PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2012)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3316

ORIGINAL REPORT

Impact of physician preferences for homeopathic or conventional medicines on patients with musculoskeletal disorders: results from the EPI3-MSD cohort

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ABSTRACT

Objective The **objective** of this study was to assess the effect of physician practicing preferences (PPP) in primary care for homeopathy (Ho), CAM (Complementary and alternative medicines) with conventional medicine (Mx) or exclusively conventional medicine (CM) on patients with musculoskeletal disorders (MSDs), with reference to clinical progression, drug consumption, side effects and loss of therapeutic opportunity.

Methods The EPI3-MSD study was a nationwide observational cohort of a representative sample of general practitioners (GP) and their patients in France. Recruitment of GP was stratified by PPP, which was self-declared. Diagnoses and comorbidities were recorded by GP at inclusion. Patients completed a standardized telephone interview at inclusion, one, three and twelve months, including MSD-functional scales and medication consumption.

Results 1153 MSD patients were included in the three PPP groups. Patients did not differ between groups except for chronicity of MSDs (>12 weeks), which was higher in the Ho group (62.1%) than in the CM (48.6%) and Mx groups (50.3%). The twelve-month development of specific functional scores was identical across the three groups after controlling for baseline score ($p > 0.05$). After adjusting for propensity scores, NSAID use over 12 months was almost half in the Ho group (OR, 0.54; 95%CI, 0.38–0.78) as compared to the CM group; no difference was found in the Mx group (OR, 0.81; 95% CI: 0.59–1.15).

Conclusion MSD patients seen by homeopathic physicians showed a similar clinical progression when less exposed to NSAID in comparison to patients seen in CM practice, with fewer NSAID-related adverse events and no loss of therapeutic opportunity. Copyright © 2012 John Wiley & Sons, Ltd.

KEY WORDS—musculoskeletal disease; cohort; homeopathy; exposure to NSAID; pharmacoepidemiology

Received 27 January 2012; Revised 10 May 2012; Accepted 01 June 2012

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INTRODUCTION

Musculoskeletal disorders (MSDs) are a leading reason for consultation in primary care. As these disorders tend to become chronic, available treatments are largely symptomatic in nature partially explaining physician and patient preferences for homeopathy (Ho) and complementary and alternative medicine (CAM).[1–4] There is a paucity of information on how Ho and CAM modifies patients' exposure to conventional drugs used in MSDs, non-steroidal anti-inflammatory drugs (NSAID) and analgesics. There is a lack of comparable non-CAM users in such study groups. In France, Ho is the most frequently used type of CAM, exclusively prescribed by physicians, mostly general practitioners (GP), and reimbursed by the National Health Insurance as with all other conventional drugs. The objective of this population-based cohort study was to assess the effects of physician practicing preferences (PPP) in primary care for Ho, CAM with conventional medicine (Mx) or solely conventional medicine (CM) on patients with MSD regarding clinical progression, quality of life, effectiveness and treatment side effects within the EPI3-MSD cohort. This study assesses the effect of physician practicing preferences (PPP) for the above three modalities of practice on exposure to NSAIDs in MSD patients.

METHODS

Study design and population

The EPI3 study was a one-year longitudinal observational survey of a representative sample of GP and their patients nationwide, conducted in France between March 2007 and July 2008. It aimed to describe patients from primary care by reasons for consultation, comorbidities and drug exposure. The study population was drawn from a two-stage sampling detailed elsewhere.[5] First, GP were randomly selected and invited from the French national directory of physicians. GP sampling was stratified according to PPP categorized in three groups: strictly conventional medicine practitioners (CM), who declared themselves never or rarely using Ho or CAM; physicians declaring using CAM regularly in a mixed practice (Mx); and registered homeopathic GP (Ho) who mainly prescribe homeopathic medicines. Physicians were classified under one of three categories after consenting to participate in the survey via short telephone questionnaires. Sampling of physicians continued until sampling ratios reached 2:1 and 3:2 for the Mx and Ho groups, respectively, relative to CM, in order to account for the variety of practices, especially in the Mx group, which does not represent a single professional entity.[6] The second stage of sampling consisted of randomly selecting a one-day of consultation for each participating physician to survey all patients attending the practice on that day.

