

Treatment Adherence and Persistence with Oral Second-generation Antipsychotics in Patients with Schizophrenia in Spain and Denmark

Charlotte Emborg¹, Kristian Tore Jørgensen², Mats Rosenlund³, Kenneth Starup Simonsen², Peter McMahon³, Anna-Greta Nylander², Jing Wang-Silvanto⁴, Julio Bobes⁵

¹Department of Clinical Medicine - Psychosis Research Unit, Aarhus University, Aarhus, Denmark; ²H. Lundbeck A/S, Valby, Denmark;

³IQVIA Solutions Sweden AB, Solna, Sweden; ⁴Otsuka Pharmaceutical Europe Ltd., Wexham, UK; ⁵Department of Psychiatry, University of Oviedo, Oviedo, Spain

Background

Schizophrenia is a heterogeneous and burdensome disease with a broad range of symptoms that can lead to loss of functioning and patient autonomy. Today, most patients with schizophrenia are treated with oral second-generation antipsychotics (SGAs); however, lack of treatment adherence and persistence may represent important treatment challenges which may lead to increased risk of relapse and hospitalization.^{1,2}

Objectives

The objective of the study was to investigate treatment adherence and treatment persistence of oral SGAs in patients with schizophrenia by using antipsychotic prescription data from databases in Denmark and Spain. Treatment adherence and persistence with oral SGAs were investigated in patients overall and in patients early in disease (defined as patients ≤ 35 years of age).

Results

Overall results for patients with schizophrenia

- Overall 2889 patients with schizophrenia were included from Spain (mean age 50 years, 41% women) and 31308 patients from Denmark (mean age 45 years, 42% women) (Table 1).
- As the Danish National Prescription Registry does not capture all drug prescriptions for patients newly diagnosed with schizophrenia (≤ 2 years after a schizophrenia diagnosis) and for patients in forensic care (equalling a total of 7587 patients overall and 4521 patients ≤ 35 years of age) these patients were not included in the description of antipsychotic treatment patterns. The remaining analysed study population comprised a total of 23721 patients (6384 patients age ≤ 35 years).
- On average, 2507 patients (87%) were prescribed antipsychotics (ATC group N05A) per year in Spain and each patient was prescribed a mean of 1.9 different antipsychotics. The majority of these patients were prescribed oral SGAs (n=1965 patients, 78%) (Table 1). In Denmark, 18788 patients (79% of 23721 patients) were prescribed antipsychotics, each patient was prescribed a mean of 1.7 different antipsychotics, and the majority were prescribed oral SGAs (n=14510, 77%).
- The mean PDC for patients who were prescribed oral SGAs was 84% in Spain and 80% in Denmark (Figure 1).
- In Spain, the proportion of patients who discontinued oral SGAs within 6 months and 12 months of follow-up were 20% and 33%, respectively. In Denmark, 25% and 40% discontinued oral SGAs within 6 and 12 months of follow-up, respectively (Figure 2).

Results for patients age ≤ 35 years at study entry

- In Spain, 605 patients were age ≤ 35 years at study entry (mean 32 years, 26% women), while in Denmark, 10905 patients were age ≤ 35 years (mean 28 years, 42% women) (Table 1).
- On average per year in Spain, 509 (84%) patients age ≤ 35 years were prescribed antipsychotics (mean 1.9 different antipsychotics prescribed per year), among which 406 (80%) were prescribed oral SGAs. In Denmark, 5212 (82%) were prescribed antipsychotics (mean 1.8 different antipsychotics prescribed per year) among which 4504 patients (86%) were prescribed oral SGAs (Table 1).
- Patients age ≤ 35 years who were prescribed oral SGAs had a mean PDC of 80% in Spain and 77% in Denmark (Figure 1).
- The proportions of patients age ≤ 35 years who had discontinued their oral SGA treatment within 6 and 12 months were 25% and 40% in Spain and 37% and 56% in Denmark, respectively (Figure 2).

