Pharmacopsychose ou psychose?

Place des troubles psychotiques induits par le cannabis

Pr Vincent Laprévote

CLIP Centre de Liaison et d'Intervention Précoce, CPN, Nancy, France

INSERM U 1114 Neuropsychologie cognitive et physiopathologie de la schizophrénie, Strasbourg-Nancy, France

D'où tu parles?

CLIP

Nancy : 300 000 habitants, 50 000 étudiants

Centre Psychothérapique de Nancy

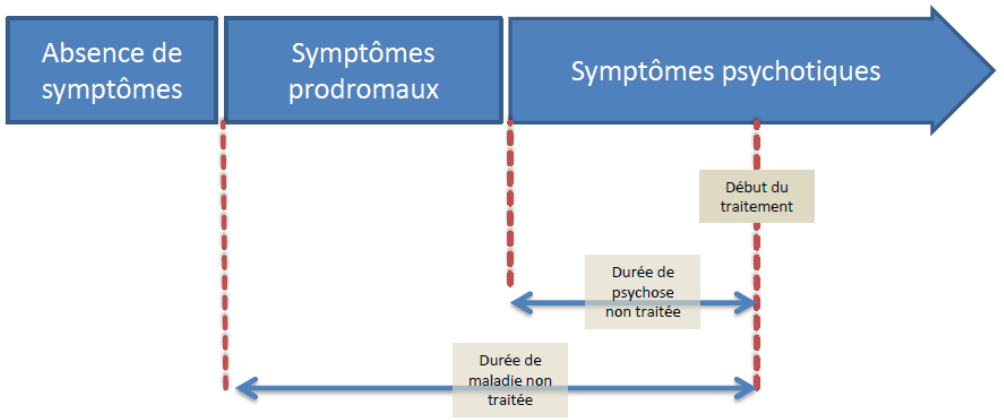
12-25 ans

CLIP

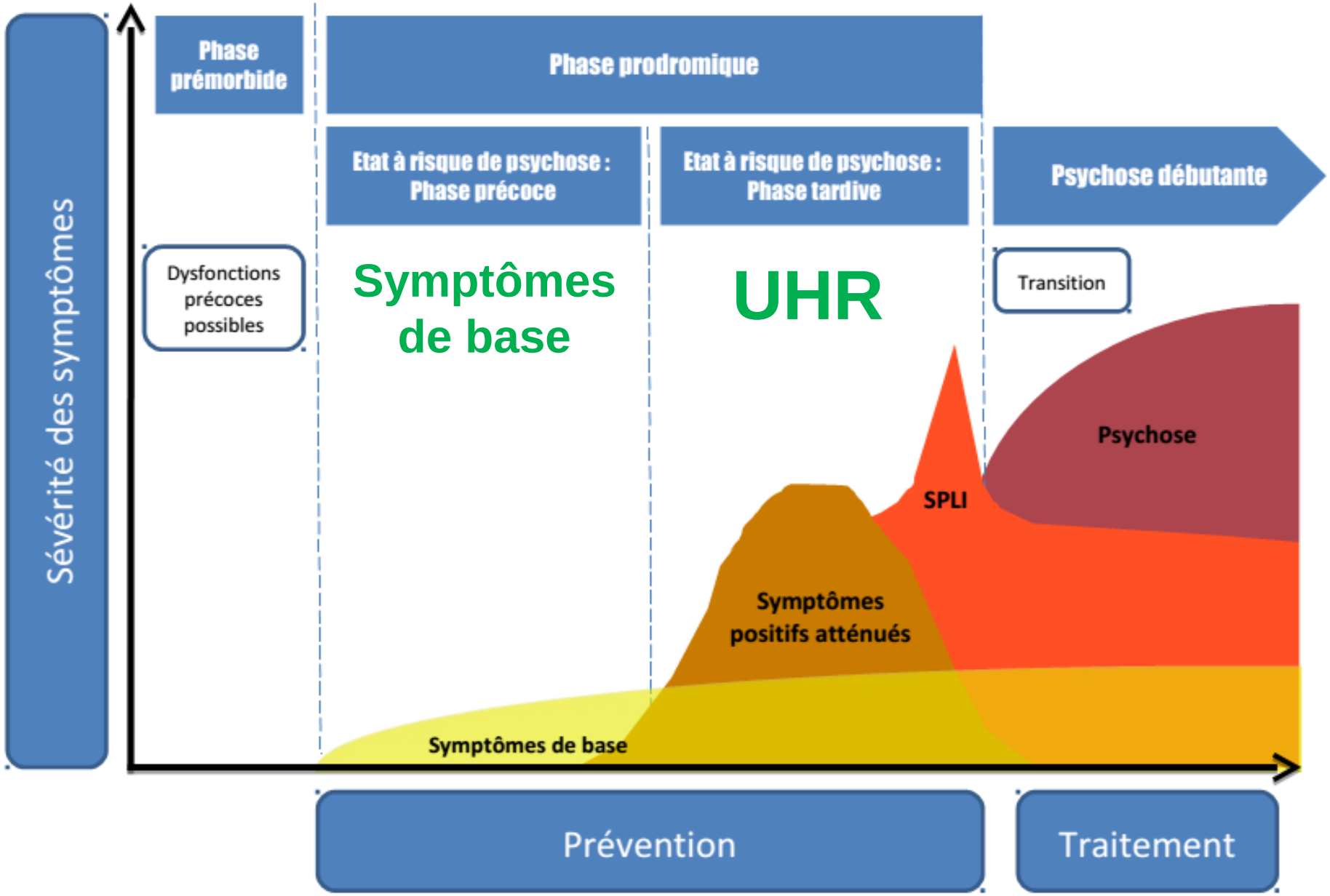
ELDO RADO

Maison des Ados

Pourquoi intervenir précocement?



- Réduire la durée de psychose non traitée voire la durée de maladie non traitée
- Favoriser l'engagement dans les soins et améliorer le pronostic
- Permettre un accès aux soins hors conditions de crise



D'après Fusar Poli et al. 2013

Stage	Definition		
	Symptoms	Functioning	Neurocognition
0	No current symptoms; increased risk of disorder	No historical change	Normal to mild deficits
1a	Mild or nonspecific symptoms (QIDS 0-11)	Mild functional change/decline; GAF 70-100	Mild neurocognitive deficits or relatively normal profile
1b	Moderate but sub-threshold symptoms (QIDS 11-20, YMRS >9, attenuated psychotic symptoms)	Functional decline to caseness (GAF <70)	Moderate neurocognitive changes, particularly in attention, learning, or executive function (e.g., 0.5-1.0 SD decrement relative to premorbid IQ)
2	Full-threshold disorder with moderate to severe symptoms (QIDS >20, YMRS >15, meets CAARMS/SIPS criteria)	Functional decline (GAF <50)	Neurocognitive deficits (1.0-1.5 SD decrements relative to premorbid IQ)
3	Incomplete remission or relapse	Persistent functional decline (GAF <40)	Persistent decrement in neurocognition (>1.5 SD relative to premorbid IQ), including social cognition
4	Severe, unremitting or refractory illness	Poor treatment effectiveness despite persistently intensive interventions (GAF <30)	Similar to stage 3, with poor treatment effectiveness despite persistently intensive interventions

QIDS – Quick Inventory of Depressive Symptomatology, YMRS – Young Mania Rating Scale, CAARMS – Comprehensive Assessment of At Risk Mental States, SIPS – Structured Interview of Psychosis-risk Syndromes, GAF – Global Assessment of Functioning

Shah et al, World Psychiatry, 2020

1. CANNABIS ET TROUBLES PSYCHOTIQUES

Augmentation du risque de Troubles psychotiques

- 10 études de cohortes sur le sujet ont retrouvé une association significative (ECA, NEMESIS, swedish cohort, Dunedin, Christchurch, EDSP, NPMS, Rossler et al., California, ALSPAC)

  (Pour une revue, voir Gage et al. 2016)

- Moore et al. 2007 (sur 8 de ces cohortes) :

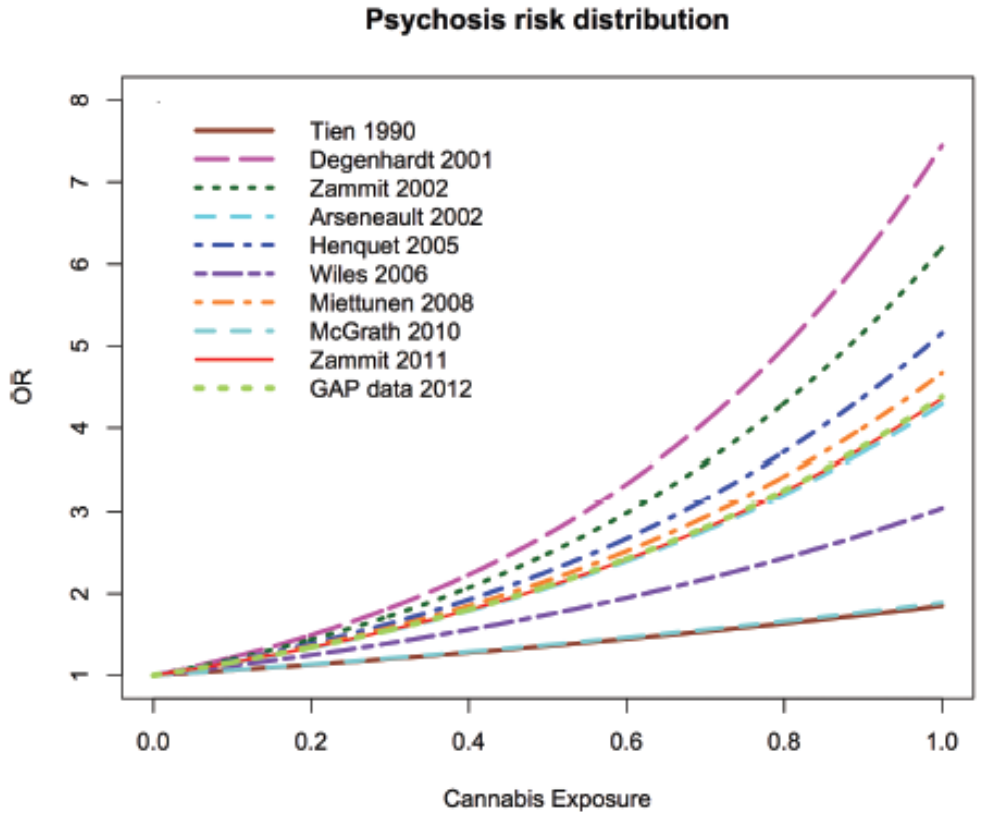
Exposition au cannabis et trouble psychotique : **OR=1.4** (IC 95% 1.2-1.65)

