

Survey of Forged Prescriptions to Investigate Risk of Psychoactive Medications Abuse in France

Results of OSIAP Survey

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Abstract

Objective: To describe patterns of drug diversion from 2001 to 2004 in France and to define different profiles of forged prescriptions.

Methods: Data from a national cross sectional survey carried out each year since 2001 were analysed. A national network of community pharmacies is requested to collect suspect prescriptions during two periods each year in May and November. Data included were date, age and sex of the patient, type of prescription form, drugs and criteria of suspicion.

Results: Between 2001 and 2004, a sample of 1710 abnormal prescription forms were analysed. These concerned women in 54% of cases. The average age of those sampled was 47 years. Sixty-one percent of the 597 varieties of medication belonged to the anatomic therapeutic chemical (ATC) nervous system class. The most frequently involved drugs were benzodiazepines and benzodiazepine analogues (flunitrazepam, zolpidem) or opioids (buprenorphine, morphine). Multiple correspondence analysis underlined two opposite profiles for suspicious prescriptions: (i) specific prescription forms for scheduled drugs presented by men aged <45 years involving drugs for the nervous system and presenting the criteria of stolen, falsified and abnormal prescriptions; and (ii) prescription forms presented by women aged >45 years involving cardiovascular and muscular-skeletal system drugs, presenting the criteria of alteration to the prescription.

Conclusion: Analysis of data collected from community pharmacies in the OSIAP (Ordonnances Suspectes Indicateur d'Abus et de Pharmacodépendance) survey gives information about patterns of diversion of medication in France. This system is able to evaluate the impact of measures implemented in order to decrease the misuse of drugs and able to identify new patterns of drug diversion. Identification of profiles of suspicious 'prescription forms' could help pharmacists to better identify abnormal prescriptions. A European project has recently been implemented to extend this kind of survey to other countries in Europe.

Background

Data concerning the risk of drug abuse are usually supplied by experimental and clinical studies. However, they often prove insufficient when the drug is widely used in real life. Drug abuse involves not only addicts, but also a significant part of the population who are not usually considered as addicts (e.g. long-term abusers of benzodiazepines who become dependent after many years of use). Most of the data concerning drug abuse or diversion in real life come from case reports or observations from epidemiological studies about the addict population. In the US, the Drug Abuse Warning Network (DAWN)^[1] monitors drug-related hospital emergencies and drug-related deaths to track the impact of drug use, misuse and abuse in the country. This system covers all types of drugs: illegal drugs, prescription and over-the-counter medication or combinations of alcohol with other drugs. In other countries, epidemiological evaluations of substance abuse are based on the collection of data from different sources, for example, police or healthcare systems. These sources provide information about cases of drug abuse that have resulted in a crisis in the individual's life.

To obtain specific information on the potential for abuse of psychoactive drugs, the French network of Centers for Evaluation and Information on Pharmacodependence (CEIP) was created in 1990.^[2] The aims of this network are: (i) to ensure the collection and the evaluation of clinical data concerning the abuse or dependence on drugs in France; (ii) to ensure training courses and refresher courses about pharmacodependence for health professionals; and (iii) and to perform experimental, clinical and epidemiological studies.^[3-6] Following the reports by Bergman and colleagues,^[7,8] the French CEIP network has launched a prescription forgeries survey involving several community pharmacy networks.^[9-11] This system provides information about potential abuse of marketed drugs in France. In contrast with systems like DAWN, data obtained by the survey of falsified or forged prescriptions are complementary since they concern drug requests in the everyday life of the patient. Moreover, since

community pharmacies have direct access to the dependent population, this kind of survey may also serve as a signal to help detect new patterns of use.

In France, since 2001, the collection of suspicious prescriptions has been performed by the French CEIP network, through a systematic periodic survey, called OSIAP (Ordonnances Suspectes Indicateur d'Abus et de Pharmacodépendance), among sentinel community pharmacies. This survey allows the identification of drugs liable to be diverted and to determine the ranking of the most diverted drugs at the regional and national levels when compared with sales data for these drugs.^[12]

The aim of the present study was to describe patterns of drug diversion from data collected in the OSIAP survey from 2001 to 2004 in France, and to define different profiles of forged prescription forms according to criteria of suspicion.

Methods

Presentation of the OSIAP Survey

The principle of data collection concerning prescription forgery has been previously described.^[9,10] Since 2001, data have been collected during two 1-month periods each year, i.e. May and November. During these two periods, a network of community pharmacies is requested to identify and collect data concerning suspect prescriptions. Pharmacies participate on a voluntary basis: they represented 7% in 2001 and 8% in 2004 of all community pharmacies in France (1600 pharmacies in 2004 out of a total of 20 000 in France). The whole of France is covered.

Prescription forgeries are defined as follows:

- a false prescription, such as a prescription written on a stolen form, a counterfeit prescription (copies);
- a forged prescription (any falsification of an initial true prescription: addition of a drug, modification of number of packages, dose or duration of treatment); and
- an abnormal prescription that varies from national prescription guidelines (a prescription inconsistent with good medical practice, resulting from the insistent requests of the patient).

