

## ORIGINAL PAPER

# Utilization of psychotropic drugs by patients consulting for sleeping disorders in homeopathic and conventional primary care settings: the EPI3 cohort study

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**Background:** Utilization of sedative hypnotic drugs for sleeping disorders (SD) raises concerns, particularly among older people. This study compared utilization of conventional psychotropic drugs for SD among patients seeking care from general practitioners (GPs) who strictly prescribe conventional medications (GP-CM), regularly prescribe homeopathy in a mixed practice (GP-Mx), or are certified homeopathic GPs (GP-Ho).

**Methods:** This was a French population-based cohort study of GPs and their patients consulting for SD, informed through the Pittsburgh sleep quality index (PSQI) questionnaire. Information on psychotropic drugs utilization was obtained from a standardized telephone interview at inclusion, one, three and 12 months.

**Results:** 346 patients consulting for SD were included. Patients in the GP-Ho group experienced more often severe SD (41.3%) than patients in the GP-CM group (24.3%). Adjusted multivariate analyses showed that patients who chose to be managed by GP-Ho were less likely to use psychotropic drugs over 12 months as opposed to the GP-CM group, with Odds ratio (OR) = 0.25; 95% confidence interval (CI): 0.14 to 0.42. Patients in the GP-Mx group also used less psychotropic drugs but the result was not statistically significant (OR = 0.67; 95% CI: 0.39–1.16). Rates of clinical improvement of the SD did not differ between groups.

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**Conclusions:** Patients with SD who chose to consult GPs certified in homeopathy consumed less psychotropic drugs and had a similar evolution of their condition to patients treated with conventional medical management. This result may translate in a net advantage with reduction of adverse events related to psychotropic drugs. *Homeopathy* (2015) ■, 1–6.

**Keywords:** Insomnia; Homeopathy; Primary care

## Introduction

Sleeping disorders (SD) are highly prevalent worldwide and represent a leading reason for consultation in primary care.<sup>1,2</sup> Widespread utilization of sedative hypnotic drugs raises serious risk concerns, particularly among older people as shown in systematic reviews.<sup>3,4</sup> The prevalence of SD in homeopathic care also ranks high, only surpassed by low-back pain.<sup>5</sup> Patients who seek homeopathic care differ from those seen in conventional medicine, but the diagnostic make-up of their consultations has been described as similar.<sup>6</sup> The efficacy of homeopathic care has shown inconsistent results in systematic reviews of SD,<sup>7,8</sup> but its potential to reduce psychotropic drug utilization has been raised.<sup>9</sup> In France, homeopathy is practiced exclusively by physicians and is partly reimbursed by the National Health Insurance. This situation provided the opportunity to compare utilization of psychotropic drugs for SD between patients who seek care with physicians who prescribe exclusively conventional medications (GP-CM), regular prescribers of homeopathy within a mixed practice (GP-Mx), or certified homeopathic GPs (GP-Ho), and to assess in parallel the clinical evolution of their SD in a population-based one-year cohort study.

## Materials and methods

### Study design and selection of study subjects

This cohort study was conducted in France between 2007 and 2008 within the nationwide EPI3 survey of primary care practice in a representative sample of GPs and their patients.<sup>1</sup> The 'EPI3' survey included three epidemiological follow-up cohort studies of common reasons for consultation in primary care, one of which focused on patients with SD (the remaining being musculoskeletal disorders and respiratory infections). The sample was drawn using a two-stage sampling process. First, a random sample of GPs was drawn from the French National Directory of Physicians in primary care. Sampling of GPs was stratified according to their declaration of prescribing preferences, obtained by telephone at the time of recruitment and categorized into three groups: strictly prescribers of conventional medications (GP-CM) who declared never or rarely prescribing homeopathy; regular prescribers of homeopathy in a mixed practice (GP-Mx); and certified homeopathic GPs (GP-Ho). This classification of GPs by type of management served as the basis for comparing their patients. As GPs in the three groups were free to prescribe conventional and/or homeopathic drugs, this study did not

