




# Establishing a clinical high-risk program in Tunisia, North Africa: A pilot study in early detection and identification

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## Abstract

**Background:** Early identification and prevention research has provided huge advances in our understanding of early screening and identification of young people at clinical high-risk (CHR). Most of these procedures were developed in high-income countries, yet middle-income countries in North Africa such as Tunisia can benefit from these empirically-based assessment approaches.

**Methods:** Using established procedures, nine Tunisian psychiatric raters were trained on structured assessments: the CAARMS, BPRS, and SCID to high standards of interrater reliability. These raters developed a clinical high-risk program (CHiRP) in Tunisia and recruited 10 patients who were exhibiting possible signs of CHR. These patients were evaluated to determine if they met criteria for a CHR group, such as Attenuated Psychosis.

**Results:** Trained raters met the following interrater reliability criteria for the CAARMS and BPRS (ICC = .80 or greater) and the SCID (Kappa = .75 or greater). Of 10 pilot patients, six were classified as CHR and belonging to the Attenuated Psychosis Group. One of the six patients converted to psychosis 3 months after study entry for a conversion rate of 17% which is comparable with currently published rates globally.

**Discussion:** The first CHR program has been established in Tunisia, a middle-income country using methods developed in high income countries. Efforts aimed at assembling a group of prevention-oriented psychiatrists, obtaining administrative support, and training raters to high levels of interrater reliability were successful. The feasibility was demonstrated for screening, assessing, treating, and following-up of 10 CHR patients suggesting that conversion rates are comparable to those of Western and European countries.

## KEYWORDS

clinical assessment, clinical high risk, comprehensive assessment of at risk mental states, global mental health, middle-east North Africa, middle-income countries

## 1 | INTRODUCTION

The field of clinical high-risk (CHR) and prevention of mental illness has greatly advanced our understanding of how to most efficiently

conduct early symptom identification, the first step toward improving the functional outcomes of young people who might be at risk of developing schizophrenia or other psychotic illnesses. In addition, there is a large body of studies reporting on clinical and biological

predictors of transition (Addington et al., 2015; Bolt et al., 2019; Lee et al., 2014), the need to address non-psychotic symptoms (Woods et al., 2018), and the importance of improving functional outcomes (Beck et al., 2019). Recent studies have taught us that despite the large number of proposed risk factors, attenuated positive symptoms, global functioning, and negative symptoms show the greatest risk for conversion (Oliver et al., 2020).

The existence of several large-scale clinical and research programs has provided the theoretical and practical models needed for further advancements in the field. Guidance to the CHR field is being provided by programs such as the personal assessment and crisis evaluation (PACE); (Yung et al., 1995) clinic in Melbourne Australia, the European Prediction of Psychosis Study (EPOS) Klosterkötter et al. (2005), (Klosterkötter et al., 2005) the Pan-Canadian ACCESS Open Minds Network (Malla et al., 2019), and the North American Prodrome Longitudinal Study (NAPLS; (Addington et al., 2015). These CHR networks have well-established, scientifically tested, and published procedures describing specific strategies for early identification, intervention, and prevention of mental illness that work well in high income countries. All of these contributions are at the forefront in guiding future directions for middle-income countries seeking to establish new CHR programs.

Despite all that is known, the treatment gap for people with mental disorders has been reported to exceed 50% in all countries of the world and has approached astonishingly high rates of 90% in the least resourced countries (Patel et al., 2010). This is especially true for low/middle income countries, such as Tunisia, which are a relatively higher priority compared to high income countries with greater access to health care resources (Bruckner et al., 2011). A recent study on pathways to mental health care for people with severe mental illness has shown that the average consultation delay in Tunisia was 15 months (median of 6 months) for schizophrenia and bipolar disorder (Khiari et al., 2019). The main reason for delayed consultation among the patients was lack of awareness about the signs and symptoms of severe mental illness, as well as cultural, rather than scientific, beliefs about the origins of mental illness. In addition, one Tunisian study found an average duration of untreated psychosis of 75.38 weeks (with a median duration of 47.5 weeks) (Rebhi et al., 2019). All this research provides a remarkable foundation for the launching of new CHR programs located in middle or lower income countries, such as Tunisia.

Tunisia is located in North Africa, bordering the Mediterranean Sea, between Algeria and Libya. Tunisia has a population of ~11 Million, Tunisian Census (Recensement Général de la Population, 2017). The country belongs to the lower middle-income group according to the International Monetary Fund (IMF) and World Bank criteria (Harrigan & El-Said, 2010). The official language is Arabic. The first foreign language is French, but English is spoken among a growing number of Tunisians. Arabs form the ethnic majority and 98% of the population are Muslims.

