (2019) 39–47

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Clinical and functional long-term outcome of patients at clinical high risk (CHR) for psychosis without transition to psychosis: A systematic review

Katharina Beck [a,b], Christina Andreou [a], Erich Studerus [a], Ulrike Heitz [a,b], Sarah Ittig [a], Letizia Leanza [a,b], Anita Riecher-Rössler [a,*]

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[b] University of Basel, Division of Clinical Psychology and Epidemiology, Department of Psychology, Basel, Switzerland

Beck, K., Andreou, C., Studerus, E., Heitz, U., Ittig, S., Leanza, L., & Riecher-Rössler, A. (2019). Clinical and functional long-term outcome of patients at clinical high risk (CHR) for psychosis without transition to psychosis: A systematic review. *Schizophrenia research*, *210*, 39–47. https://doi.org/10.1016/j.schres.2018.12.047

Ultra-high risk for psychosis (UHR)

- **Intervention**: Intervento psicologico indicato in tutte le linee guida cliniche nazionali e internazionali. Trattamento preventivo è efficace → Riduzione del rischio di conversione a psicosi in pazienti seguiti in psicoterapia rispetto ai campioni di controllo (Risk Ratio=0.50 a 12 mesi di FU → riduzione del rischio del 50%; Mei et al., 2021).
- Tuttavia, informazioni limitate sul «what works for whom» → «Dodo verdict»

Contents lists available at ScienceDirect

Clinical Psychology Review

journal homepage: www.elsevier.com/locate/clinpsychrev

Review

Preventive interventions for individuals at ultra high risk for psychosis: An updated and extended meta-analysis

Cristina Mei [a,b,1], Mark van der Gaag [c,d,**,1], Barnaby Nelson [a,b], Filip Smit [c,e,f], Hok Pan Yuen [a,b], Maximus Berger [a,b], Marija Krcmar [a,b], Paul French [g], G. Paul Amminger [a,b], Andreas Bechdolf [h,i], Pim Cuijpers [c], Alison R. Yung [a,b,g], Patrick D. McGorry [a,b,*]

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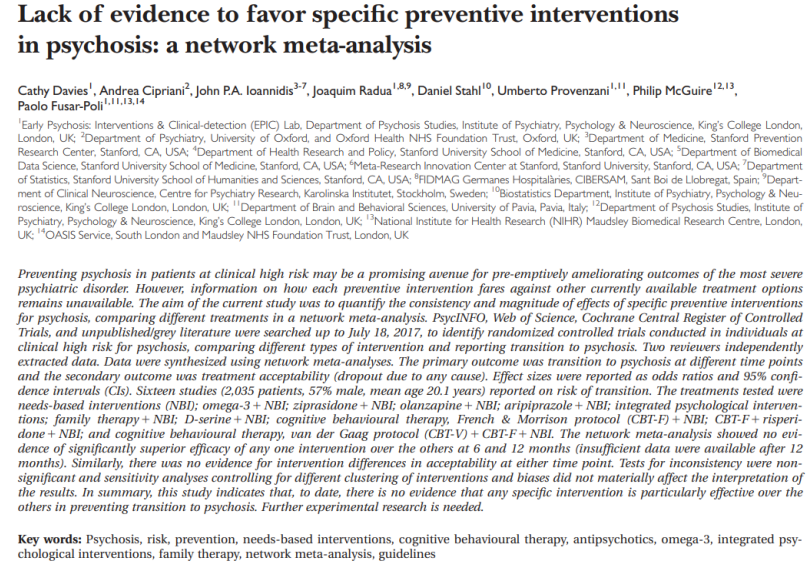
Mei, C., van der Gaag, M., Nelson, B., Smit, F., Yuen, H. P., Berger, M., Krcmar, M., French, P., Amminger, G. P., Bechdolf, A., Cuijpers, P., Yung, A. R., & McGorry, P. D. (2021). Preventive interventions for individuals at ultra high risk for psychosis: An updated and extended meta-analysis. *Clinical psychology review*, *86*, 102005. https://doi.org/10.1016/j.cpr.2021.102005



Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis

Cathy Davies[1], Andrea Cipriani[2], John P.A. Ioannidis[3-7], Joaquim Radua[1,8,9], Daniel Stahl[10], Umberto Provenzani[1,11], Philip McGuire[12,13], Paolo Fusar-Poli[1,11,13,14]