Patients were eligible for inclusion unless their health status or literacy level did not permit completion of a self-administered questionnaire. All adult patients ($\geq$18 years) with a MSD as their main reason for consultation were included. These comprised spinal disorders (ICD codes: 720–724) and non-spinal MSD, (ICD codes: 715, 719, 729, 726–728, and 782). Patients diagnosed with inflammatory, infectious or neoplastic joint diseases (main reason for consultation) were excluded from the analyses. MSD were classified as non-chronic or chronic using a twelve-week cut-off for symptom duration at inclusion as per consensus recommendations for research on MSD.[7]

Data collection

On the day selected for patients' inclusion, a trained interviewer consecutively recruited on site (i.e. in the waiting room) all eligible patients up to a maximum of 15. Consenting patients completed a self-administered questionnaire that included information presented in Table 1; health-related quality of life was assessed by the Short Form 12 (SF-12) questionnaire.[8] GP completed a medical questionnaire including the main reason for consultation and up to five other diagnoses (comorbidities). Diagnoses were coded by a trained archivist using the 9th revision of the International Classification of Diseases.

Within 72 h of being recruited, MSD patients were asked to complete a telephone interview on their current functional status, which comprised the French adaptations of the Roland-Moris questionnaire for back pain, the Quick-Dash for MSD of the upper extremities and the Lequesne for MSD of the lower extremities.[9–11] Similar interviews were repeated at one, three and twelve months; all three interviews assessed drug exposure using a standardized method called *Progressive Assisted Backward Active Recall* (PABAR).[12] Briefly, patients were given upon recruitment a booklet detailing the interview including a list of commonly used drugs for MSD. The period of reference for drug exposure was the previous month at the one-month interview and the past two months at three and twelve-month interviews. Drugs reported by patients were entered by the interviewer in a database that automatically assigned drugs their corresponding *Anatomical Therapeutic Chemical* (ATC) codes, revision 2009.

Loss of therapeutic opportunity for patients with MSD during the twelve-month follow-up was defined

DOI: 10.1002/pds

Table 1. Characteristics of patients at inclusion by physicians' practicing preferences[a]

		CM	Mx	Ho
%		*N* = 272	*N* = 510	*N* = 371
Female gender		64.0	64.1	77.4*
Age (years)	18–39	21.8	22.5	15.1
	40–59	39.8	39.8	38.8
	60+	38.4	37.7	46.1
Body Mass Index (kg/m^2)	<25	48.3	50.0	56.2
	25–29	32.2	32.7	31.9
	30+	19.5	17.3	11.0 *
Smoking	Never smoked	50.4	53.3	64.2
	Past smoker	23.5	26.1	20.5
	Smoker	26.1	20.6	15.3
Alcohol consumption	Rarely / never	33.8	32.6	31.9
	Once a week	54.1	56.4	55.6
	Daily	12.1	11.2	12.5
Physical activity	30 minutes +	33.6	37.7	37.1
Education	High school +	37.6	35.7	46.9*
Occupational status	Employed	49.6	47.7	42.0
	Unemployed	7.5	10.5	9.8
	Retired	42.9	41.8	48.2
Complementary medical insurance		4.2	5.4	2.5
Physician declared regular physician		85.1	83.3	58.3*
Hospitalization in previous year		23.4	17.8	17.7
Absence from work in previous year (any cause)		12.1	13.8	7.2

[a]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice (conventional and CAM); Ho, registered homeopathic physicians.
*Differences with group CM statistically significant ($p \leq 0.05$) in multiple logistic regressions including all variables in Tables 1 and 2.

first by the occurrence of anxiety and depressive disorder, and second by progressing from non-chronic MSD at inclusion to chronic MSD. The occurrence of anxiety and depressive disorder was defined as the start of a psychotropic drug treatment at any time during the twelve-month follow-up.

