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Drug treatment modalities in psychiatric inpatient practice
A 20-year comparison

■ **Abstract** *Objectives* The present study investigated whether the increased number of psychotropic agents available in Italy in the last 20 years increased the proportion of inpatients being treated with individual medication classes and the proportion receiving combined treatments with agents of the same class or of different classes. *Methods* This study was conducted in South-Verona, Italy. From the local Psychiatric Case Register (PCR) all patients consecutively admitted to the inpatient unit during the years 1981/1982, 1991/92 and 2001/02 were extracted. Drug use at discharge was derived from clinical records, while service use data were extracted from the PCR. *Results* During the six years surveyed 160 patients were admitted in 1981/82, 139 in 1991/92 and 228 in 2001/02. An increasing proportion of subjects receiving antipsychotic, antidepressant and benzodiazepine treatment at discharge was observed. In addition, we found an increasing proportion of patients receiving two or more psychotropic drugs at discharge, which accounted for almost 80 % of cases in 2001/02. The number of psychotropic agents prescribed at hospital discharge was positively correlated with the total consumption of psychotropic drugs. A relevant proportion of patients were also dispensed agents for medical conditions, yielding an average number of 3.2 prescriptions

in 2001/02. The Lavik score, a summary index of service use, indicated that subjects admitted in 1981/82 were moderate users of psychiatric services, while those admitted in 1991/92 and in 2001/02 were high users of psychiatric services. *Conclusion* This study documented emerging trends toward polypharmacotherapy and higher total doses. Additional pharmacoepidemiological research is needed to clarify both the beneficial and, potentially, adverse effects associated with these trends in psychiatric pharmacotherapy.

■ **Key words** drug treatment · epidemiology · polypharmacotherapy · inpatients

Introduction

During the last two decades new generation antidepressant (AD) and antipsychotic (AP) agents have increased the therapeutic options available for subjects with psychiatric disorders (Lawrenson et al. 2000; Santamaria et al. 2002; Mond et al. 2003; Isacsson et al. 1999). New indications have in addition broadened the use of these agents to a wide range of psychiatric conditions and symptoms. Moreover, antiepileptic (AE) agents have been increasingly prescribed to tackle psychiatric symptoms. This evolving context of care has been producing, at a national level, a progressive rise in consumption of psychotropic drugs. In Italy, from 1988 to 1996, an increase of AD sales of 53 % was recorded (Barbui et al. 1999), while the consumption of AP agents remained substantially stable from 1984 to 1994, and increased by 54 % in the subsequent five years (Barbui et al. 2001).

In addition to sales data, in recent years surveys of prescribing habits have documented emerging trends towards higher total AP doses and polypharmacotherapy (Baldessarini et al. 1995; Centorrino et al. 2002). However, these surveys have some limitations. First, prescribing habits have rarely been studied in different index years to document changes over time in drug use,

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and studies where these comparisons were carried out usually considered narrow time intervals. In these studies service use modalities, in addition to drug use modalities, have rarely been described, losing the possibility of understanding whether the use of drugs and services displayed similar or contrasting trends. A second limitation is that surveys tend to focus on specific diagnostic categories, for example on patients with a diagnosis of schizophrenia (McCue et al. 2003; Rothbard et al. 2003). Although this approach precisely describes the use of drugs in that specific condition, it systematically excludes all prescriptions issued with no reference to diagnostic labels, which may account for up to half of the total amount of drug consumption (Weiss et al. 2000; Barbui et al. 2004). On the other hand, studies not focusing on specific disorders usually describe the use of specific drug categories only, not recognizing that a relevant proportion of psychiatric patients are poly-drug users. Finally, in many studies patients are enrolled on the basis of attending a specific psychiatric service, where cases might be selected on the basis of patient-characteristics (age, diagnosis, severity of illness) or on the basis of service-characteristics (reputation, accessibility), thus generating findings of limited generalizability.

