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A National network of schizophrenia expert centres: An innovative tool to bridge the research-practice gap

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ABSTRACT

Schizophrenia is probably the most severe psychiatric disorder with much suffering for the patients and huge costs for the society. Efforts to provide optimal care by general practitioners and psychiatrists are undermined by the complexity of the disorder and difficulties in applying clinical practice guidelines and new research findings to the spectrum of cases seen in day-to-day practice. An innovative model of assessment aimed at improving global care of people with schizophrenia provided by the French national network of schizophrenia expert centres is being described. Each centre has established strong links to local health services and provides support to clinicians in delivering personalized care plans. A common set of assessment tools has been adopted by the ten centres spread over the whole French territory. A web application, e-schizo⁵ has been created to record data in a common computerized medical file. This network offers systematic, comprehensive, longitudinal, and multi-dimensional assessments of cases including a medical workup and an exhaustive neuropsychological evaluation. This strategy offers an effective way to transfer knowledge and share expertise. This network is a great opportunity to improve the global patient care and is conceived as being an infrastructure for research from observational cohort to translational research.

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1. Introduction

Schizophrenia is probably the most severe psychiatric disorder [40]. Patients with schizophrenia exhibit a wide range of symptoms from a variety of domains. The cardinal features are delusions, hallucinations, formal thought disorder, disorganized or abnormal motor behaviour and negative symptoms. In addition to these symptoms, the disorder is, to variable degrees, accompanied by a broad spectrum of cognitive impairments [27], which strongly reduces functional outcome [21,36] and to medical comorbid disorders, which require specific assessment and treatment [2]. The onset of the disorder occurs in adolescence or early adulthood, its course is usually chronic with different stages from early prodromes to chronic and severe handicap. In addition, up to 40% of people suffering from schizophrenia attempt suicide at least once, with estimates of about 5–15% for completed suicide [52]. Schizophrenia is the third most disabling illness of the central nervous system worldwide with a global cost of 23.7 millions disability-adjusted life years (DALYs) [14].

Despite treatment advances over the past decades, schizophrenia is still associated with a chronic relapsing course, marked functional impairment in a substantial proportion of patients, and remains often unrecognized or misdiagnosed leading to delayed treatments. Moreover, recent systematic reviews indicated that subjects suffering from schizophrenia have a reduced life expectancy of 15–20 years compared with the average general population, mostly because of increased medical comorbid diseases, as well as reduced access to medical treatment and to healthcare services [48,63].

Recent systematic reviews and practice guidelines have been proposed to optimize the pharmacological management of schizophrenia [24,25,46]. While, several studies have shown that psychosocial interventions such as cognitive behavioral therapy, cognitive remediation therapy, psycho-education programs, family intervention, social skills, training programs, and case management or assertive community treatment for people with schizophrenia, as an adjunct to medications can reduce psychotic symptoms and relapse risk and improve patients' long-term outcomes [32,61]. Particularly, neuropsychological assessment and rehabilitation have gained much interest in recent years, but very few patients have access to a comprehensive neuropsychological assessment. In addition, systematic assessment of comorbid medical disorder is required as well as management of diet and of physical activity in order to improve the overall prognosis.

Due to the heterogeneity of schizophrenia, as well as the evolution through successive stages [41], personalized medicine, based on individual data to determine treatment choices including pharmacological agents, psycho-social strategies, and lifestyle measures [51] need to be implemented. In addition, strategies to reduce duration of untreated psychosis (DUP) for people with first-episode psychosis are widely advocated as a plausible way in which patient outcomes and experience of services may be improved [46].

Unfortunately, due to inadequate training of psychiatrists, lack of systematic evaluation in clinical practice and/or limited availability and access to different models of effective treatments, the dissemination of the recommendations in usual practice within mental health services is slow and patchy [43]. This leads to elevated relapse rates (80% of patients relapse within 5 years) [35,60], long duration of untreated psychosis [39], high levels of adverse effects such as movement disorders, weight gain, cardiac and sedative problems, and increased risk of developing somatic diseases and early death [10].

In France, based on the above findings, the need to reduce DUP, to improve diagnosis and personalized treatment of schizophrenia led both the Ministry of Research and the Ministry of Health to

support the development of a national network of schizophrenia Expert Centres under the aegis of FondaMental foundation (<http://www.fondation-fondamental.org>), a scientific foundation created in 2007. This paper describes how the FondaMental foundation used this opportunity to introduce a new model to implement Expert Centre enabling systematic and standardized assessment of patients suffering from schizophrenia, and to enhance collaborations between Expert Centres and local clinicians (general practitioners and general psychiatrists) who provide the first point of contact with health services for most individuals with schizophrenia. The Expert Centres offer wide access for all schizophrenia subjects with few barriers for referral and no biases towards treatment-refractory cases. Their goals are to provide reliable systematic multi-dimensional assessments of subjects leading to personalized therapeutic recommendations, all shared with the patients, their relatives and the referring clinicians. These Expert Centres are also conceived as an infrastructure for research as they enable to follow-up large size cohorts, to build large and shared databases and biobanks, and to facilitate the implementation of research projects. The links between care and research also enable the efficient transfer of innovation into clinical practice and the implementation of the quality of care.

The following sections outline the rationale for the Expert Centres and include discussions of key elements of the assessment process.