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Preventing psychosis in patients at clinical high risk may be a promising avenue for pre-emptively ameliorating outcomes of the most severe psychiatric disorder. However, information on how each preventive intervention fares against other currently available treatment options remains unavailable. The aim of the current study was to quantify the consistency and magnitude of effects of specific preventive interventions for psychosis, comparing different treatments in a network meta-analysis. PsycINFO, Web of Science, Cochrane Central Register of Controlled Trials, and unpublished/grey literature were searched up to July 18, 2017, to identify randomized controlled trials conducted in individuals at clinical high risk for psychosis, comparing different types of intervention and reporting transition to psychosis. Two reviewers independently extracted data. Data were synthesized using network meta-analyses. The primary outcome was transition to psychosis at different time points and the secondary outcome was treatment acceptability (dropout due to any cause). Effect sizes were reported as odds ratios and 95% confidence intervals (CIs). Sixteen studies (2,035 patients, 57% male, mean age 20.1 years) reported on risk of transition. The treatments tested were needs-based interventions (NBI); omega-3 + NBI; ziprasidone + NBI; olanzapine + NBI; aripiprazole + NBI; integrated psychological interventions; family therapy + NBI; D-serine + NBI; cognitive behavioural therapy, French & Morrison protocol (CBT-F) + NBI; CBT-F + risperidone + NBI; and cognitive behavioural therapy, van der Gaag protocol (CBT-V) + CBT-F + NBI. The network meta-analysis showed no evidence of significantly superior efficacy of any one intervention over the others at 6 and 12 months (insufficient data were available after 12 months). Similarly, there was no evidence for intervention differences in acceptability at either time point. Tests for inconsistency were non-significant and sensitivity analyses controlling for different clustering of interventions and biases did not materially affect the interpretation of the results. In summary, this study indicates that, to date, there is no evidence that any specific intervention is particularly effective over the others in preventing transition to psychosis. Further experimental research is needed.

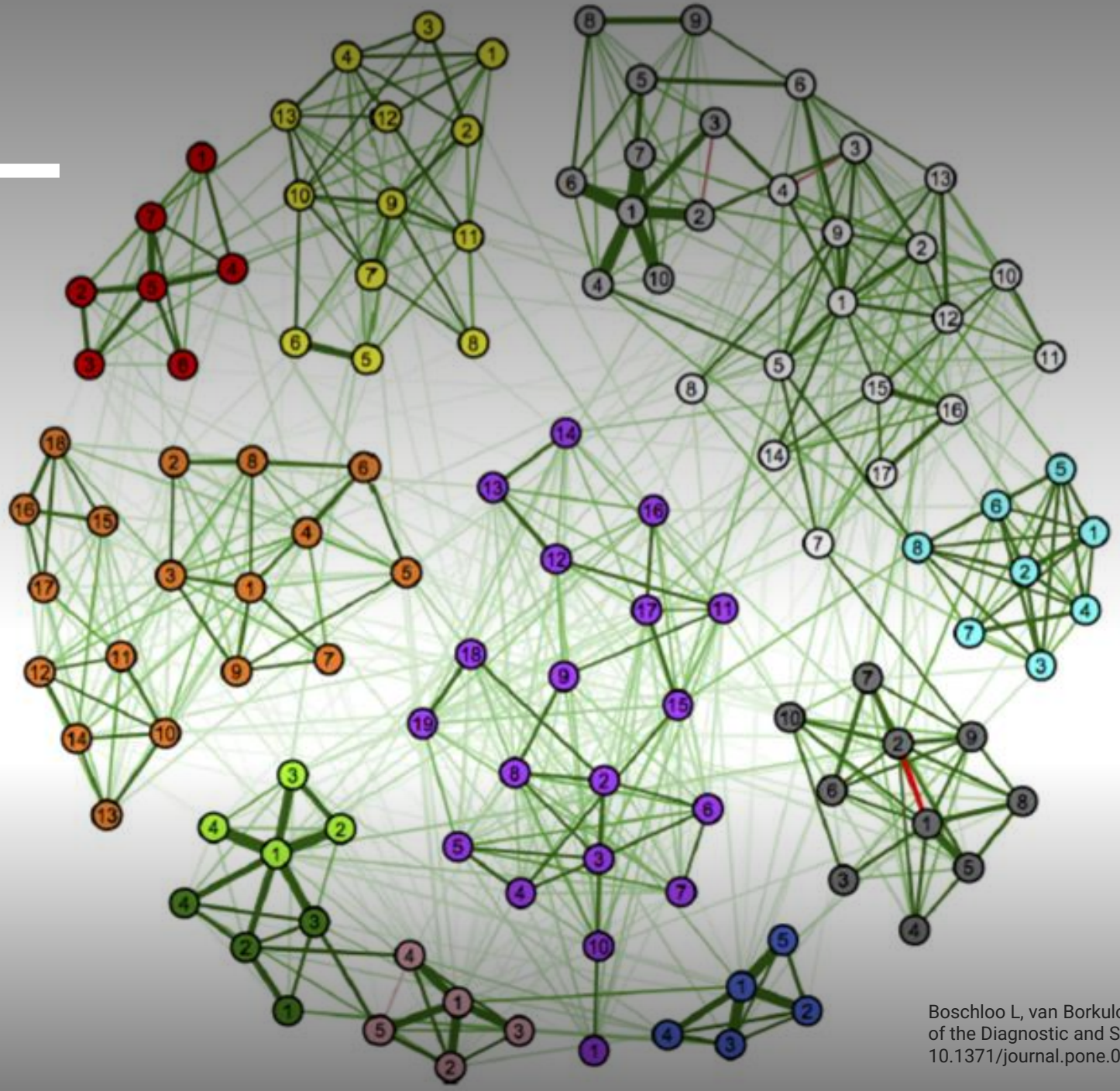
Key words: Psychosis, risk, prevention, needs-based interventions, cognitive behavioural therapy, antipsychotics, omega-3, integrated psychological interventions, family therapy, network meta-analysis, guidelines