In the present survey of prescribing behaviors we took advantage of the presence of a Psychiatric Case Register (PCR), operating since 1978, in the area of South-Verona (Tansella and Burti 2003). The Italian system of psychiatric care is an ideal setting for implementing and using PCRs, since individuals with psychiatric problems living in a specific catchment area are followed by the psychiatric service of that area, usually a community-based network of in- and out-patient facilities; subjects seeking psychiatric care outside the catchment area are always referred to their catchment area. In this system, PCRs routinely and prospectively collect service use data on unselected populations of typical patients seeking psychiatric care. In this study we used the South-Verona PCR to compare the rate and dose of psychotropic drugs prescribed at hospital discharge in three index periods in the last 20 years. We assessed whether the increased availability of psychotropic agents in the last 20 years increased the proportion of inpatients being treated with individual medication classes and the proportion receiving combined treatments with agents of the same class or of different classes. Service use data were in addition considered to understand whether drug and service use modalities showed similar or contrasting trends over time.

Methods

◼ Setting

This study was conducted in South-Verona (about 100,000 inhabitants), an area that includes part of the city of Verona and three neighboring small towns. The main agency providing psychiatric care for the adult population is the South-Verona community mental health service (CMHS), which is run by the Section of Psychiatry, Department of Medicine and Public Health of the University of Verona. The CMHS is a unitary service, in which great emphasis is given to communication between all staff members and to integration between the various clinical activities. The CMHS comprises one inpatient unit located in the general hospital and a network of outpatient and community facilities (Tansella and Burti 2003). The inpatient unit is an open ward of 16 beds located in the academic general hospital which has about 1000 beds. It is a traditional hospital ward, similar to all other medical wards in the hospital and patients can be admitted on a voluntary or compulsory basis.

Since 1978, the year of implementation of the Italian psychiatric reform, the South-Verona Psychiatric Case Register (PCR) routinely records, for all subjects in contact with the CPS, socio-demographic characteristics, ICD-10 diagnoses, past psychiatric and medical history, clinical data, admissions and outpatient contacts (Amaddeo et al. 1997). The PCR also records details of patients who leave the catchment area, and those who die. The PCR, however, does not routinely collect information on prescriptions of psychotropic drug.

The style of working privileges a psychosocial approach, with strong emphasis on continuity of care and rational drug use (Tansella et al. 1998). To assure continuity of care, inpatients are treated by the same clinical team which provides outpatient community care, and pharmacological treatments, dispensed during the acute inpatient phase, are usually continued at discharge. In addition to psychotropic drugs, a comprehensive system of outpatient community interventions, based on patients' needs, are usually developed and implemented after the admission episode (Tansella et al. 1998). No major changes have occurred in the organization of the CMHS in the last 25 years. However, during this period the community service gradually developed: more staff was available for out-patient and community care, and rehabilitative activities increased. On the other hand the number of hospital beds remained stable (Tansella et al. 1998).

◼ Patients

From the South-Verona PCR all patients consecutively admitted to the inpatient unit during the years 1981/1982, 1991/92 and 2001/02 were extracted. Using the PCR patient code (a code that uniquely identifies individuals) and the date of admission we identified the corresponding clinical records. Clinical records were manually reviewed by two members of the research team (AC and DL) to gather information on the type and dose of psychotropic agents prescribed at discharge. Agents prescribed for medical disorders were also recorded. From the PCR, for each included subject, we extracted the number of outpatient contacts, the number of days in day-care facilities and the number of bed days in psychiatric ward, in the six months before and after the index admission. In order to obtain a cumulative measure of service use, the Lavik index of total consumption of service was constructed using the following principles: 1 outpatient consultation = 1 weight point; 1 day in day-care facility = 2 weight points; 1 day in inpatient service = 3 weight points (Lavik 1983).