2. Implementation and development of the Schizophrenia Expert Centres

2.1. Rationale

The national network of Expert Centres is envisioned as an innovative health and research care system composed of a network of specialized teams. Each team is composed of psychiatrists, psychologists, neuropsychologists and nurses, all specialised in care and research for schizophrenia that will support - but not replace - the existing health system. The Schizophrenia Expert Centres are required to first provide a comprehensive systematic assessment of patients with a probable diagnosis of schizophrenia, using a shared e-medical tool, to elaborate psychiatric and somatic diagnoses, to give advice on personalized treatment strategies, to monitor the evolution of the disorder through yearly follow-up consultations (Fig. 1) and last to propose to patients to participate to large collaborative research projects. This integrated approach aims to:

- accelerate access to specialists for all subjects suffering from schizophrenia, as well as subjects at risk;
- promote a personalized medicine approach by a systematic and thorough investigation of schizophrenia, to improve detection and prevention of somatic and psychiatric comorbidities, to offer personalized recommendations for pharmacological, psychosocial and lifestyle care, to prospectively evaluate the impact of treatments recommended for the individual and to identify risk factors for relapse;
- reduce delays between illness onset, accurate diagnosis and introduction of appropriate treatment;
- enhance concordance between evidence-based medicine guidelines and clinical practice;
- disseminate knowledge and skills on new diagnostic tools and therapeutic strategies.

Ten regional Expert Centres have been opened so far across France, and are widely distributed all over the country. Clinical team members from each centres have monthly meetings to

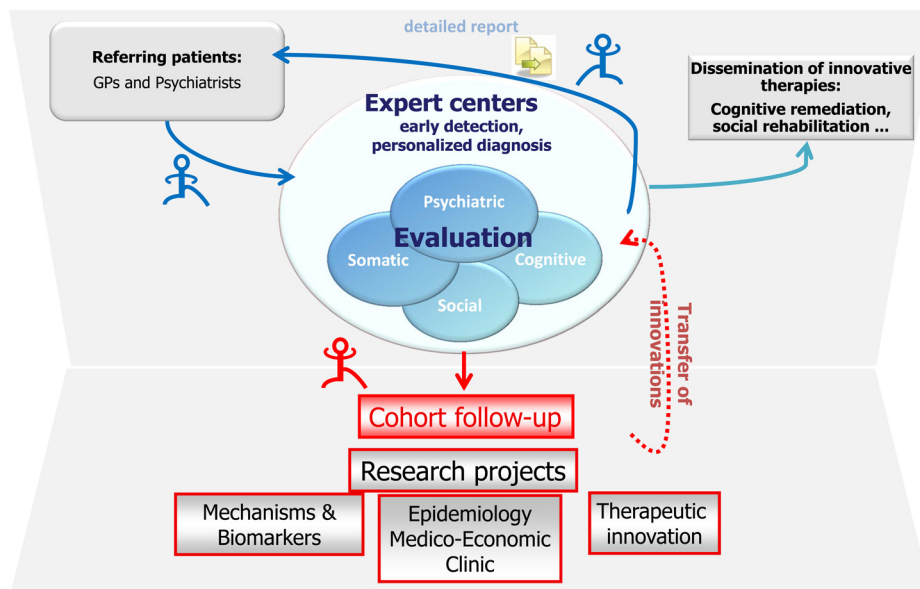


Fig. 1. Representation of the network.

ensure good interrater reliability, to provide training in new therapeutic interventions, to initiate new research studies and to discuss with advocacy groups a range of anti-stigma campaigns.

2.2. Site selection

Sites must be affiliated to an academic centre already actively involved in the treatment of patients suffering from schizophrenia, as well as in research on schizophrenia and having the will to integrate the network.

2.3. Working groups and training

A multidisciplinary team formed a working group to ensure the coordination of the network. This group have been in charge of the selection of the instruments for the clinical assessment, have followed up the quality controls, and are in charge of organising regular meetings of the network to measure interrater assessment, as well as clinical training, to disseminate innovative therapeutic strategies as well as therapeutic guidelines.

3. Centre activity

3.1. Referral criteria and eligibility for assessment

Patients assessed in Expert Centres are referred by their general practitioner or psychiatrist, who will receive a detailed evaluation report along with suggestions for therapeutic interventions.

The goal is to provide a 'personalized medicine' approach to general population of schizophrenia patients. Comprehensive assessment is offered to increase adherence, prevent relapse, and restore social functioning in order to improve the long-term prognosis.

Exclusion criteria for referral are minimal, and all patients who purportedly meet diagnostic criteria for any schizophrenia or schizo-affective disorder can benefit from this examination. However, the examination of those referred during a psychotic relapse is postponed until they have reached at least partial remission and/or the patient is able to participate to the assessment.

To date, 82% of subjects referred to the expert Centres received full clinical and neuropsychological assessments. The majority of

subjects who were not fully assessed after the screening phase did not meet criteria for a diagnosis of schizophrenia or schizo-affective disorder. At the end of the evaluation, all patients receive a detailed personalized care program.

3.2. Data collection: electronic healthcare record system and national database

A web-based application, e-schizo[®] was developed by the FondaMental foundation to collate assessment data for clinical monitoring and research purposes. Access to the system is carefully regulated and approval was obtained from the ethical committee and the committee in charge of the safety of computerized databases (CNIL). The XML format is used to transfer data from e-schizo[®] into an anonymous national database. This database has the same structure as that used by other Expert Centres networks (working on bipolar disorders, Asperger syndrome or resistant depression) also allowing clinical comparisons between these different disorders [28] as well as observational cohort follow-up. Quality controls of the data are regularly performed by the research assistants.