Can we take what we know about CHR in high-income countries and apply those CHR models in Tunisia given the economic and

cultural differences? Why Tunisia? Tunisia was one of the leading countries behind the Arab Spring, whose peaceful transition from an autocratic government to a democratically elected President and Parliament is considered a model for other Arab countries. Tunisia has, since its independence in 1956, established and improved a public health care system giving access to health care to all citizens (El-Said & Harrigan, 2014). The main entry point into the health care system are the primary health care centres evenly distributed throughout the country. As of 2015, 2123 primary health care centres existed in Tunisia (Carte Sanitaire, 2016). However, mental health was not one of the priorities of health politics during the first decades after independence. In 1992, a National Program of Mental Health under the guidance of the WHO was implemented. The main objective was the integration of mental health services into the general health system and particularly into the primary care services (Douki et al., 2005). The National Mental Health Strategy, adopted in 2013, explicitly states as one of its objectives the establishment of programs for early intervention in psychiatry to improve prognosis, and reinforces the call to anchor mental health care in primary care, Ministry of Health (Revue des programmes nationaux, 2017). Moreover, a recent reform of the specialist training of doctors has established family medicine as requiring 3 years of specialist training which includes a compulsory 6 months (2 months per year) training in Psychiatry-by Decree (Décret n° 2011-4132, 2011). These efforts raised awareness of the importance of detection and treatment of mental health disorders among future family physicians many of whom aim to work within the primary care structure. All these factors will greatly facilitate collaboration with primary care physicians and attempts to establish a clinical high-risk program (CHiRP).

This project was designed to test the feasibility of developing a CHiRP program aimed at identifying and assessing youth to determine if they meet CHR criteria. The project aims were to: (a) train a group of Tunisian psychiatric professionals at Razi Hospital (Tunis) to screen and conduct clinical assessments at high levels of reliability using established scales, such as the CAARMS, the BPRS, and the SCID-5 and (2) develop a CHR program using as a guiding principle the well-established and empirically-based practices for CHR programs from around the world.

## 2 | METHODS

### 2.1 | Subjects

The sample consisted of 10 patients, 70% male, whose average age was 19.8 (5.0) and who had an average education of 11.1 (2.8) years in the Tunisian school system. All patients were single, never married and were living in Tunis, Tunisia. The 10 patients that were recruited and enrolled in the study were evaluated by the members of the CHiRP Clinical Assessment Team. This study was approved by the Internal Review Board at Razi Hospital and complied with the ethical standards detailed in the Declaration of Helsinki (Association, 2001).

## 2.2 | Procedures

### 2.2.1 | CHiRP: Razi Hospital—La Manouba, Tunis, Tunisia

The CHiRP was initiated in May 2018 through the impetus of Early Career Psychiatry Residents belonging to the Tunisian Association of Young Psychiatrists. The project proposal was supported by the Directors of the Departments of Adult Psychiatry and Child and Adolescent Psychiatry of Razi Hospital, La Manouba, and Mongi Slim Hospital, La Marsa. A core group comprised of a four-member Steering Committee provided research and clinical supervision for the assessment and treatment team. Several members of the Razi Hospital treatment staff, who have primary roles elsewhere within the hospital, rotate into the CHiRP service. The latter stages of the project were supported by a Fulbright Scholar grant awarded to Joseph Ventura. The CHiRP Assessment Team of nine raters (six psychiatric residents and three Lecturers in Psychiatry, two Junior and one Senior) requested referrals of possible CHR patients from outpatient clinicians at Razi Hospital as well as from primary care physicians and school nurses within the community.

### 2.2.2 | Assessment and intervention

Referrals consisted of help-seeking individuals who were screened and assessed by the CHiRP Team using the comprehensive assessment of at risk mental states (CAARMS) to determine their CHR status, the BPRS and the SCID-5. The classification of CHR positive or CHR negative was made through an assessment team consensus which served as an additional training and quality assurance procedure beyond the initial didactic training and the patients were followed. Treatments were provided, such as CBT, supportive psychotherapy, and medication management, for example, anxiolytics, anti-depressants. Additional interventions included Cognitive Remediation Training and psychoeducation for patients and families.