compare patients by the type of prescription issued but only by the type of physician (prescribing preferences) they had chosen to consult. The second-stage sampling consisted of a one-day survey of all patients attending the medical practice of each participating GP during which a trained research assistant surveyed all patients in the waiting room. For this cohort study, consenting adult patients consulting for SD were invited to participate in a baseline telephone interview within 72 h of recruitment, which included the French adaptation of the Pittsburgh sleep quality index (PSQI) questionnaire.<sup>10</sup> Patients scoring on this scale (PSQI score  $\geq 1$ ) were then invited to follow-up interviews at one, three and 12 months. Primary SD was defined as no motive reported for the SD in the PSQI questionnaire. Severity of the SD at baseline was obtained from the PSQI as a result of being associated with one or more of the following complications: difficulty staying awake while driving, eating meals or engaging in social activities one or more times a week, or having problems maintaining sufficient enthusiasm to get things done (somewhat or persistent problem).

### Information collected

At inclusion, GPs completed a medical questionnaire for each patient surveyed, including all drugs (conventional and homeopathic) prescribed that day. All consenting participants completed a self-administered questionnaire at inclusion (waiting room), collecting information on socio-demographics, lifestyle, history of hospitalization in the previous 12 months, and whether the physician consulted was the patient's regular physician or not. Follow-up telephone interviews included PSQI scores at one and three months, and patient's history of drug utilization (conventional and homeopathy) and injuries (resulting from a fall, motor vehicle collision, practice of sports, or occupationally-related, all of which pertinent to SD and use of psychotropic drugs) up to 12 months. Drug utilization, whether prescribed, obtained over the counter or from the family pharmacy, was assessed using a standardized method known as Progressive Assisted Backward Active Recall (PABAR), previously validated against medical prescriptions.<sup>11,12</sup> Drugs were automatically recorded using the anatomical therapeutic chemical classification index (ATC), 2009 revision.

### Outcomes and statistical analysis

Three outcomes were assessed at follow-up. The main outcome, consumption of psychotropic drugs for SD, was defined at each interview interval (one, three and 12

months) as the proportion of patients declaring at least one utilization since the previous interview of drugs belonging to the ATC classes N05B (anxiolytics), N05C (hypnotics and sedatives) or N06A (antidepressants) prescribed to treat their SD. The two other outcomes were persistence of the SD as reported by the PSQI questionnaire (score  $\geq 1$ ) at the one-month and three-month follow up, and reporting of any injury resulting from a fall, motor vehicle collision, sport, or occupation at any time during the entire 12-month follow up.

Differences at baseline between GP-CM, GP-Mx and GP-Ho groups were performed using chi-square test on proportions. A propensity score was computed for each participant in the study on their probability of belonging to either GP-Mx or GP-Ho groups compared to the GP-CM group, according to all variables listed in Table 1. All three outcomes were compared across the three groups using the GP-CM group as the reference in logistic regression adjusted for baseline characteristics (propensity score) and stratified for the severity of the ADD at baseline. All

