



## Original Article

# Cost-effectiveness of treating first-episode psychosis: five-year follow-up results from an Italian early intervention programme

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### Abstract

**Aim:** Early intervention programmes are expected to result in the reduction of illness severity in patients with schizophrenia, and contain health-care costs by reducing hospital admissions and improving the social functioning of patients. This study aimed to investigate the cost-effectiveness of treatment in an early intervention programme in comparison to standard care.

**Methods:** Retrospective analysis of data prospectively recorded in an urban area (Milan, Italy). Twenty-three patients from an early intervention programme and 23 patients from standard care with first-episode psychosis were evaluated on their use of services over a 5-year period. The Health of the Nation Outcome Scale was used to measure clinical status.

**Results:** Significant changes with respect to initial assessment were

recorded on the Health of the Nation Outcome Scale, with larger effect sizes in the early intervention programme than in the standard care group. Consequently, the cost-effectiveness ratio per reduced score of severity was lower in the early intervention programme than in standard care (€ 4802 vs. € 9871), with an incremental cost-effectiveness ratio, or net saving of € –1204 for every incremental reduced score of severity. Over time, greater recourse to hospital and residential facilities to obtain comparable improvement in symptoms resulted in a steady cost increase for the patients in standard care.

**Conclusions:** Allocation of funds to specialized early intervention programmes is the best alternative, as it can save costs by reducing the use of hospitals and residential facilities, and may produce net savings of costs in the long term.

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## INTRODUCTION

Schizophrenia is a chronic and severe disorder, which negatively impacts the lives of affected patients and their families.<sup>1–3</sup> Costs for patients, their families and the society largely depend on costs for care although additional costs arise from lost productivity (because of unemployment and work absences for both patients and the relatives caring for them), informal care, involvement of criminal justice services and costs related to social security.<sup>4–6</sup>

Early detection and early interventions (EIs) in patients with psychosis aim to limit the most damaging outcomes of co-morbidity, namely, including depression, substance abuse and vocational disruption, so as to reduce the risk of social drift of the patient.<sup>7,8</sup> These measures are expected to prevent the development of a chronic course,<sup>9,10</sup> and maximize the chances of social and occupational functioning.<sup>11,12</sup>

From a theoretical standpoint, early intervention programmes (EIPs) are expected to decrease illness severity of schizophrenia and hence contain

healthcare costs by reducing the number of hospital admissions and by improving patients' social functioning thus lessening the burden of informal care by relatives. Some evidence exists on the effectiveness of phase-specific early interventions for people with psychosis,<sup>10,13,14</sup> by increasing rates of remission and decreasing admission rates and hospital stays.<sup>15,16</sup> However, precise evidence on the cost-effectiveness of such programmes is limited.<sup>17</sup> Two studies found significantly better social functioning and symptomatic outcome after the first year of treatment in patients treated by EI services compared with historical matched groups who received treatment-as-usual, with lower costs in EIPs because of lower inpatient costs.<sup>16,18</sup>

More recently, data from the Early Psychosis Prevention and Intervention Centre (EPPIC), in Melbourne, Australia, demonstrated significantly better social and symptomatic outcomes among a cohort 8 years after initial 2-year EPPIC treatment compared with a historical treatment-as-usual group, with significantly lower costs for treatment per annum in the EPPIC group.<sup>17</sup>

To date, no study has analysed data on patients who underwent a full 5-year specialized protocol of care in an EI service, with this period arguably being the most critical as far as the long-term follow-up is concerned.<sup>17,19</sup>

This paper summarizes data on the cost-effectiveness of treatment as part of the *Programma2000*, a comprehensive programme operating in Italy since 1999,<sup>20</sup> which provides focused intensive treatment at the onset of psychosis, by comparing patients treated with standard care (SC) – or treatment-as-usual – in the same health district (Milan). Prospectively collected data concerning a 5-year interval, from assessment at inception to the final end point, were used in the study.

## METHODS

### The setting

*Programma2000* was established in a health-care catchment area of inner Milan (Italy), which provides services to approximately 200 000 inhabitants. The focus area has a dedicated Community Mental Health Center (CMHC) open 9 h a day, 5 days a week, throughout the year.<sup>20</sup>

The main inclusion criteria are: first, contact with any public mental health service of the catchment area for a first episode of psychosis with a duration of untreated psychosis (DUP)  $\leq 24$  months, for people aged 17–30 years old.

