Transition in care in persons with antidepressant prescription in naturalistic conditions

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Background. Few studies have explored transition to psychiatric care in persons treated by antidepressants in primary care.

Objective. To assess the rates of transition in care after a dispensing of antidepressant and the characteristics associated with transition from primary to psychiatric care.

Methods. A follow-up study of persons starting antidepressant treatment was carried out on a representative sample of the 2005–07 French Social Security Insurance national database. Prescribers were categorized as GPs, hospital practitioners (as a proxy for public psychiatrist), private psychiatrists and other private specialists. Transition in care was defined as a prescription of psychotropic drugs by a prescriber belonging to a category different from that of the index antidepressant prescriber.

Results. Eighty per cent of incident antidepressant treatments were initiated by a GP and 28% of persons transited in care. The most frequent pattern was transition from a GP to a hospital practitioner (8%) or to a private psychiatrist (5%). Transition to psychiatric care was independently associated with younger age and markers of illness severity (psychiatric chronic illness status, duration of the index antidepressant treatment >6 months and prescription of other classes of psychotropic drugs). Almost all treatments with antipsychotics or mood stabilizers were initiated after the transition to a specialist.

Conclusions. Transition to psychiatric care seemed coherent with distribution of tasks between primary and secondary care according to illness severity. Further studies using detailed clinical information are required to assess not only the clinical appropriateness of psychiatric referral but also lack of referral in antidepressant users.

Keywords. Antidepressant, primary care, referral, secondary care.

Introduction

GPs play a growing role in the initiation of antidepressant treatments.\textsuperscript{1} Although most persons treated by antidepressants are currently managed in primary care,\textsuperscript{2–5} some of them require specialized mental health care. Pathways to psychiatric care and characteristics associated with psychiatric referral have been explored by several studies.\textsuperscript{6–9} However, few studies have explored transition to specialized care in persons treated by antidepressants.\textsuperscript{10} Considering the marked increase in antidepressant prescriptions in the general population,\textsuperscript{11,12} it is of interest to explore how persons using these drugs are managed in real-life settings, particularly regarding their pattern of transition from primary care to mental health care.

The objectives of this study were to assess the rates of transition in care after a dispensing of antidepressant and the characteristics associated with transition from primary to psychiatric care.

Methods

Design and setting

A follow-up study of persons starting antidepressant treatment was performed using a fixed cohort. Data were drawn from the 2005–07 French Social Security Insurance (SSI) national database, which includes data on community claims for reimbursement of drugs on the market.\textsuperscript{13} Owing to space and memory constraints, information on health care consumption of the whole sample of SSI beneficiaries (nearly 75% of the French general population) is conserved only for 2 years. The present study was carried out on a database called ‘Echantillon Généraliste des Bénéficiaires’ (EGB) (meaning Generalist Sample of Beneficiaries) including a representative sample of 1% of persons insured by the SSI for whom information on health care consumption is conserved up to 20 years.\textsuperscript{14} The randomization criterion is the SS identification number. The identification of persons included in the EGB sample
is protected by an anonymization process with two cryptographic levels, a procedure conforming to French data protection legislation.

**Sample**

Persons from the EGB sample considered in the present study fulfilled the following inclusion criteria: (i) aged $\geq 18$ years; (ii) incident dispensing of antidepressant in 2005–06, defined as no dispensing of antidepressant in the prior 6 months; (iii) at least two dispensings of antidepressant over the follow-up period in order to exclude persons with only one prescriber over the follow-up.

**Characteristics of psychiatric referral in France**

In France, GPs are in theory the gatekeepers to psychiatric care. However, referral by a GP is not strictly mandatory. All persons aged 16–25 years have direct access to psychiatrists. Other persons may directly consult private psychiatrists without GP referral if they pay extra costs (which can be refunded by private insurance schemes). They may also directly consult a hospital psychiatrist as outpatient psychiatric treatment is free of charge in community mental health care centres.

**Type of prescriber and transition in care**

Only prescribers of psychotropic drugs were considered in the present study. For each dispensing of psychotropic drug, the specialty of private practice prescribers (including GPs and private psychiatrists) was identified by a specific code in the SSI database. Hospital practitioners (including public psychiatrists) were all identified with a single code irrespective of their specialty. As only prescribers of psychotropic drugs were included in the present study, we considered that the category ‘hospital practitioners’ was a proxy for public psychiatrists. We used the following categorization of prescribers: (i) GPs, (ii) hospital practitioners, (iii) private psychiatrists and (iv) other private specialists.