**Table 1** Baseline characteristics of patients with sleeping disorders by type of medical practice\* (N = 346)

|  | GP-CM<br>(N = 84)<br>% | GP-Mx<br>(N = 119)<br>% | GP-Ho<br>(N = 143)<br>% |
|--|------------------------|-------------------------|-------------------------|
| <b>Gender (female)</b>                               | 75.0                   | 74.8                    | 76.9                    |
| <b>Age (years)</b>                                   |                        |                         |                         |
| 18–39  | 17.9                   | 25.2                    | 23.1                    |
| 40–59  | 42.9                   | 48.7                    | 45.5                    |
| 60+  | 39.3                   | 26.0                    | 31.5                    |
| <b>Education</b>                                     |                        |                         |                         |
| High school completed                                | 45.2                   | 55.5                    | 55.9                    |
| <b>Smoking</b>                                       |                        |                         |                         |
| Non smoker   | 50.3                   | 51.2                    | 52.6                    |
| Past smoker  | 23.0                   | 22.6                    | 24.9                    |
| Current smoker                                       | 26.7                   | 26.2                    | 22.5                    |
| <b>Body mass index (BMI)</b>                         |                        |                         |                         |
| <25  | 52.2                   | 53.5                    | 69.6 <sup>‡</sup>       |
| 25–29  | 30.4                   | 31.1                    | 21.1 <sup>‡</sup>       |
| 30+  | 17.4                   | 15.4                    | 9.3 <sup>‡</sup>        |
| <b>Alcohol consumption</b>                           |                        |                         |                         |
| Less than once a week                                | 39.8                   | 37.3                    | 31.8                    |
| Once a week  | 48.5                   | 51.9                    | 54.3                    |
| Daily  | 11.7                   | 10.8                    | 13.9                    |
| <b>Complementary health insurance</b>                | 9.5                    | 5.9                     | 4.2                     |
| <b>Hospitalization last 12 months</b>                | 28.6                   | 25.2                    | 19.6                    |
| <b>GP declared as the regular treating physician</b> | 79.8                   | 84.0                    | 42.0 <sup>‡</sup>       |
| <b>Sleeping disorder<sup>†</sup></b>                 |                        |                         |                         |
| Primary  | 80.9                   | 77.3                    | 83.9                    |
| Severe   | 24.3                   | 34.4                    | 41.3                    |

\* Type of medical practice according to physicians' prescribing preferences: GP-CM, conventional medicine; GP-Mx, mixed, conventional and homeopathic practice; GP-Ho, registered homeopathic physicians.

<sup>†</sup> Primary SD defined as no specific motive reported for sleeping disorders in the PSQI; Severity of sleeping disorders defined as reporting one or more of the following from the PSQI: problems staying awake during activities once a week or more or lack of enthusiasm (somewhat or a very big problem).

<sup>‡</sup> Difference with GP-CM group statistically significant ( $p < 0.05$ ) by chi-square test.

analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, North Carolina, USA).

The study was approved by the French National Data-Protection Commission (CNIL) and the French National Medical Council (CNOM). Participating physicians received compensation fees for their participation. Patients were not compensated for their participation in the study.

## Results

### Study population

A total of 346 patients corresponding to the definition of SD responded to at least one follow-up interview and were included in the cohort, which represents 45.5% of patients invited to participate. The proportion of patients included who completed their follow-up interviews up to 12 months was 79.8%. As previously reported for the EPI3 study, participants were represented slightly more often by females (79.7%) than non-participants (72.6%), but were very similar otherwise.<sup>13</sup>

Compared to the GP-CM group, patients who consulted a GP-Ho were younger, more educated and had a lower body mass index (BMI), only the latter reaching statistical significance (Table 1). In addition, GP-Ho participants were less likely than participants in the GP-CM group to have been hospitalized in the year prior to their inclusion in the study (respectively 19.6% and 28.6%) and to report the attending GP as their regular physician (respectively 42.0% and 79.8%), again only the latter reaching statistical significance. The proportion of primary SD was similar across the three groups, ranging from 77.3% to 83.9%, but the proportion of severe SD was higher in the GP-Ho than in the GP-CM groups (respectively 41.3% and 24.3%), a difference that did not reach statistical significance. Overall, no significant difference was observed between patients of the GP-Mx and GP-CM groups. In terms of homeopathic drug prescription at baseline, the proportions of patients receiving at least one prescription in the groups GP-CM, GP-Mx and GP-Ho were 0.8%, 7.8% and 65.4%, respectively.

### Evolution of SD

In the GP-CM group, almost one third (30.6%) and over one half (51.6%) of patients did not score for SD using the PSQI questionnaire at one- and three-month follow ups, respectively (Table 2). In the two remaining groups, rates were higher at one month but lower at three months as opposed to the GP-CM group. None of those differences were statistically significant after controlling for potential confounding factors using the propensity score.

As for the reporting of injuries during the 12-month follow up it was roughly twice as high in the GP-CM group with 15.9% than in the other two groups. Multivariate comparison showed a risk of injuries in the GP-Mx group 67% lower (OR = 0.33; 95% CI: 0.10–1.03) and of borderline significance. The lower rate also observed in the GP-Ho group (OR = 0.57; 95% CI: 0.21–1.52) was not statistically significant.