3.3. Assessment procedure and report

3.3.1. Pre-screening

Before participating in the full assessment, patients are interviewed by a psychiatrist at the expert centre during a screening phase (one hour) in order to:

- confirm the high probability of diagnosis of schizophrenia spectrum disorder meeting DSM-5 criteria [4] and assess the need to perform the full evaluation;
- inform the patient of the formal assessment procedure and schedule the appointments. Patients with schizophrenia who consent to participate in the assessment protocol (and who were not currently experiencing an acute psychotic episode) are then invited to complete the assessment procedure over a period of about 2 days.

3.3.2. Standardized assessment package

Each Expert Centre has been agreed and been trained to use the same package of assessment tools for the initial visit and for the

follow-up. Tables 1 and 2 provide a list of the self and observer-rated measures included in each of these visits. This battery contains assessment of psychiatric diagnoses, symptoms and dimensions, as well as systematic search for somatic disorders and a thorough neuropsychological assessment, and overall level of functioning. In addition, we measure the social and economic impact of these clinics. Socio-demographic and major clinical and neuropsychological variables of subjects who received a full assessment are summarized in Tables 3 and 4.

We attach great importance to neuropsychological assessment because cognition has been firmly established as a predictor of real-world community functioning [20] as well as the ability to perform everyday living skills in assessment settings [17,54].

This is a wide-ranging psycho-bio-social assessment that systematically explores all potential aspects of the presentation and factors that influence course and outcome. The measures are relevant for clinical purpose as well as research and provide useful evaluations for research studies.

3.3.3. Clinical report

At the end of each evaluation, the full description of the assessment is given to the patient, and if required to his relative. A personalized care program is proposed taking into account the information derived from the clinical assessments and medical work up. Importantly, management strategies can be revised during the follow-up done on a yearly basis, not only according to changes in individual patient needs but also in keeping with

Table 1
Systematic data recorded during the initial visit in the schizophrenia expert center. All patients with a confirmed or a suspected diagnosis of schizophrenia receive a complete clinical psychiatric evaluation based on the Structured Clinical Interview for DSM-IV—Patient Edition [19].

Sociodemographical data	Age, sex, marital status, educational level, number of children, living alone
Medico-economic data	Global assessment of functioning scale [66] Quality of life: S-QoL [5], EQ5D [56] Working status (labor force, unemployed) and number of unworked weeks in the previous year Monthly income and source(s) of income Number of consultations in the previous year for non-psychiatric issues Number of consultations in emergencies in the previous year Personal and Social Performance Scale (PSP) Dental care frequency
Current and lifetime symptomatology and severity	Positive And Negative Symptoms Scale (PANSS) scores (positive, negative and general symptomatology of schizophrenia) [31] Number and duration of hospitalisations in psychiatric healthcare departments (months) Age at first hospitalisation and duration of first hospitalisation (weeks) Age at first antipsychotic treatment – Age at psychosis onset = duration of untreated psychosis Number and duration of psychotic episodes CGI: Clinical Global Impression Aggressive behavior (Buss et Perry autoquestionnaire [11]) Insight Heteroquestionnaires: SUMD [3,57] Self-reported questionnaires: Birchwood et al. [9] and Beck Cognitive Insight Scale (BCIS) [18,55]
Current and lifetime mood symptomatology	Calgary Depression Score (CDSS heteroquestionnaire) [1] Young Mania Rating Scale (YMRS) Manic score [72] Current suicidal ideations and suicidal history
Previous and current psychiatric comorbidities and risk factors	Anxiety disorders (generalized anxiety disorder, post-traumatic stress disorder, social phobia, specific phobia) Obsessive-compulsive disorder (Yale-Brown autoquestionnaire) [45] Eating disorders (anorexia, bulimia, binge eating disorder) History of childhood attention deficit/hyperactivity disorder (Wender Utah Rating Scales [WURS-25] [12]) Childhood Trauma Questionnaire (CTQ) [53] Familial psychiatry history
Current and lifetime addictive comorbidities	Tobacco smoking behaviour: age at first cigarette, number of daily smoked cigarette, previous tobacco cessation attempts, nicotine dependence (Fagerström Test for Nicotine Dependence [FTND] [26]) Cannabis, alcohol, caffeine and other substances (including drugs) consumption Daily Internet consumption (hours) (Problematic Internet Use Questionnaire [PIUQ 12] [16,30]) Pathological gambling (South Oaks Gambling Screen [SOGS] [34])
Somatic comorbidities	Cardiovascular, immunologic, gastro-entologic, neurologic comorbidities, Familial somatic history
Physical examination	Tension, weight, height (body mass index), ECG, waist circumference, hear rate
Biological data	Compleat blood count C-reactive protein Hepatic enzymes (ASAT, ALAT, Gamma-GT, PAL) LDL and HDL cholesterol, triglycerides Drugs' blood dosages TSH ultrasensitive Ionogram (Na, K, urea, creatinine) Uricemia Glycemia Ferritinemia Prolactinemia
Pharmacological treatment	Previous and current pharmacological treatments Tolerance: Barnes [68], Simpson and Angus scale of extrapyramidal symptoms [33], Abnormal Involuntary Movements Scale (AIMS) [71] Observance and adherence: (BARS [heteroquestionnaire], self-reported questionnaire [MARS] [44]) Sexual side-effects

Table 2

Systematic neuropsychological assessment provided during the initial visit in the schizophrenia expert center.

