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Six months functional response to early psychosis intervention program best predicts outcome after three years

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ABSTRACT

Background: Not all patients respond well to early interventions for their psychosis. The present study's goal was to evaluate whether patients' responses in the first six months of treatment in a specialised three-year programme could predict final outcomes.
Methods: 206 early psychosis patients were assessed at baseline, using a large set of sociodemographic and clinical variables, and then monitored for 36 months. Among those variables, changes in their Global Assessment of Functioning (GAF) scores during the first six months were used to predict outcomes after three years.
Results: Changes in GAF scores during the first six months were the only variables that predicted every symptom of functional outcome. GAF scores were also always the first or second most important predictor for every outcome. This finding held for both high- and low-functioning patients at baseline.
Conclusions: Predicting poor long-term outcomes after only six months should help clinicians to improve treatments.

1. Introduction

Early intervention is now widely seen as a standard approach to treating psychotic disorders. Early identification, reducing the duration of untreated psychosis (DUP) and reinforcing treatment adherence are some of its main goals (Conus et al., 2010; Golay et al., 2016; Malla et al., 2002; Sheitman et al., 1997). Case management interventions is an essential ingredient of most programs (Marshall et al., 2004). Case-management has progressively developed during the last decades and the responsibility of clinicians assuming such positions in early intervention programs is to facilitate patient's engagement, conduct clinical assessment, plan treatment in collaboration with psychiatrists, facilitate linkage with available treatment resources, collaborate with families, and provide psychoeducation or crisis intervention (Alameda et al., 2016; Lamb, 1980; Marion-Veyron et al., 2013). Despite the recognised effectiveness of early intervention, not all patients reach favourable symptomatic or functional outcomes at the end of their programme and service disengagement in the context of early psychosis remains a high stake issue (Edwards et al., 2002; Golay et al., 2020; Robinson et al., 2004). Indeed, about a fifth of patients with recent-onset schizophrenia have persistent psychotic symptoms and experience disability, suffering and family burden (Edwards et al., 2002). Stratification tools are needed to personalize prevention strategies at an early stage. The goal is to improve patient response to treatment and counteracting the functional deficits that critically affect their long-term quality of life (Fournier et al., 2020).

Recent studies in large representative cohorts of early psychosis (EP) patients showed that functional impairment is prevalent in patients with EP and that the longitudinal course of functioning in the early stage of psychotic illness remains under-studied (Chang et al., 2018; Hall et al., 2019; Hodgekins et al., 2015). These studies also revealed the heterogeneous courses of socio-occupational functioning during EP, with distinct functional trajectories. In particular, Chang et al. (2018) reported that approximately half of the patients displayed a persistently

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poor trajectory over three years, suggesting that socio-occupational impairment had been an unmet therapeutic need in the early phase of their illness. This is in line with the critical period hypothesis, suggesting that symptoms during the first two or three years are important for long-term prognosis (Birchwood et al., 1998). However, another recent study suggested that long-term prognosis can be predicted much sooner—as early as one year after the first psychotic episode (Simonsen et al., 2017). This suggests that factors that could predict poor outcomes could be identified early during treatment, allowing the adjustment of therapeutic strategies. More importantly, there is a need to test if considering the dynamic of change of certain variables rather than their cross sectional value is a better approach for the identification of patients at risk of poor evolution. In a neighbouring field, it has been shown, for instance, that increase in patient weight during the first month of treatment with second-generation antipsychotics predicted longer-term weight gain (Vandenberghe et al., 2018); following the same rationale, the present study's goal was to investigate whether changes in global functioning within the first six months of a specialised EP intervention programme could predict various outcomes after three years. The 6-months timeframe was chosen to ensure case-managers had enough time to meet patients several times after a first hospitalisation. Specifically, this 6-months period from the first admission of our programme was chosen as the best time point on clinical grounds to observe the initial changes in our population: in this interval, case-managers are able to establish and stabilise the basis of the alliance, have contacted the relevant partners in the patient's network, have planned the initial therapeutic goals and have clarified the intensity of the intervention or the need for an intensive mobile intervention. In order to take advantage of the longitudinal cohort follow-up, we also used mid-programme outcomes (after 18 months).