### Psychotropic drug utilization for SD

Psychotropic drug utilization at baseline was high in patients of the GP-CM (76.8%) and the GP-Mx (71.1%) groups and remained high until the end of the follow-up. Utilization in the GP-Ho group was lower (40.3%) and also remained stable during follow-up. After controlling for baseline characteristics, consumption of psychotropic drugs for SD was significantly lower in both the GP-Ho group (OR = 0.25; 95% CI: 0.14–0.42) and the GP-Mx group (OR = 0.67; 95% CI: 0.39–1.16) compared to the GP-CM group, reaching statistical significance only in the GP-Ho group. This effect was not modified by the severity of SD at baseline, with similar results when restricting the comparison to severe cases only (GP-Ho: OR = 0.21; 95% CI: 0.12–0.37, and GP-Mx: OR = 0.67; 95% CI: 0.37–1.23).

### Discussion

The results of this population-based, prospective cohort study showed that patients who saw an homeopathic physician for SD used conventional psychotropic drugs at a frequency that was only 25% that of patients seen in conventional medical practice, after controlling for baseline differences which included a higher proportion of severe SD in patients in the GP-Ho group. The lower use of psychotropic drugs in the GP-Ho group of patients did not change once stratified by its severity at baseline. At the same time, observed rates of persistence of SD and of injuries did not differ between groups.

In the context of the present study, homeopathy is practiced by GPs qualified in conventional medicine who have access to available diagnostic and therapeutic resources recommended for the treatment of SD in primary care.<sup>14</sup> The physicians represented by the GP-Ho group practiced

a distinct type of management and patient–physician interaction in itself may account for the results observed. Patients' characteristics associated to seeking care from a GP-Ho such as a greater proportion of younger patients with higher education and lower BMI, can be interpreted as both a drawing consultation force and a result of homeopathic care itself.<sup>15</sup>

Another important difference between patients from the GP-Ho group compared to the remaining two groups was the low proportion (42.0%) declaring the attending physician as their regular GP, nearly half of that observed for the GP-CM and GP-Mx groups (79.8% and 84.0%, respectively). One potential explanation for this difference might be that some patients who seek homeopathic care for SD do so after a subjective perception of failure to improve with the treatment prescribed by their regular physician, an effect that has been observed elsewhere.<sup>16</sup> However, the influence of prior healthcare on our results could not be assessed and such explanation remains speculative.

The results of our study cannot be interpreted as evidence of comparative effectiveness between conventional and homeopathic care as they result from the observation of patients who were free to choose one or the other type of management. Efforts were made to control for differences between groups at baseline but residual confounding cannot be excluded.

The category of GPs who declared themselves as regular prescribers of homeopathy without being qualified as homeopathic practitioners (GP-Mx) became an interesting group as it allowed the observation of patients in a naturally-occurring mixed setting combining homeopathic and conventional medicine. That group differed little from the GP-CM group, which might indicate that it was mostly the type of management rather than the type of prescription that could explain the results. Patients in the GP-