Statistical analysis

Differences between CM, Mx and Ho groups at baseline were assessed by multivariate logistic regression analyses for dichotomized categorical data, and by ANCOVA for continuous data (SF-12 scores), controlling for all variables. A propensity score was computed for each subject in the study indicating their probability to belong to Mx or Ho compared to the CM group according to their baseline characteristics, using all descriptive variables available from polytomic logistic regression analyses. All longitudinal analyses included the propensity score to control for differences between the groups and were performed separately for non-chronic and chronic MSD patients at inclusion.

Functional scores were standardized at 100 points from their original scales. The functional scores to assess disease progression used the 72-h interview (baseline value), against which scores at one, three and twelve months were compared. Comparison of score progression between the CM, Mx and Ho groups used multivariate ANOVA for repeated measures adjusting for baseline functional score, age, gender and propensity score. Changes on functional scores were individually categorized as improved, if their twelve-month functional score was 12.5 points (standardized over 100) higher than their baseline value, and not improved otherwise.[13] Proportions of non-improved patients were compared among the three groups of patients in multiple logistic regression analyses adjusted similarly as above.

Patients' exposure to NSAID (ATC codes beginning with M01A) and analgesics (ATC codes beginning with N02A and N02B) in the Mx and Ho groups were compared to the CM group. Drug exposure in each class was first dichotomized as exposed or not exposed at least once in any of the three time intervals, and groups were further compared using logistic regressions adjusting for baseline functional score, age, gender and propensity score. Second, rates of exposure were computed in each group as the number of different drug treatments reported by patients summed over the three time intervals and reported per 100 patient-years. Rates and their 95% confidence intervals were adjusted for propensity score.

Odd ratios obtained by logistic regressions were computed to assess the relation between the occurrence of either anxiety or depressive disorder and the type of practice.

DOI: 10.1002/pds

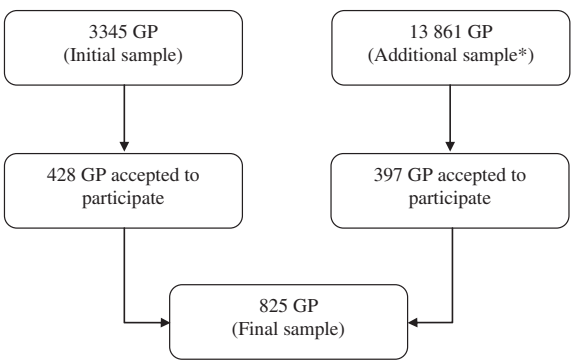
All analyses were performed using SAS version 9.1.

The study was approved by the French National Data-Protection Commission (CNIL) and the French National Council of Physicians (CNOM). Participating physicians were compensated but not patients.

RESULTS

The sequential recruitment of physicians (Figure 1) was done by random stratified sampling from the doctor phone directory. The geographical distribution of participating physicians spanned all 22 regions of France. Their median age was 52, 80% were males, 52% worked in solo practice and 78% practiced fee-for-service in addition to the general health insurance regime, characteristics that were close to national statistics data on medical manpower in France.[14] Recruitment of patients is summarized in Figure 2. Slightly more participants were female (68.3%) than nonparticipants (66.7%), most often older than 60 years (44.1% versus 42.5%), less often smokers (20.2% versus 22.1%), and with MSD more often chronic at inclusion (52.7% versus 44.1%). Patient distribution by PPP grouping was similar between nonparticipants and participants with 23.6% of the cohort recruited by CM-GP, 44.2% by Mx-GP and 32.2% by Ho-GP, which corresponded to the recruitment scheme planned.