Handedness	Edinburgh Handedness Inventory [50]
Cognitive complaint	Subjective Scale to Investigate Cognition in Schizophrenia (STICSS)[67]
IQ, premorbid intelligence and General Cognitive Functioning	Wechsler Adult Intelligence Scale (3rd, 4th edition) [69,70] Similarities Matrix reasoning Information Digit span Coding Arithmetic Picture completion Letter-number sequencing IQ and Index scores estimation following the Ward's seven subtest short form [42,62] f-NART [47]
Attention/Vigilance	The Continuous Performance Test-Identical Pairs: MCCB Version [49]
Executive function	TAP (Tests of Attentional Performance) [73] Alertness Divided attention Flexibility Go/NoGo 1 Go/NoGo 2 Six element test (SET) [65] Trail Making Test [58,59] Verbal Fluency Test [13]
Memory and learning	California Verbal Learning Test [15] Doors test [6] Working memory index (WAIS)
Social cognition	V-LIS [8]

updates to recommended treatment algorithms based on empirical research findings.

The individual care plan is multifaceted and may include the rationale for the selection of a particular antipsychotic drug based on a detailed risk-benefit assessment, plus options for using a combination of relapse prevention and health improvement strategies such as psycho-social treatment and lifestyle recommendations including improvement in sleep and circadian rhythm, diet and physical activity, tobacco cessation.

3.3.4. Follow-up assessments

Every year (for 3 to 5 years), the patient is re-evaluated to prospectively record any significant changes that have occurred including clinical progress but also periods of hospitalization and/or medical sick leave. Positive, negative and disorganized symptomatology, cognitive functioning, residual symptoms, mood, suicide attempts and ideation, professional and social functioning, resource utilization, treatments (including side effects, therapeutic adherence), sleep quality, physical activity and insight are monitored.

The majority of clinical measures in the initial assessment are repeated annually (including sections of the Structured Clinical Interview for DSM disorders (SCID) interview to examine changes in diagnosis and comorbidities and evaluation of inter-episodic functioning) and then every two years, which is suitable interval between measurements to avoid a learning effect, a subgroup of neuropsychological assessments is also repeated.

3.4. Research:scientific issues

The electronic healthcare record system for each Expert Centre is connected to a national database recording all the data on this large cohort of cases called "FondaMental advanced centers of expertise in Schizophrenia", FACE-SZ, which allows prospective

Table 3

Socio-demographic and major clinical variables of the 603 patients with schizophrenia who received a full-time evaluation at the Schizophrenia Expert Centers (at January 2015).

Socio-demographic characteristics, n (%)	
Sex (female)	159 (26.4)
Age (years), mean (SD)	32.89 (9.85)
Academic level (education level > 12 years)	12.13 (2.77)
Unemployed	392 (65)
Monthly income < 1000 \$	428 (603)
Unworked weeks in the previous year, mean (SD)	21 (17)
Mean cost per year per patient (\$)	26574
Illness characteristics, mean (SD)	
Age at onset (years)	21.75 (7.8)
Duration of untreated psychosis (years)	1.32 (3.34)
Illness duration (years)	9.9 (9.3)
PANSStotal score	69.75 (18.74)
PANSSpositive score	14.46 (5.42)
PANSSnegative score	20.83 (7.33)
PANSSgeneral score	34.44 (10.06)
Lifetime number of depressive episodes	2.6 (2.5)
Lifetime number of psychotic episodes	3.2 (3.0)
Lifetime number of suicide attempts	1.5 (1.8)
Insight (SUMD score)	4.7 (0.1)
Insight (Birchwood score)	8.14 (2.05)
Aggressiveness (Buss & Perry total score)	66.82 (18.39)
Mood, mean (SD)	
YMRS score	2.45 (3.98)
CDSSscore	3.6 (4.0)
Illness severity	
CGI score, mean (SD)	4.42 (1.1)
Number of lifetime hospitalizations, mean (SD)	3.0 (2.7)
Lifetime duration of hospitalization, mean (SD)	4.9 (5.4)
Functioning characteristics	
GAF score, mean (SD)	48.5 (12.8)
S-QoL score, mean (SD)	65.27 (28.1)
Current substance disorders and addictions, n (%)	
Daily tobacco smoking	324 (53.7)
Cannabis abuse or dependence	50 (8.3)
Alcohol abuse or dependence	35 (5.8)
Current treatment, n (%)	
Total number of psychotropic drugs, mean (SD)	1.83 (1.4)
Second generation antipsychotic	580 (96.2)
First generation antipsychotic	82 (13.6)
Antipsychotic polytherapy	183 (30.4)
SSRI treatment	101 (16.6)
Benzodiazepines	126 (20.9)
Anticholinergic drug	103 (17.1)
Antipsychotic dose (CPZ100eq), mean (SD)	5.7 (3.78)
Compliance and adherence to treatment, mean (SD)	
BARSscore	90.35 (17.92)
MARS score	6.7 (0.1)
Treatment side-effects, n (%)	
Parkinsonism (Simpson and Angus score 1)	41 (6.8)
Objective akathisia (Barnes score 2)	112 (18.6)
Metabolic variables, n (%)	
BMI, mean (SD)	26.6 (5.1)
Hypertension	67 (34.2)
High fasting glucose	37 (19.7)
Hypertriglyceridemia	56 (28.4)
High waist circumference ^a	111 (58.7)

PANSS: Positive and Negative Symptoms Scale for Schizophrenia; SGA: second generation antipsychotic; FGA: first generation antipsychotic; CGI: Clinical Global Impression Scale; S-QoL: Subjective Quality of Life; MARS: Medication Adherence Rating Scale; BARS: Brief Adherence Rating Scale; SUMD: Scale of Unawareness of Mental Disorder; YMRS: Young mania Rating Scale; CDSS: Calgary Depression rating Scale for Schizophrenia.