All patients who are referred to *Programma2000* receive a prompt admission in treatment (within 24 h), and undergo a comprehensive, multidimensional evaluation with a package of standardized assessments aimed at evaluating general psychopathology, level of functioning and associated impairment, disability and cognitive deficits.<sup>20,21</sup>

Proposed interventions include individual pharmacotherapy, psychoeducational and motivational sessions, cognitive-behavioural psychotherapy (CBT), individual family psychoeducation and therapeutic support group activities (e.g. anxiety management, social problem-solving, assertive training, substance abuse prevention, etc.), various social group activities (e.g. musical group, multimedia group, computer training sessions, language courses, empowerment group), and other support activities (concerning employment, school, compliance with medication, recreational planning).<sup>20</sup> Hospital admissions, when necessary, are negotiated with the two General Hospital Psychiatric Units (GHPUs) operating in the same area. The beds available for hospital treatment were 11 per 100 000 when the study was conducted.

All interventions are free of charge for admitted patients and are financed through a special grant from the Lombardy Regional Authority. The length of care under the programme is set at 5 years from the time of initial assessment.

The comparison group included patients treated in SC. By SC, we mean any specialized mental health provision not offering interventions specifically aimed at treating the first-episode of psychosis.

To make the comparison with SC services, the study included public outpatient and inpatient psychiatric facilities operating in the same catchment area (Milan and the surrounding health district), which provide services to approximately 400 000 inhabitants. There were two GHPUs and four CMHCs involved in the study.

All public psychiatric facilities are open 24 h a day, with staff on duty at night; pharmacotherapy and individual supportive psychotherapy are the main treatment methods for patients with psychosis.<sup>22,23</sup> Co-morbidity for substance abuse is treated in cooperation with a dedicated team, which is external to the psychiatric service and works as part of Drug Addiction Services.<sup>23</sup> School support, vocational (re)habilitation and competency training generally are not offered to patients with psychosis in SC, and in the health district covering the Lombardy Regional Authority complex care packages were rarely provided in SC.<sup>24</sup> A specific protocol of care is not active for patients with psychosis

at their first episode. Patients are seen within 7–15 days from the request for intervention: they receive a clinical interview to ascertain diagnosis and co-morbidity, and are prescribed pharmacotherapy and individual supportive psychotherapy.<sup>25</sup> Contacts are one-two per month, unless a patient requires more frequent visits. In this case, patients are usually admitted to day-hospital or community residential or semi-residential facilities. In these settings, generic group therapy and social skills training are provided as adjunctive treatment. For patients with acute illness, admissions are negotiated with the GHPUs operating in the same area. The beds available for hospital treatment were 10 per 100 000 when the study was performed. Families receive information on the illness and psychological support when needed, but structured psychoeducation and family therapy are not provided.<sup>25</sup>

### Participants

All patients enrolled in Programma2000 who were diagnosed with schizophrenia or related disorders (International Classification of Diseases–10 codes: F20 and F21–29)<sup>26</sup> with DUP  $\leq 24$  months, and who completed the 5-year treatment by the end of September 2008, were evaluated and included in the study ( $n = 23$ ).

The comparison group came from a parallel study investigating severity and costs in patients diagnosed with schizophrenia. This group includes 23 patients who received public psychiatric services in the same health district but in different units, were treated for a first episode of psychosis and were diagnosed with schizophrenia or a related disorder (in line with Programma2000). To select this sample, we examined clinical records for SC patients who complied with inclusion and exclusion criteria, including age (17–30 years old) and DUP ( $\leq 24$  months) limits, and completed a five-year treatment by the end of September 2007. At the end of September 2008, 23 SC patients met the criteria, resulting in a matched group in terms of sample size.

In both groups, a co-morbid, persistent substance-dependence disorder was an exclusion criterion, however substance use/abuse without dependence was not.

Patients in both groups were treated for 5 years, and there were no dropouts.

The institutional review boards of the involved services approved the study, and all patients gave their informed consent.