Patients consulting a Ho-GP were more often older, non-smoking females with higher education and a lower body mass index than those seen by CM-GP, differences that were statistically significant after taking into account all other factors (Table 1). In addition, Ho-GP were considered less often as the regular treating physician by their patients (58.3%) than CM-GP (85.1%). Otherwise, no difference was observed between the Mx and CM groups. Regarding MSD, higher prevalence



*At the end of recruitment in July 2008, an additional sample of 13 861 GP were contacted to ensure a representative sample of GP from all types of primary care practice in France (strictly allopaths, homeopaths, mixed practice)

Figure 1. Recruitment of GP

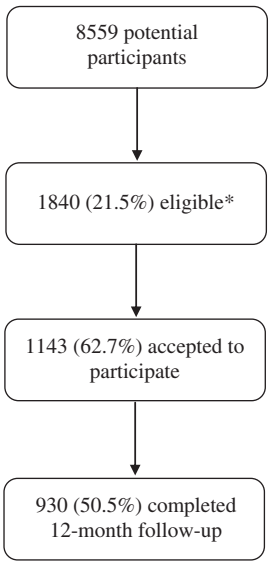


Figure 2. Recruitment of patients (*adults consulting mainly for a MSD)

of chronic disorders (≥12 weeks at inclusion) were found in in the Ho group (60.8%) as compared to CM (50.4%) and Mx (52.1%) groups (Table 2). No other difference was observed for comorbidities or quality of life. All further analyses were stratified according to the MSD chronicity status at inclusion.

Figure 3 captures the standardized functional scores for MSD progression. In both non-chronic and chronic MSD, Ho patients showed better functional scores at baseline. Adjusting for this difference and the propensity score yielded similar improvement in the three groups with repeated-measures ANOVA ($p > 0.5$). As expected, improvement was gradual but less pronounced among chronic patients. Greatest improvement was observed in non-chronic patients for the first month of follow-up. More chronic patients did not improve (32.1%, 42.0% and 31.6% in the CM, Mx and Ho groups, respectively) as compared to non-chronic (16.4%, 19.8% and 20.4%, respectively) (Table 3). Regarding MSD progression, non-chronic patients were comparable to chronic patients across the three PPP groups.

Table 4 shows distribution of patients taking NSAID across the three PPP groups. In all three PPP groups, the proportion of users reached its maximum at one-month to drop again between one and three-month of follow-up in non-chronic patients, whereas NSAID consumption remained relatively stable over time in chronic patients. Lower use of NSAID was observed at all follow-ups of non-chronic and chronic MSD patients in the Ho in comparison to the CM group; differences which were most pronounced among chronic patients in the first three months of follow-up.

DOI: 10.1002/pds

Table 2. Comparability of musculoskeletal disorders at inclusion by physicians' practicing preference[a]

		CM	Mx	Ho
	%	*N* = 272	*N* = 510	*N* = 371
MSD	Spine	55.9	55.9	50.4
	Upper limb	23.6	27.7	29.4
	Lower limb	23.2	16.1	19.7
Chronicity (duration of episode ≥12 weeks at inclusion)		50.4	52.1	60.8*
Physical therapy in previous year				
At least one session		18.7	17.2	17.1
Number of sessions (median)		15	15	15
Comorbidity at inclusion				
Another MSD		2.6	2.0	2.7
Anxio-depressive disorder		11.0	6.3	10.0
Sleep disorders		1.8	2.0	2.7
Cardiovascular or respiratory disorder		24.6	27.3	25.3
Digestive disorder		4.0	7.3	7.0
Quality of life (SF12)				
Mental score (mean, SE[b])		42.3 (1.2)	43.1 (1.0)	43.0 (1.0)
Physical score (mean, SE[b])		41.2 (1.3)	41.3 (1.0)	42.3 (1.1)

[a]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice, conventional and CAM; Ho, registered homeopathic physicians.
[b]Means and standard errors (SE) obtained by covariance analyses adjusting for variables in Tables 1 and 2.
*Differences with group A statistically significant ($p \leq 0.05$) in multiple logistic regressions including all variables in Tables 1 and 2.