Chez ceux qui ont un usage plus fréquent : **OR=2.09** (IC 95% 1.54-2.84)

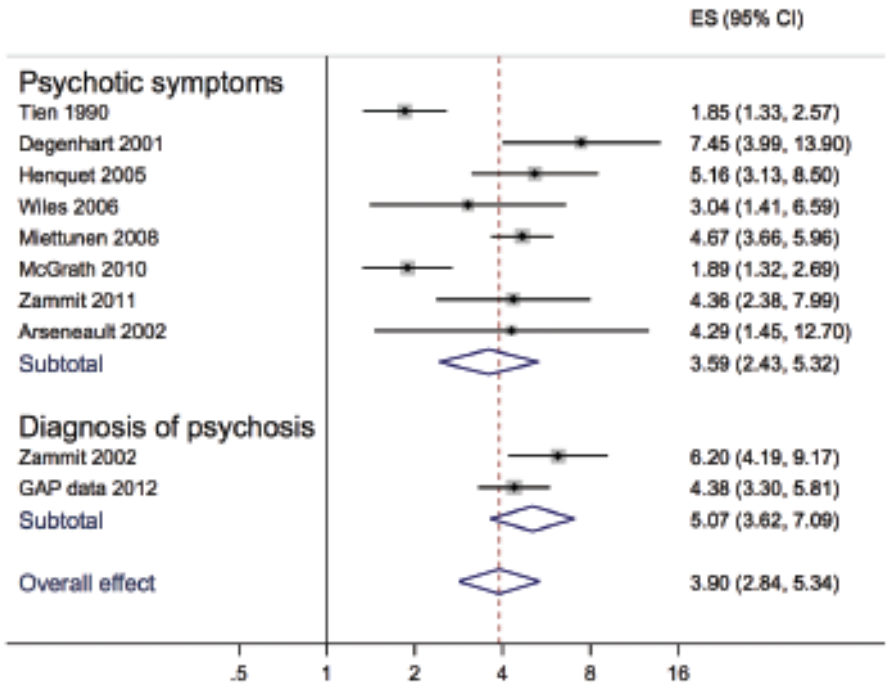
Effet de l'exposition

Marconi et al. Schiz Bull, 2016

Méta analyse sur 10 études. Ayant des données sur la consommation de cannabis avant l'apparition de la psychose en utilisant un critère de dose (fréquence/quantité consommée) et la survenue de psychose comme critère de jugement



OR médian pour tout usage de cannabis : 1.97 (1.68 to 2.31)
Groupe top 20% : 3.40 (2.55 to 4.54).



Autres facteurs liés aux consommations

- Age de début des consommations :

  En population générale, début avant 17 ans Vs Début après 17 ans : plus haut risque de symptômes positifs **OR=9,5** (p=0,0001) Ruiz-Veguilla et al. 2013

- Les variétés de cannabis fortement dosées en THC sont plus à risque de psychose (Di Forti et al, 2015)

Facteurs modulant le risque de psychose

- Antécédents familiaux de troubles psychotiques :

  Arendt et al (2008) : 2,5 fois plus de risques de développer une psychose induite par la cannabis chez les enfants d'une mère souffrant de schizophrénie

- Violence intra familiale

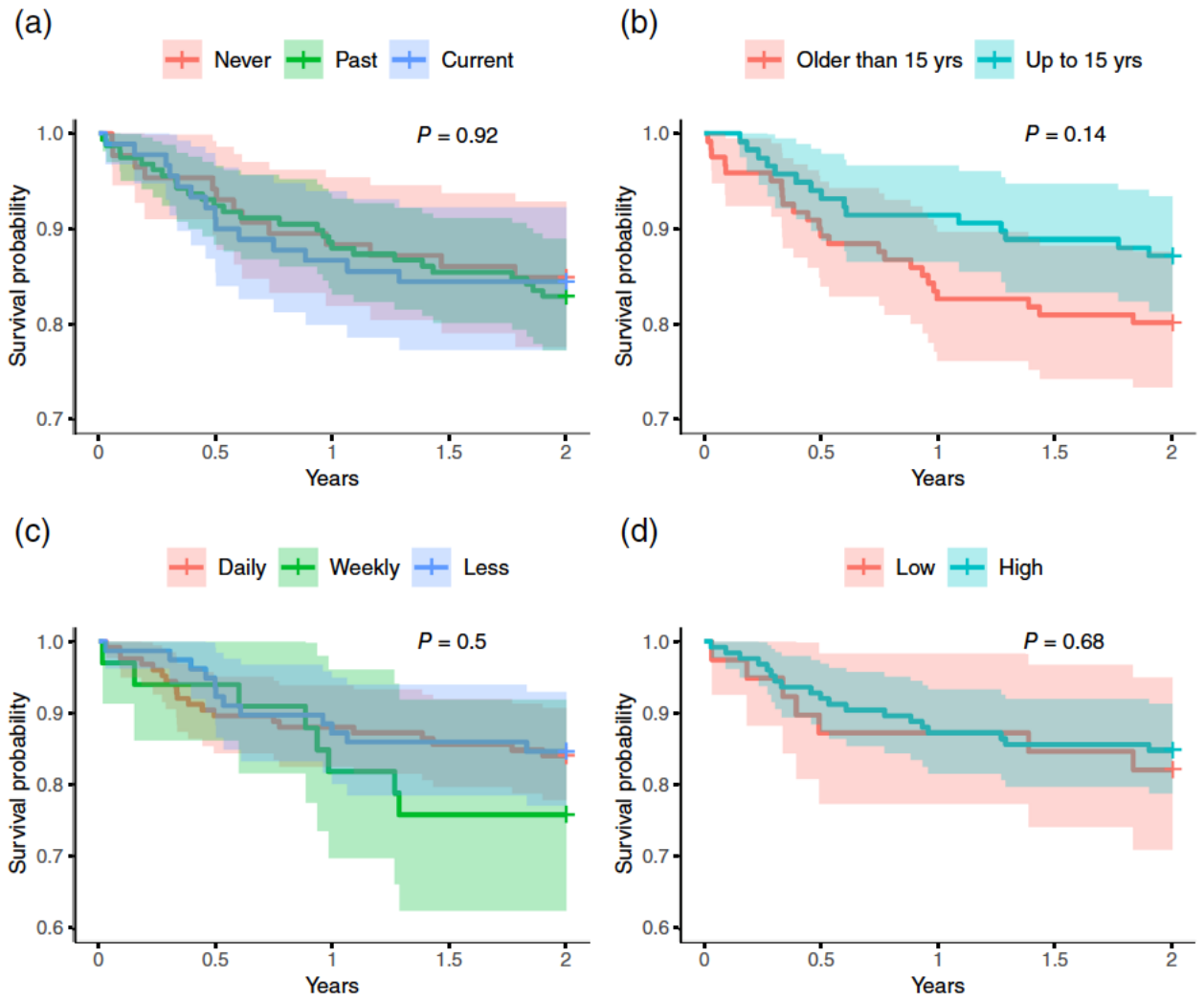
  Histoire personnelle de maltraitance ou trauma dans l'enfance + cannabis : OR de 11,9 à 20,9 pour le risque de troubles psychotiques

- Vulnérabilité génétique

  COMT (locus RS4680) allèle Val/Val + usage de cannabis : OR=10,9 pour les troubles psychotiques (Caspi et al. 2005)

  AKT1 (locus RS 2494732) : génotype c/c : OR=7,23 pour les troubles psychotiques si consommation quotidienne de cannabis (di Forti et al. 2012)

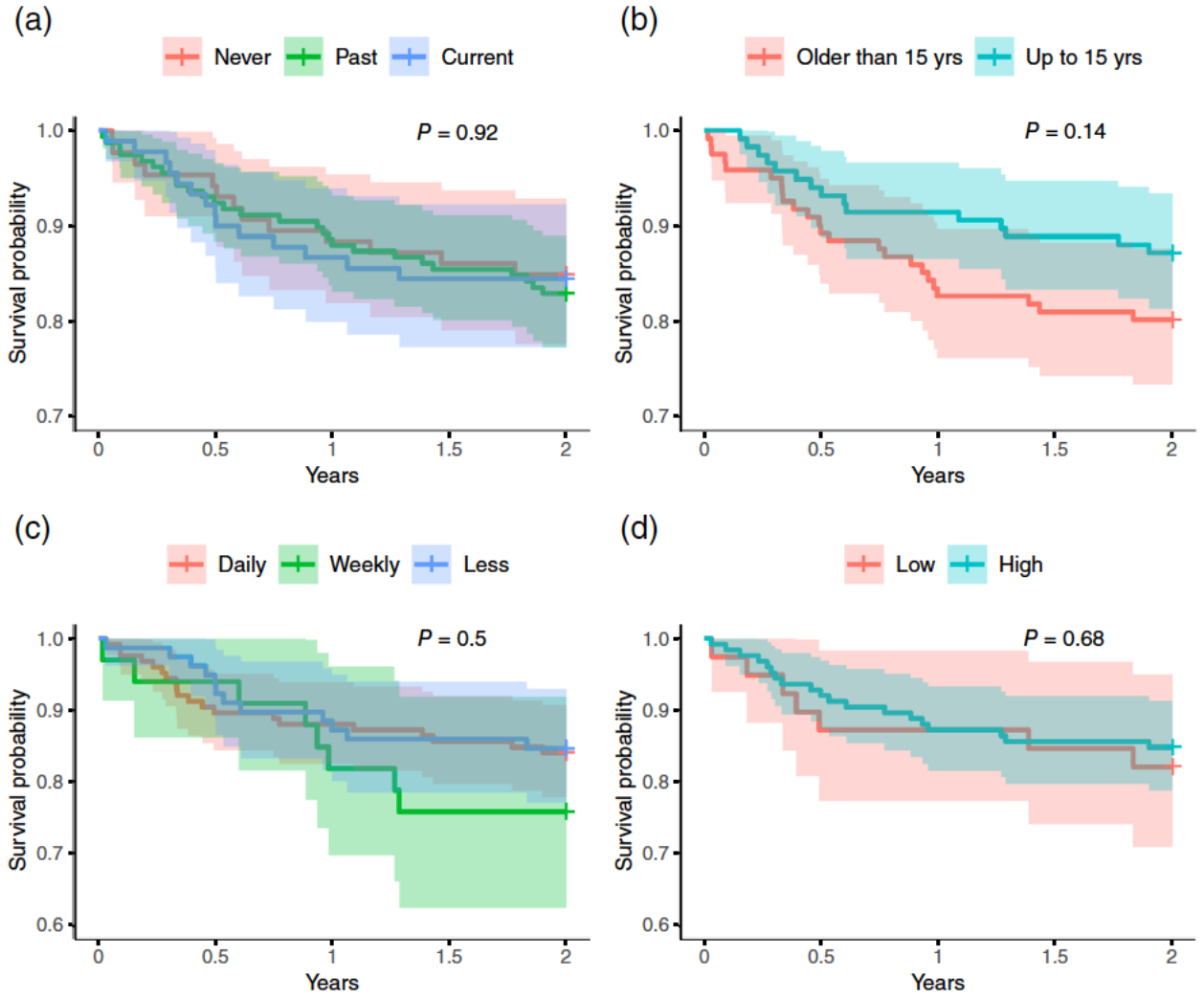
Risque de transition chez les patients CHR-P