### Effectiveness measures

Patients enrolled in the Programma2000 undergo a detailed assessment protocol<sup>20</sup> that uses various psychiatric scales, but patients enrolled in SC were not assessed in detail. Both groups were assessed on the Health of the Nation Outcome Scales (HoNOS),<sup>27</sup> which is a widely used measure of outcome developed for routine use in mental health services. The treating clinicians assigned the scores on the HoNOS.

HoNOS consists of 12 subscales, each using the 5-point Likert scale (from 0, 'no problem', to 4, 'severe/very severe'). Scores can be totalled to a theoretical maximum of 48 points. Cut-offs used to determine the clinical status of patients have been proposed and validated in the Italian setting.<sup>28</sup> For the purpose of this study, as an effectiveness measure, we used the average per patient total score reduction between entry and 5-year follow-up and the reliable change index (RC). RC refers to the extent to which an observed change falls beyond the range attributable to the measurement error: RC was set at 7, in accordance with the suggested threshold for severe patients.<sup>28</sup> On the basis of the percentage of patients achieving RC, the number needed to treat (NNT) was calculated as such:  $100/(\text{Percent Improved Programma2000} - \text{Percent Improved in SC})$ . Suggested thresholds for interpreting NNT are: small = 8.8; medium = 3.6; large = 2.3.<sup>29</sup>

The interrater reliability as measured by the intraclass correlation coefficient for the HoNOS at 5-year follow-up was found to be 0.771 (95% confidence interval (CI): 0.605–0.888) in the index group (Programma2000), and 0.710 (95% CI: 0.498–0.858) in the control (SC) group. Despite the larger CI in the SC group, reliability estimates did not differ ( $\chi^2 = 0.274$ , degrees of freedom (d.f.) = 1,  $P = 0.60$ ), according to Hakstian and Whalen.<sup>30</sup>

### Costs

Treatment costs were calculated by multiplying the different items of services used by each patient times their unit costs. Only direct health-care costs falling on the Italian National Health Service were analysed. These are grouped into three types of treatment: CMHCs interventions (outpatient costs), inpatient care (use of psychiatric acute beds and day hospital admissions), and time spent living in community residential and semi-residential facilities (residential costs). The records on items of services used were made available by the Department of Health of the Lombardy Region, while unit costs

were derived from a previous study, based on 10 psychiatric service centres of the Lombardy Region.<sup>31</sup> All unit costs were expressed at 2006 constant prices in Euros, €, in order to avoid influence of yearly price increases. In the sensitivity analysis, patient costs were discounted at 3% and 5% rates.

### Data analyses

The index (Programma2000) and the contrast (Standard Care) groups were compared with respect to clinical effectiveness (reduction of HoNOS scores after 5 years; number of patients with RC) and costs (total, outpatient interventions, hospital and residential facilities admissions). In addition, the profile of costs was calculated across the 5 years of treatment for each patient.

All data were coded and analysed using the Statistical Package for Social Science for Windows (SPSS Inc., Chicago, IL, USA), version 13. Categorical data were analysed in inter-group comparisons with chi-squared or Fisher's exact test, when appropriate. Student's *t*-test was used to compare age. Analysis of covariance was used to compare HoNOS scores at the 5-year follow-up, taking HoNOS scores at the initial assessment as covariate. The Mann-Whitney test and the Wilcoxon signed rank test were used to compare ordinal variables and costs. The non-parametric Friedman test for repeated measures (with the Dunn multiple comparison test for further

post hoc comparisons) was used to compare costs over time. All tests were two-tailed, with  $\alpha = 0.05$ .

For HoNOS, effect sizes of statistically significant differences were expressed through Hedges' *g* (a bias corrected version of Cohen's *d*) with 95% CI: for intervention costs, the area under the receiver operating characteristic area (area under the curve, AUC) was used; when 95% CIs are both above 0.500 (equiprobability), the effect size of the difference can be considered statistically reliable.<sup>29</sup>

## RESULTS

### General characteristics of the sample

The two samples did not differ at entry by age, sex, educational and/or occupational level, or diagnosis, nor did HoNOS scores differ at assessment (Table 1).

The patients of Programma2000 were treated on average for 4.8 years (1756 days), while those of the control group for 5.1 year (1863 days).