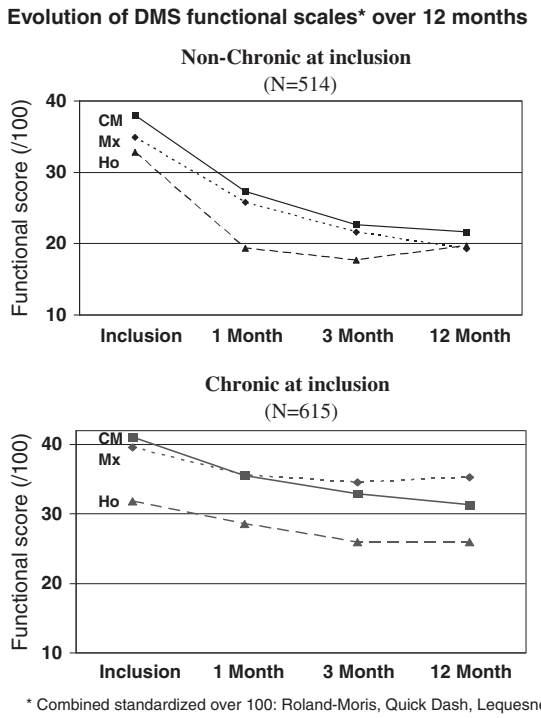


Figure 3. Comparability of musculoskeletal disorders twelve-month development of functional scores by physicians' prescription preference

Table 3. Comparability of musculoskeletal disorders improvement of functional scores[a] at the end of twelve-month follow-up by physicians' practicing preference[b]

	CM	Mx	Ho
	N = 272	*N* = 510	*N* = 371
Non-chronic at inclusion[c]			
% Not improved	16.4	19.8	20.4
Odds ratio No-improvement (95% CI)[d]	1.0 (−−)	1.49 (0.75–2.96)	1.62 (0.72–3.61)
Chronic at inclusion[c]			
% Not improved	32.1	42.0	31.6
Odds ratio No-improvement (95% CI)[d]	1.0 (−−)	1.55 (0.93–2.60)	1.34 (0.73–2.48)

[a]Functional scores (Roland-Morris, Quick Dash and Lequesne) standardized over 100 points; improvement defined as a minimum positive change of 12.5 points over 100 from baseline.
[b]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice (conventional and CAM); Ho, registered homeopathic physicians.
[c]Chronicity at inclusion defined as duration of 12 weeks or more at inclusion.
[d]Odds ratios obtained from logistic regressions controlling for age, gender, functional score at baseline and propensity score.

Table 4. Changes in **NSAID**[a] consumption as declared by MSD patients followed over twelve months by physicians' practicing preference[b]

% with at least one NSAID at follow-up	CM	Mx	Ho
Non-Chronic MSD			
1 month (*N* = 132)	45.4	36.2	34.8
3 months (*N* = 241)	19.8	22.3	15.0
12 months (*N* = 141)	24.6	22.5	17.7
Three periods (*N* = 514)	**54.03**	**46.2**	**38.0**
Probability three periods	1.0	0.78	0.58
OR (95% CI)[c]	(−−)	(0.50–1.22)	(0.35–0.95)
Chronic MSD			
1 month (*N* = 134)	33.0	27.7	15.5
3 months (*N* = 262)	35.9	24.8	14.4
12 months (*N* = 219)	25.7	30.7	18.7
Three periods (*N* = 615)	**48.8**	**41.5**	**28.6**
Probability three periods	1.0	0.81	0.56
OR (95% CI)[c]	(−−)	(0.52–1.24)	(0.35–0.90)

[a]Non-steroidal anti-inflammatory drugs excluding acetylsalicylic acid.
[b]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice (conventional and CAM); Ho, registered homeopathic physicians.
[c]Odds ratios comparing with CM category obtained from logistic regressions controlling for age, gender, functional score at baseline and propensity score; 24 subjects with missing information not included in the analysis.