◼ Statistical analysis

Categorical data are expressed as numbers and percentages of the overall population with a 95 % confidence interval (CI), while continuous data are expressed as means of the overall population with a 95 % CI. Psychotropic agents' daily doses in milligrams were converted into multiples of the Defined Daily Dose (DDD) for each drug by dividing the prescribed daily dose (PDD) by the DDD (PDD/DDD). The DDD is the international unit of drug utilization approved by the World Health Organization for drug use studies (WHO 2003). It is a theoretical unit of measurement defined as the assumed average maintenance daily dose for a drug, used for its main indication in adults. Expression of drug use in terms of multiples of DDDs allows to calculate, for each patient, a cumulative measure of drug consumption taking into account the concurrent use of more than one agent. In this case, for example the concurrent use of two antipsychotic agents, the sum of each agent's PDD/DDD ratio provides an overall estimate of drug consumption. This methodology is routinely

used to calculate national drug consumption statistics (Santamaria et al. 2002; Mond et al. 2003; Andretta et al. 2004; Ciuna et al. 2004) and to provide descriptions of drug use in selected catchment areas (Italian Collaborative Study Group on the Outcome of Severe Mental Disorders 1999; Barbui et al. 2002). A PDD/DDD ratio of one indicates that the dose prescribed is equal to the DDD of that drug; a ratio greater than one indicates a dosage higher than the standard dose, while a ratio lower than one means a low dose.

Linear regression analysis was run to investigate predictors of AP, AD and BDZ dose regimens. The following independent variables were inserted into the model: gender (male = 0, female = 1), age (years), length of illness (years), length of current admission (days), diagnosis (other = 0, psychosis = 1), number of agents prescribed (of the same class), Lavik index, admission in 2001/02 (no = 0, yes = 1). A non-parametric bootstrap method of statistical accuracy was used, assuming that the observed distribution of the present sample was a good estimate of the true population distribution (Efron 1986).

Results

During the six years surveyed there were 160 patients admitted in 1981/82, 139 in 1991/92 and 228 in 2001/02. The distribution of patients by sociodemographic and clinical characteristics, presented in Table 1, revealed that there were more young subjects, with a shorter length of illness, in 1981/82, and that there were more subjects with a diagnosis of psychosis in 1991/92 and 2001/02.

Trends in psychotropic drug prescriptions at discharge are presented in Table 2. AP agents were prescribed at discharge in more than 60 % of subjects in 2001/02, as compared with less than 52 % in 1991/92 and less than 47 % in 1981/82; similarly, the proportion of those receiving two or more AP agents at discharge progressively rose, accounting for slightly less than 20 % in 2001/02. AD agents were prescribed at discharge in more than 53 % of subjects in 2001/02, as compared with less than 26 % in 1991/92 and 20 % in 1981/82; however, the proportion of those receiving two or more AD remained very low in the three time periods surveyed (Table 2). BDZ were prescribed at discharge in around 65 % of subjects in 2001/02 and in 1991/92, as compared with less than 36 % in 1981/82; the proportion of those receiving two or more BDZ at discharge progressively rose, accounting for more than 23 % of subjects in 2001/02. Overall, the proportion of those receiving two or more psychotropic agents at hospital discharge progressively rose, accounting for almost 80 % of subjects in 2001/02. While the use of anticholinergic agents decreased, the use of antiepileptic drugs progressively increased, as well as the use of agents for medical conditions. Finally, the proportion of those receiving two or more agents belonging to any drug class progressively rose, accounting for more than 85 % of subjects in 2001/02. The average number of agents received at hospital discharge was 1.85 (SD 0.93) in 1981/82, 2.10 (SD 1.06) in 1991/92 and 3.19 (SD 1.70) in 2001/02.

AP were prescribed at doses slightly below the DDD in 1981/82 and in 1991/92, and at doses corresponding to their DDD in 2001/02; in contrast, the mean dose of AD agents progressively rose, and that of BDZ progressively