Methods

- Schizophrenia diagnosis and antipsychotic prescription data were available from electronic medical records from the Spanish Longitudinal Patient Database (an IQVIA database) comprising a representable sample of 124 psychiatry clinics in Spain, and from the Danish National Patient Register and the Danish National Prescription Registry in Denmark.
- Patients with a diagnosis of schizophrenia (Spain ICD-9: 295.0-295.6, 295.8-295.9; Denmark ICD-10: F20.00 – F20.99) were included in the study and followed from the start of 2013 to end of 2016 or from their first diagnosis of schizophrenia if documented after January 1st 2013.
- Antipsychotic treatment adherence and persistence were estimated using prescription data issued by one of 124 psychiatry clinics (Spain) or at prescriptions filled and dispensed at community pharmacies (Denmark).
- Antipsychotic treatment adherence was defined as the proportion of days covered (PDC) by drug supply for each antipsychotic treatment episode (Number of days drug

supply / Numbers of days between first prescription to last prescription dates*100) within a max period of one year. PDC was not calculated for antipsychotic drugs prescribed only once, and drug supply from the last recorded prescription was excluded. PDC was capped at 100%. Number of days' supply for each prescription is according to prescribed daily dose, or if missing, number of defined daily doses (DDD) prescribed.

- Antipsychotic treatment persistence was estimated for each treatment and described as the proportion of patients with a treatment discontinuation within 6 and 12 months after the start of follow-up or treatment initiation, whichever came later. A treatment discontinuation was defined as the first day of a ≥ 60 days treatment gap for each treatment.
- Treatment adherence and persistence were investigated in all patients overall and in patients ≤ 35 years old at study entry.

Table 1

	Spain		Denmark	
	Overall	Age ≤ 35 years	Overall	Age ≤ 35 years
Total number of patients (%)	2889 (100%)	605 (21%)	31308 (100%)	10905 (35%)
Age, mean years (SD)	49.9 (14.6)	31.6 (4.7)	44.5 (15.3)	28.0 (5.4)
Women, n (%)	1170 (40.5%)	158 (26.1%)	13201 (42.2%)	4533 (41.6%)
Analysed study population*	2889 (100%)	605 (100%)	23721 (76%)	6384 (59%)
Patients prescribed APs (N05A), n (% of analysed study population)	2507 (86.8%)	509 (84.1%)	18788 (79.2%)	6384 (81.6%)
Number of different APs prescribed, mean number per year (SD)	1.92 (1.30)	1.88 (1.35)	1.70 (0.88)	1.75 (0.95)
Patients prescribed oral SGAs, n (% of patients prescribed APs)	1965 (78.4%)	406 (79.8%)	14510 (77.2%)	4504 (86.4%)

APs, antipsychotics; SD, standard deviation; SGA, second-generation antipsychotics
*In Denmark, patients newly diagnosed with schizophrenia (≤ 2 years after a schizophrenia diagnosis) and patients in forensic care (equalling a total of 7587 patients overall and 4521 patients ≤ 35 years of age) were not included in the description of AP treatment patterns. The remaining analysed study population comprised a total of 23721 patients (6384 patient age ≤ 35 years).

Figure 1. Adherence: Proportion of days covered by drug supply in patients on oral second-generation antipsychotic therapy in the total population and in the younger population