Transition in care was defined as prescription of psychotropic drugs by a prescriber belonging to a category different from that of the index antidepressant prescriber, e.g. transition from a GP to a psychiatrist. Hence, this definition did not include transition from one prescriber to another prescriber of the same category, e.g. change from a GP to another GP. We used a broad definition of transition including prescription of any psychotropic drugs by a specialist and not only prescription of an antidepressant. This choice was motivated by the fact that patients treated by antidepressant may be referred to a specialist when they present with refractory mood or anxiety symptoms but also with unexpected reactions to antidepressant treatment, such as occurrence of a manic switch or of psychotic symptoms. In such cases, the specialist is likely to stop the antidepressant treatment and to initiate other treatments, such as mood stabilizers or antipsychotics. As we wished to explore the proportion of persons who initiated such a treatment after transition, excluding the persons who did not continue the antidepressant treatment after transition would have biased the sample towards selection of persons less likely to be prescribed such psychotropic drugs. Patients were considered to have transited irrespective of the existence of subsequent prescriptions of psychotropic drugs by the index prescriber. Transition in care was explored over the whole follow-up (during and after the index episode of antidepressant treatment).

**Psychotropic treatment**

Psychotropic drugs were classified using the WHO Anatomical Therapeutic Chemical (ATC) index and categorized as: (i) antidepressants, (ii) anxiolytics/hypnotics, (iii) antipsychotics and (iv) mood stabilizers (see Table 1).

Duration of antidepressant treatment episode was categorized as (i) ‘short’ if $<168$ days (defined hereafter as $<6$ months), (ii) ‘long’ if $\geq 168$ days (defined hereafter as $\geq 6$ months). The method used to calculate duration of antidepressant treatment episode has been previously described. Briefly, duration was calculated irrespective of the types of antidepressants prescribed, i.e. without taking into account the event of switching from an antidepressant product to another over the episode. Since dispensings are for a maximum of 28 days, discontinuation of antidepressant treatment was considered to have occurred in the event of non-renewal 56 days after the last dispensing (i.e. the 28-day period following a 28-day period with antidepressant treatment).

**Other variables of interest**

The EGB database includes data on demographic characteristics: age, gender and welfare benefit for persons with very low income (couverture maladie universelle complémentaire, CMU-C). Diagnoses or indication for prescribing are not collected in this database. The status ‘long-duration disease’ may be used as a proxy for presence of a serious chronic illness. This status, which gives access to treatment free of charge, is restricted to persons presenting with a chronic and costly disease (e.g. disabling stroke, cancer, psychosis). In the present study, this characteristic was categorized as ‘no chronic illness’ versus ‘psychiatric chronic illness’ versus ‘other chronic illness’.

**Statistical methods**

Analyses were performed using STATA 11. We investigated the characteristics of patients with or without transition from a GP to a private psychiatrist or a hospital practitioner (as a proxy for public psychiatrist) using Cox proportional hazards regression
models. Person-days of follow-up were calculated from the first dispensing date of an antidepressant by a GP to the first dispensing date of a psychotropic drug by a private psychiatrist or a hospital practitioner or to the end of the follow-up period. Hazard ratios (HR) and 95% confidence intervals (CIs) were estimated using the Efron approximation to handle events occurring at the same time in different patients (ties).

The following demographic and clinical variables were a priori entered in the multivariate models (i.e. not selected on the basis of findings of prior univariate analyses); hence, the HR for a given variable was adjusted for all the other variables: (i) age categorized into seven categories, (ii) gender, (iii) welfare benefit, (iv) chronic illness status, (v) duration of index episode of antidepressant treatment, (vi) other classes of psychotropic drugs. HR for linear trend was calculated for age, giving the effect size of the increased probability of transition for moving from one category to the next.

Results

Characteristics of the sample

The 19,975 patients fulfilling the inclusion criteria had a mean age of 50.7 years (SD 17.5) and 68.1% were females. The median duration of follow-up was 830 days (interquartile range 647–979, range 365–1089). Around one-third (n = 6388; 32%) presented with a single episode of antidepressant treatment, a quarter (n = 5345; 26.8%) with two episodes and nearly half (n = 8242; 41.3%) with three episodes or more (maximum 15).