2. Material and methods

2.1. Participants

The Treatment and early Intervention in Psychosis Programme (TIPP) is a specialised EP programme run by Lausanne University Hospital's Department of Psychiatry, in Switzerland (Baumann et al., 2013). Inclusion criteria are being aged from 18 to 35, living in the hospital's catchment area (population about 350,000) and meeting the criteria for psychosis as defined by the 'psychosis threshold' subscale in the Comprehensive Assessment of At-Risk Mental States (CAARMS) instrument (Yung et al., 2005). This psychotic disorder threshold is defined as frank psychotic symptoms such as delusions, hallucinations and thought disorder persisting for longer than one week and with a frequency of at least 3-6 times a week for longer than one hour each time or daily for less than 1 h each time. This is a standard and widely used criteria for first episode psychosis threshold (Nelson et al., 2014).

Patients with psychosis related to intoxication or an organic brain disease, an IQ < 70, or who have been taking antipsychotic medication for more than six months are referred to other programmes. Patients can be referred in several ways: general practitioners, families, private psychiatrists, psychiatric institutions, the Psychiatry Liaison Service and other Lausanne University Hospital departments (e.g. emergency, psychiatry) can all contact the TIPP team, who will conduct an initial assessment by email or telephone. A multidisciplinary team (including psychiatrists and case management nurses) ensures the accuracy of inclusion criteria before admitting patients. The TIPP rationale is based on the principles of both case management interventions and assertive community treatment undertaken in outpatient settings. Patients are seen at least 100 times over the three-year programme, primarily by their case manager but also by a resident physician or an intern in psychiatry. A consultant psychiatrist supervises each case.

All patients treated within the TIPP are fully assessed at baseline, after two months, 6 months and then prospectively every six months in order to monitor outcomes and adjust treatments. A specially designed questionnaire (the TIPP Initial Assessment Tool: TIAT; available online; Service of General Psychiatry D.o.P., 2021) is completed for all patients enrolled in the programme by case managers. It allows assessment of demographic characteristics, past medical history, exposure to life events as well as symptoms and functioning. It is completed on the basis of information gathered from patients and their family over the first weeks of treatment and can be updated during follow up if new information emerges. Follow-up assessments exploring various aspects of treatment and co-morbidities as well as evolution of psychopathology and functional level are conducted by a psychologist and by case managers at baseline, after 2, 6, 12, 18, 24, 30 and 36 months in treatment. Symptoms assessment are conducted by a psychologist who is independent of patients' treatment and had received standardized training. For three years, case managers are available to each patient up to twice a week. An Intensive Case Management team can provide additional support and treatment at any time during the treatment period. TIPP case managers remain involved, however, to ensure continuity of care. This study was carried out in accordance with the Declaration of Helsinki and was approved by the Human Research Ethics Committee of the Canton of Vaud (CER-VD; protocol #2020-00272). Access to clinical data was granted for research purposes allowing the data generated during patient follow-up were used in the study. Consequently, all patients who received treatment within this programme could be included in this study.

2.2. Clinical assessments

Case managers and an experienced psychologist performed detailed evaluations of patients' using interviews and the TIAT questionnaire. The DUP was defined as the time between the onset of the psychotic symptoms defined by the CAARMS and admission to the TIPP. Patients' socioeconomic statuses were subdivided into low, intermediate and high (Chandola and Jenkinson, 2000). Premorbid functional level was evaluated using the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982). The Global Assessment of Functioning (GAF) instrument was used to assess functional levels at baseline, and changes between the six-month GAF assessments (ΔGAF 0–6 months) and baseline were also computed. A positive difference score indicated improvement in global functioning during the first six months of the follow-up. We focused on change in global functioning because this measure provides a broader picture of functioning, including the impact of symptomatology and social and professional functioning, and because it is easy to administer by clinicians. Its 1-100 scoring allows for a finer discrimination than other global scores with limited range. Insight into the illness was categorised as complete, partial or absent (Conus et al., 2007). Severity of illness at baseline was assessed using the Clinical Global Impression scale (CGI; Guy, 1976). Diagnosis results from an expert consensus discussed at 18 and 36 months, based on the DSM-IV criteria using the information from medical reports from treating psychiatrists, as well as from the TIPP-assigned psychiatrist and case manager. In this study, we used the latest consensus diagnostic available. Past diagnosis of substance abuse/dependence was rated according to DSM-IV.