^a > 94 cm for male and > 80 cm for female.

and observational cohort follow-up and comparative-effectiveness studies. Quality control of the variables is ensured continuously by the research assistant of the FondaMental foundation. During the systematic work up, blood samples (serum, plasma, DNA, RNA) are

Table 4

Neuropsychological variables of the 603 patients with schizophrenia who received a full-time evaluation at the Schizophrenia Expert Centers (at January 2015).

Cognitive domains	Neuropsychological tests	Variable	Mean	SD		
Cognitive complaint	Subjective Scale to Investigate Cognition in Schizophrenia (SSTICS)	Total SSTICS score	36.53	13.79		
IQ premorbid IQ	Wechsler Adult Intelligence Scale (Ward's seven subtest short form) f-NART estimated premorbid IQ	Estimated IQ	85.98	15.03		
		NART-based Premorbid IQ	104.77	8.57		
Attention vigilance	The Continuous Performance Test-Identical Pairs	3 trials mean D prime	2.31	0.68		
Executive functions	TAP (Tests of Attentional Performance)	Alertness (index)	0.0028	0.68		
		Divided attention (% omissions)	3.68	4.06		
		Flexibility (global index)	7.98	12.00		
		Flexibility (speed-accuracy trade-off)	2.60	9.16		
		Go/NoGo 1	GONOGO1 (% hit)	19.46	1.69	
		Go/NoGo 2	GONOGO1 (% false alarms)	1.67	2.04	
			GONOGO1 (% omissions)	0.53	1.69	
		Six element test (SET)	GONOGO2 (% hit)	23.16	2.50	
			GONOGO2 (% false alarms)	1.34	3.01	
		Trail Making Test	GONOGO2 (% omissions)	0.83	2.50	
			SET (Total score)	803.68	244.01	
			SET (Total errors)	7.51	5.10	
		Verbal Fluency Test	TMT A time	43.34	21.59	
			TMT B time	105.41	61.94	
			TMT B perseverative errors	0.15	0.57	
		Memory learning	California Verbal Learning Test	Total correct (phonemic fluency) 2 mins	18.13	6.63
				Total correct (semantic fluency) 2 mins	24.46	7.60
		Memory learning	Doors test	List A trials 1 to 5 (total)	46.76	12.66
				Short-delay free recall	9.31	3.54
Short-delay cued recall	9.98			3.26		
Long-delay free recall	9.83			3.51		
Long-delay cued recall	10.03			3.46		
Discriminability (correct recogn. & false alarms)	92.44			9.49		
Total correct (A & B parts)	15.47			4.38		
Working memory index (WAIS)	86.65			14.73		
Digit span forwards	5.93			1.13		
Digit span backwards	4.30			1.16		

also stored in the biobank for future biological research. As the Expert Centres are conceived as being an infrastructure for care and for research, patients are offered the opportunity to participate to multi-site research programs on biology (genetic, immune-inflammation), brain-imaging, cognition as well as epidemiological and cost analysis programs and clinical trials.

4. Discussion

The schizophrenia Expert Centres network has been developed to better inform the patients on their ongoing disorder and to assist clinicians, by allowing a depth clinical work up and providing practical, evidence-based recommendations. There are many challenges faced by the Expert Centres.

The use of standardized clinical and neuropsychological examinations increase the diagnostic stability [23,64], which has important implications for management care and for the longitudinal course of the disease. Although there are some very successful examples of personalized medicine, especially in oncology, relatively few such examples exist in psychiatry [51]. The use of recommendations has been shown to improve clinical outcomes [7], while, adherence to guidelines for the management of schizophrenia remains poor in real world.

One of the missions of the Expert Centres is to improve early diagnosis by reducing the duration of untreated psychosis (DUP). Several studies have shown that the average length of time from the onset of psychotic symptoms to first treatment ranges between 364 and 721 days [39] and reported an association between long DUP and poor outcome for symptoms, quality of life and treatment response [29,38]. In addition, the Expert Centres emphasize the role of improved public

knowledge regarding mental health, particularly when dealing with severe disorders like schizophrenia. Indeed, it has been shown that information campaigns designed to reduce the DUP must be aimed at the general population as well as specific target groups [37].

In terms of clinical research, the French network is conceived as being a research infrastructure that will enable observational cohort follow-up. This large prospective cohort will be a tool for studying the trajectories of patients moving across stages of disorder. Identifying stages of the illness and the factors associated with the transition from one stage to the other, will improve the preventive approach of schizophrenia care [41]. Studies estimating utilization of services, healthcare, societal costs and quality of life of patients suffering from schizophrenia will also be performed. Furthermore, national and international academic collaborators or industry partners may have access to data collected, which will increase the number of scientific publications.