### Effectiveness

In both groups, after a 5-year period there were significant changes on the HoNOS compared with initial assessment (Wilcoxon signed rank test:  $z = -3.408$ ,  $P = 0.001$  in Programma2000;  $z = -2.960$ ,  $P = 0.003$  in SC). There were larger effect sizes in the Programma2000 than in the SC group (Table 2).

TABLE 1. Socio-demographic and clinical characteristics of the sample

	Programma2000 <i>n</i> = 23 (%)	Standard Care <i>n</i> = 23	Statistics
Age (SD)	24.5 (3.9)	25.8 (3.6)	$t = -1.16$ , d.f. = 44, $P = 0.25$
Sex			$\chi^2 = 0.00$ , d.f. = 1, $P = 1.00$
Male	16 (69.6)	17 (73.9)	
Female	7 (30.4)	6 (26.1)	
Educational qualification			$\chi^2 = 0.82$ , d.f. = 1, $P = 0.365$
Lower than high school diploma	12 (52.2)	16 (69.6)	
High school diploma or higher	11 (47.8)	7 (30.4)	
Marital status			$\chi^2 = 0.27$ , d.f. = 1, $P = 0.60$
Single	22 (95.7)	20 (87.0)	
Married	1 (4.3)	3 (13.0)	
Occupational status			$\chi^2 = 1.493$ d.f. = 1, $P = 0.22$
Student/housewife/unemployed	17 (73.9)	12 (52.2)	
Part-time/fully Employed	6 (26.1)	11 (47.8)	
Diagnoses (ICD-10 codes)			$\chi^2 = 0.80$ , d.f. = 1, $P = 0.37$
F20	15 (65.2)	12 (52.2)	
F21-29	8 (34.8)	11 (47.8)	
HoNOS at assessment (SD)	16.26 (6.77)	13.47 (4.06)	M-W = 189.00, $P = 0.096$

All data: mean (SD), or *n* (%), according to their nature.

d.f., degrees of freedom; HoNOS, Health of the Nation Outcome Scales; ICD, International Classification of Diseases; M-W, Mann-Whitney U test; SD, standard deviation.

TABLE 2. Outcome after 5 years of treatment

	Programma2000		Standard Care	
	<i>n</i> = 23	Effect size (95%CI)	<i>n</i> = 23	Effect size (95%CI)
HoNOS behavioural problems				
Pre-treatment	1.82 (1.80)	-0.77	2.17 (1.61)	-0.85
Post-treatment	0.65 (1.11)*	(-1.37; -0.17)	0.95 (1.18)*	(-1.45; -0.25)
HoNOS general impairment				
Pre-treatment	1.95 (1.39)	-0.73	0.95 (0.92)	0.22
Post-treatment	0.91 (1.41)*	(-1.33; -0.13)	1.21 (1.34)	(-0.36; 0.80)
HoNOS clinical symptoms				
Pre-treatment	5.91 (2.77)	-1.15	5.08 (2.72)	-0.57
Post-treatment	2.95 (2.28)*	(-1.77; -0.52)	3.65 (2.18)	(-1.16; 0.02)
HoNOS psychosocial problems				
Pre-treatment	6.56 (3.46)	-0.88	5.26 (2.43)	-0.67
Post-treatment	3.47 (3.48)*	(-1.48; -0.27)	3.56 (2.59)*	(-1.26; -0.07)
HoNOS total score				
Pre-treatment	16.26 (6.77)	-1.27	13.47 (4.06)	-0.85
Post-treatment	8.00 (5.94)*	(-1.91; -0.64)	9.39 (5.29)*	(-1.45; -0.25)
% changes in HoNOS from entry to 5-year follow-up				
Mean (SD)		-37.5% (65.2%)		-19.3% (72.2%)
Median (interquartile range)		-54.5 (63.3)		-22.2 (66.6)
HoNOS cut-offs at 5 years ( <i>n</i> , %)				
No severe symptoms (= 0)		1 (4.3%)		0 (0%)
Light severe symptoms (1-7)		13 (56.5%)		10 (45.3%)
Moderately severe symptoms (8-14)		6 (26.1%)		9 (39.1%)
Severe symptoms (15-21)		2 (8.7%)		4 (17.4%)
Very severe symptoms ( $\geq 22$ )		1 (4.3%)		0 (0%)
HoNOS RC ( <i>n</i> , %)		14 (60.9%)		8 (34.8%)

\*Wilcoxon signed rank test, post-treatment versus pre-treatment,  $P < 0.05$ .