Type of prescribers

GPs were most often the index prescribers of antidepressant treatment (n = 16,150; 80.9%), followed by hospital practitioners (n = 1864; 9.3%), private psychiatrists (n = 1164; 5.8%) and other private specialists (n = 797; 4%). Over the follow-up period, most

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**Table 1** Comparison of patients with and without transition to private psychiatrist or hospital practitioner after index prescription of antidepressant (AD) by a GP analyses. Cox survival multivariate analyses

<table>
<thead>
<tr>
<th>Only GP, N = 12,900 (82.8%)</th>
<th>Private psychiatrist, N = 1079 (6.9%)</th>
<th>Hospital practitioner, N = 1593 (10.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–24</td>
<td>506 (3.9)</td>
<td>56 (5.2)</td>
</tr>
<tr>
<td>25–34</td>
<td>1865 (14.5)</td>
<td>255 (23.6)</td>
</tr>
<tr>
<td>35–44</td>
<td>2908 (22.5)</td>
<td>304 (28.2)</td>
</tr>
<tr>
<td>45–54</td>
<td>2711 (21.0)</td>
<td>262 (24.3)</td>
</tr>
<tr>
<td>55–64</td>
<td>1902 (14.7)</td>
<td>127 (11.8)</td>
</tr>
<tr>
<td>65–74</td>
<td>1353 (10.5)</td>
<td>48 (4.5)</td>
</tr>
<tr>
<td>≥75</td>
<td>1655 (12.8)</td>
<td>27 (2.5)</td>
</tr>
</tbody>
</table>

| aHR linear trend (95% CI)    | Reference                            | 0.76 (0.73–0.79) P < 0.01 | 0.95 (0.92–0.98) P < 0.01 |
| Gender men                   | 3849 (29.8)                          | 362 (33.6)                | 558 (35.0)                |
| aHR (95% CI)                 | Reference                            | 1.1 (0.9–1.2) P = 0.42    | 1.1 (1.0–1.2) P = 0.16    |
| Welfare benefit              | 1190 (9.2)                           | 98 (9.1)                  | 215 (13.5)                |
| aHR (95% CI)                 | Reference                            | 0.6 (0.5–0.8) P < 0.01    | 1.3 (1.1–1.5) P < 0.01    |
| Serious chronic illness      |                                      |                          |                                        |
| Psychiatric                  | 233 (1.8)                            | 81 (7.5)                  | 134 (8.4)                 |
| aHR (95% CI)                 | Reference                            | 1.6 (1.2–2.0) P < 0.01    | 2.2 (1.8–2.7) P < 0.01    |
| Other                        | 2476 (19.9)                          | 117 (10.8)                | 510 (34.2)                |
| aHR (95% CI)                 | Reference                            | 0.8 (0.5–0.8) P = 0.01    | 2.0 (1.8–2.2) P < 0.01    |
| Duration of first AD episode |                                      |                          |                                        |
| ≥6 months                    | 2196 (17.0)                          | 298 (27.6)                | 361 (22.7)                |
| aOR (95% CI)                 | Reference                            | 1.9 (1.6–2.1) P < 0.01    | 1.4 (1.2–1.5) P < 0.01    |
| Other drugs over follow-up   |                                      |                          |                                        |
| Anxiolytics/hypnotics         | 10,838 (84.0)                        | 1032 (95.6)               | 1485 (93.2)               |
| aHR (95% CI)                 | Reference                            | 3.5 (2.6–4.6) P < 0.01    | 2.1 (1.8–2.6) P < 0.01    |
| First-generation AP           | 1031 (8.0)                           | 258 (23.9)                | 449 (28.2)                |
| aHR (95% CI)                 | Reference                            | 2.3 (1.9–2.6) P < 0.01    | 2.5 (2.2–2.8) P < 0.01    |
| Second-generation AP         | 250 (1.9)                            | 140 (12.9)                | 195 (12.2)                |
| aHR (95% CI)                 | Reference                            | 3.0 (2.4–3.7) P < 0.01    | 2.3 (1.9–2.7) P < 0.01    |
| Mood stabilizers             | 322 (2.5)                            | 131 (12.1)                | 155 (9.7)                 |
| aHR (95% CI)                 | Reference                            | 2.2 (1.8–2.7) P < 0.01    | 1.9 (1.6–2.3) P < 0.01    |