Etude EU-GEI : 334 UHR et 67 volontaires sains
Suivi 2 ans

Chester et al. 2023, Psychiatry and Clinical neuroscience

Risque de transition chez les patients CHR-P



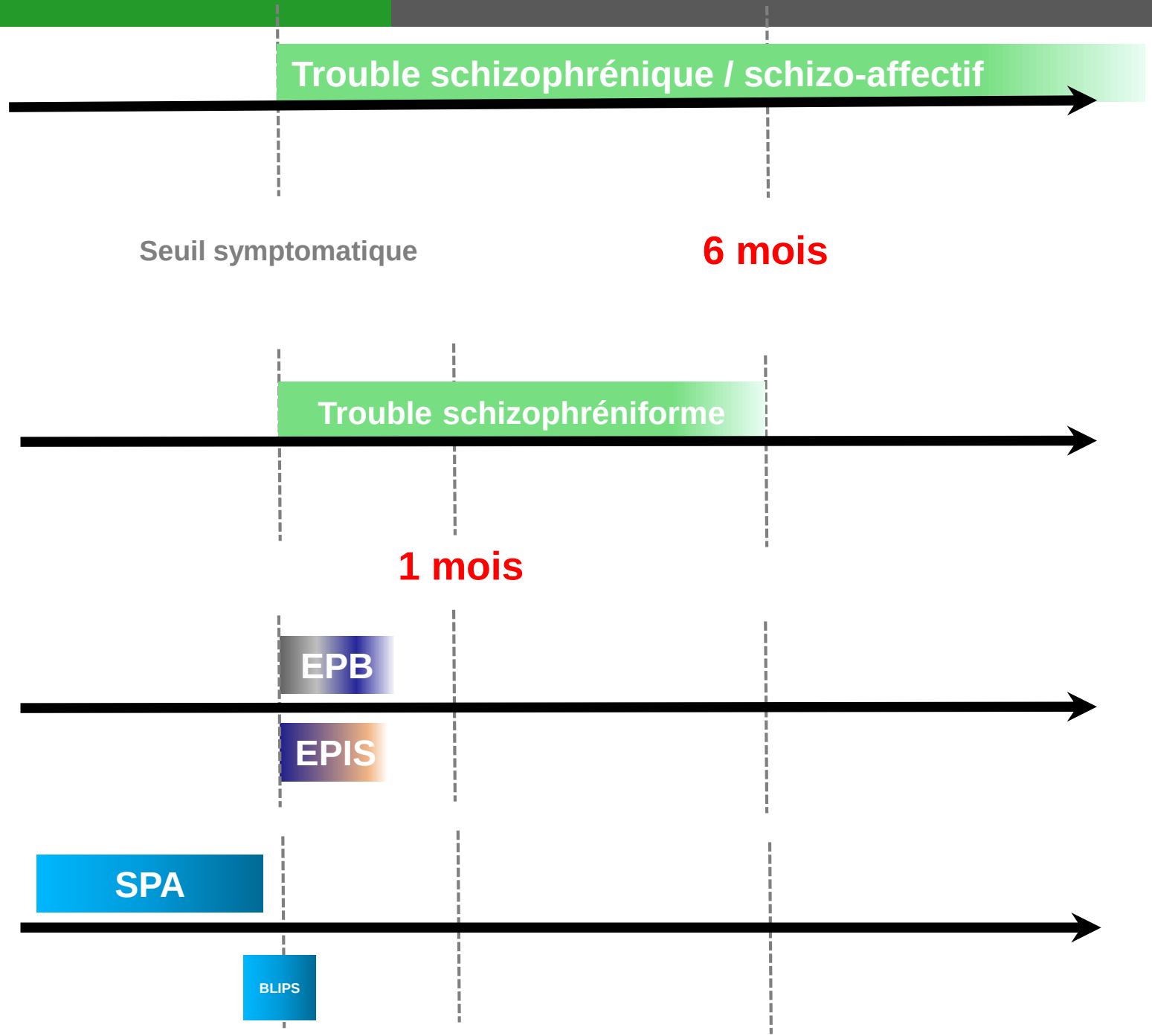
Etude EU-GEI : 334 UHR et 67 volontaires sains
Suivi 2 ans

Inclusion and exclusion criteria

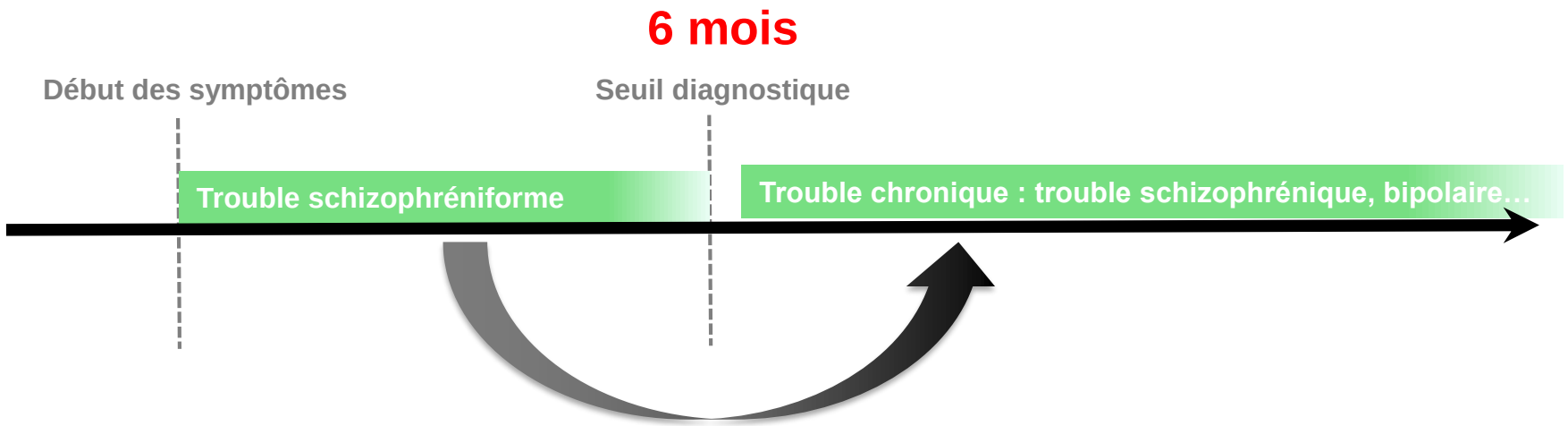
The study guidelines recommended that participants should be 16–35 years old. While most of the sample (95.0%) was in this age range, a few sites included individuals who were slightly older ($n = 3$) or younger ($n = 14$) than this range as the local clinical services for CHR subjects used a slightly broader age range. Exclusion criteria were: previous diagnosis of a psychotic disorder, as defined by the Structural Clinical Interview for DSM Disorders[30]; exceeding the 'Psychosis Threshold' or 'Antipsychotic Treatment Threshold', defined by the CAARMS[29]; an estimated IQ < 60 as measured by the shortened WAIS[31]; being unwilling to give a blood or saliva sample for genetic analysis. In addition, CHR subjects were excluded if their psychotic symptoms could be explained by an organic disorder or substance misuse, and HC were excluded if they met CAARMS criteria for the CHR state. Written, informed consent was provided by all participants.