Being exposed to at least one NSAID during the twelve-month follow-up was more than 40% lower in that group compared with the CM group with an adjusted OR of 0.58 (95% CI: 0.35–0.95) and 0.56 (95% CI: 0.35–0.90) for non-chronic and chronic MSD, respectively. The odds of being exposed to NSAID was also around 20% lower in the Mx compared to the CM for both chronic and non-chronic MSD patients, but the differences were not statistically significant.

DOI: 10.1002/pds

High prevalence of analgesic consumption was found across all patients' categories and remained relatively stable over time (Table 5). Compared to CM, lower use in the Ho group reached statistical significance only among those patients with chronic MSD (OR: 0.40; 95% CI: 0.20–0.82) and borderline significance in the Mx group (OR: 0.54; 95% CI: 0.27–1.08). Regarding the number of drugs declared per 100 patient-years, the lower NSAID-users proportion in the Ho group also translated to lower exposure rates (Table 6). Patients with non-chronic and chronic MSD in the Ho group consumed on average less NSAID, with differences of −39.3 (38.4% less) and −58.6 (49.8% less) treatments per 100 patient-years compared to the CM group ($p < 0.001$). For analgesics, the only significant difference was observed for chronic MSD with −84.7 (25.3% less) treatments per 100 patient-years. In the Mx group, no difference was observed for NSAIDs consumption; however, Mx patients with non-chronic MSD consumed significantly more analgesics than the CM group, surpassing +75.5 (24.4% more) treatments per 100 patient-years.

The probability of reporting NSAID-related adverse effects during exposure, with or without treatment interruption, did not differ between Mx and Ho groups versus the CM group with an OR of 1.09 (95% CI: 0.59–2.03) and 0.95 (95% CI: 0.44–2.02), respectively, after adjusting for age, gender, chronicity, functional score at baseline and propensity score.

Finally, for the occurrence of anxiety and depressive disorder during follow-up, the frequency of use of psychotropic drugs were comparable across the three PPP groups (CM, Mx and Ho) with a non-negligible result of 10% (OR: 1.27; 95% CI: 0.75–2.14 in the Mx group and OR: 0.96; 95% CI: 0.53–1.75 in the Ho group taking the CM group as reference).

Table 5. Changes in **analgesic**[a] consumption, as declared by MSD patients followed over twelve months, by physicians' practicing preference[b]

% with at least one analgesic at follow-up	CM	MP	Ho
Non-Chronic MSD			
1 month ($N = 132$)	76.9	66.3	60.9
3 months ($N = 241$)	71.3	66.9	70.0
12 months ($N = 141$)	69.1	61.8	65.5
Three periods ($N = 514$)	**88.7**	**78.9**	**83.7**
Probability three periods	1.0	0.53	0.69
OR (95% CI)[c]	(−−)	(0.35–1.18)	(0.33–1.45)
Chronic MSD			
1 month ($N = 134$)	75.7	68.8	59.0
3 months ($N = 262$)	70.9	66.4	57.8
12 months ($N = 219$)	79.8	67.1	67.6
Three periods ($N = 615$)	**90.4**	**83.1**	**77.6**
Probability three periods	1.0	0.54	0.40
OR (95% CI)[c]	(−−)	(0.27–1.08)	0.20–0.82

[a]All classes of narcotic and non-narcotic analgesics.
[b]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice (conventional and CAM); Ho, registered homeopathic physicians.
[c]Odds ratios comparing with CM category obtained from logistic regressions controlling for age, gender, functional score at baseline and propensity score; 24 subjects with missing information not included in the analysis.