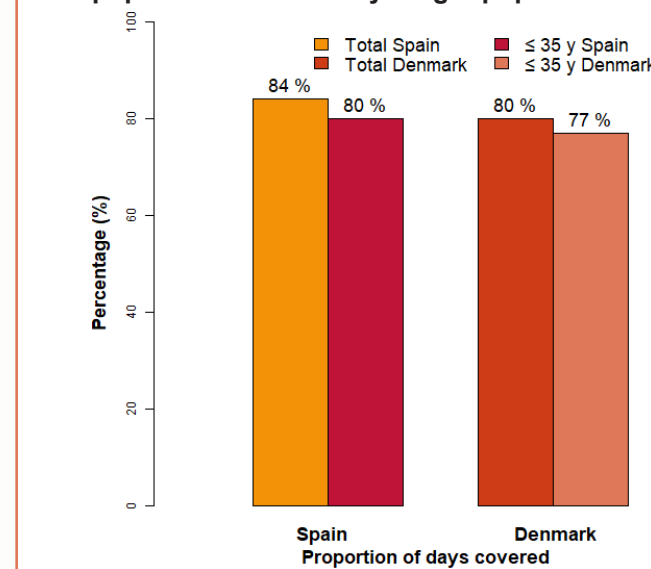
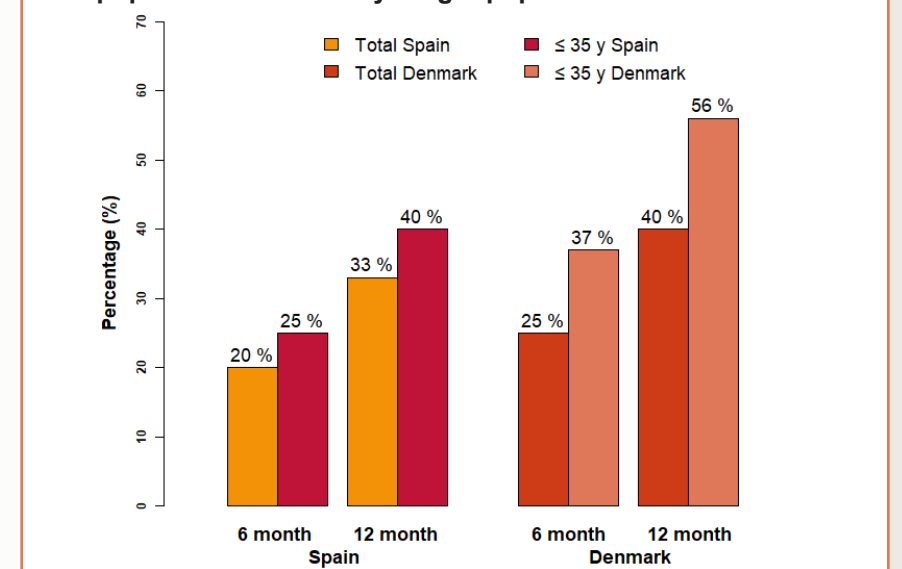


Figure 2. Persistence: 6 and 12 months discontinuation rates in patients on oral second-generation antipsychotic therapy in the total population and in the younger population



Limitations

- In Denmark, forensic patients and patients during their first 2 years after first diagnosis of schizophrenia were excluded because their drug prescriptions are not captured by the Danish National Prescription Registry used in this study.
- In Spain, the included patients were all seen in specialist psychiatry clinics and these may not represent all patients with schizophrenia.
- In both countries, adherence and persistence were estimated from prescription data on issued prescriptions in Spain and filled prescriptions in Denmark. Since it was not possible to assess if patients actually took their medication, the true adherence and persistence may have been lower than estimated in this study.
- The reason for each patient to discontinue treatment with oral SGAs could not be identified from the available data. Known factors related to treatment discontinuation are inadequate efficacy or occurrence of adverse events.^{3,4}

Conclusions

- Results from Spain and Denmark indicated that the majority of patients with schizophrenia are predominantly receiving oral SGA therapy, and that these patients in general have about 80% of days covered by drug supply enabling a good treatment adherence.
- A relatively large proportion of patients with schizophrenia discontinued their oral SGA therapy within one year of follow-up after treatment initiation. In both Spain and Denmark treatment discontinuation was observed to be more pronounced in younger patients than in patients overall, with 56% of patients age ≤ 35 years discontinuing their oral SGA therapy within one year in Denmark.
- These results highlight the unmet need for alternative oral antipsychotics to improve treatment persistence and meet the needs of individual patients with schizophrenia.
- Further research on the reasons behind the relatively low treatment persistence is warranted.

References

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