All data: mean (SD), or *n* (%), according to their nature.

CI, confidence interval; HoNOS, Health of the Nation Outcome Scales; RC, reliable change index; SD, standard deviation.

The type of treatment (Programma2000 vs. SC) did not produce a significant effect on HoNOS scores at the 5-year follow-up after controlling for the HoNOS scores at initial assessment: ( $F(1,43) = 0.55, P = 0.57$ ). However, at the 5-year follow-up, patients in Programma2000 reported a larger absolute decrease, being 8.3 in Programma2000 (95% CI = 4.3-12.1) and 4.1 in SC (95%CI = 1.6-6.5) (Mann-Whitney  $U = 177.00, z = -1.92, P = 0.054$ ).

Patients with RC  $\geq 7$  constituted 60.9% ( $n=14$ ) in Programma2000 and 34.8% in SC ( $\chi^2 = 2.17, d.f. = 1, P = 0.14$ ). The NNT, on the basis of RC, was 3.8 (i.e. 4), which is close to a medium effect.

After 5 years of treatment, 14 patients (60.8%) in Programma2000 were determined to have no or minimal severe symptoms on the HoNOS; the corresponding figure in the SC group was 10 (43.4%) ( $\chi^2 = 0.78, d.f. = 1, P = 0.37$ ).

### Costs analysis

Average costs per patient over 5 years were quite similar, being € 39 671 for the index and € 42 810 for

the contrast group (Table 3). The average cost per day of treatment was € 22.6 and € 23.0, respectively.

In Programma2000, allocation of costs was: outpatient care = 77.4%, inpatient care = 9.9%, residential facilities care = 12.7%. The corresponding figures in SC were: 59.1%, 25.6% and 15.3%, respectively.

Patients in Programma2000 were marginally less likely to be treated in day hospital (Fisher's exact test  $P = 0.109$ ) and, on average, had been hospitalized for shorter periods. Therefore their hospital costs were far lower than the SC group (€ 3928 vs. € 10 969; respectively) (Mann-Whitney  $U = 207.00, z = -2.33, P = 0.019$  (AUC = 0.609, but 95%CI = 0.444-0.773) (Table 3).

Patients in Programma2000 were also marginally less likely to have been admitted to semi-residential facilities (Fisher's exact test  $P = 0.165$ ), so costs for semi-residential facilities care, too, were also lower in Programma2000 in comparison to the SC group, though this did not reach statistical significance (Mann-Whitney  $U = 198.00, z = -1.71, P = 0.086$ ).

## Costs of early intervention in psychosis

TABLE 3. Cost-analysis of treatment over 5 years, early intervention in psychosis (Programma2000) versus Standard Care

	Programma2000 <i>n</i> = 23			Standard Care <i>n</i> = 23		
	<i>n</i> (%)	Days of use*	Mean (SD)	<i>n</i> (%)	Days of use*	Mean (SD)
Outpatient interventions						
Total outpatient costs	23 (100)	n.a.	30 701 (19 789)	23 (100)	n.a.	25 292 (32 910)
Inpatient interventions						
Hospital inpatient care	9 (39)	242	3 928 (6 631)	13 (56)	542	9833 (19 794)
Day hospital care	0 (-)	0	0.0 (0.0)	4 (17)	64	1136 (2 341)
Total inpatient costs			3 928 (6 631)			10 969 (20 065)
Residential care						
Residential facilities	1 (4)	546	3 072 (14 732)	1 (4)	734	4130 (19.805)
Semi-residential facilities	3 (13)	376	1 970 (9 181)	8 (35)	1121	2419 (7 527)
Total residential care costs			5 042 (17 221)			6549 (20 688)
Total costs of care	23 (100)		39 671 (35 089)	23 (100)		42 810 (72 155)

\*Days of use are intended as days of utilization of the specific facility (length of stay), and are expressed as the total amount for all patients across all the 5 years. Days of use are n.a. for outpatient interventions, since costs for these are not calculated by day of use. Data expressed in Euros at constant year 2006 prices – costs over 5 years, mean per patient (SD). n.a., not available; SD, standard deviation.