## 2.3 | Clinical assessment measures

CAARMS (Yung et al., 2005). The CAARMS is a semi-structured interview designed for use by raters who are sufficiently trained to evaluate a patient's clinical status. In the current study, we used the CAARMS – Brief; (Fusar-Poli, Cappucciati, Borgwardt, et al., 2016; Yung et al., 2010) which includes four primary positive symptom subscales: unusual thought content, non-bizarre ideas, perceptual abnormalities and disorganized speech. Scores for each CAARMS positive symptom subscale range from zero to six. Ratings of frequency and distress are needed for the classification into a clinical high risk group, such as the Vulnerability Group, Attenuated Psychosis Group, brief intermittent limited psychotic symptoms (BLIPS), and was used for follow-up evaluation at 3 and 6 months.

Brief Psychiatric Rating Scale (BPRS) (Ventura et al., 1993) This 24-item version contains clinically relevant symptoms, such as suicidality and elevated mood. The BPRS is used to examine initial severity levels in positive, negative, depression-anxiety, and manic symptoms and to evaluate change over time (Ventura et al., 2000). In this study, the BPRS assessment provided an additional way to evaluate whether CHR patients were in fact not fully psychotic and thus considered in the CHR range. BPRS ratings were conducted as part of the initial interview with the CAARMS and at the three and six-month follow-up points.

Structured Clinical Interview for DSM-5 Clinician Version (SCID-5-CV) (First et al., 2016). The SCID-5 is a semi-structured instrument used to gather the relevant symptom and psychiatric history data needed to make a DSM-5 diagnosis (American Psychiatric et al., 2013). The SCID-5 has been shown to be reliable and valid (Shankman et al., 2018), but needs to be administered by a clinician or trained mental health professional who is familiar with the DSM-5 diagnostic criteria. The SCID-5 CV is organized in modules that allow for the gathering of information needed to make a range of diagnoses.

## 2.4 | Establishing interrater reliability through rater training

A series of in-person training workshops were held in English by the lead author (J.V.) during two visits in Tunis during November 2017 and May 2018, followed up by virtual meetings. The aim of the rater training courses was to instruct the assessment team on the reliable use of the CAARMS, BPRS, and SCID-5 CV (Ventura et al., 1993; Ventura et al., 1998). Standardized videotaped interviews were rated by each of the nine trainees who then participated in training sessions during which their ratings were discussed and compared to “Gold Standard” ratings. All the diagnostic and symptom rating forms were collected for the calculation of interrater reliability.

## 2.5 | Didactic and “live” cases

During didactic training, the nine Tunisian psychiatric raters achieved interrater reliability standards for the CAARMS and the 24-item BPRS, minimum standard of an ICC = .80 or greater, and for the SCID-5 CV achieved minimum Kappa scores of .75 or greater for symptom presence and Kappa scores of .85 or greater on diagnostic classification (Table 1).

The 10 patients who were recruited and assessed by the CHiRP team who exhibited signs of clinical high risk were formally assessed using the CAARMS – Brief and classified in one of the following groups: Genetic Vulnerability, Attenuated Psychotic Group, or Brief Limited Intermittent Psychotic Symptoms or BLIPS (Table 2). The CAARMS includes the Social and Occupational Functioning Scale (SOFAS) which is rated from 0 to 100. The SOFAS was used to assess initial and current levels of functioning to determine whether the patient met criteria for a 30% drop in functioning within the past year.

**TABLE 1** Interrater reliability ICC and kappa scores for the didactic training phase of rater training for nine CHiRP raters on the CAARMS, BPRS, and SCID-5

	CAARMS (mean kappa) 30% drop/CHR classification		BPRS (median ICC) symptom assessment	SCID-5 (mean kappa) symptoms/diagnostic present/absent classification	
Average Interrater Reliability	0.87	0.91	0.85	0.73	0.94

Note: The didactic training for the Comprehensive Assessment of At Risk Mental States (CAARMS)-Brief included four videos, the Brief Psychiatric Rating Scale (BPRS) (ICC) and Structured Clinical Interview for DSM (SCID)-5 (Kappa) included six videos for each measure. The SCID-5 kappa scores were calculated for overall sensitivity and specificity and for agreement on diagnostic classification.

**TABLE 2** Ten pilot case patients who were enrolled in the clinical high-risk program–Razi Hospital (CHiRP) that were evaluated with the CAARMS at baseline, 3 months, and 6 month follow-up assessments

Baseline assessment							
CHR pilot patients	Sex	Age	Ed	CHR type	SOFAS score highest/current	SOFAS % drop	Transition 3 months/6 months
01	M	22	12	Attenuated	90/55	39%	No/No
02	M	20	14	Attenuated	91/55	40%	No/No
03	M	32	17	Attenuated	90/60	33%	Yes/
04	M	6	10	Attenuated	91/55	40%	No <sup>1</sup>
05	M	9	9	Attenuated	86/50	42%	No/No
06	F	17	12	CHR neg	–	–	–
07	M	17	10	Attenuated	92/62	32%	No <sup>2</sup>
08	F	6	10	CHR neg	–	–	–
09	F	16	10	CHR neg	–	–	–
10	F	23	7	CHR neg	–	–	–

Note: <sup>1</sup> follow-up status unknown, <sup>2</sup> Not yet reached the 6-month follow-up point, and CHR neg = CHR negative.