During data-collection periods (May and November), participating pharmacies fill in a specific form, where they indicate the following data for each suspicious prescription identified by the pharmacy staff:

- date, age and sex of the patients;
- location of pharmacy: rural (<2000), urban (2000–99 999) and unit-urban ($\geq 100\,000$);
- type of prescription form (simple form, specific prescription form for scheduled drugs, prescription form for chronic disease and hospital prescription form);
- criteria of suspicion (modification of the prescription, over-writing on the prescription form, suspect writing, spelling mistakes, photo or copy of prescription form, stolen prescription form, overlapping prescription, abnormally prescribed dose, prescriptions not obeying prescriptions rules, i.e. non-rational prescriptions and inconsistencies); and
- name of drug(s) involved in the falsification and comments.

Data concerning the patient and the prescriber remain strictly anonymous. However, when possible, pharmacists make an anonymous copy of the suspicious prescription form. These copies and forms for collecting data are sent to the regional CEIP at the end of the study period. Finally, all data concerning the OSIAP survey are checked, recorded and analysed to establish patterns of drug diversion each year. For the purpose of our study, we used all prescriptions recorded during surveys from 2001 to 2004, excluding several prescriptions where the exact name of drug or the specified criteria of suspicion were lacking or if at least they were not readable. All drugs were coded according to the Anatomic Therapeutic Chemical (ATC) classification.

Data Analysis

The analysis was conducted using SAS® 9.1 statistical software.

The first step was a descriptive analysis of OSIAP from 2001 to 2004, in terms of characteristics of patients, pharmacies, drugs involved and criteria of suspicion.

Secondly, we performed a multiple correspondence analysis (MCA) to identify profiles of suspect prescription forms according to the characteristics of the patients: either specific or non-specific prescription forms for scheduled drugs, location of pharmacy and drugs. The purpose of the MCA is to produce a simplified representation of the information in large frequency tables.^[13–15] This method could be considered as an extension of simple correspondence analysis to more than two variables; it is carried out on an indicator matrix with cases as rows and categories of variables as columns. All information about similarities is presented on the same graph, which allows the representation of different profiles. The row and column totals of the relative frequencies matrix are called the row mass and column mass. Inertia is defined as the total Pearson Chi-squared (χ^2) for the two-way table divided by the total sum. This method decomposes the overall χ^2 statistic by identifying a small number of dimensions in which the deviations from the expected values can be represented. We chose two dimensions and we included two categories of variables: active variables (represented in the figures in blue), which helped determine the positioning of the prescription forms in the factorial axis, and additional variables (represented in the figures in red), which described the profiles. Variables that encoded the criteria of suspicion were additional variables.

Results

Characteristics of OSIAP

A total of 1944 prescriptions were available (their number rose from 409 in 2001 to 607 in 2004). After exclusion of reports where the exact name of the drug or the criteria of suspicion were lacking, we retained 1710 prescription forms for our analysis. Patients were 47 ± 19 years old (\pm standard deviation) and women in 54% of cases. Men were younger than women (43 ± 18 years vs 51 ± 19 years, respectively; $p < 0.0001$). Most of prescriptions were presented in pharmacies in urban zones (57%) compared with unit-urban zones (33%) and rural

Table I. Anatomic Therapeutic Chemical (ATC)-level 1 classes of drugs reporting OSIAP collection from 2001 to 2004