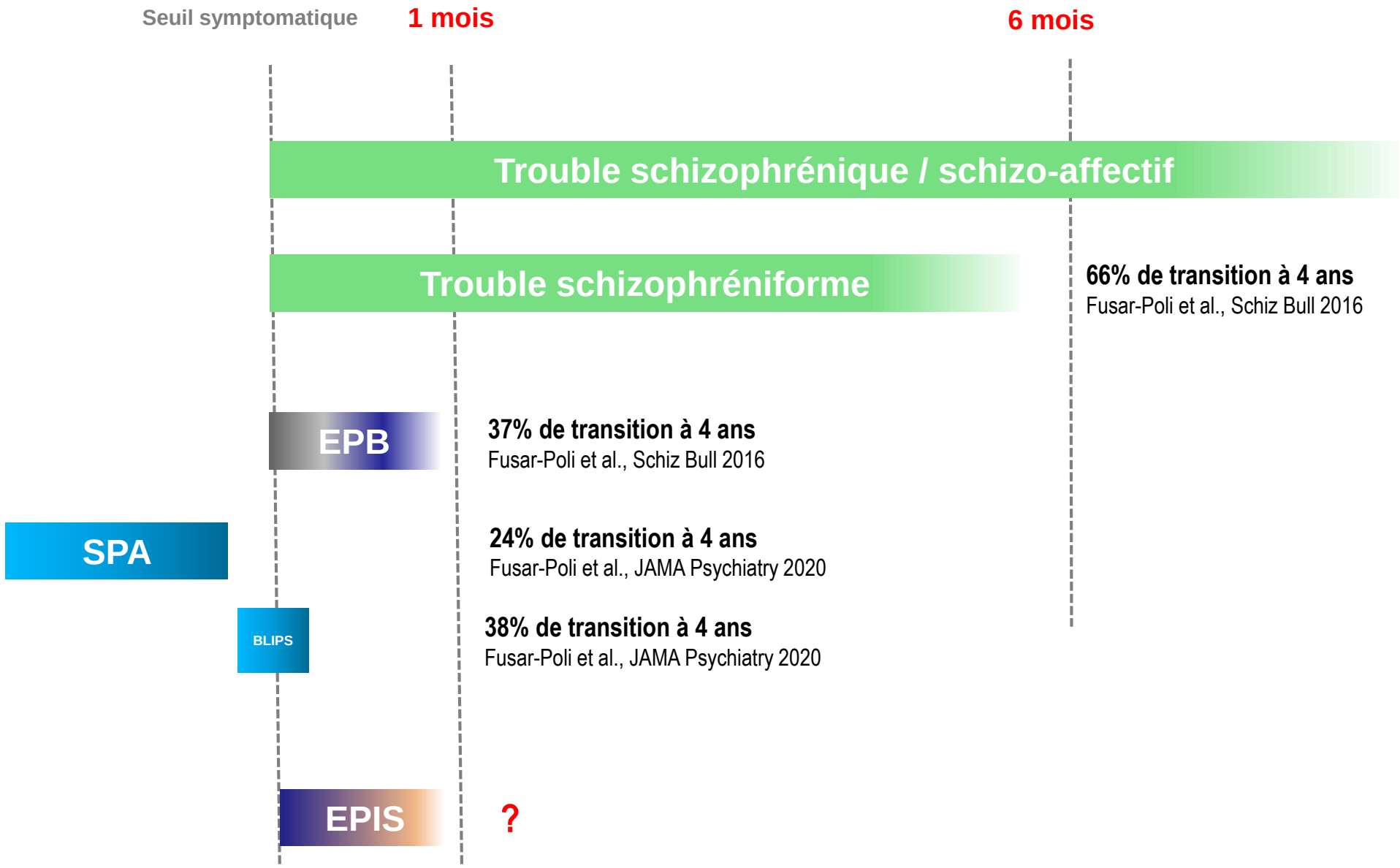
Chester et al. 2023, Psychiatry and Clinical neuroscience

2. EPISODES PSYCHOTIQUES INDUITS PAR UNE SUBSTANCE


Trouble schizophrénique / schizo-affectif
Seuil symptomatique
6 mois
Trouble schizophréniforme
1 mois
EPB
EPIS
SPA
BLIPS

Transition


6 mois
Début des symptômes
Seuil diagnostique
Trouble schizophréniforme
Trouble chronique : trouble schizophrénique, bipolaire…

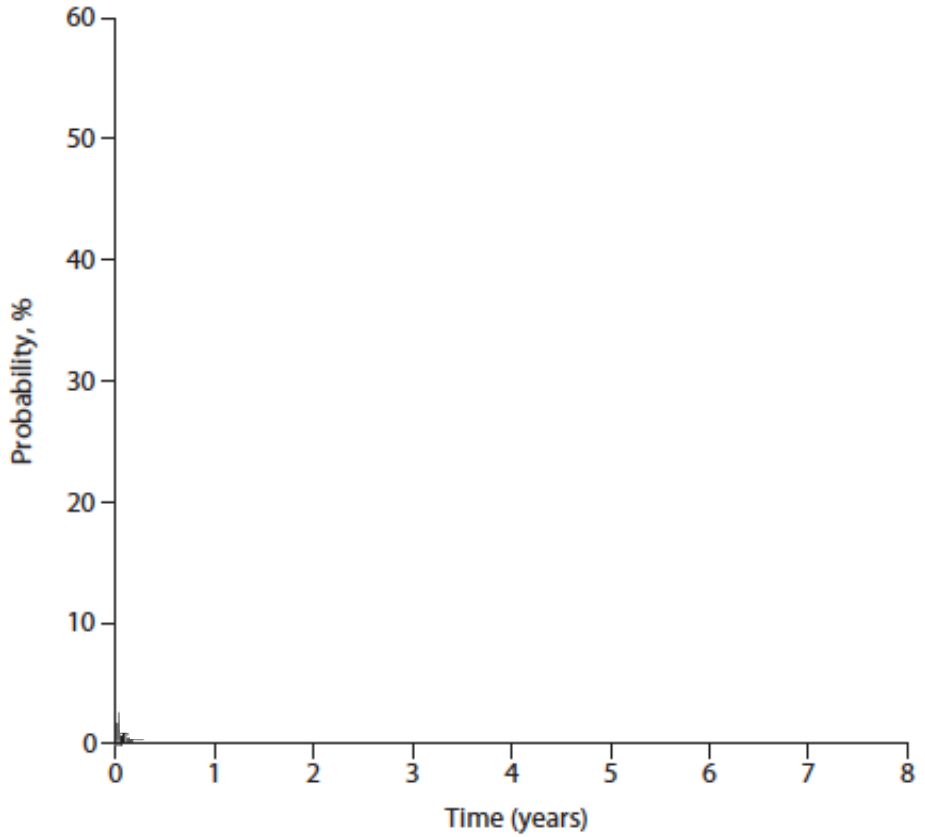

Seuil symptomatique
1 mois
6 mois
Trouble schizophrénique / schizo-affectif
Trouble schizophréniforme
66% de transition à 4 ans
Fusar-Poli et al., Schiz Bull 2016
EPB
37% de transition à 4 ans
Fusar-Poli et al., Schiz Bull 2016
SPA
24% de transition à 4 ans
Fusar-Poli et al., JAMA Psychiatry 2020
BLIPS
38% de transition à 4 ans
Fusar-Poli et al., JAMA Psychiatry 2020
EPIS
?

ORIGINAL RESEARCH

Substance-Induced Psychoses Converting Into Schizophrenia: A Register-Based Study of 18,478 Finnish Inpatient Cases

Jussi A. Niemi-Pynttäri, MD; Reijo Sund, DSocSc; Hanna Putkonen, MD, PhD; Helena Vorma, MD, PhD; Kristian Wahlbeck, MD, PhD; and Sami P. Pirkola, MD, PhD

Figure 1. Cumulative Probability of Receiving a Schizophrenia Spectrum Disorder Diagnosis (N = 18,478)



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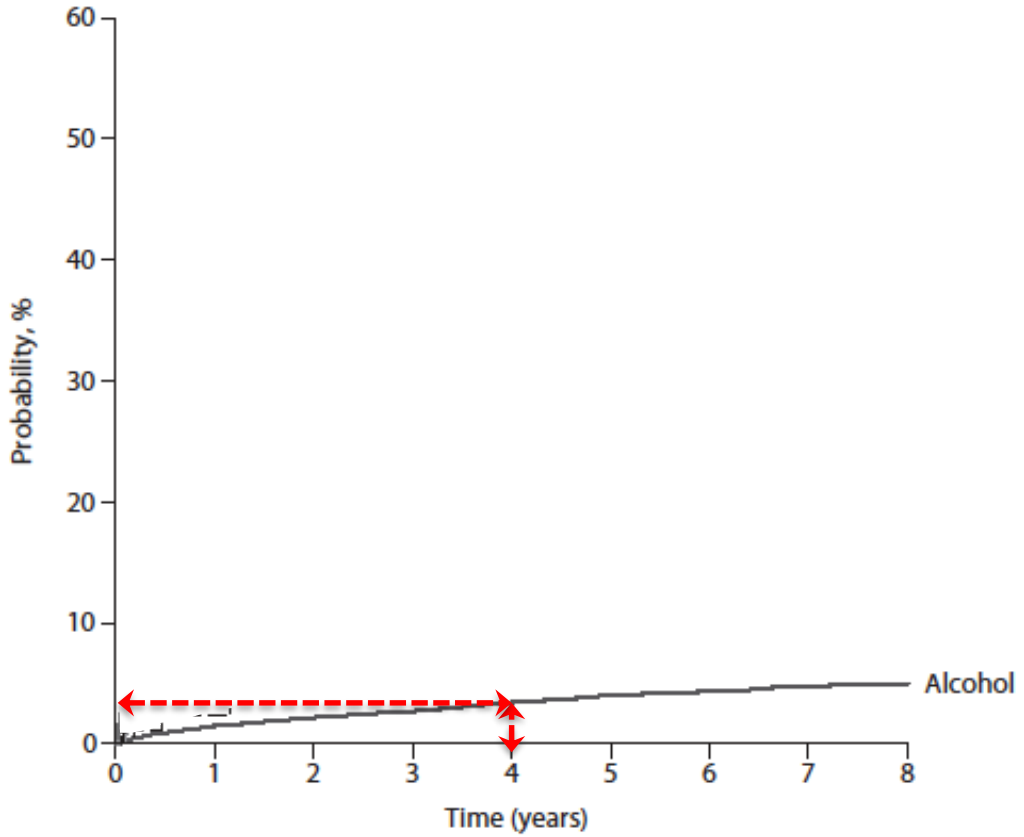

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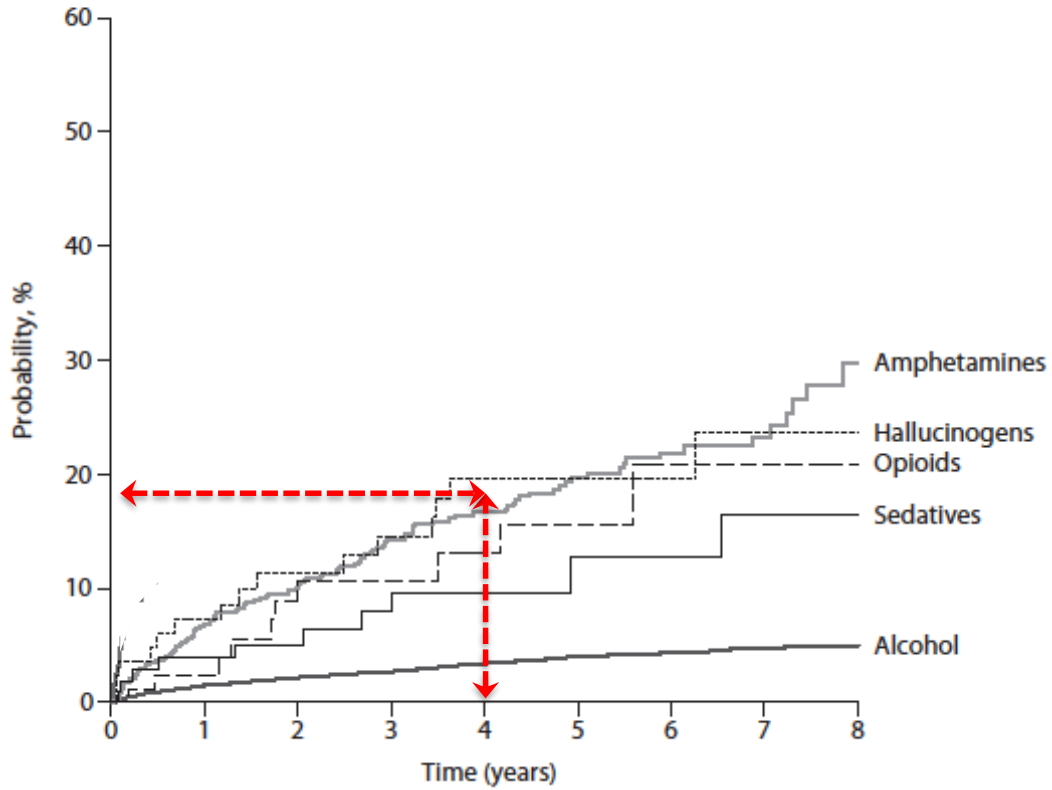