The classification of CHR cases was made via consensus which served as an additional training and quality assurance procedure.

The CAARMS reliability was calculated for “live” cases for the 30% Drop and the CHR classification. We used a kappa score to determine the degree of agreement on the classification of CHR Type which was a kappa of 0.83. Of the 10 CHR positive “live” cases, six were classified as belonging to the Attenuated Group with a high level of interrater reliability (Table 2).

### 2.5.1 | Community outreach

Two community outreach workshops were conducted by the members of CHiRP that were geared toward primary care physicians and school nurses. Both took place at Razi Hospital. The aim of these workshops was to raise awareness about CHR signs and symptoms through the presentation of didactic material and clinical cases so health professionals could identify potential CHR patients. During these meetings, participants were trained on how to screen for CHR cases using the Prodromal Questionnaire–Brief (PQ-B) (Loewy et al., 2011; Savill et al., 2018).

As part of the community outreach efforts, we created an adapted Arabic version of the PQ-B by following the standard

procedures of adaptation of questionnaires. These were: (a) translation and back-translation of the original questionnaire, (b) establishing a preliminary version by comparing the translated and back translated versions with the help of a group of psychiatrists and linguists, (c) debriefing through pilot testing with members of the target population to identify potential difficulties or unclear terms, and (d) finalization of the adapted version using the results of the debriefing sessions to develop the PQ-B: Arabic Version. To obtain a copy of the PQ-B Arabic Version, please e-mail Uta Ouali, M.D. (co-author) at <uta.ouali@gmail.com>.

## 3 | RESULTS

Of the 10 pilot patients in the study, six met CAARMS CHR positive symptom criteria and were classified in the Attenuated Psychosis Group (Table 2) while four were CHR negative. One of those six cases was classified as both Attenuated and in the Vulnerability Group. That patient had a first degree relative with a history of psychiatric disorder and met criteria for a 30% Drop in the SOFAS. BPRS ratings of the symptoms in the psychotic cluster (Unusual Thought Content, Hallucinations, and Conceptual Disorganization) were all in the subclinical range, that is, rating scale scores of 1–3 confirming the CHR and non-

psychotic levels of symptoms. All six of the CHR positive patients were re-assessed at the three-month and six-month follow-up points. At the three-month follow-up, one of the six CHR positive patients converted to schizophrenia for a transition rate of 17%. Patients who did not convert at 3 months did not convert at 6 months, and none of the CHR negative patients converted to CHR positive at 3 months.

Of the six CHR-positive patients, five were treated with medication, such as anti-depressants, anti-anxiety agents, and were provided supplements, such as omega-3 Fatty acids. The majority received CBT and one patient received Cognitive Rehabilitation Training. All six received supportive psychotherapy and medication management. The four patients who were CHR-negative received supportive psychotherapy and follow-up. One of the four patients was treated with CBT and anti-depressants.

The initial community outreach meeting was attended by 23 primary care physicians who were very interested in being able to identify clinical high risk patients. The second session was attended by 18 elementary to high school nurses. Both groups of health professionals showed a great deal of interest in the topic and were willing to make referrals. The school nurses in particular asked many questions and provided several examples of students they had seen and asked if those individuals might have been CHR cases. Thus far, the group of nurses have referred one adolescent for evaluation, but that person did not fall within the CHR group. Follow-up meetings are planned to coincide with further developments on the CHiRP at Razi Hospital, Tunis, Tunisia.

## 4 | DISCUSSION

This study demonstrated the feasibility of developing and implementing a CHiRP in Tunis, Tunisia, an Arabic Country in the Middle East North Africa (MENA) region. Well-established and scientifically based methods from young adult mental health projects and services around the world provided a model for CHiRP. We demonstrated the feasibility of using methods in a middle-income country that had been developed in high-income countries, for example, the United States, Australia and the United Kingdom to identify and evaluate patients potentially at CHR. On December 16, 2019, our CHiRP was officially recognized by the Early Intervention in Mental Health Association (also known as the International Early Psychosis Association; IEPA) as the first Clinical High Risk (CHR) program in Africa. In addition, CHiRP is one of the few CHR programs in the Arab World that combines early detection and identification, reliability-based assessments by trained raters, several empirically-based treatments, and follow-up assessments.