Also, the network has established strong links with neuroscience laboratories to allow investigation of underlying disease mechanisms and biomarkers.

At the European level, the national network of schizophrenia expert centres is involved in many international collaborations such as the EU-GEI project (European Network of National Schizophrenia Networks studying Gene-Environment Interactions) (<http://www.eu-gei.eu>) or OPTIMISE project (Optimization of Treatment and Management of Schizophrenia in Europe) (<http://www.optimisetrial.eu>).

In addition, the Expert Centres infrastructure follows the recommendations of the ROAMER project (<http://www.roamer-mh.org>), which has been created to build the roadmap for Mental Health Research in Europe [22]. ROAMER has

recommended to support existing infrastructure for research, and has emphasized the need to share biological, psychological, epidemiological, public health, social and economic data with other research teams in Europe and around the world.

Finally, another mission devoted to the Expert Centres is to raise awareness and inform public opinion and authorities through conferences, radio broadcasts, newspaper articles, distribution of written material, organization of information days for GPs, psychiatrists and paramedical personnel. This can contribute to reduce stigma and discrimination, and to facilitate treatment and adaptations for social and occupational insertion of patients.

5. Conclusions

This French schizophrenia network offers an efficient and effective way to transfer knowledge and share expertise as the referrer can appreciate the rationale underpinning suggested treatment protocols and more readily apply such principles and approaches to other cases. This network is also a great opportunity to avoid or minimize illness progression towards chronicity, to safeguard opportunities for significant health improvement as well as to enhance successful socio-professional reintegration (Tables 1 and 2).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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References