2.3. Outcomes

Functional characteristics after 18 months or at the end of the programme were assessed using the Modified Vocational Status Index and the Modified Location Code Index while living independently (MVSI & MLCI; Tohen et al., 2000). Patients were considered as *living independently* based on their MLCI score (head of household or living alone, living with a partner or peers, or living with their family with minimal supervision). Patients were considered as *working* at based on the MVSI (in paid or unpaid, full- or part-time employment, being an active student in school or university, head of household with an employed partner (homemaker), or a full or part-time volunteer). Functional recovery after three years or 18 months was defined as a GAF score > 60.

Symptomatic remission at the end of the programme or after 18 months was defined by the last Positive And Negative Syndrome Scale assessment score in the last year of the programme, following Andreasen's Criteria (mild or lower (≤3) score on the following items: delusion, unusual thought content, hallucinatory behaviour, conceptual disorganization, mannerisms, blunted affect, social withdrawal & lack of spontaneity; Andreasen et al., 2005). The number of hospitalisations during the programme was calculated from patients' medical records. Insight into the illness was categorised as complete, partial or absent (Conus et al., 2007). Therefore, our study included seven dichotomous outcomes: work activity (MVSI), living independently (MLCI), working & living independently combined, functional recovery (GAF > 60), symptomatic remission, repeated hospitalisation during programme and full insight recovery.

2.4. Statistical analysis

A series of logistic regression models were estimated to predict the various outcomes. ΔGAF 0–6 months and other important baseline variables (age, sex, socioeconomic status, DUP, Premorbid Adjustment Scale, Clinical Global Impression at baseline, and diagnosis) were introduced as predictors. To compare the relative importance of different independent variables, differences in Nagelkerke's R squared were computed with each variable removed. Finally, because ΔGAF 0–6 months was negatively correlated to baseline functioning, we also checked whether scores could predict outcomes for higher-functioning and lower-functioning patients at baseline; participants were split in to below- and above median subgroups based on their baseline GAF score. Models for all outcomes were re-estimated using baseline GAF and ΔGAF 0–6 months as predictors.

3. Results

A total of 206 patients was included. Sample characteristics are shown in Table 1. Patients were predominantly male (61.2%) with an average age of 24.4 years. Among the patients, 57.8% had a diagnostic of Schizophrenia, 10.7% of Brief schizophreniform disorder, 11.7% of Schizoaffective disorder, 8.3% of Major depression with psychotic features, 8.3% of Bipolar disorder and 9.2% another diagnostic. A total of 18 patients (8.7%) left the programme before the end of the three year period. Among them, 6 (33.3%) fulfilled the definition of "disengagement" (patients actively refusing any contact with the treatment facility or that were not traceable despite extensive efforts).

Results of the logistic regression models for the three-year outcomes are presented in Table 2. ΔGAF 0–6 months was the only variable that predicted all the other outcome variables: having a work activity (MVSI), living independently (MLCI), working & living independently combined, functional recovery (GAF > 60), symptomatic remission, repeated hospitalisation during programme, and full insight recovery. It was also always the first or second most important predictor of every outcome according to ΔR^2. Baseline GAF also predicted every three-year outcome except symptomatic remission when other variables were taken into account. DUP and socioeconomic status predicted several but not every aspect of recovery (DUP predicted working & living independently combined and symptomatic remission; socioeconomic status predicted work activity (MVSI) and working & living independently combined). Diagnosis only predicted working & living independently combined.