The project aim was to establish a CHR program at Razi Hospital which would be facilitated by the existing infrastructure consisting of clinical and research expertise, psychoeducation about mental illness, and the need for reduction of stigma that blocks access to services (Ouali et al., 2020). Establishing interrater reliability as the first step in forming the assessment team of diagnostic and symptom assessment raters was facilitated by their training as psychiatry residents and

senior lecturers. Although a standard Arabic validated version is available of the full CAARMS (Braham et al., 2014), the CHiRP raters preferred to use the English version of the CAARMS-Brief. The raters translated the CAARMS to the patients in a Tunisian Arabic dialect, which was more familiar to this young patient population. Further, because neither an Arabic version of the BPRS nor the SCID has been published, the English language versions were used by the raters who then spoke Tunisian Arabic. These assessment measures were used to screen and assess 10 patients, 6 of whom were CHR positive and then re-assessed at followed up. One of the six patients transitioned to having schizophrenia at the 3-month follow-up assessment point. This very preliminary 17% transition rate is generally consistent with what has been reported in the CHR literature for Western and European countries (Fusar-Poli et al., 2012; Fusar-Poli, Cappucciati, Rutigliano, et al., 2016; Salazar de Pablo et al., 2020).

The outreach and education campaign will continue to be used to inform primary care physicians and school nurses to reduce the stigma that delays getting help to promote the utilization of psychiatric services. The long-term goal is to reduce the incidence of schizophrenia and other major psychotic disorders to the lowest rate possible through early detection and early intervention.

There is agreement in the field that the CHR syndrome has become increasingly associated with significant patient distress, impairment and family psychological burden whether or not transition occurs to a major psychiatric disorder (Addington 2019). Even CHR symptoms that are at sub-psychotic levels are disruptive and interfere with social and role functioning (Olvet et al., 2015). Differences in symptom and functional outcomes highlight the need for early, targeted intervention that can be individualized for local cultural norms in CHR individuals. The emphasis on the importance of targeting functioning is in line with the significance that “fulfilling one's social role” plays in Arab society. In traditional Arab society, the role of males is to be the “head of household” and the provider for the family, whereas women care for the children and the household. Although these traditional roles in Tunisia have changed considerably in recent years, not fulfilling one's expected social role can still be a source of shame for the family and adds to the stigma attached to mental disorders (Ouali et al., 2020). This view supports the emphasis on treatment that leads to functional improvement rather than a sole emphasis on the reduction in the transition rate to psychosis (Cornblatt et al., 2012).

The project was successful in advancing the skills of Tunisian psychiatrists, mental health professionals, and researchers for studying and using treatment approaches many of which are empirically based interventions. The CHiRP program is comparable in several ways, in both structure and organization, to other CHR programs in North America, Australia and Europe. However, certain elements of CHiRP are still under development, such as supported employment and supported education (SEE) services and group therapy interventions.

The CHiRP program was designed to serve as a model program that could be re-created in other MENA counties, such as neighbouring Morocco or Algeria. Indeed, Algeria's and Morocco's health systems share many features with the Tunisian health system as all

are partly based on the French model and whose culture and language share many commonalities (Benmebarek, 2017; Landrault & Amine, 2020).

In conclusion, despite economic, training and cultural differences between Western and North African societies and mental health systems, there are many shared humanistic and societal similarities (Zahid & Ohaeri, 2010) which could and should be the basis for improving mental health in the Arab world.

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## CONFLICT OF INTEREST

Joseph Ventura obtained funding from the US Fulbright Scholar Foundation (PS00286537) to support travel, accommodations, and the basic components of the research program. Dr. Ventura trained and supervised the assessment team who conducted eligibility assessments of CHR patients. Drs. Ventura, Ouali, and Jourini trained and supervised research staff on the data collection process and the daily research data collection operations. Drs. Ventura, Ouali, Jouini, Aissa, Larnaout, Nefzi, Ghazzai, Jelili, Fekih-Romdhane designed elements of the study, screened and evaluated patients, complied and coded raw data such as patient assessments, created and managed data bases, and preformed literature searches. Drs. Ouali and Prof Nacef provided administrative support and supervised the clinical conduct of the Razi Hospital team of clinical psychiatrists (co-authors) who enrolled and treated the patient-subjects. All of the authors participated in interrater reliability data process. All authors prepared, read and commented on the initial drafts, and approved the final manuscript.

## DATA AVAILABILITY STATEMENT

The authors do not have permission to share this data.

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