aAdjusted hazard ratio (95% CI).
bBenefit for persons with very low income (couverture maladie universelle complémentaire).
cLong duration disease status giving access to treatment free of charge (see text).
dBenzodiazepines, carbamates and others.
eAntipsychotics.
fAmisulpride, aripiprazole, clozapine, olanzapine and risperidone.
gLithium, sodium divalproate, valpromide, carbamazepine, lamotrigine, oxcarbazepine and topiramate.
patients \((n = 18324; 91.7\%)\) had at least one prescription of psychotropic drugs by a GP, \(3901 (19.5\%)\) by a hospital practitioner, \(2595 (13\%)\) by a private psychiatrist and \(1675 (8.4\%)\) by another private specialist. In the latter case, the three most frequent specialties were neurologists \((n = 524; 2.6\%)\), rheumatologists \((n = 262; 1.3\%)\) and cardiologists \((n = 106; 0.5\%)\).

**General pattern of transition**

Most persons \((n = 14317; 71.7\%)\) had a single type of prescriber: only GPs \(n = 12900 (64.6\%)\), only hospital practitioners \(n = 634 (3.2\%)\), only private psychiatrists \(n = 517 (2.6\%)\) and only other private specialists \(n = 266 (1.3\%)\). For persons \((n = 5658; 28.3\%)\) with at least two types of prescriber over the follow-up period, the pattern of index transition is given in Figure 1. Half of the patients with antidepressant first prescribed by GPs transited to a hospital practitioner and one-third to a private psychiatrist. Most patients with antidepressant first prescribed by a specialist transited to a GP. The median duration between the index dispensing of antidepressant and the index transition was 139 days (interquartile range 45–349).

**Characteristics associated with transition from a GP to a psychiatrist**

Cox survival multivariate analyses comparing patients with and without transition are shown in Table 1. A linear trend was found in the association between age and transition, i.e. the younger the patient, the higher the probability of transition. Welfare benefit was less frequent in patients who transited to private psychiatrists and more frequent in those who transited to hospital practitioners. Compared to patients without transition, patients with transition were more likely to present with a chronic illness status. Those who transited to private psychiatrists were more likely to present with a chronic psychiatric illness status and less frequently with the other chronic illness status, while patients who transited to hospital practitioners presented more frequently with both chronic psychiatric and other chronic illness status.

Antidepressant treatment was more frequently of long duration in patients with transition and they were more likely to be prescribed other classes of psychotropic drugs. We explored which classes of psychotropic drugs were initiated after the transition during the index episode of antidepressant in patients who transited to a private psychiatrist \((n = 467)\) or to a hospital practitioner \((n = 581)\). Half of anxiolytics/hypnotics were initiated after transition \((private n = 234, 51.8\%; hospital n = 287, 53.2\%)\). Most antipsychotics and mood stabilizers were initiated after transition (FGAPs: private \(n = 96, 76.4\%; hospital n = 120, 72.3\%; SGAPs: private \(n = 46, 80.1\%; hospital n = 59, 86.8\%\); mood stabilizers: private \(n = 48, 88.9\%; hospital \(n = 46, 82.1\%)\).

As patients were included in the cohort after the first dispensing of antidepressant treatment by a GP, we cannot exclude that some of them were misclassified as transiting to a specialist since they were already prescribed psychotropic drugs by private or hospital psychiatrists before the index date. We performed further analyses in the sample of persons \((n = 12580)\) with index dispensing by a GP and with data available on dispensing of psychotropic drugs for the 3-month period preceding the index data. Of the persons who did not transit to a specialist \(24 (0.2\%)\) and \(226 (2.2\%)\) were prescribed a psychotropic drug before the index data by a private psychiatrist or a hospital practitioner, respectively. These proportions were \(34 (4.1\%)\) and \(21 (2.5\%)\) for those who transited to a private psychiatrist and \(5 (0.4\%)\) and \(140 (11.3\%)\) for those who transited to a hospital practitioner. After exclusion of the 448 patients \((3.6\%)\) who had a dispensing by a specialist before the index date, the direction and the size of the associations were similar (data not shown). The only exception was the association between gender and transition to a hospital practitioner who became significant \((aHR = 1.1, 95\% CI 1.0–1.2, P = 0.05)\).