Results for mid-programme outcomes after 18 months were very similar (Table 3). ΔGAF 0–6 months was the only variable that predicted all 18-months outcome variables. It was also always the first or second most important predictor of every outcome according to ΔR^2.

ΔGAF 0–6 months was negatively correlated with baseline GAF ($r = -0.608$, $p < .001$). Baseline GAF was rarely associated with outcomes within either the above- or below-median patient subgroups. However, ΔGAF 0–6 months could predict most outcomes in the different subgroups (Table 4). In the below-median subgroup, 23.8% of patients with a ΔGAF 0–6 months of 20 or below reached Functional recovery (GAF > 60) after 3 years, whereas this rose to 46.5% among those with ΔGAF 0–6 months over 20 ($\chi2(1) = 5.225$, $p = .022$). The pattern was the same at mid-programme (22.6% vs 44.1%; $\chi2(1) = 4.831$, $p = .028$). In the above-median subgroup, 54.3% of patients with a ΔGAF 0–6 months of 20 or below reached Functional recovery (GAF > 60) after 3 years, whereas this reached 100.0% of those with ΔGAF 0–6 months over 20 (Fisher's exact test, $p = .020$). At mid-programme, this pattern was less evident however (51.7% vs 85.7%, Fisher's exact test, $p = .120$). Finally, it should be noted that lifetime substance abuse (alcohol - $\chi2(1) = 7.906$, $p = .005$, cannabis - $\chi2(1) = 5.012$, $p = .025$ & other substances - $\chi2(1) = 5.663$, $p = .017$) and lifetime substance addiction (alcohol - $\chi2(1) = 7.592$, $p = .006$ & cannabis - $\chi2(1) = 11.648$, $p = .001$) were significantly more frequent in the below-median subgroup. However, lifetime substance abuse and lifetime substance addition did not differ between patients with below-median ΔGAF 0–6 months (≤10.00) and above-median ΔGAF 0–6 months (>10.00) with the exception of alcohol abuse who was slightly more frequent when ΔGAF 0–6 months was above-median ($\chi2(1) = 4.111$, $p = .043$).

Table 1
Sample characteristics ($N = 206$).

Characteristics	
Age, Mean (SD), year	24.55 (4.79)
Sex, % (N), male	61.2 (126)
Socioeconomic status, % (N)	
Low	17.0 (35)
Intermediate	45.1 (93)
High	37.9 (78)
DUP, Median (IQR), days	103.00 (504.25)
Age of onset, Mean (SD), year	23.12 (5.20)
Premorbid Adjustment (PAS)	0.31 (0.17)
CGI baseline, Mean (SD)	4.60 (1.36)
GAF baseline, Mean (SD)	42.89 (16.96)
GAF 2 months, Mean (SD)	49.39 (15.18)
GAF 6 months, Mean (SD)	54.10 (14.99)
GAF 12 months, Mean (SD)	56.82 (15.51)
GAF 18 months, Mean (SD)	58.93 (14.63)
GAF 24 months, Mean (SD)	58.63 (15.67)
GAF 30 months, Mean (SD)	59.76 (15.90)
GAF 36 months, Mean (SD)	59.71 (16.23)
ΔGAF 0–6 months, Mean (SD)	11.20 (16.90)
Diagnosis, % (N)	
Schizophrenia	57.8 (119)
Brief schizophreniform disorder	10.7 (22)
Schizoaffective disorder	11.7 (24)
Major depression	2.4 (5)
Bipolar disorder	8.3 (17)
Others	9.2 (19)
Lifetime substance abuse (DSM), % (N)	
Alcohol	22.6 (45)
Cannabis	33.8 (68)
Other substances	13.1 (27)
Lifetime substance addiction (DSM), % (N)	
Alcohol	8.0 (16)
Cannabis	27.5 (55)
Other substances	6.8 (14)
Insight at presentation, % (N)	
Absent	31.0 (62)
Partial	42.5 (85)
Complete	26.5 (53)

4. Discussion

The present study investigated whether early changes in the global functioning of patients treated using a specialised EP intervention programme could predict a series of outcomes at the end of that three-year programme. Overall, our results suggest that after only six months of treatment, initial changes in patients' GAF scores predict a variety of long-term symptomatic and functional outcomes. This adds support to

Table 2
Prediction of three-year outcomes.