In contrast, outpatient treatment was more intensive in Programma2000 than in SC, which is reflected in the higher costs for outpatient interventions: (€ 30 701 vs. € 25 292: AUC = 0.733, 95% CI = 0.583–0.884).

### Cost-effectiveness of early treatment

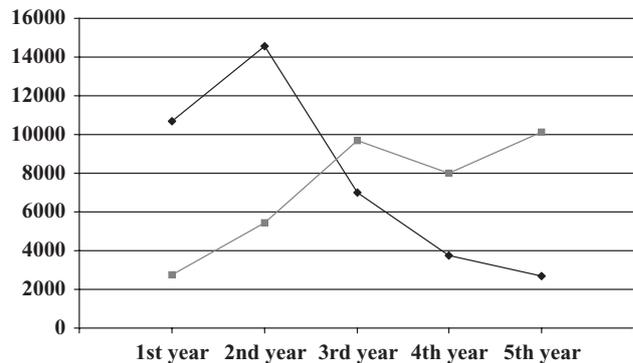
The average cost per score of reduction on the HoNOS scale was € 4802 for the Programma2000 group and € 9871 for the SC group. Being more cost-effective, the incremental cost-effectiveness ratio (ICER) of Programma2000 over SC is € –1204 per incremental score of reduction, which means that a net saving of € 1204 per score is achieved if patients are treated with an EIP instead of a SC programme.

Similarly, the average cost per patient with a RC is € 65 173 with EI and 115 982 with SC; the ICER is € –8468 per patient with RC, which is a significant net saving.

### Costs of treatment over time and sensitivity analysis

Average costs were higher in the first 2 years of treatment for patients in Programma2000, after which they decreased (Friedman test's  $P = 0.0001$ , post-hoc Dunn's  $P < 0.05$  from assessment to the fourth and fifth year), whereas they increased smoothly over time among patients in SC (Friedman test's  $P = 0.0281$ , Dunn's  $P > 0.05$  in all comparisons), concurrently to a higher chance of hospitalization (Fig. 1).

FIGURE 1. Overall costs of treatment over time, from assessment to 5-year follow-up in early intervention in psychosis (Programma2000 vs. Standard Care) – Data expressed in Euros at 2006 constant prices. ◆, Programma 2000 (*n* = 23); ■, Standard Care (*n* = 23).



As the cost profiles over the 5-year treatment are different between the two groups, the average per patient cost, discounted at 3% or 5% annually compounded, would be somewhat lower for the SC group (because many costs occur in the last years, contrary to Programma2000), but the cost-effectiveness ratio would still favour the Programma2000 group (€ 4520 vs. € 8646 per reduced score, if discounted at 3%, and € 4639 vs. € 9127, if discounted at 5%, with an ICER of € –988 and € –1075, respectively).

### DISCUSSION

The main finding of this study is that patients with first-episode psychosis enrolled in an EIP in Milan,

Italy, showed a better improvement at the 5-year follow-up than those enrolled in SC. The potential bias of a 'floor effect' in the changes of pre- to post-treatment scores on the HoNOS cannot be disregarded, because patients in SC were marginally less severe at initial assessment than those in the Programma2000, and so had less room for improvement at the 5-year follow-up. However, at the 5-year follow-up a larger number of patients in the SC group had HoNOS scores in the moderately severe to very severe range (56.5%) compared with those in the Programma2000 (39.1%). Thresholds for symptoms severity are based on absolute values and do not depend on relative size with respect to initial assessment.