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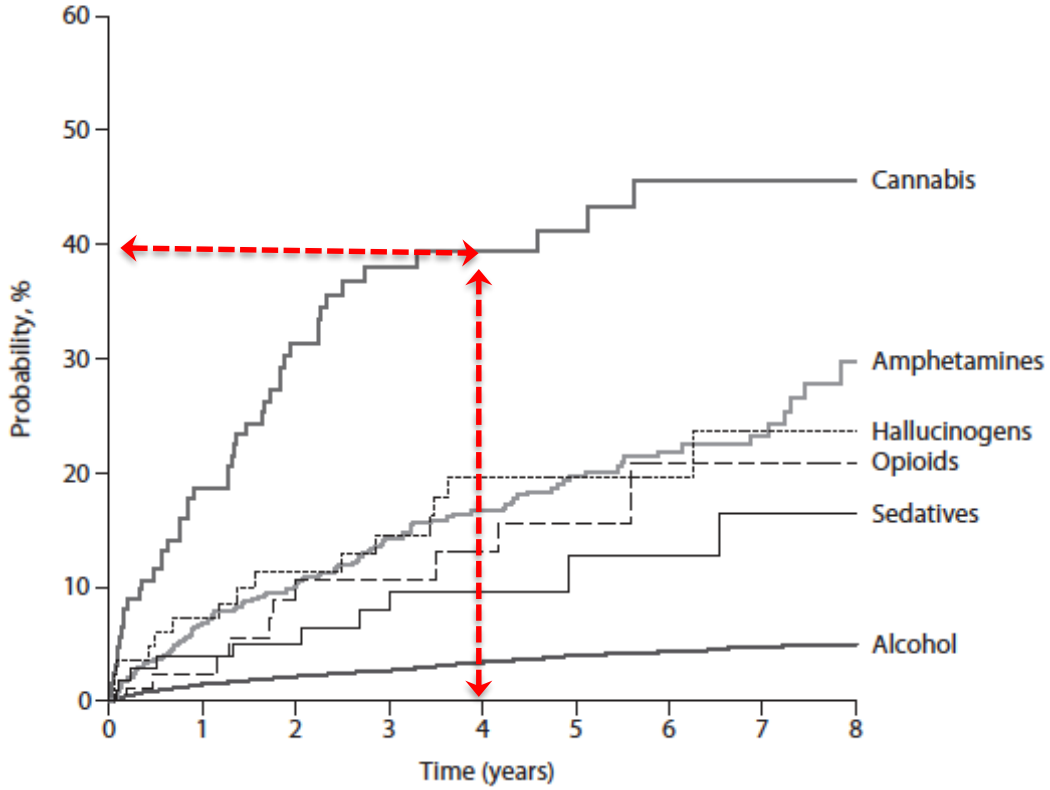
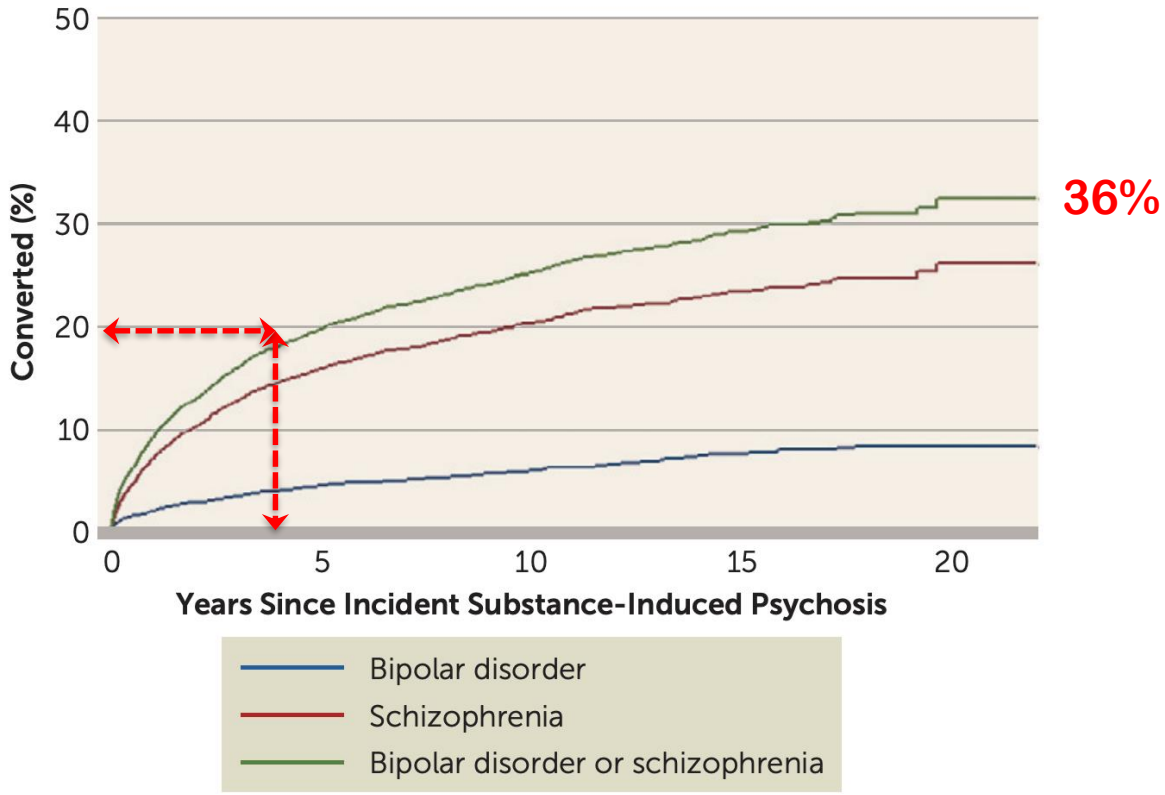


Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis

Marie Stefanie Kejser Starzer, M.D., Merete Nordentoft, Dr.Med.Sc., Carsten Hjorthøj, Ph.D., M.Sc.

Am J Psychiatry 175:4, April 2018

FIGURE 1. Rates of Conversion to Schizophrenia and Bipolar Disorder Following Incident Substance-Induced Psychosis in a Registry Study (N=6,788)



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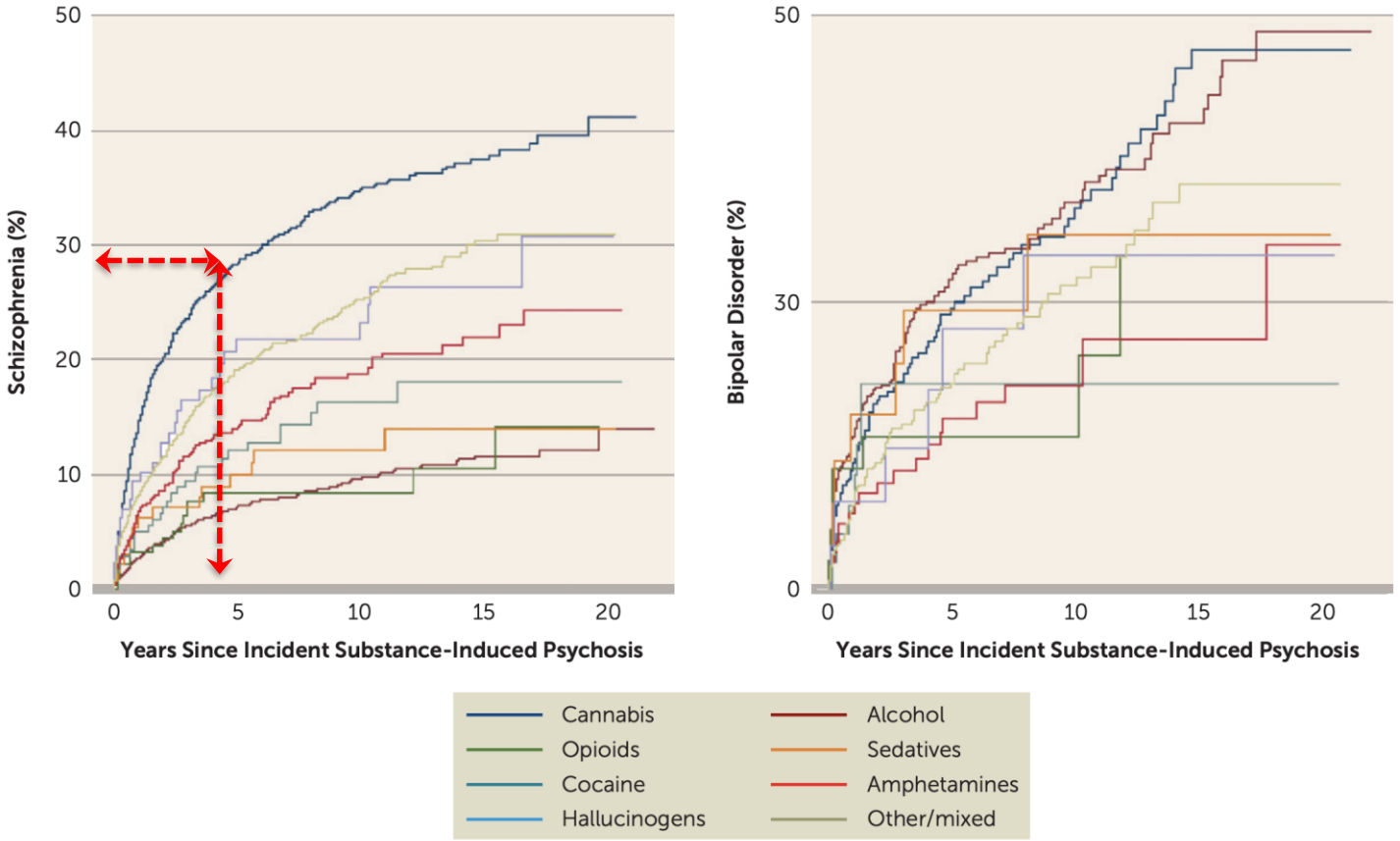
Am J Psychiatry 175:4, April 2018