Outcomes after three years	Work activity (MVSI)			Living independently (MLCI)			Working & living independently combined			Functional recovery (GAF > 60)			Symptomatic remission			Repeated hospitalisation during programme			Full insight recovery		
	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed
Predictors																					
Age	0.980	0.634	0.001	**1.107**	**0.011**	**0.043**	0.996	0.934	0.000	1.009	0.812	0.000	1.055	0.347	0.008	0.972	0.433	0.004	1.018	0.634	0.001
Sex	0.806	0.619	0.001	0.838	0.627	0.001	0.804	0.640	0.002	0.906	0.790	0.000	1.204	0.729	0.001	1.011	0.976	0.000	1.137	0.723	0.001
Socioeconomic status	**3.070**	**0.001**	**0.078**	0.882	0.611	0.002	**2.815**	**0.003**	**0.060**	0.919	0.722	0.000	0.921	0.827	0.000	0.981	0.936	0.000	1.550	0.080	0.001
DUP[a]	0.642	0.095	0.015	0.698	0.085	0.019	**0.503**	**0.018**	**0.033**	0.829	0.395	0.003	**0.526**	**0.041**	**0.043**	0.861	0.447	0.003	0.753	0.189	0.020
PAS Premorbid Adjustment	0.492	0.601	0.001	0.471	0.493	0.003	0.370	0.505	0.003	**0.041**	**0.007**	**0.040**	1.207	0.907	0.000	0.402	0.371	0.005	1.304	0.815	0.011
CGI baseline	**1.705**	**0.022**	**0.030**	1.294	0.226	0.009	1.456	0.129	0.014	0.762	0.203	0.008	0.881	0.711	0.001	1.050	0.813	0.001	1.534	0.053	0.025
GAF Baseline	**1.139**	**<0.001**	**0.191**	**1.042**	**0.039**	**0.028**	**1.144**	**<0.001**	**0.170**	**1.066**	**0.002**	**0.057**	1.051	0.122	0.022	**0.938**	**0.001**	**0.064**	**1.078**	**0.001**	**0.047**
ΔGAF 0–6 months	**1.074**	**<0.001**	**0.113**	**1.038**	**0.012**	**0.043**	**1.107**	**<0.001**	**0.194**	**1.055**	**<0.001**	**0.078**	**1.052**	**0.025**	**0.053**	**0.936**	**<0.001**	**0.142**	**1.038**	**0.009**	**0.093**
Diagnostic	–	0.055	0.068	–	0.299	0.044	–	**0.046**	**0.079**	–	0.131	0.052	–	0.366	0.160	–	0.231	0.045	–	0.132	0.048
Schizophrenia	Ref. category			Ref. category			Ref. category			Ref. category			Ref. category			Ref. category			Ref. category		
Brief schizophreniform disorder	1.261	0.739	–	5.192	0.050	–	0.713	0.648	–	0.374	0.141	–	1.644	0.651	–	0.961	0.948	–	0.765	0.665	–
Schizoaffective disorder	0.284	0.107	–	1.743	0.319	–	0.216	0.096	–	1.128	0.822	–	0.475	0.327	–	1.748	0.276	–	6.789	0.006	–
Major depression	9.474	0.038	–	4.035	0.239	–	5.388	0.127	–	7.366	0.091	–	0.000	1.000	–	0.310	0.316	–	1.750	0.566	–
Bipolar disorder	0.199	0.078	–	2.253	0.297	–	0.108	0.033	–	4.182	0.072	–	$1.7*10^9$	0.999	–	1.168	0.812	–	1.708	0.497	–
Others	1.690	0.448	–	1.408	0.574	–	2.540	0.193	–	1.099	0.878	–	5.747	0.053	–	0.246	0.045	–	1.053	0.934	–
Model summary (Nagelkerke R^2)	Total $R^2 = 0.437$			Total $R^2 = 0.237$			Total $R^2 = 0.460$			Total $R^2 = 0.340$			Total $R^2 = 0.427$			Total $R^2 = 0.261$			Total $R^2 = 0.229$		
N included in model (% missing)	181 (12.1)			181 (12.1)			181 (12.1)			194 (5.8)			98 (52.4)			202 (1.9)			174 (15.5)		