(World Psychiatry 2018;17:196–209)

Davies, C., Cipriani, A., Ioannidis, J. P. A., Radua, J., Stahl, D., Provenzani, U., McGuire, P., & Fusar-Poli, P. (2018). Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, *17*(2), 196–209. https://doi.org/10.1002/wps.20526

(Alcuni dei) limiti

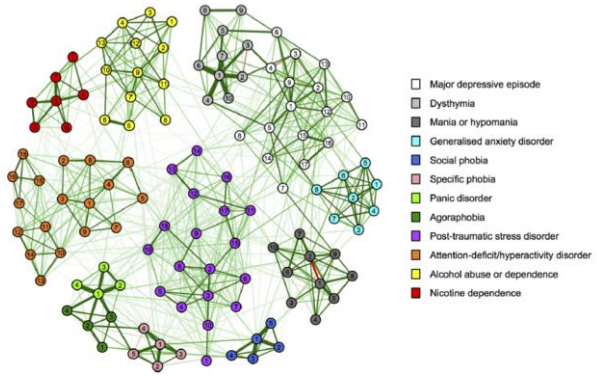
- «Detection paradox» (van Os et al., 2017).
- Efficacia degli interventi preventivi → specifica per transizione a psicosi e, in parte, sintomi positivi. Futuri trials (e meta-analisi) necessari per sintomatologia negativa, sintomi depressivi, qualità della vita, funzionamento (sebbene il loro decorso clinico sia favorevole nel tempo; Salzar de Pablo et al., 2022).
- Comorbidità: 78% UHR ha una doppia diagnosi con un disturbo non psicotico (prevalentemente disturbi depressivi, d'ansia e di personalità) → UHR è una popolazione estremamente eterogenea (Solmi et al., 2023).
- «Rischio pluripotente» (McGorry et al., 2018) → da UHR a una pluralità di esiti clinici (psicosi, disturbi depressivi, disturbi di personalità, disturbi bipolari, remissione).



- Major depressive episode
- Dysthymia
- Mania or hypomania
- Generalised anxiety disorder
- Social phobia
- Specific phobia
- Panic disorder
- Agoraphobia
- Post-traumatic stress disorder
- Attention-deficit/hyperactivity disorder
- Alcohol abuse or dependence
- Nicotine dependence

Boschloo L, van Borkulo CD, Rhemtulla M, Keyes KM, Borsboom D, Schoevers RA. The Network Structure of Symptoms of the Diagnostic and Statistical Manual of Mental Disorders. PLoS One. 2015 Sep 14;10(9):e0137621. doi: 10.1371/journal.pone.0137621. PMID: 26368008; PMCID: PMC4569413.