Table 1 Socio-demographic characteristics of the sample

	1981/1982 (N = 160) N (%)	1991/1992 (N = 139) N (%)	2001/2002 (N = 228) N (%)
Gender			
Male	81 (50.63)	57 (41.01)	111 (48.68)
Female	79 (49.38)	82 (58.99)	117 (51.32)
Age			
18–35	57 (35.63)	51 (36.69)	52 (22.81)
36–45	42 (26.25)	33 (23.74)	49 (21.49)
46–55	24 (15.00)	26 (18.71)	56 (24.56)
56–65	21 (13.13)	11 (7.91)	36 (15.79)
> 65	16 (10.00)	18 (12.95)	35 (15.35)
Marital status			
Single	58 (36.48)	60 (43.48)	91 (41.55)
Married	67 (42.14)	46 (33.33)	78 (35.62)
Widowed	15 (9.43)	9 (6.52)	19 (8.68)
Separated	19 (11.95)	23 (16.67)	31 (14.16)
Education			
No education	11 (7.24)	9 (6.57)	6 (3.05)
5 years	81 (53.29)	45 (32.85)	59 (29.95)
8 years	38 (25.00)	54 (39.42)	75 (38.07)
> 8 years	22 (14.47)	29 (21.17)	57 (28.93)
Living conditions			
Alone	26 (16.77)	32 (23.53)	42 (19.72)
With a partner	110 (70.97)	91 (66.91)	101 (47.42)
With family members	11 (7.10)	7 (5.15)	58 (27.23)
In residential facilities	8 (5.16)	6 (4.41)	12 (5.63)
ICD-10 diagnosis			
Psychosis	36 (23.38)	43 (31.62)	68 (29.82)
Affective disorders	53 (34.42)	50 (36.76)	93 (40.79)
Neurotic disorders	18 (11.69)	8 (5.88)	14 (6.14)
Personality disorder	13 (8.44)	17 (12.50)	30 (13.16)
Other	34 (22.08)	18 (13.24)	23 (10.09)
Length of illness			
< 1 year	36 (24.83)	24 (18.32)	0 (–)
1–5 years	26 (17.93)	41 (31.30)	14 (15.22)
6–10 years	29 (20.00)	16 (12.21)	18 (19.57)
11–15 years	22 (15.17)	16 (12.21)	17 (18.48)
16–20 years	13 (8.97)	12 (9.16)	14 (15.22)
> 20	19 (13.10)	22 (16.79)	29 (31.52)
Length of admission			
1–10 days	74 (46.25)	83 (59.71)	98 (43.36)
11–20 days	48 (30.00)	35 (25.18)	69 (30.53)
21–30 days	19 (11.88)	11 (7.91)	25 (11.06)
> 30	19 (11.88)	10 (7.19)	34 (15.04)

fell (Table 3). Overall, the mean dose of psychotropic drugs received at hospital discharge increased from 1.77 DDD in 1981/82 to 2.23 DDD in 2001/02.

Trends in service use are presented in Table 4. While the mean number of outpatient contacts and the mean number of days spent in day-care facilities progressively rose, the mean number of bed days in a psychiatric ward in the six months before and after admission was stable. The Lavik score indicated that subjects admitted in 1981/82 were moderate users of psychiatric services,

Table 2 Number of patients receiving psychotropic and non-psychotropic agents in 1981/1982, 1991/1992 and 2001/2002

	1981/1982		1991/1992		2001/2002	
	n/N	% (CI)	n/N	% (CI)	n/N	% (CI)
Antipsychotic agents	75/160	46.88 (38.9, 54.9)	72/139	51.80 (43.1, 60.3)	139/228	60.96 (54.3, 67.3)
Two or more antipsychotic agents	8/75	10.66 (4.71, 19.93)	5/72	6.94 (2.29, 15.46)	24/139	17.26 (11.38, 24.59)
Antidepressive agents	33/160	20.63 (14.6, 27.7)	35/139	25.18 (18.2, 33.2)	122/228	53.51 (46.8, 60.1)
Two or more antidepressive agents	1/33	3.03 (0.07, 15.75)	1/35	2.85 (0.07, 14.91)	1/122	0.81 (0.02, 4.48)
Benzodiazepines	57/160	35.63 (28.2, 43.5)	91/139	65.47 (56.9, 73.3)	151/228	66.23 (59.6, 72.3)
Two or more benzodiazepines	5/57	8.77 (2.90, 19.29)	19/91	20.87 (13.06, 30.66)	35/151	23.17 (16.70, 30.73)
Two or more psychotropic agents*	48/119	40.33 (31.44, 49.71)	69/127	54.33 (45.26, 63.19)	170/216	78.70 (72.63, 83.96)
Anticholinergic agents	16/160	10.00 (5.8, 15.7)	6/139	4.32 (1.6, 9.15)	12/228	5.26 (2.7, 9.0)
Antiepileptic agents	10/160	6.25 (3.0, 11.1)	7/139	5.04 (2.0, 10.1)	38/228	16.67 (12.0, 22.1)
Agents for medical disorders	19/160	11.88 (7.3, 17.9)	26/139	18.71 (12.5, 26.1)	103/228	45.18 (38.5, 51.8)
Two or more agents belonging to any class**	70/127	55.11 (46.04, 63.94)	84/129	65.11 (56.22, 73.29)	189/221	85.52 (80.17, 89.88)