Table 6. NSAID and analgesic consumption per 100 patient – years followed over twelve months by physicians' prescription preference[a] ($N = 1153$)

Number of drugs declared per 100 patient – years (95% confidence interval)[b]	CM	MP	Ho
Non-Chronic MSD			
NSAID	102.4	120.5	63.1*
	78.7–126.1	95.4–145.6	32.5–93.7
Analgesics	309.7	385.2*	256.4
	265.8–353.5	351.8–418.6	209.4–303.4
Chronic MSD			
NSAID	117.6	113.7	59.0*
	89.6–145.6	91.3–136.1	34.5–83.5
Analgesics	335.2	357.0	250.5*
	292.9–377.5	322.0–392	211.5–289.5

[a]Physicians' practicing preferences: CM, conventional medicine; Mx, mixed practice (conventional and CAM); Ho, registered homeopathic physicians.
[b]Number of different drugs consumed over twelve months declared by 100 patients; means adjusted for propensity score.
*Comparison with CM category: $p < 0.05$.

DISCUSSION

We believe the EPI3-MSD study is the first to provide information about the impact of PPP for Ho and other modalities of CAM on MSD patients. This survey assessed differences between patients with chronic and non-chronic MSD while reporting also on exposure to NSAID. One other study evaluated the impact of Ho on conventional drug exposure in MSD patients[15] but lacked comparability between groups. In a recent trial, Brien and colleagues concluded that, rather than homeopathic remedies, homeopathic consultations are associated with clinically relevant benefits for patients with rheumatoid arthritis,[16] but again it lacked a comparison arm, along with low efficacy and high drop-out rates. It was therefore difficult to distinguish and attribute potential benefits to either homeopathic medicines or the consultation alone.[17] In France, GP practicing Ho and CAM share similar reimbursement schemes with other GP, which allow comparing patients' drug exposures using grouping by PPP. Our results showed that patients with chronic MSD seen by homeopathic GP, used 50% and 25% less NSAID and analgesics, respectively, than patients seen by conventional GP over one-year follow-up. These large differences in drug exposure did not entail any significant clinical difference

DOI: 10.1002/pds

on the progression of functional status, considered the usual outcome of interest in MSD, at the end of follow-up.

In the EPI3-MSD population survey, MSD were among the first five reasons for primary care consultation, similar to national statistics reported in France.[14] Patients visiting homeopathic GP were more often older and more educated women with less lifestyle risk factors than those consulting conventional primary care physicians as previously reported.[2,3,18,19] However, the magnitude of these differences was not so large as to undermine our capacity to control for the above confounding variables. Nevertheless, differences in two other variables could have potentially biased the comparison in the opposite direction. First, more patients in the Ho group were chronic at inclusion, as reported elsewhere for patients with chronic pain.[1–4]

The results highlighted comparable progression of functional status exhibited by MSD patients across the three groups over the one-year follow-up. Treatment effectiveness was perceived as similar, quantified by standard measurement instruments, controlling for baseline differences and stratifying by chronicity status, the single most important confounder for MSD progression.[20] The concept of *competing drug exposure* induced by PPP extends beyond the doctors' office, to patients' preferences as mentioned above, and also to potentially improve patients' compliance to medical advice of remaining active in spite of the pain, one of the leading messages from clinical guidelines for MSD.[21,22] Here, PPP was not analyzed as a confounding factor on treatment effect but as a stratification factor of the treatment itself.[23,24] We suggest that in this situation, PPP differences would rather reflect changes in the risk–benefit balance between different leading options, than a biased estimation of treatment effect.[25,26]

MSD are a common indication for homeopathic treatment but their efficacy beyond the placebo effect is yet to be proved.[27,28] The fact that homeopathic medicines are generally devoid of adverse effects and that MSD treatments are largely symptomatic in nature makes them good alternatives to drugs with a higher potential to cause side effects.[29,30] In France, Ho is practiced exclusively by physicians and removing Ho from the reimbursement schedule will have to account for the cost of increased gastrointestinal (GI) risk by each switch to an NSAID. For example, using a rate of 0.5 GI events per 100 person-year in patients with chronic MSDs, and our estimated replacement rate of 40 switches to NSAID per 100 patient-year, would add 0.2 GI events per 100 patients with chronic MSD.[31] Besides the increased risk from switches, an increased number of multiple and high-dose NSAID users with an increase of previous history of GI problems among switchers is also likely to occur, all three factors being leading risk factors.[32]