**Table 2** Follow-up of patients with sleeping disorders by type of medical practice\* (N = 346)

|   | GP-CM<br>N = 84 | GP-Mx<br>N = 119 | GP-Ho<br>N = 143   |
|---|-----------------|------------------|--------------------|
| <b>Evolution of sleeping disorders</b>                        |                 |                  |                    |
| Patients reporting none (%) at:                               |                 |                  |                    |
| 1-month follow up   | 30.6            | 38.6             | 34.1               |
| 3-month follow up   | 51.6            | 45.5             | 37.9               |
| Odds ratio (95% CI) <sup>†</sup> vs GP-CM                     | 1.0             | 0.94             | 0.72               |
| Sleeping disorder persisting at 3 months                      | –               | (0.56–1.57)      | (0.42–1.22)        |
| <b>Occurrence of any injury<sup>‡</sup></b>                   |                 |                  |                    |
| Patients reporting at least one in the 12-month follow up (%) | 15.9            | 6.9              | 9.5                |
| Odds ratio (95% CI) <sup>†</sup> vs GP-CM                     | 1.0             | 0.33             | 0.57               |
| Injury at 12 months   | –               | (0.10–1.03)      | (0.21–1.52)        |
| <b>Psychotropic drug for sleeping disorders</b>               |                 |                  |                    |
| Patients reporting at least one utilization (%) at:           |                 |                  |                    |
| Baseline  | 76.8            | 71.1             | 40.3               |
| 1-month follow up   | 80.8            | 67.3             | 41.1               |
| 3-month follow up   | 71.0            | 63.3             | 41.9               |
| 12-month follow up  | 66.7            | 65.5             | 42.9               |
| Odds ratio (95% CI) <sup>†</sup> vs GP-CM                     | 1.0             | 0.67             | <b>0.25</b>        |
| 12-month utilization  | –               | (0.39–1.16)      | <b>(0.14–0.42)</b> |

The bold numbers (0.25 (0.14 – 0.42) indicate a statistically significant result

\* Type of medical practice according to physicians' prescribing preferences: GP-CM, conventional medicine; GP-Mx, mixed, conventional and homeopathic practice; GP-Ho, registered homeopathic physicians.

<sup>†</sup> Odds ratios obtained by logistic regression using propensity score including all variables in Table 1.

<sup>‡</sup> Any injury resulting from a fall, motor vehicle collision, sport, or occupation.



Mx group also used less psychotropic drugs, indicating that patients' preference for homeopathy might also play an important role as suggested by some authors.<sup>17,18</sup>

The potential impact of a lower utilization of psychotropic drugs without significant effect on the clinical evolution of SDs as observed in this study might translate into a net advantage with lower incidence of adverse effects related to benzodiazepine utilization in older adults.<sup>9</sup> This is of particular interest from a public health viewpoint and therefore worth exploring further in future research.

### Strengths and limitations

While appended to a population health survey, this study provided a unique opportunity to assemble a pool of potential patients seen in primary care, with no selection criteria applied prior to the invitation to join this cohort study. The distribution of physicians and patients participating to the EPI3 general survey has been shown to be close to what is known about medical demography and reasons for consultation in France.<sup>1</sup> A strength of this study was also the variety of information collected at baseline, covering socio-demographic and clinical characteristics using a validated instrument. Drug utilization was obtained from patient interviews using a methodology that had been previously validated, although not specifically for psychotropic drugs.<sup>11,12</sup> The quality of psychotropic drug reporting could not have differed much across the three groups of patients, as they were unaware of the specific hypotheses regarding drug consumption. The methodology has shown excellent recall capacity up to two-year follow up and has the advantage of identifying drugs purchased over the counter and from the family pharmacy, which are not accounted for in prescription databases and potentially represent an important source of psychotropic drug utilization.<sup>19</sup>

One of the main limitations of this study was the low participation rate, at 45% of eligible patients. Although generally considered acceptable for a general health survey of this type, in which patients are asked to participate in a one-year follow-up study, the participation rate leaves the results open to potential selection bias. Differences between participants and non-participants have been reported to be small and participation rates to be almost identical across the three groups of GPs, which made comparison biases unlikely.<sup>13</sup>

The low sample size was a limitation to detect differences in the outcomes between groups. For psychotropic drug utilization this was not an issue as differences were very large. For SD persistence rates and injury rates however, comparison between groups lacked statistical power. Although not statistically significant, all differences were in favor of the GP-Ho group with less persistence of the SD and less injuries.

### Conclusion

Patients with SD who chose to consult GPs certified in homeopathy consumed less psychotropic drugs, with an evolution of their condition that was not statistically

different from patients treated with conventional medical management. This result may translate in a net advantage with reduction of adverse events related to psychotropic drugs.

### Authors' contributions

All authors are members of the scientific committee that developed the study protocol and the analyses plan, discussed and interpreted the results and revised the manuscript. MR drafted the manuscript. LBG supervised all operational aspects of the study including recruitments, data collection and management. MR supervised data analyses and the preparation of the manuscript.

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