**Discussion**

Antidepressant treatment was initiated by a GP in 80% of persons and was prescribed only by a GP for
65% of them. More than a quarter of persons transited to another type of prescriber over the follow-up period, with a median time to transition of 5 months. The most frequent pattern for the first transition was from a GP to a hospital practitioner (8%) or to a private psychiatrist (5%). Characteristics independently associated with transition from a GP to a hospital practitioner or a private psychiatrist were younger age, psychiatric chronic illness status, duration of index antidepressant treatment >6 months and dispensing of other classes of psychotropic drugs. Almost all treatments of antipsychotics or mood stabilizers were initiated after the transition to a psychiatrist.

Our findings are very close to those obtained in a comparable study on antidepressant users carried out on a Dutch administrative database, reporting a 5% transition rate from GP to psychiatrist over the index episode of antidepressant and a median time to transition of 4 months. The main differences between the studies are that only transition over the index episode and prescribers of antidepressants were considered in the Dutch study, possibly excluding persons with psychiatric adverse effects of antidepressant treatment (such as manic switch) leading to psychiatric referral. In accordance with prior studies, we found that transition to psychiatric care was higher in younger persons, with an inverse dose-response relationship between age and transition, which was particularly marked for transition to private psychiatrists. This may be explained by differences between younger and older persons regarding the severity of the disorder requiring antidepressant treatment or by the fact that the threshold severity for psychiatric referral is higher in elderly persons. Males had a greater likelihood for transition to psychiatric care as in prior studies. Other characteristics independently associated with transition to psychiatric care might be considered as markers of illness severity, a factor that has consistently been found to predict referral in prior studies. Duration of antidepressant treatment, which was also associated with psychiatric referral in the Dutch study, is indeed likely to reflect the existence of recurrent, chronic or refractory symptoms rather than differences in application of guidelines, as suggested by a study carried out in this sample showing that a long duration of index antidepressant treatment was associated with a higher risk of relapse. In accordance with prior findings, patients with a comorbid somatic illness were less likely to transit to private psychiatrists. However, the converse association was found for hospital practitioners, may be as a consequence of the inclusion of specialists other than psychiatrists in this category. A noteworthy finding was that antipsychotics and mood stabilizers, which can be considered as markers of severe mental illness, were seldom prescribed in persons treated only by GPs and were most frequently initiated after the transition to a specialist. In spite of the growing use of these drugs, GPs may still consider their initiation as a specialized task.

Strengths and limitations
This study was carried out in a large cohort representative of the general population, with all dispensings of psychotropic drugs and all changes of prescribers documented over the follow-up period. The findings should be interpreted in the light of potential limitations. Specialists other than psychiatrists prescribing psychotropic drugs may have been included in the category hospital practitioner. However, the profile of persons with transition to a hospital practitioner was very close to that of persons with transition to a private psychiatrist, except regarding the higher frequency of welfare benefit and chronic somatic illness in persons transiting to a hospital practitioner.

Transition in care was documented by prescription of psychotropic drugs by a new prescriber. Hence, as the proportion of private psychiatrists practising only psychotherapy is relatively high in France, we could have underestimated the frequency of persons who transited to a psychiatrist. Our definition of transition also implies that we could not assess whether patients were referred to the new prescriber by the index one or were self-referred.

Since no information on diagnosis was available, indications for antidepressant prescribing might have been for psychiatric illnesses other than depression such as anxiety disorder, as well as for somatic illnesses. Furthermore, we cannot rule out that some antidepressant users did not present with any clinical indication for these treatments.

Since patients were selected on the basis of a 6-month pre-treatment period without antidepressant dispensing, persons with pre-existing episodes of antidepressant prescribing were included. This selection bias may have favoured the inclusion of persons at higher risk of relapse/recurrence. Hence, it might have contributed to increasing the proportion of persons with transition to a specialist.

Conclusions
In spite of the relatively free access to private or public mental health professionals in France compared for example to UK or the Netherlands, transition to psychiatric care was the exception rather than the rule in persons with an index prescription of antidepressant by a GP. Hence, in developed countries, patients' characteristics might play a greater role than health care organization regarding psychiatric referral. In our study, transition to psychiatric care seemed coherent with distribution of tasks between primary and secondary care, at least regarding illness severity. These
findings suggest that referral to secondary care generally met the patients’ needs. However, further studies providing more detailed clinical information are necessary to assess not only the appropriateness of psychiatric referral but also lack of referral in antidepressant users. The latter issue is particularly crucial regarding assessment of unmet needs in elderly persons as the likelihood of transition to psychiatric care decreases with age irrespective of illness severity.

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Conflicts of interests: none.

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