Network analysis



- Disturbi mentali come sistemi complessi (Borsboom et al., 2021; Robinaugh et al., 2020)
- Disturbi mentali non sono «causati» da una variabile latente (per esempio, la presenza di un disturbo psicotico genera i deliri e le allucinazioni)
- I disturbi mentali **sono** le interconnessioni tra variabili (sintomi, variabili psicologici, ambientali) all'interno di un network → «feedback loop» tra sintomi.
- Sistemi nosologici principali: sintomi intercambiabili
- Approccio network: ogni sintomo ha il proprio peso all'interno della struttura e contribuisce in modo specifico al mantenimento dello stato di attivazione psicopatologica
- «Psicopatologia» → stato stabile di un network densamente connesso (Borsboom, 2017)

Network analysis

- Identificare: (a) nodi centrali all'interno del network, (b) sintomi ponte (per esempio, un sintomo che collega i sintomi d'ansia con i sintomi depressivi), (c) indici di attendibilità (stabilità) della rete, (d) possibili «arcipelaghi di sintomi» e sintomi isolati.
- Comorbidity: «flesh and bones of psychopathology» (Borsboom, 2017)

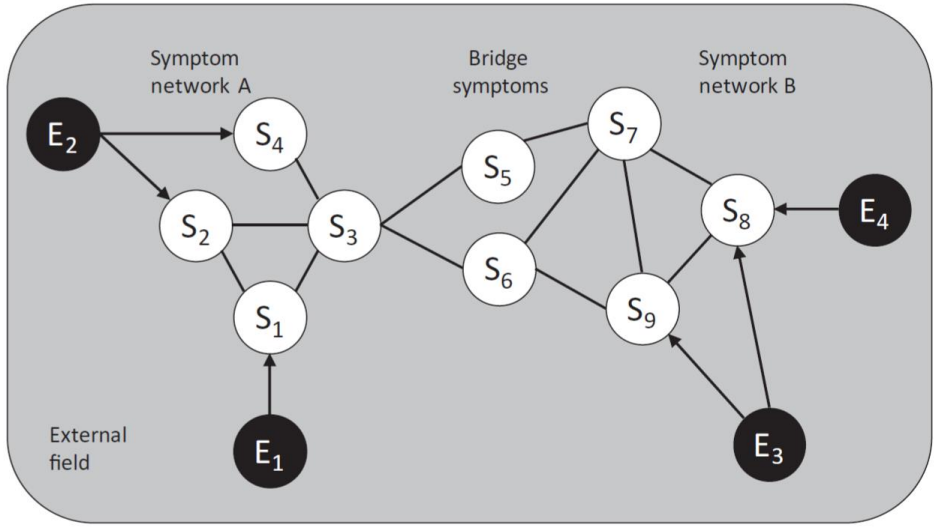
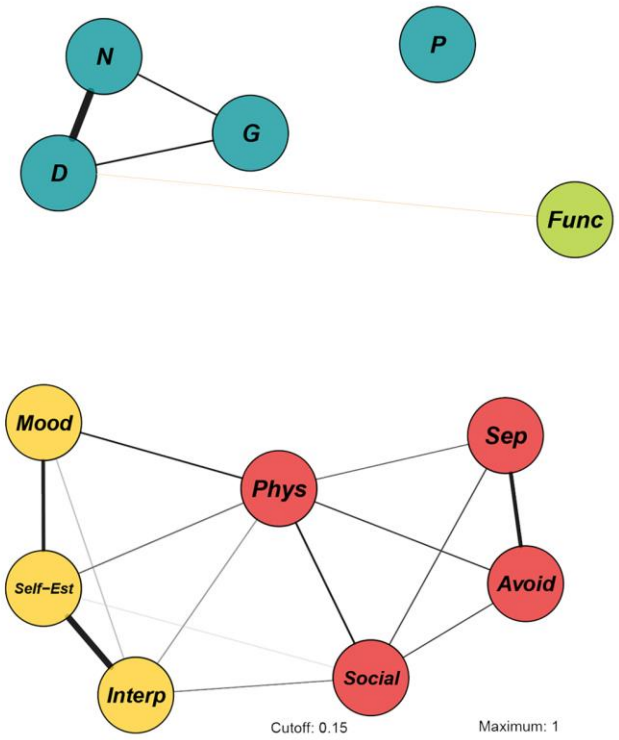


Figure 2 Two disorders (A and B) that are connected through bridge symptoms (S_5 and S_6) which play a role in both networks. Although the association of symptoms will be strongest within each network, structural overlap between the disorders is unavoidable, and as a result comorbidity will arise.