- [1] Addington D, Addington J, Maticka-Tyndale E, Joyce J. Reliability and validity of a depression rating scale for schizophrenics. *Schizophr Res* 1992;6(3):201–8.
- [2] Altamura AC, Serati M, Albano A, Paoli RA, Glick ID, Dell'Osso B. An epidemiologic and clinical overview of medical and psychopathological comorbidities in major psychoses. *Eur Arch Psychiatry Clin Neurosci* 2011;261:489–508.
- [3] Amador XFSD. The scale to assess unawareness of mental disorder. New York: Columbia University and New York Psychiatric Institute; 1990.
- [4] American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th ed., Arlington, VA: American Psychiatric Publishing; 2013.
- [5] Auquier P, Simeoni MC, Sapin C, Reine G, Aghababian V, Cramer J, et al. Development and validation of a patient-based health-related quality of life questionnaire in schizophrenia: the S-QoL. *Schizophr Res* 2003;63(1–2):137–49.
- [6] Baddeley A, Emslie H, Nimmo-Smith I. Doors and people. Oxford: Harcourt Assessment; 1994.
- [7] Bauer MS, Biswas K, Kilbourne AM. Enhancing multiyear guideline concordance for bipolar disorder through collaborative care. *Am J Psychiatry* 2009;166:1244–50.
- [8] Bazin N, Brunet-Gouet E, Bourdet C, Kayser N, Falissard B, Hardy-Bayle MC, et al. Quantitative assessment of attribution of intentions to others in schizophrenia using an ecological video-based task: a comparison with manic and depressed patients. *Psychiatry Res* 2009;167(1):28–35.
- [9] Birchwood M, Smith J, Drury V, Healy J, Macmillan F, Slade M. A self-report insight scale for psychosis: reliability, validity and sensitivity to change. *Acta Psychiatr Scand* 1994;89(1):62–7.
- [10] Brown S, Mitchell C. Predictors of death from natural causes in schizophrenia: 10-year follow-up of a community cohort. *Soc Psychiatry Psychiatr Epidemiol* 2012;47:843–7.
- [11] Buss AH, Perry MP. The aggression questionnaire. *J Pers Soc Psychol* 1992;63:452–9.
- [12] Caci HM, Bouchez J, Bayle FJ. An aid for diagnosing attention-deficit/hyperactivity disorder at adulthood: psychometric properties of the French versions of two Wender Utah Rating Scales (WURS-25 and WURS-K). *Compr Psychiatry* 2010;51(3):325–31.
- [13] Cardebat D, Doyon B, Puel M, Goulet P, Joannette Y. Formal and semantic lexical evocation in normal subjects. Performance and dynamics of production as a function of sex, age and educational level. *Acta Neurol Belg* 1990;90:207–17.
- [14] Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS, et al. Grand challenges in global mental health. *Nature* 2011;475:27–30.
- [15] Delis DC, Kramer JH, Kaplan E, Ober BA. California verbal learning test, 2nd ed., San Antonio, TX: The Psychological Corporation; 2000 [Adult Version].
- [16] Demetrovics Z, Szeredi B, Rozsa S. The three-factor model of Internet addiction: the development of the Problematic Internet Use Questionnaire. *Behav Res Methods* 2008;40(2):563–74.
- [17] Evans JD, Heaton RK, Paulsen JS, Palmer BW, Patterson T, Jeste DV. The relationship of neuropsychological abilities to specific domains of functional capacity in older schizophrenic patients. *Biol Psychiatry* 2003;53:422–30.
- [18] Favrod J, Zimmermann G, Raffard S, Pomini V, Khazaal Y. The Beck Cognitive Insight Scale in outpatients with psychotic disorders: further evidence from a French-speaking sample. *Can J Psychiatry* 2008;53(11):783–7.
- [19] First SR, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV axis I disorders, patient edition (SCID-P), version 2. New York: New York State Psychiatric Institute, Biometrics Research; 1995.
- [20] Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? *Am J Psychiatry* 2012;153:321–30.
- [21] Green MF, Helleman G, Horan WP, Lee J, Wynn JK. From perception to functional outcome in schizophrenia: modeling the role of ability and motivation. *Arch Gen Psychiatry* 2012;69:1216–24.
- [22] Haro JM, Ayuso-Mateos JL, Bitter I, Demotes-Mainard J, Leboyer M, Lewis SW, et al. ROAMER: roadmap for mental health research in Europe. *Int J Methods Psychiatr Res* 2014;23(Suppl. 1):1–14.
- [23] Harvey PD. Clinical applications of neuropsychological assessment. *Dialogues Clin Neurosci* 2012;14:91–9.
- [24] Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthøj B, Gattaz WF, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 1: update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. *World J Biol Psychiatry* 2012;13:318–78.
- [25] Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthøj B, Gattaz WF, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 2: update 2012 on the long-term treatment of schizophrenia and management of antipsychotic-induced side effects. *World J Biol Psychiatry* 2013;14:2–44.
- [26] Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for nicotine dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict* 1991;86(9):1119–27.
- [27] Heinrichs RW, Zakzanis KK. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychology* 1998;12:426–45.
- [28] Henry C, Etain B, Mathieu F, Raust A, Vibert JF, Scott J, et al. A French network of bipolar expert centres: a model to close the gap between evidence-based medicine and routine practice. *J Affect Disord* 2011;131:358–63.
- [29] Hill M, Crumlish N, Clarke M, Whitty P, Owens E, Renwick L, et al. Prospective relationship of duration of untreated psychosis to psychopathology and functional outcome over 12 years. *Schizophr Res* 2012;141:215–21.
- [30] Kern LAD. French adaptation of the Problematic Internet Use Questionnaire. *Evol Psychiatr* 2012. <http://dx.doi.org/10.1016/j.evopsy.2012.07.002>.
- [31] Lancon C, Reine G, Llorca PM, Auquier P. Validity and reliability of the French-language version of the Positive and Negative Syndrome Scale (PANSS). *Acta Psychiatr Scand* 1999;100(3):237–43.
- [32] Larsen TK, McClashan TH, Johannessen JO, Friis S, Guldborg C, Haahr U, et al. Shortened duration of untreated first episode of psychosis: changes in patient characteristics at treatment. *Am J Psychiatry* 2001;158:1917–9.
- [33] Lejoyeux M, Gorwood P, Stalla-Bourdillon A, Ades J. [Translation and application of the Simpson and Angus Scale of extrapyramidal symptoms]. *Encephale* 1993;19(1):17–21.
- [34] Lesieur HR, Blume SB. The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. *Am J Psychiatry* 1987;144(9):1184–8.
- [35] Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Salanti G, et al. Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. *Lancet* 2012;379:2063–71.
- [36] Lipkovich IA, Deberdt W, Csernansky JG, Sabbe B, Keefe RS, Kollack-Walker S. Relationships among neurocognition, symptoms and functioning in patients with schizophrenia: a path-analytic approach for associations at baseline and following 24 weeks of antipsychotic drug therapy. *BMC Psychiatry* 2009;14:9–44.
- [37] Lloyd-Evans B, Crosby M, Stockton S, Pilling S, Hobbs L, Hinton M, et al. Initiatives to shorten duration of untreated psychosis: systematic review. *Br J Psychiatry* 2011;198:256–63.
- [38] Malla AK, Norman RM, Manchanda R, Ahmed MR, Scholten D, Harricharan R, et al. One year outcome in first episode psychosis: influence of DUP and other predictors. *Schizophr Res* 2002;54:231–42.
- [39] Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Croudace T. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Arch Gen Psychiatry* 2005;62:975–83.
- [40] McGlashan TH. The profiles of clinical deterioration in schizophrenia. *J Psychiatr Res* 1998;32:133–41.
- [41] McGorry P, Keshavan M, Goldstone S, Amminger P, Allott K, Berk M, et al. Biomarkers and clinical staging in psychiatry. *World Psychiatry* 2014;13:211–23.