CI Confidence Interval
* Antidepressive agents, antipsychotic agents and benzodiazepines
** Antidepressive and antipsychotic agents, benzodiazepines, anticholinergic and antiepileptic agents, and agents for medical disorders

Table 3 Mean dose prescribed at hospital discharge, expressed as multiples of the defined daily dose of antipsychotic agents, antidepressant agents and benzodiazepines

	1981/1982		1991/1992		2001/2002	
	N	mean DDD (CI)	N	mean DDD (CI)	N	mean DDD (CI)
Antipsychotic agents	73	0.85 (0.64, 1.05)	72	0.73 (0.61, 0.86)	139	1.01 (0.88, 1.14)
Antidepressive agents	32	0.86 (0.74, 0.97)	35	1.01 (0.85, 1.17)	110	1.51 (1.39, 1.64)
Benzodiazepines	57	2.03 (1.76, 2.29)	90	1.81 (1.52, 2.10)	133	1.26 (1.10, 1.43)
All psychotropics	116	1.77 (1.49, 2.04)	126	2.00 (1.73, 2.26)	213	2.23 (2.03, 2.44)

DDD Defined Daily Dose; *CI* Confidence Interval

Table 4 Service use in the six months before and after admission

	1981/1982 (N = 160) mean (CI)	1991/1992 (N = 139) mean (CI)	2001/2002 (N = 228) mean (CI)
Outpatient contacts in the six months before admission	2.21 (1.42, 3.00)	4.56 (3.44, 5.68)	6.03 (3.81, 8.25)
Outpatient contacts in the six months after admission	4.15 (3.38, 4.91)	9.45 (7.79, 11.11)	11.31 (8.75, 13.87)
Days in day-care facilities in the six months before admission	0.10 (0.0, 0.24)	7.17 (3.04, 11.29)	8.76 (3.41, 14.11)
Days in day-care facilities in the six months after admission	0.70 (0.33, 1.06)	9.68 (5.28, 14.07)	20.09 (11.92, 28.26)
Bed days in psychiatric ward in the six months before admission	2.50 (1.10, 3.90)	2.98 (1.01, 4.95)	2.98 (1.43, 4.53)
Bed days in psychiatric ward in the six months after admission	9.40 (6.14, 12.65)	8.03 (4.79, 11.27)	8.62 (5.59, 11.65)
Lavik index of total consumption of services	43.69 (32.04, 55.34)	80.79 (57.95, 103.6)	109.91 (81.56, 138.2)

CI Confidence Interval

while those admitted in 1991/92 and in 2001/02 were high users of psychiatric services.

To investigate factors associated with AP, AD and BDZ discharge dose, multivariate analysis was applied (Table 5). After patients' sociodemographic and clinical characteristics were controlled for, admission in 2001/02 was positively associated with higher AD dose and lower BDZ dose. In contrast, admission in 2001/02, in comparison with admission during the previous two index periods, was not associated with higher AP doses. The number of AP and BDZ agents prescribed at hospital discharge was positively associated with total AP and BDZ discharge dose.