Borsboom D. (2017). A network theory of mental disorders. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, *16*(1), 5–13. https://doi.org/10.1002/wps.20375

Lo Buglio G, Pontillo M, Cerasti E, Polari A, Schiano Lomoriello A, Vicari S, Lingiardi V, Boldrini T, Solmi M. A network analysis of anxiety, depressive, and psychotic symptoms and functioning in children and adolescents at clinical high risk for psychosis. Front Psychiatry. 2022 Oct 28;13:1016154. doi: 10.3389/fpsyt.2022.1016154. PMID: 36386985; PMCID: PMC9650363.



- Presenza di tre «arcipelaghi di sintomi»:
- 1) Sintomi depressivi e di ansia. Il nodo «sintomi fisici» (sintomo di ansia) → connesso a tutti gli altri sintomi depressivi e di ansia;
- 2) Sintomi psicotici attenuati (sintomi positivi esclusi) e funzionamento;
- 3) Sintomi positivi.

Future directions

- Network analysis come **strumento per la diagnosi** → no presenza assenza di una condizione, ma specifiche inter-relazioni tra variabili che consentano di differenziare una condizione clinica da altre
- Network analysis **beyond symptoms** → Funzionamento psicologico dell'individuo e meta-analisi sull'analisi network
- **«Mapping»** (Es. studio precedente), **«Zooming»** (Es. single-case su un single case/cohort con N molto elevato di misurazioni ripetute), e **«Intervening»** (Es. Intervento guidato da una valutazione network – Network versus non-network).

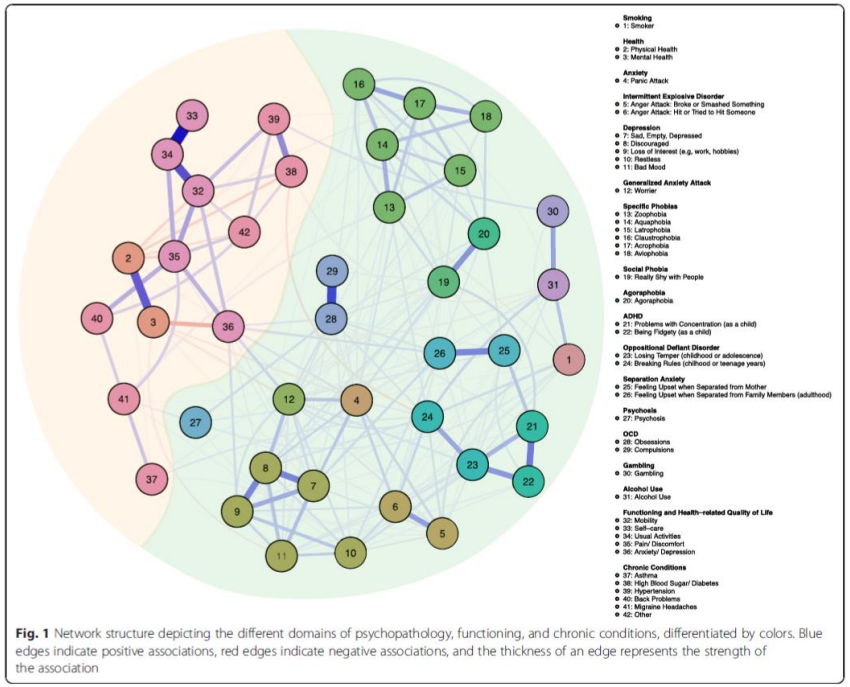


Fig. 1 Network structure depicting the different domains of psychopathology, functioning, and chronic conditions, differentiated by colors. Blue edges indicate positive associations, red edges indicate negative associations, and the thickness of an edge represents the strength of the association

Isvoranu, A. M., Abdin, E., Chong, S. A., Vaingankar, J., Borsboom, D., & Subramaniam, M. (2021). Extended network analysis: from psychopathology to chronic illness. *BMC psychiatry*, *21*(1), 119. https://doi.org/10.1186/s12888-021-03128-y