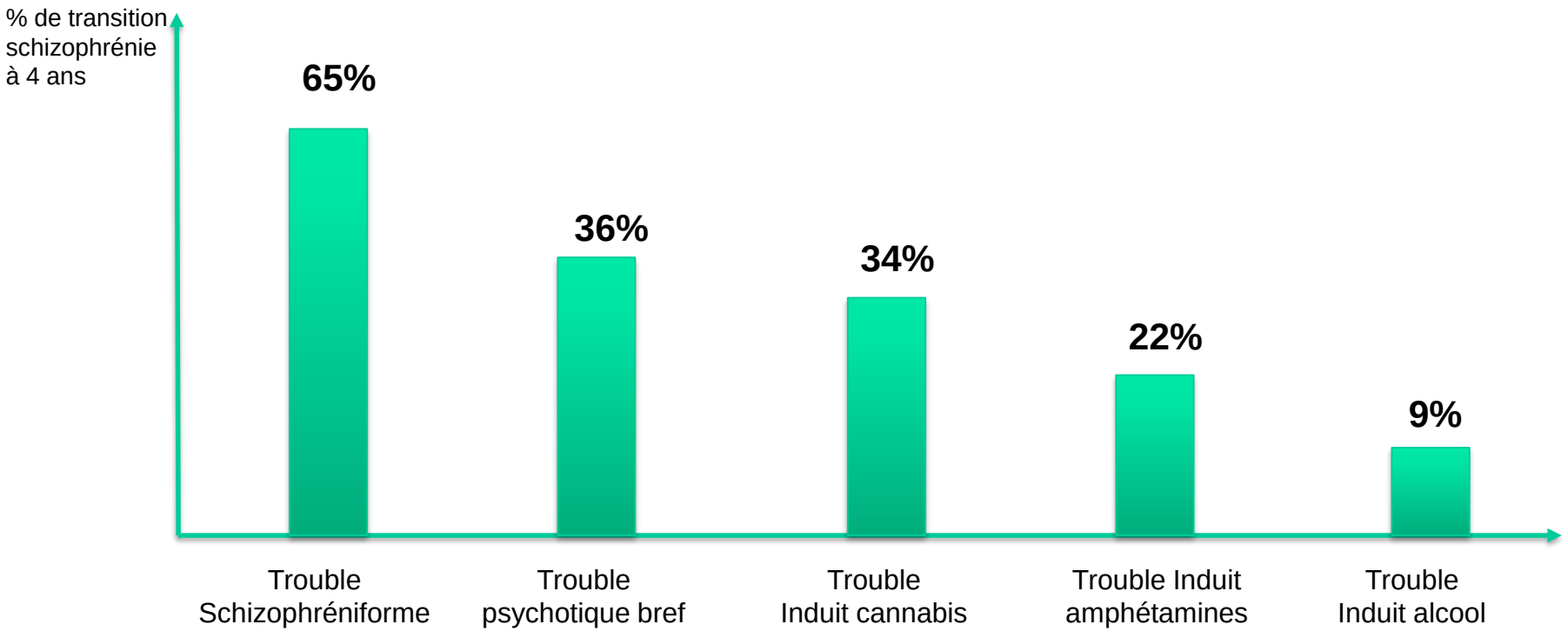
FIGURE 2. Rates of Conversion to Schizophrenia and Bipolar Disorder Following Incident Substance-Induced Psychosis, by Substance, in a Registry Study (N=6,788)



Schizophrenia Bulletin vol. 46 no. 3 pp. 505–516, 2020
doi:10.1093/schbul/sbz102
Advance Access publication 16 October 2019

Transition of Substance-Induced, Brief, and Atypical Psychoses to Schizophrenia: A Systematic Review and Meta-analysis

Benjamin Murrie[1], Julia Lappin[2,3], Matthew Large[2], and Grant Sara[*,4,5]



3. QUI VA FAIRE LA TRANSITION?

BRITISH JOURNAL OF PSYCHIATRY (2007), 190, 105–111. doi: 10.1192/bjp.bp.105.015784

Stability of early-phase primary psychotic disorders with concurrent substance use and substance-induced psychosis

CAROL L. M. CATON, DEBORAH S. HASIN, PATRICK E. SHROUT, ROBERT E. DRAKE, BOANERGES DOMINGUEZ, MICHAEL B. FIRST, SHARON SAMET and BELLA SCHANZER

Suivi à un an des admissions aux urgences psychiatriques pour épisode psychotique : 186 patients en psychose primaire, 99 patients en psychose induite par une substance

Facteurs de conversion vers une psychose primaire :

- Antécédents familiaux de troubles psychiques
- Moins bonne adaptation prémorbide
- Moins d'insight

Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis

Marie Stefanie Kejser Starzer, M.D., Merete Nordentoft, Dr.Med.Sc., Carsten Hjorthøj, Ph.D., M.Sc.

Am J Psychiatry 175:4, April 2018

TABLE 3. Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Incident Substance-Induced Psychosis in a Registry Study

	Schizophrenia				Bipolar disorder			
Variable	Converted (N)	Hazard Ratio	95% CI	p	Converted (N)	Hazard Ratio	95% CI	p
Substance inducing the psychosis								
Alcohol	183	1 (ref.)			144	1 (ref.)		
Opioids	12	0.78	0.43–1.40	0.40	7	0.72	0.34–1.55	0.41
Cannabis	433	2.17	1.77–2.66	<0.001	90	1.49	1.07–2.08	0.02
Sedatives	13	1.94	1.10–3.42	0.02	7	0.67	0.31–1.44	0.30
Cocaine	22	0.84	0.54–1.33	0.47	5	0.70	0.28–1.76	0.45
Amphetamines	97	1.23	0.94–1.61	0.12	20	0.83	0.50–1.37	0.46
Hallucinogens	23	1.28	0.82–1.98	0.28	6	1.24	0.53–2.87	0.62
Mixed or other substances	391	1.48	1.21–1.81	<0.001	82	0.93	0.68–1.27	0.65
Earlier diagnoses								
Substance use disorder	467	1.19	1.05–1.37	0.009	191	1.08	0.85–1.38	0.52
Attention deficit hyperactivity disorder	31	1.02	0.71–1.46	0.93	7	1.27	0.59–2.74	0.54
Personality disorder	229	1.29	1.09–1.52	0.002	115	1.46	1.13–1.89	0.004
Unipolar depression	106	1.10	0.89–1.36	0.36	77	2.03	1.54–2.67	<0.001
Anxiety disorder	45	0.95	0.70–1.29	0.73	38	1.59	1.11–2.27	0.01
Autism	≤4[a]	0.41	0.13–1.27	0.12	≤4[a]	1.04	0.14–7.64	0.97
Eating disorder	17	1.73	1.05–2.87	0.03	≤4[a]	0.75	0.27–2.07	0.58
Self-harm before substance-induced psychosis	177	0.80	0.68–0.95	0.01	80	0.95	0.72–1.24	0.71
Self-harm after substance-induced psychosis	124	1.92	1.58–2.34	<0.001	40	1.60	1.13–2.27	0.008
Age at incident substance-induced psychosis (years)								
≤15	11	0.36	0.20–0.66	0.001	0			
16–25	639	1 (ref.)			103	1 (ref.)		
26–30	179	0.74	0.63–0.88	0.001	38	0.99	0.68–1.44	0.96
31–35	119	0.59	0.48–0.73	<0.001	30	0.87	0.57–1.32	0.51
36–40	99	0.60	0.47–0.75	<0.001	32	1.05	0.68–1.61	0.82
41–50	102	0.32	0.25–0.40	<0.001	71	1.14	0.79–1.64	0.48
≥51	29	0.12	0.08–0.18	<0.001	87	1.69	1.16–2.44	0.006
Male	980	1.58	1.35–1.86	<0.001	228	0.68	0.54–0.85	0.001

[a] Danish laws regarding data protection do not allow reporting of cell counts <4 but >0.

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

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

Regional update

Cannabis induced psychosis and subsequent psychiatric disorders

Dharav Shah, Prabhat Chand*, Mrunal Bandawar, Vivek Benegal, Pratima Murthy

Dept. of Psychiatry, National Institute of Mental Health And Neuro Sciences (NIMHANS), Bangalore 560029, India