Note. a = test statistics were based on log10 (+ 1) transformed data because of extreme positive skewness; OR = Odds ratio; $p = p$-value; statistically significant coefficients are in bold.

Table 3
Prediction of 18 months outcomes.

Outcomes after three years	Work activity (MVSI)			Living independently (MLCI)			Working & living independently combined			Functional recovery (GAF > 60)			Symptomatic remission			Repeated hospitalisation during programme			Full insight recovery		
	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed	OR	p	ΔR^2 if removed
Predictors																					
Age	0.924	0.067	0.017	**1.077**	**0.037**	**0.030**	**0.908**	**0.041**	**0.025**	0.993	0.857	0.000	0.941	0.178	0.015	0.892	0.010	0.039	1.077	0.051	0.023
Sex	2.020	0.100	0.014	0.871	0.684	0.001	1.866	0.169	0.011	1.464	0.352	0.004	1.522	0.344	0.007	1.250	0.569	0.002	1.509	0.262	0.008
Socioeconomic status	1.257	0.432	**0.003**	1.023	0.919	0.000	1.268	0.457	0.003	0.889	0.661	0.001	0.996	0.989	0.000	1.267	0.363	0.004	1.285	0.304	0.006
DUP[a]	1.045	0.862	0.001	0.788	0.223	0.010	0.759	0.317	0.006	0.998	0.995	0.000	0.748	0.249	0.011	0.848	0.439	0.003	0.679	0.075	0.019
PAS Premorbid Adjustment	0.269	0.328	0.005	0.700	0.724	0.001	0.208	0.294	0.006	0.117	0.101	0.013	0.200	0.245	0.011	0.152	0.094	0.015	8.170	0.064	0.021
CGI baseline	0.697	0.161	0.010	1.234	0.277	0.008	0.868	0.594	0.002	0.908	0.695	0.001	1.039	0.881	0.000	0.986	0.952	0.000	1.492	0.073	0.020
GAF Baseline	**1.077**	**0.003**	**0.050**	1.036	0.060	0.024	**1.104**	**<0.001**	**0.089**	**1.118**	**<0.001**	**0.114**	**1.061**	**0.016**	**0.050**	**0.933**	**0.002**	**0.058**	**1.088**	**0.000**	**0.096**
ΔGAF 0–6 months	**1.073**	**<0.001**	**0.097**	**1.041**	**0.004**	**0.061**	**1.090**	**<0.001**	**0.146**	**1.100**	**<0.001**	**0.040**	**1.058**	**0.001**	**0.106**	**0.920**	**0.000**	**0.179**	**1.040**	**0.007**	**0.046**
Diagnostic	–	**0.024**	**0.068**	–	0.995	0.003	–	0.400	0.028	–	0.186	0.000	–	0.147	0.077	–	0.123	0.069	–	0.168	0.079
Schizophrenia	Ref. category			Ref. category			Ref. category			Ref. category			Ref. category			Ref. category			Ref. category		
Brief schizophreniform disorder	3.444	0.094	–	1.132	0.837	–	0.924	0.911	–	0.860	0.842	–	0.847	0.841	–	0.380	0.199	–	1.933	0.293	–
Schizoaffective disorder	1.700	0.409	–	0.885	0.808	–	1.629	0.499	–	0.857	0.795	–	0.903	0.875	–	1.757	0.283	–	3.514	0.027	–
Major depression	6.994	0.084	–	0.635	0.663	–	12.062	0.036	–	7.832	0.090	–	5.092	0.187	–	0.497	0.550	–	$1.6*10^9$	0.999	–
Bipolar disorder	13.385	0.003	–	0.771	0.720	–	1.689	0.624	–	5.623	0.074	–	5.782	0.053	–	0.829	0.803	–	1.123	0.892	–
Others	1.815	0.357	–	0.990	0.986	–	1.909	0.363	–	0.485	0.292	–	5.338	0.066	–	0.077	0.019	–	0.545	0.326	–
Model summary (Nagelkerke R^2)	Total $R^2 = 0.470$			Total $R^2 = 0.125$			Total $R^2 = 0.436$			Total $R^2 = 0.472$			Total $R^2 = 0.304$			Total $R^2 = 0.342$			Total $R^2 = 0.300$		
N included in model (% missing)	191 (7.3)			189 (8.3)			189 (8.3)			190 (7.8)			132 (64.1)			202 (1.9)			180 (12.6)		