Discussion

In this study trends in the rate and dose of psychotropic drugs prescribed at patient discharge in the last 20 years were analyzed. In Italy in this period selective serotonin-reuptake inhibitors and newer antidepressants became available, as well as second-generation antipsychotic agents and non-benzodiazepine hypnotics, thus increasing the number of psychotropic agents available in the treatment of psychiatric conditions (Andretta et al. 2004; Ciuna et al. 2004). A PCR was used to identify all patients discharged during three index periods, and all

Table 5 Determinants of antipsychotic, antidepressant and benzodiazepine dose: linear regression analysis (bootstrapped 95 % CIs, 5000 repetitions)

Explanatory variable	Antipsychotic discharge dose		Antidepressant discharge dose		Benzodiazepine discharge dose	
	coefficient	Bias corrected 95 % CI	coefficient	Bias corrected 95 % CI	coefficient	Bias corrected 95 % CI
Gender (male = 0, female = 1)	−0.1549	−0.3342, 0.0373	0.0346	−0.1820, 0.2803	−0.2985	−0.6207, 0.0004
Age (years)	−0.0060	**−0.011, −0.0013**	−0.0052	−0.0135, 0.0022	−0.0032	−0.0126, 0.0077
Length of illness (years)	0.0036	−0.0043, 0.0127	−0.0028	−0.0124, 0.0066	0.0123	−0.0018, 0.0272
Length of current admission (days)	0.0013	−0.0011, 0.0084	0.0053	−0.0006, 0.0111	0.0030	−0.0014, 0.0093
Diagnosis (other = 0, psychosis = 1)	0.1380	−0.0805, 0.3246	−0.1558	−0.4791, 0.1399	0.0164	−0.3169, 0.3523
Number of agents of the same class prescribed at discharge	0.8572	**0.4407, 1.331**	0.6096	0.0, 1.0184	1.2984	**0.8324, 1.7200**
Lavik index	0.0007	**0.0003, 0.0011**	−0.0001	−0.0007, 0.0006	0.0001	−0.0005, 0.0009
Admission in 2001/2002 (no = 0, yes = 1)	0.0930	−0.1366, 0.3368	0.7013	**0.4526, 0.9632**	−0.7924	**−1.1679, −0.429**
Constant term	0.1930	−0.4292, 0.8228	0.4806	−0.1171, 1.1362	0.8297	0.0414, 1.665

Positive coefficients indicate that explanatory variables included in the model were correlated with higher doses; positive upper and lower limits of confidence intervals indicate a statistically significant positive association. Negative coefficients indicate that explanatory variables included in the model were correlated with lower doses; negative upper and lower limits of confidence intervals indicate a statistically significant negative association. *CI* Confidence Interval

prescriptions issued to this unselected sample of typical patients were recorded. No restriction to a specific diagnostic category or psychotropic drug class was imposed, the purpose being to show whether the increased availability of psychotropic agents increased the proportion of inpatients being treated with individual medication classes and the proportion receiving combined treatments with agents of the same class or of different classes. Service use data were in addition extracted from the PCR to investigate whether drug and service use showed similar trends.

The analysis highlighted an increasing proportion of subjects receiving AP, AD and BDZ treatment at discharge, and an increasing rate of subjects receiving AE and agents for medical disorders. Only the use of anticholinergic agents declined, although the small number of prescriptions limits the confidence of this finding, which cannot be attributed to the more favorable side-effect profile of newer AP agents, since the decline was observed before the introduction of these agents (Isacsson et al. 1999). The increasing use of BDZ was an unexpected finding, since the introduction of new AD agents, strongly supported in the pharmacological treatment of many anxiety disorders, should have theoretically caused a decreasing rate of BDZ users. Although BDZ users did not decline, a declining trend was observed in the average dose, expressed as multiples of the DDD, of BDZ prescribed at hospital discharge. In contrast, the average dose of AP and AD progressively increased. This leads to the hypothesis that incrementing the use of AD agents does not represent a public health tool for reducing the number of BDZ users, although it might represent a tool for reducing the total amount of BDZ consumption. This hypothesis is further supported by the multivariate analysis, which showed that, after controlling for several independent variables, patients admitted in 2001/02 were more likely to receive higher AD doses and lower BDZ doses. Obviously, these data need repli-

cation and confirmation from specific studies carried out in larger samples of patients enrolled in different settings and contexts of care, as well as from the analysis of national AD and BDZ sales data in different countries.