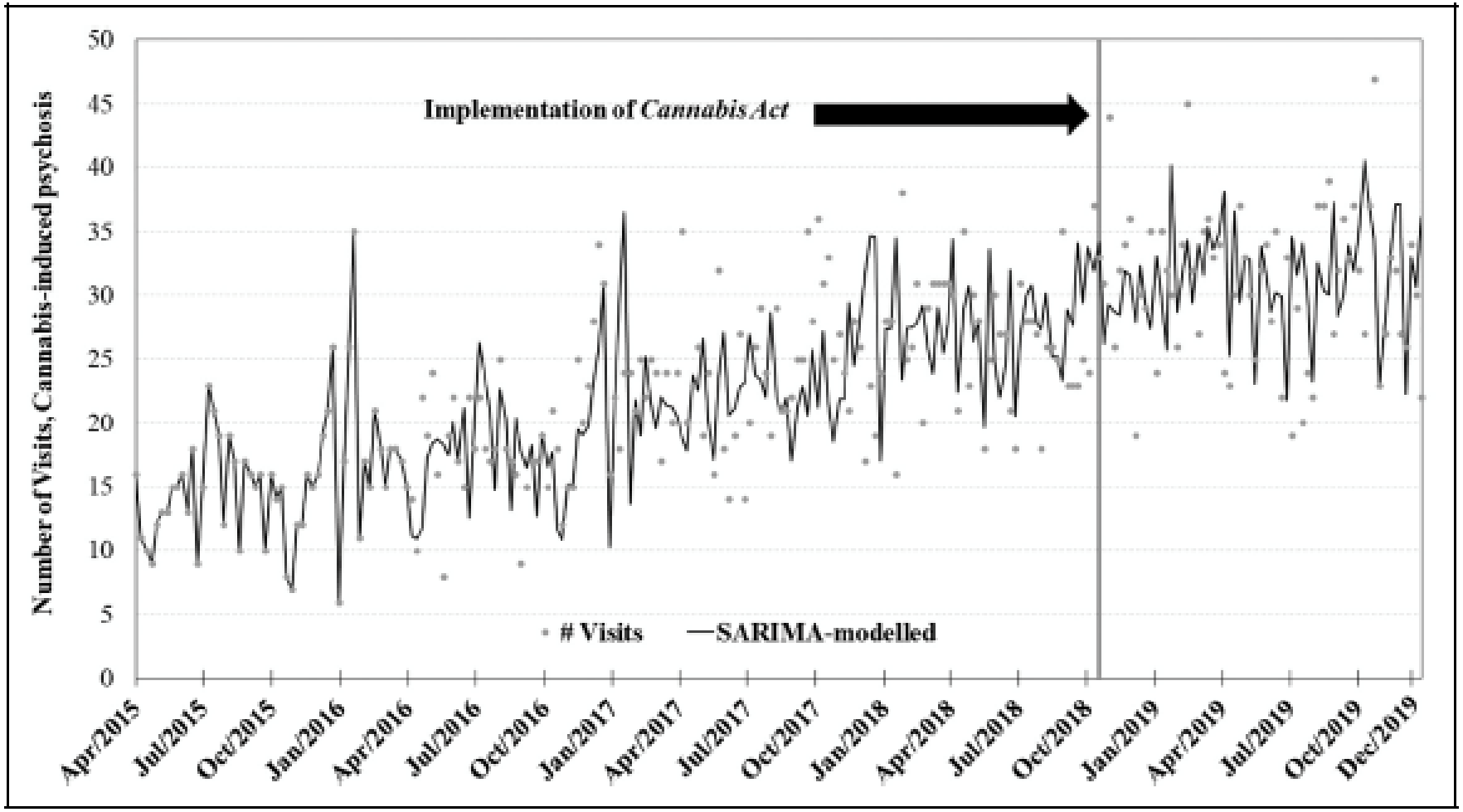
57 dossiers de psychose induite par cannabis

Aucune rechute si arrêt du cannabis

Mauvais pronostic :

- Jeune âge de début pour le cannabis
- Jeune âge de début des troubles psychotiques
- Antécédent familial de trouble psychotique
- Statut marital ou socio-économique

La légalisation augmente-t-elle le risque?



Callaghan et al.
The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie
2022, Vol. 67(8) 616-625

4. LE RISQUE EXISTE-T-IL POUR DE SIMPLES SYMPTÔMES PSYCHOTIQUES ?

Schizophrenia Research 157 (2014) 266–270

Contents lists available at ScienceDirect

Schizophrenia Research

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

Change in cannabis use in the general population: A longitudinal study on the impact on psychotic experiences

W.A. van Gastel [a,b,c,1], A. Vreeker [a,*,1], C.D. Schubart [a,d], J.H. MacCabe [e], R.S. Kahn [a], M.P.M. Boks [a]

[a] Brain Center Rudolf Magnus, University Medical Center Utrecht, Department of Psychiatry, HP. B01.206, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands
[b] Department of Psychiatry, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands
[c] Department of Sexology & Psychosomatic Obstetrics and Gynaecology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands
[d] Department of Psychiatry, Tergooi Hospital, Hilversum, The Netherlands
[e] Department of Psychosis Studies, Institute of Psychiatry, King's College, London, UK

Cohorte de 705 usagers de cannabis de 18-27 ans (recrutés par annonce dans coffee shops)
Mesure des consommations de cannabis et des expériences de psychose par la Community Assessment of Psychic Experiences (CAPE)
En moyenne, 16,4 mois entre 2 mesures

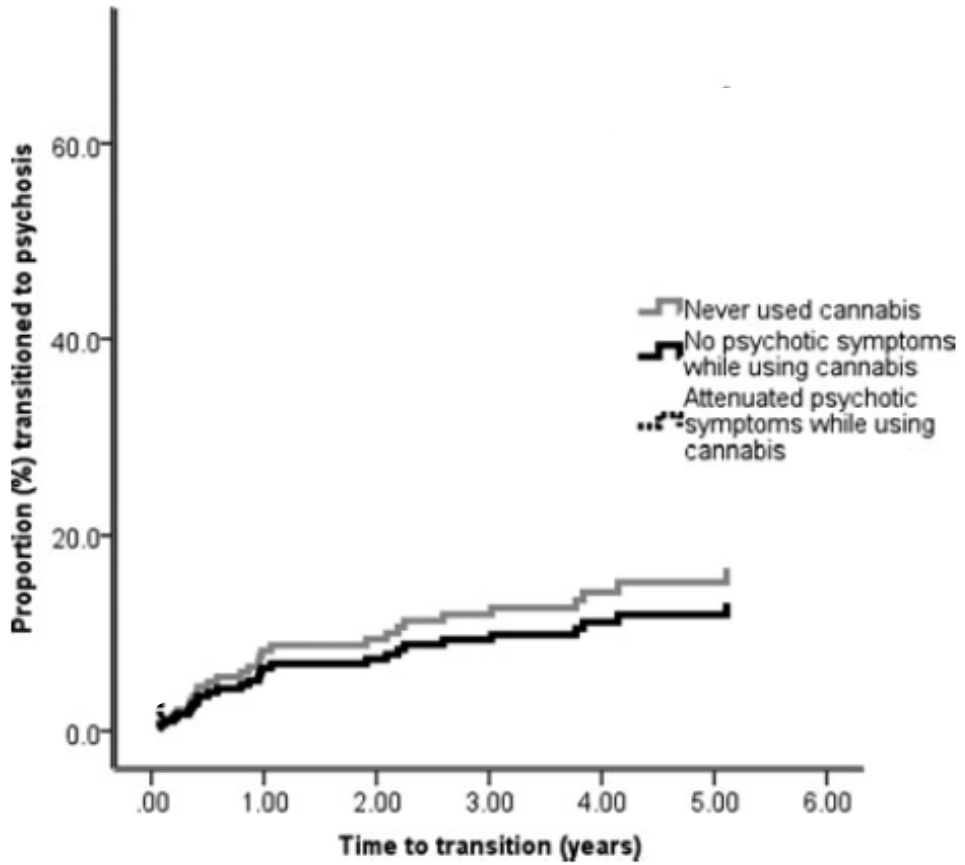
La diminution de la consommation de cannabis chez 249 patients prédit la diminution de la symptomatologie psychotique ($\beta = -0.096$, $p = 0.01$)

Psychological Medicine, Page 1 of 11. © Cambridge University Press 2016
doi:10.1017/S0033291716002671

ORIGINAL ARTICLE

Cannabis-induced attenuated psychotic symptoms: implications for prognosis in young people at ultra-high risk for psychosis

M. J. McHugh[1,2*], P. D. McGorry[1,2], A. R. Yung[3], A. Lin[4], S. J. Wood[1,5,6], J. A. Hartmann[1,2] and B. Nelson[1,2]



Psychological Medicine, Page 1 of 11. © Cambridge University Press 2016
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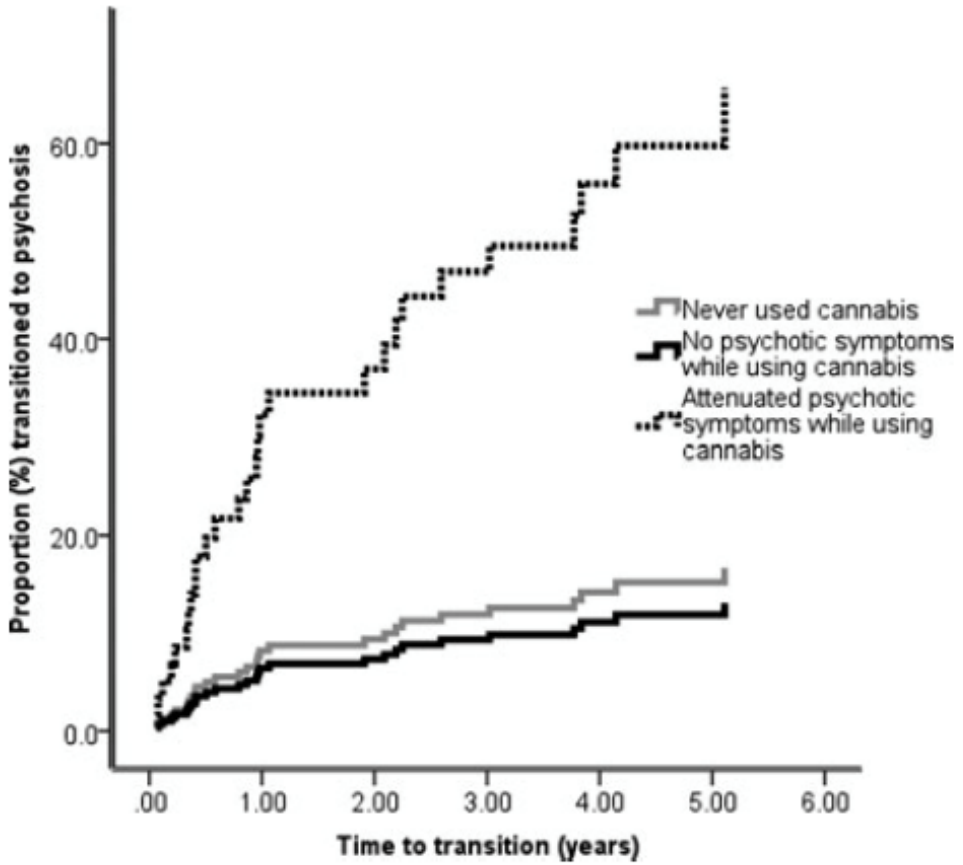


6.QUELLE CONDUITE À TENIR?

Comment distinguer un trouble induit d'un trouble primaire?