Note. a = test statistics were based on log10 (+ 1) transformed data because of extreme positive skewness; OR = Odds ratio; *p* = p-value; statistically significant coefficients are in bold.

the hypothesis that relying on dynamic changes, rather than on static variables, is a more suitable means of estimating patients' potential outcomes, and that early changes in functional levels are more reliable than any other baseline characteristic.

Among patients with higher baseline functional levels, and despite limited scope for potential improvements, post hoc analyses showed that ΔGAF 0–6 months was still a good predictor of 18 months and three-year outcomes. This suggests that our findings may be generalisable to most patients, regardless of their functional level when entering the programme. This variable may therefore prove to be a useful tool for the early detection of patients at risk of poorer outcomes and who may have special needs during the programme or require adjustments to their treatment. Some strategies (such as TREAT at EPPIC/ORYGEN) have been explicitly implemented within early intervention programmes to ensure prompt action when facing delayed recovery in patients with EP (Thien et al., 2018). Individuals with persistent positive symptoms at 12 weeks are presented to the TREAT panel to implement intensive support and treatment adjustments for promoting a better recovery (Thien et al., 2018). Our study confirms that discerning early changes in GAF scores could be helpful in the very early identification of subgroups of EP patients whose recovery would involve special treatment needs.

Otherwise, baseline GAF scores were strong predictors of various outcomes and revealed a strong autoregressive structure to functional recovery. Patients' relative functioning rankings remained quite similar throughout the programme. In other words, patients with the lowest initial functioning scores are also likely to be among the lowest functioning individuals at the end of the programme. Although a previous study reported that patients on a good functional trajectory might also have good functional outcomes at follow-up, it also reported a subgroup of patients with greater difficulties at treatment programme entry but an ability to recover quickly and reach good functional outcomes (Hall et al., 2019). This subgroup included more female, Caucasian subjects with higher socioeconomic status, a higher IQ, higher executive functioning, better premorbid adjustment scale scores and a history of lower rates of substance use than the subgroup with poor functional trajectories and outcomes. This suggests that the predictive value of the baseline GAF score might also depend on patients' characteristics, but further investigations will be required to better identify such subgroups.

DUP and socioeconomic status predicted several but not all aspects of recovery. Although shortening the DUP is a key goal in early intervention strategies, its predictive value for outcomes has been questioned (Golay et al., 2016; Polari et al., 2011). The DUP's limited predictive value for outcomes in previous studies was likely linked to problems of definition that did not consider adherence to treatment: when the end of the DUP is defined as the start of adherence to proper treatment, the DUP's predictive power is greater. In the present study, DUP was also competing with several other important variables explaining the lion's share of outcome variance. Considering that the DUP predicted working & living independently combined and symptomatic remission better than other variables did, efforts to shorten the DUP should continue, both through early detection and the development of engagement strategies.