We found an increasing proportion of patients receiving two or more psychotropic drugs at discharge, which accounted for almost 80 % of cases in 2001/02, as compared with slightly more than 40 % twenty years before. No specific pattern of drug combinations was observed, although 60 % of those receiving two or more antipsychotics received simultaneous treatment with conventional and atypical agents. According to a recent survey comparing psychotropic drug prescribing patterns in acute psychiatric wards across Europe, the mean number of psychotropic agents prescribed per patient ranged from 1.73 in Germany to 3.21 in Spain (Bowers et al. 2004). These findings have implications, because we noticed that the number of psychotropic agents prescribed at hospital discharge, as already reported by other authors (Italian Collaborative Study Group 1999), was positively correlated with the total consumption of psychotropic drugs. This was confirmed by the multivariate analysis which highlighted that, after controlling for patient variables, the number of AP and BDZ agents prescribed was positively associated with the dose of AP and BDZ received, respectively.

It would be of clinical interest to understand the reasons why the rate and dose of psychotropic agents prescribed at patient discharge is on the increase. It might be the reflection, at a local level, of the increase in drug sales observed at a national level. A progressive rise in consumption of psychotropic agents has been observed in most western countries, and this has likely contributed to the increasing rate of subjects receiving treatment. A second contributing factor is severity of illness. Patients admitted in 2001/02 could have been more severely ill than those admitted during the previous two

index intervals. Although a direct measurement of severity of illness was not feasible in this study, given its retrospective design, the number of inpatient bed days in the six months before and after the index admission was not different in the three time periods, possibly reflecting similar psychopathological conditions. Length of index admission, another proxy indicator of severity of illness, was not different in the three periods. The lack of changes in quantitative aspects of inpatient care may well be due to the fact that the capacity of hospital facilities did not increase over the years, in spite of the increasing number of South-Verona patients seeking care. However, the three cohorts of subjects differed with respect to sociodemographic and clinical characteristics, and the use of day-care facilities and the number of outpatient contacts suggested a rise in service use, as also suggested by the Lavik index, a cumulative index of service consumption. These differences might reflect differences in patients' needs and clinical status, which might have ultimately contributed to determining different prescribing habits, or might reflect differences in service availability, admission criteria, staff availability or changes in prescribing recommendations. Longitudinal monitoring of service utilization in South-Verona showed that, after the implementation of the 1978 psychiatric reform, the implementation of a community-based system of psychiatric care produced a consistent increase in outpatient care, home visits and other community contacts (Tansella et al. 1998).

In addition to psychotropic drugs, a relevant proportion of patients were also dispensed agents for medical conditions, yielding an average number of 3.2 prescriptions in 2001/02, as compared with an average number of 1.85 prescriptions twenty years previously. These data do not specifically reflect the situation of patients with mental disorders, since similar trends have been observed in other patient populations. Lernfelt and colleagues, who investigated changes in drug treatment among elderly men and women over a 29-year period between 1971 and 2000 in Gothenburg, Sweden, showed that the proportion of drug users in the population increased from 60% to 79% in men and from 76% to 88% in women; the average number of drugs increased from 2.8 to 3.5 in men and from 2.8 to 4.0 in women (Lernfelt et al. 2003). These findings, as pointed out by the authors, could not be attributed to an increased morbidity but may be due to a better access to medical care or represent also a sign of overtreatment. In addition, it is possible that in the present sample of psychiatric patients the detection of medical diagnoses has become increasingly accurate, thus leading to an increased number of psychiatric patients receiving treatment for medical disorders. The finding that patients with psychiatric disorders receive an average number of drugs similar to that recorded among elderly men and women highlights a potentially serious emerging problem of polypharmacy involving agents belonging to different pharmacological classes, with possible negative consequences in terms of drug interactions and treatment adherence (Nosé et al. 2003).

Additional pharmacoepidemiological research is needed to clarify both the beneficial and, potentially, adverse effects associated with these trends in psychiatric pharmacotherapy. Empirical evidence for the efficacy of combining agents of the same pharmacological class or of different classes of psychotropic drugs is very limited (Miller and Craig 2002; Freudenreich and Goff 2002), and future trials are needed to test whether combination of agents provides additional benefits over monotherapy. In the meantime, clinicians should be warned that each patient should ideally be prescribed a limited number of agents, preferably in a single dosage form and at the lowest possible effective dose.

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