As therapists in both settings are likely to follow the same guidelines for pharmacotherapy, the additional reported benefits are supposed to come from the intensive outpatient care programme offered in Programma2000, based on psychotherapy, psychoeducation, social support and competency training.<sup>7,20</sup> SC usually does not provide this type of treatment,<sup>23,25</sup> which is costly and primarily produces indirect effects on the quality of life and family burden. The intensive outpatient treatment in Programma2000 also succeeded in reducing hospital admission rates and use of day hospital, although statistical differences were at a trend level only because of the small sample size. These results are consistent with the aim of deinstitutionalization and better community care. However, in Italy, there are large differences among areas concerning the provision and the quality of care for people with mental disorders. In particular, the frequency and intensity of psychosocial interventions – the major strength in the treatment package of Programma2000 – was uneven across different geographical areas.<sup>32</sup>

Total treatment costs were similar between the two groups over a 5-year treatment period. Outpatient costs were higher in the Programma2000 than in the SC group, but they were compensated by lower hospital costs and, marginally, residential care costs. The Programma2000 costs were concentrated and higher in the first 2 years of treatment, decreasing thereafter, while the SC group costs increased year after year. Data after the fifth year of treatment are being collected to assess whether Programma2000 patients have consolidated their lower level of severity and continue to have lower costs than the SC group.

A similar trend (higher costs than SC at settlement, but cost savings at follow-up) was observed in a recent theoretical cost-effectiveness analysis using data from Outreach and Support in South London.<sup>33</sup> Similarly, another theoretical probabilistic model,

based on data from real studies, found higher costs at the start of treatment in EIPs than in SC, but lower costs in the long run at 3 years.<sup>34</sup> Finally, results based on real data from the Lambeth Early Onset service and compared with SC in the same area (south London) provide evidence of the cost-effectiveness of EIPs, with findings similar to the Programma2000. Costs were higher for outpatient interventions and lower for hospital-based interventions in the EI service than in SC, although overall, differences between the services were not statistically significant.<sup>35</sup> Even the Danish OPUS study, which found no clear clinical benefits at a 5-year follow-up after 2-year treatment in EI service, still showed that differences in inpatient services favoured EI over SC.<sup>36</sup>

In fact, the main difference between Programma2000 and SC is the better allocation of resources required to achieve improvement: the ICER of Programma2000 over SC is € –1204 per incremental score of reduction, a net saving. This occurs with a wide variability across patients, as a reflection of the large variation in the clinical effectiveness of treatment at patient level (a finding already reported in Italy).<sup>37</sup>

Average yearly costs per patient were strictly comparable with past Italian studies, taking into account inflation: € 7934 in Programma2000 and € 8562 in SC; € 7500 in Tarricone *et al.*<sup>38</sup> € 7025 in Garattini *et al.*<sup>37</sup> Indirect costs attributable to schizophrenia are known to be consistently higher than direct care costs,<sup>38</sup> but this was not the study purpose.

### Limitations and strengths

The small sample size is the main limitation of this study, which precludes multivariate analyses. Nevertheless socio-demographic variables did not differ between the two compared groups, so it is unlikely that an interaction effect has resulted. Another issue are the significant differences in the provision of psychiatric care across Italy,<sup>32</sup> which limits the possibility of generalizing the results of this study.

In this research, clinicians assigned the scores on the HoNOS, which may have affected overall rating, however any bias would have occurred in both settings, so should not be relevant with respect to the final results. A greater limitation is the lack of detailed information at assessment for patients in SC: standard assessments are not conducted as part of public psychiatric services in Italy. We had to rely entirely on the HoNOS, which was not designed to cover all the aspects of outcomes, but principally reflect the staff's view of the situation.<sup>39</sup> However, it

has cross-cultural validity and the ability to predicting a wide range of outcomes, including admissions, bed days and psychiatric contacts,<sup>40,41</sup> relevant to the aims of this study. Furthermore, we have data on a sample of patients who received 5 years of treatment, with continuity of care and no dropout. Therefore, we can be confident that results are not affected by bias due to selective assessment.

### CONCLUSIONS

This is the first study on costs of EIP services emanating from a non-Anglo-Saxon or Scandinavian country: its is entirely based on real costs data, calculated patient by patient, and cover a total direct health care period of 5 years. The study results are consistent with the assumption that the provision of phase-specific, tailored interventions in psychosis might relieve the burden of illness for patients, their families and, potentially, society at large, because of better use of resources. Therefore, a reallocation of funds that could allow for the increased application of intensive early intervention treatment in psychosis might be opportune, especially because the most expensive specialized outpatient care programmes can ultimately save on costs by reducing the use of hospital and residential facilities, thus producing net cost savings in the long term.

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