Critères DSM-5 Trouble psychotique induit par une substance

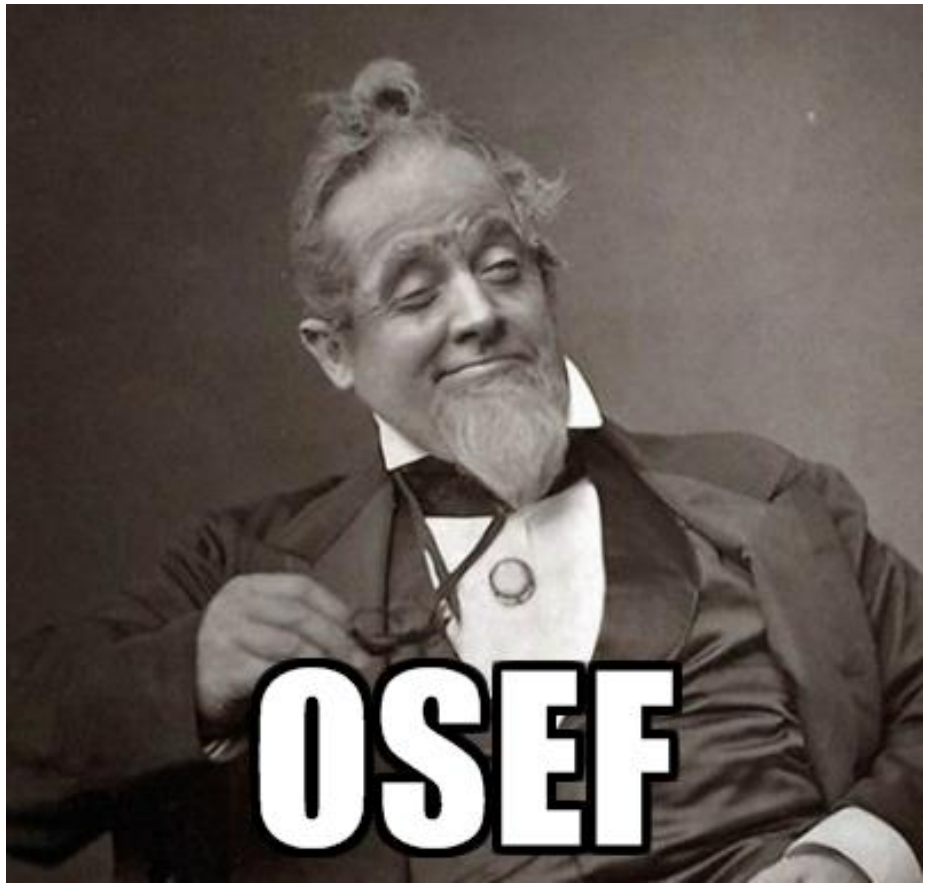
A. Présence d'au moins un des deux symptômes, parmi
- •Hallucinations
- •Idées délirantes

B. Preuve de 1 et 2 :
1. Critère A apparu au moment ou peu après la prise ou le sevrage d'une substance (médicament, drogue/intoxication...);
2. Cette substance (ou son sevrage) peut expliquer les symptômes du critère A

C. Un trouble psychiatrique qui n'est pas induit par une substance n'expliquerait pas mieux les symptômes psychotiques; c'est-à-dire qu'il n'y a pas:
- •Symptômes présents avant la prise de la substance ou l'intoxication
- •Symptômes présents longtemps après la prise de la substance ou l'intoxication
- •Présence d'indices orientant vers un trouble psychiatrique primaire

D. Présence de symptômes en dehors d'un syndrome confusionnel

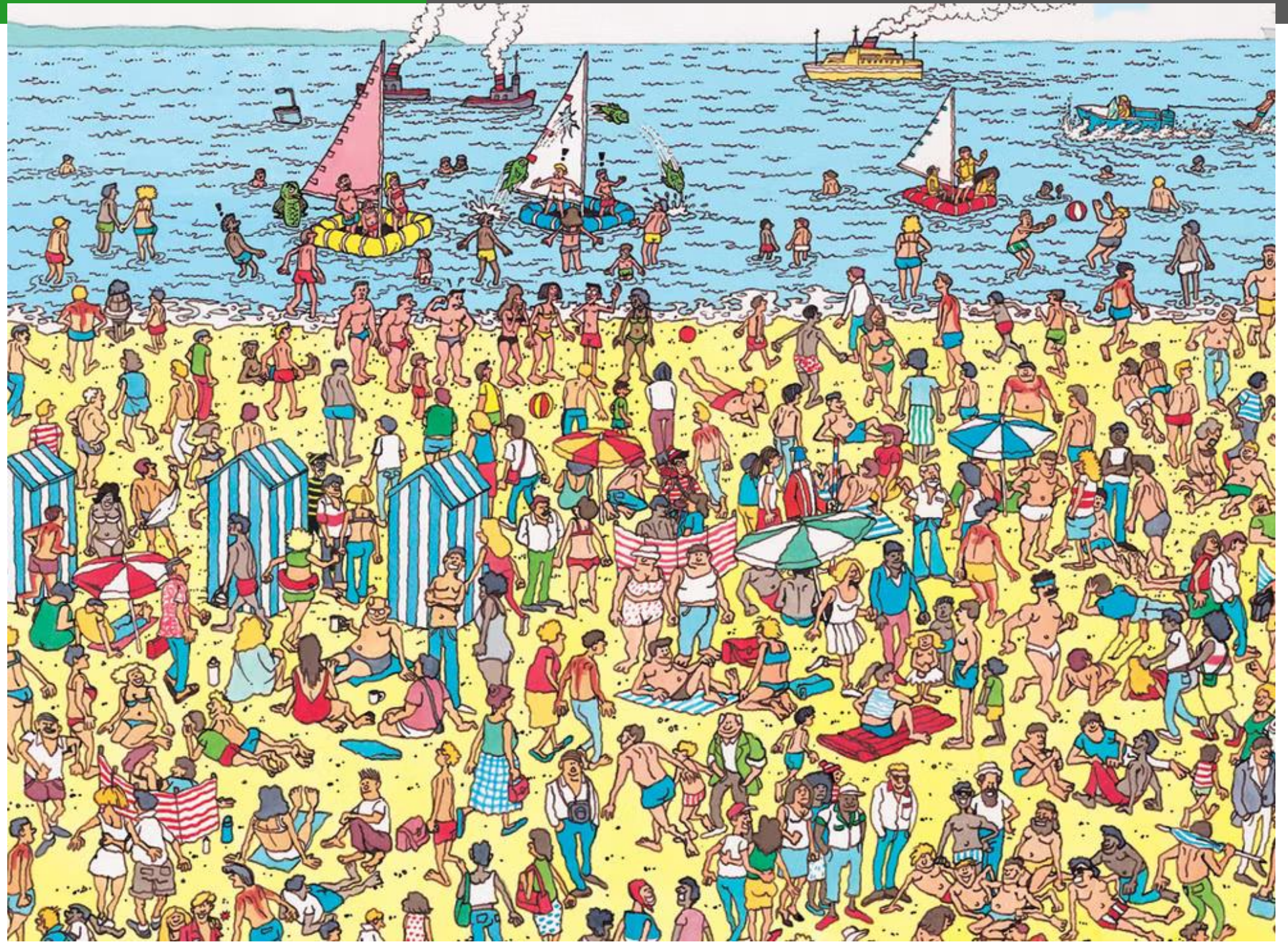
E. Altération du fonctionnement (professionnel, social), détresse clinique


OSEF

Pharmacopsychose

Pharmacopsychose

Oublie ce mot



Comparative Study > Am J Psychiatry. 2011 Jul;168(7):742-8.
doi: 10.1176/appi.ajp.2011.10071051. Epub 2011 Mar 31.

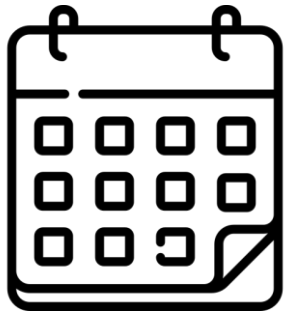
A prospective 2-year study of emergency department patients with early-phase primary psychosis or substance-induced psychosis

Robert E Drake [1], Carol L M Caton, Haiyi Xie, Eustace Hsu, Prakash Gorroochurn, Sharon Samet, Deborah S Hasin

217 patients with early-phase primary psychosis plus substance use
134 patients with early-phase substance-induced psychosis
psychiatric emergency departments at 5 hospitals in Upper Manhattan

	Assessment										p		
	Baseline		6 Months		12 Months		18 Months		24 Months				
Group and Treatment or Service	N	%	N	%	N	%	N	%	N	%	Group Difference at Baseline	Average Time Trend	Group-by-Time Interaction
Antipsychotic medication											<0.001	<0.001	0.139
Primary psychosis group	175	81	121	65	95	55	91	53	85	52			
Substance-induced psychosis group	67	50	30	31	14	16	13	16	10	13			
Outpatient mental health treatment											0.079	0.232	0.004
Primary psychosis group	20	9	46	25	39	23	45	26	49	30			
Substance-induced psychosis group	8	6	12	12	9	10	5	6	3	4			
Outpatient substance abuse treatment											0.016	0.057	0.531
Primary psychosis group	6	3	6	3	5	3	8	5	5	3			
Substance-induced psychosis group	7	5	11	11	12	14	15	18	8	10			
Outpatient dual disorders treatment											0.090	0.005	0.530
Primary psychosis group	18	8	24	13	24	14	19	11	26	16			
Substance-induced psychosis group	4	3	8	8	10	11	9	11	6	8			
Psychiatric hospitalization											0.010	0.331	0.945
Primary psychosis group	9	4	27	15	15	9	19	11	18	11			
Substance-induced psychosis group	1	1	3	3	1	1	0	0	2	3			

Suivi



Minimum
2 ans

Réactivité

Suivi intensif
dans la cité

Si possible TCC

Intervention précoce

Traitement

Recommandations pour premiers épisodes psychotiques (exemple : NICE 2014)

Minimum un an de traitement

Recommandations pour les UHR (exemple : EPA 2015)

Pas de traitement systématique mais seulement en fonction des symptômes

Usage du cannabis

- Médicaments :
  - Pas de traitement spécifique
- Attitude :
  - Pas dans la confrontation mais plutôt le conseil
  - Réduction des dommages
- Programme psychothérapeutique :
  - Les programmes spécifiquement adaptés n'ont pas fait la preuve de leur efficacité par rapport aux programmes classiques
  - Intérêt du double suivi
  - Entretien motivationnel

En résumé

Episode psychotique induit à suivre comme un premier épisode psychotique

C'est un double diagnostic : les deux troubles sont prioritaires

Maintien du traitement antipsychotique ?

Merci

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