Strengths and limitations

To our knowledge, the EPI3-MSD is the largest cohort study of homeopathic care conducted in the context of medical general practice on a representative sample of patients consulting for MSD. Its large number of participating physicians and patients ensured best representation of clinical practices in primary care from across France. The distribution of physicians' individual characteristics differed only slightly from published French national statistics.[14] MSD patients were identified from a large sample of patients consulting for any reason in primary care, thus minimizing selection bias from direct sampling of MSD patients. Differences between participants and non-participants were small and participation rate was almost identical across the three PPP groups. Also, our SF-12 scores were very close to those reported in three previous European population surveys of MSD patients.[33,34]

Another advantage was the quality of the data combining medical information on diagnoses and patients' information on drug utilization over one year follow-up. Drug exposure was obtained from patients' interviews using a previously validated methodology.[12] Discrepancies in NSAID exposure, as declared by patients and physicians, are known to partially reflect consumption of over-the-counter drugs.[35] This deliberate choice was thought to better reflect the real exposure to MSD drugs. However, our assessment provided only a rough estimate of the true drug exposure. All three interviews conducted on patients covered only five of the twelve-month follow-up and therefore likely to underestimate true exposure. Nonetheless, the fact that identical methods were used in all patients, blinded to the physician PPP, reduced the possibility of a bias in the comparison of exposures.

The present analysis was restricted to patients consulting for MSD in order to optimize our observations of NSAID and analgesics use. However, these drugs are not specific to MSD, and the differences observed in patients' utilization reflected both PPP for the treatment of this type of disorders, alongside their comorbidities. Yet, the three groups of patients showed very similar comorbidity profiles. Another factor, independent of PPP, is the preference of patients for drugs available without prescription. In this study, drug exposure was based on patients' self-declaration of drug consumption, therefore including drugs either available over-the-counter or from the family medicine cabinet. The large

DOI: 10.1002/pds

differences observed in patients' NSAID utilization between the groups reflected a combination of preferences from physicians and patients.

CONCLUSION

MSD patients seen by GP with prescription preferences for Ho showed a similar clinical progression of their MSD, assessed by specific standardized functional scales, with less exposure to NSAID compared to patients seen by conventional medical practitioners. This effect has an impact on the risk–benefit balance between homeopathic treatment and NSAID, with fewer reports of NSAID-related adverse events, no significant cost on long-term functional outcomes and no loss of therapeutic opportunity.

KEY POINTS

- The EPI3-MSD was the largest cohort study of homeopathic care conducted in the context of medical general practice on a representative sample of patients consulting for MSDs.
- Patients with MSD seen by GP with prescribing preferences for Ho showed a similar clinical progression of their MSD, assessed by specific standardized functional scales, with less exposure to NSAID when compared to patients seen by conventional medical practitioners.
- Patients seen by Ho- and Mx-GP represent 4% and 20% of patients, respectively, in France, a scenario that would have considerable impact on population health and healthcare costs.

CONFLICT OF INTEREST

All authors, members of the LA-SER network, have no commercial or other interest in a drug or other factors mentioned in this study and therefore declare no competing interest.

ACKNOWLEDGEMENTS

Laboratoires Boiron, France, sponsored this independently run study published by the authors. The sponsor had no role in the design, management, data collection, analyses, interpretation and writing of the manuscript or the decision to publish our findings.

Lamiae Bensouda-Grimaldi was the recipient of a research fellowship from INSERM (French National Institute of Health and Medical Research) at the time of the study. The authors wish to thank Djamila Abed and Rémi Sitta for their technical contribution in data analyses.

AUTHORS' CONTRIBUTIONS

All authors are members of the scientific committee that developed and approved 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.

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