- [42] Meyers JE, Zelling MM, Kockler T, Wagner M, Miller RM. A validated seven-subtest short form for the WAIS-IV. *Applied Neuropsychol* 2013;20(4):249–56.
- [43] Michie S, Pilling S, Garety P, Whitty P, Eccles MP, et al. Difficulties implementing a mental health guideline: an exploratory investigation using psychological theory. *Implementation Sci* 2007;26:2–8.
- [44] Misdrahi D, Verdoux H, Llorca PM, Bayle FJ. [Therapeutic adherence and schizophrenia: the interest of the validation of the French translation of Medication Adherence Rating Scale (MARS)]. *Encephale* 2004;30(4):409–10.
- [45] Mollard E, Cottraux J, Bouvard M. [French version of the Yale-Brown Obsessive Compulsive Scale]. *Encephale* 1989;15(3):335–41.
- [46] National Institute for Health Clinical Excellence. Psychosis and schizophrenia in adults: treatment and management. National Clinical Practice Guideline 82. London: National Institute for Health Clinical Excellence; 2014.
- [47] Nelson HE, O'Connell A. Dementia: the estimation of premorbid intelligence levels using the New Adult Reading Test. *Cortex* 1978;14:234–44 [French adaptation: Mackinnon A, Mulligan R. Estimation de l'intelligence pré-morbide chez les francophones. *Encephale* 2005;31:31–43].
- [48] Nordentoft M, Wahlbeck K, Hällgren J, Westman J, Osby U, Alinaghizadeh H, et al. Excess mortality, causes of death and life expectancy in 270,770 patients with recent onset of mental disorders in Denmark, Finland and Sweden. *PLoS One* 2013;8(1):e55176.
- [49] Nuechterlein KH, Green MF. MCCB–MATRICS Consensus Cognitive Battery–Manual. Matrics Assessment Inc. (In MATRICS assessment battery with permission of Barbara Comblatt, Biobehavioral Technologies, Inc.); 2006.
- [50] Oldfield RC. The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia* 1971;9:97–113.
- [51] Ozomaro U, Wahlestedt C, Nemeroff CB. Personalized medicine in psychiatry: problems and promises. *BMC Med* 2013;11:132.
- [52] Palmer BA, Pankratz VS, Bostwick JM. The lifetime risk of suicide in schizophrenia: a reexamination. *Arch Gen Psychiatry* 2005;62:247–53.
- [53] Paquette D, Laporte L, Bigras M, Zoccolillo M. [Validation of the French version of the CTQ and prevalence of the history of maltreatment]. *Sante Ment Que* 2004;29(1):201–20.
- [54] Patterson TL, Goldman S, McKibbin CL, Hughes T, Jeste DV. UCSD Performance-Based Skills Assessment: development of a new measure of everyday functioning for severely mentally ill adults. *Schizophr Bull* 2001;27:235–45.
- [55] Pedrelli P, McQuaid JR, Granholm E, Patterson TL, McClure F, Beck AT, et al. Measuring cognitive insight in middle-aged and older patients with psychotic disorders. *Schizophr Res* 2004;71(2–3):297–305.
- [56] Prieto L, Sacristan JA, Hormaechea JA, Casado A, Badia X, Gomez JC. Psychometric validation of a generic health-related quality of life measure (EQ-5D) in a sample of schizophrenic patients. *Curr Med Res Opin* 2004;20(6):827–35.
- [57] Raffard S, Trouillet R, Capdevielle D, Gely-Nargeot MC, Bayard S, Laroi F, et al. [French adaptation and validation of the scale to assess unawareness of mental disorder]. *Can J Psychiatry* 2010;55(8):523–31.
- [58] Reitan RM. The relation of the Trail Making Test to organic brain damage. *J Consult Psychol* 1955;19:393–4.
- [59] Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Mot Skills* 1958;8:271–6.
- [60] Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry* 1999;56:241–7.
- [61] Rummel-Kluge C, Kissling W. Psychoeducation in schizophrenia: new developments and approaches in the field. *Curr Opin Psychiatry* 2008;21:168–72.
- [62] Ryan JJ, Ward LC. Validity, reliability, and standard errors of measurement for two seven-subtest short forms of the Wechsler Adult Intelligence Scale-III. *Psychol Assess* 1999;11(2):207–11.
- [63] Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Arch Gen Psychiatry* 2007;64:1123–31.
- [64] Salvatore P, Baldessarini RJ, Tohen M, Khalsa HM, Sanchez-Toledo JP, Zarate Jr CA, et al. McLean-Harvard International First-Episode Project: two-year stability of ICD-10 diagnoses in 500 first-episode psychotic disorder patients. *J Clin Psychiatry* 2011;72:183–93.
- [65] Shallice T, Burgess PW. Deficits in strategy application following frontal lobe damage in man. *Brain* 1991;114:727–41 [Adaptation used: Garnier C, Enot-Joyeux F, Jokic C, Le Thiec F, Desgranges B, Eustache F. Une évaluation des fonctions exécutives chez les traumatisés crâniens : l'adaptation du test des six éléments. *Rev Neuropsychol* 1998;8(3):385–414].
- [66] Startup M, Jackson MC, Bendix S. The concurrent validity of the Global Assessment of Functioning (GAF). *Br J Clin Psychol* 2002;41(Pt 4):417–22.
- [67] Stip E, Caron J, Renaud S, Pampoulova T, Lecomte Y. Exploring cognitive complaints in schizophrenia: the subjective scale to investigate cognition in schizophrenia. *Compr Psychiatry* 2003;44(4):331–40.
- [68] Swift RH, Harrigan EP, Cappelleri JC, Kramer D, Chandler LP. Validation of the behavioural activity rating scale (BARS): a novel measure of activity in agitated patients. *J Psychiatr Res* 2002;36(2):87–95.
- [69] Wechsler D. WAIS-III: administration and scoring manual. San Antonio, TX: Pearson; 1997.
- [70] Wechsler D. WAIS-IV administration and scoring manual. San Antonio, TX: Pearson; 2008.
- [71] Whitty PF, Owoeye O, Waddington JL. Neurological signs and involuntary movements in schizophrenia: intrinsic to and informative on systems pathology. *Schizophr Bull* 2009;35(2):415–24.
- [72] Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry* 1978;133:429–35.
- [73] Zimmermann P, Fimm B. Testatterie zur Aufmerksamkeitsprüfung (TAP), Version 2.3. Handbuch. Wurselen: Psytest; 2010.