Some factors only predicted functional outcomes. In particular, premorbid functioning was only associated with functional recovery. This result was not surprising given that a recent study found that Premorbid functioning had no predictive effect for remission (Simonsen et al., 2017). Moreover, socioeconomic status predicted a return to employment. With this in mind, new sociopolitical strategies must be implemented to better protect the professional status or employment of patients who develop psychosis (Dutoit et al., 2014). Finally, diagnosis only predicted working & living independently combined, which was in line with a previous study reporting the weak predictive value of diagnoses (Hall et al., 2019). In our opinion, these findings make a case for a multi-dimensional rather than a categorical or rules-based approach to diagnosis in psychiatry. Another study also recently suggested that combining symptom-dimensional scores for EP with a categorical diagnosis, rather than relying on diagnosis alone, improved the accuracy of predicting time to first remission (Ajnakina et al., 2018).

This study had some limitations. First, our sample size was moderate, and further research should attempt to replicate our results in larger samples. Second, our results only suggest that treatment should be adjusted, but not how. It should also be highlighted that is a naturalistic study and as these individuals were not improving, they likely did receive more intensive inputs from their case-managers. Further study is therefore required to understand more specifically how and which elements of treatment should be adjusted or added when a rapid response is absent at the beginning of an early intervention programme. Second, Panss scores were not collected at baseline and were therefore not used in the analysis. Third, even if our models included several important variables, they did not include every potential confounding factors. Indeed, for statistical reasons, our models would likely be overparametrized given our sample size. It could include change of

Table 4
Prediction of three-year and 18 months outcomes given GAF functioning at baseline.

	Work activity (MVSI)	Living independently (MLCI)	Working & living independently combined	Functional recovery (GAF > 60)	Symptomatic remission	Repeated hospitalisation during programme	Full insight recovery
Outcomes after three years							
Below median Baseline GAF (≤ 40) subgroup, N = 101							
GAF						x	
Baseline							
ΔGAF 0–6 months	x	x	x	x	x	x	x
Above median baseline GAF (> 40) subgroup, N = 105							
GAF	x		x	x			x
Baseline							
ΔGAF 0–6 months	x		x	x		x	x
Outcomes after 18 months							
Below median Baseline GAF (≤ 40) subgroup, N = 101							
GAF			x	x			x
Baseline							
ΔGAF 0–6 months	x	x	x	x	x	x	x
Above median baseline GAF (>40) subgroup, N = 105							
GAF Baseline	x		x	x	x		
ΔGAF 0–6 months	x		x	x		x	

Note. x = significant predictor.

medication during the course of program, change of symptom severity and type of symptoms (positive, negative, affective, etc.), subset of patients receiving cognitive remediation training, substance use or case-manager utilization and treatment intensity. Therefore, it is unknown whether they could provide an even better predictor of outcome than ΔGAF 0–6 months. It also seems relevant to suggest other approaches for future work. Interactions between ΔGAF 0–6 months and factors like DUP, socioeconomic status, medication, compliance, cognition and social cognition (Green, 2016; Green et al., 2000) or cognitive remediation training should also be studied to better understand the determinants of long-term outcomes. We hypothesize that the predictive value of ΔGAF 0–6 months could likely be moderated by these variables and could be higher or lower depending on the situation.

Finally, the emphasis on the dynamics of change, rather than on baseline or static variables, could be extended to variables other than functioning (e.g. psychopathology or CGI scores). ΔCGI scores were not used in the present study and the specificity of differences in functioning versus symptomatology remains to be studied, especially since GAF mixes both symptomatology and functioning. Even if they are relatively crude, we have no reason to believe ΔCGI scores could not also be used to successfully predict long-term outcome.

In conclusion, the present study reports that rapid changes in overall functioning scores during EP could predict various clinical outcomes after three years. This finding could help to tailor specific interventions for EP patients according to the early dynamics in their overall functioning. Early changes in GAF scores seem to be an effective and simple predictor of which patients might make an incomplete recovery and need adjustments to their treatment strategies as early as possible. Further studies will be required to explore such targeted intervention strategies and to specify their key determinants and relevant associations.

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CRediT authorship contribution statement

PG, RJ, and PK designed this study. PG analyzed and interpreted the data. PG, JR RJ PK and NM drafted the first version of the manuscript. AS and PC critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare no conflict of interest in relation to the subject of the study.

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