Classification of Drugs (ATC)	2001 (n = 225)		2002 (n = 385)		2003 (n = 507)		2004 (n = 593)		Total (n = 1710)	
	nb	%	nb	%	nb	%	nb	%	nb	%
Alimentary tract and metabolism	17	7.6	39	10.1	64	12.6	79	13.3	199	11.6
drugs for peptic ulcer and GORD	5	2.2	6	1.6	13	2.6	15	2.5	39	2.3
drugs for functional bowel disorders	0	0.0	2	0.5	6	1.2	8	1.3	16	0.9
laxatives	1	0.4	7	1.8	7	1.4	8	1.3	23	1.3
anti-obesity preparations	0	0.0	0	0.0	3	0.6	10	1.7	13	0.8
oral blood glucose lowering drugs	1	0.4	1	0.3	1	0.2	9	1.5	12	0.7
Cardiovascular system	26	1.6	39	10.1	68	13.4	76	12.8	209	12.2
loop diuretics	0	0.0	2	0.5	6	1.2	5	0.8	13	0.8
β -adrenoceptor antagonists	6	2.7	6	1.6	5	1.0	9	1.5	26	1.5
lipid modifying agents, plain	2	0.9	4	1.0	16	3.2	17	2.9	39	2.3
Dermatologicals	4	1.8	22	5.7	31	6.1	23	3.9	80	4.7
corticosteroids, dermatological preparations	2	0.9	5	1.3	18	3.6	10	1.7	37	2.2
Genito-urinary system	7	3.1	12	3.1	30	5.9	45	7.6	94	5.5
hormonal contraceptives for systemic use	4	1.8	4	1.0	6	1.2	11	1.9	24	1.4
androgens	0	0.0	1	0.3	5	1.0	6	1.0	12	0.7
urologicals	0	0.0	1	0.3	11	2.2	11	1.9	23	1.3
Systemic hormonal preparations	6	2.7	6	1.6	8	1.6	10	1.7	30	1.8
corticosteroids for systemic use, plain	4	1.8	2	0.5	2	0.4	2	0.3	10	0.6
thyroid preparations	2	0.9	4	1.0	6	1.2	8	1.3	20	1.2
Anti-infectives for systemic use	8	3.6	13	3.4	19	3.7	7	1.2	47	2.7
Musculo-skeletal systems	10	4.4	23	6.0	30	5.9	36	6.1	99	5.8
anti-inflammatory and antirheumatic products	6	2.7	12	3.1	19	3.7	18	3.0	55	3.2
muscle relaxants, centrally acting agents	0	0.0	7	1.8	5	1.0	3	0.5	15	0.9
Nervous system	224	99.6	322	83.6	468	92.3	550	92.7	1 564	91.5
opioids	20	8.9	30	7.8	57	11.2	69	11.6	176	10.3
other analgesics and antipyretics	18	8.0	16	4.2	28	5.5	44	7.4	106	6.2
antiepileptics	5	2.2	4	1.0	20	3.9	22	3.7	51	6.2
antipsychotics	9	4.0	8	2.1	13	2.6	10	1.7	40	2.3
anxiolytics	48	21.3	76	19.7	91	17.9	158	26.6	40	2.3
hypnotics and sedatives	86	38.2	128	33.2	143	28.2	143	24.1	500	29.2
antidepressants	12	5.3	23	6.0	49	9.7	34	5.7	118	6.9
drugs used in addictive disorders	23	10.2	29	7.5	54	10.7	55	9.3	161	9.4
Respiratory system	25	11.1	24	6.2	48	9.5	44	7.4	141	8.2
decongestants and other nasal preparations for topical use	5	2.2	4	1.0	6	1.2	5	0.8	20	1.2
adrenergics, inhalants	2	0.9	6	1.6	9	1.8	5	0.8	22	1.3
cough and cold preparations	8	3.6	4	1.0	7	1.4	8	1.3	27	1.6
antihistamines for systemic use	4	1.8	8	2.1	12	2.4	8	1.3	32	1.9

GORD = gastro-oesophageal reflux disease; **n** = number of prescriptions reported during OSIAP each year; **nb** = number of cases reported each year; **OSIAP** = Ordonnances Suspectes Indicateur d'Abus et de Pharmacodépendance; % = percentage of prescriptions reported each year.

zones (10%). This distribution remained stable over 2001–4.

Most of the suspect prescriptions (91.5%) concerned at least one drug for the nervous system (table I). Of 597 different drugs, 61.0% were ner-

vous system drugs (hypnotics 20%, anxiolytics 15%, opioids 7% and drugs used in addictive disorders 6%), 8.0% were drugs for the cardiovascular system, 8.0% were alimentary tract and metabolism drugs and 6.0% were respiratory system drugs (data not shown).

Most of the drugs were benzodiazepines or benzodiazepine analogues. Other drugs were buprenorphine used in opioid maintenance and other opioids used as analgesic drugs. From 2001 to 2004, we observed a decrease in the proportion of hypnotics (38.2% in 2001, 24.1% in 2004). This decrease was mainly due to a decrease in the number of prescriptions of flunitrazepam (table II), which remained one of the most implicated drugs for the whole 2001–4 period (11.3% of prescriptions), followed by zolpidem (10.2%), buprenorphine (8.8%), bromazepam (5.9%), paracetamol (acetaminophen) [4.4%] and zopiclone (4.1%). In contrast with flunitrazepam, we observed an increase of reports concerning clonazepam and combinations of paracetamol/codeine or paracetamol/cafeine/opium extracts, whereas combinations of paracetamol/dextropropoxyphene remained stable.

Twenty-seven percent of drugs identified were subject to specific rules of prescription as scheduled drugs. However, only half of these drugs (55%) were requested on a specific prescription form for scheduled drugs; this proportion varied from 44.2% in 2002 (this information was not systematically requested in 2001) to 66.1% in 2004.

Criteria of falsification reported by pharmacists are listed in table III. The most frequently reported were 'modification of the prescription' (37%), followed by 'suspect writing' (20%), 'writing over' (18%) and 'abnormal prescribed dose' (13%). The criterion 'stolen' was found in 8% and 'copy' in 9%. The 'modification of the prescription' increased (from 29.8% to 42.2%) as did 'copy' (from 5.3% to 12%) between 2001 and 2004.

Profiles of Suspect Prescriptions

We performed two MCA with common variables coding for sex, age, a specific prescription form for scheduled drugs or not, location of the pharmacy

and criteria of suspicion as additional variables (see codes in table IV). The first MCA explored ATC-level 1 classes of drugs, the second MCA included names of drugs.

Profiles of Suspect Prescriptions Involving ATC Classes of Drugs

The percentage of explained inertia was equal to 1.250 (percentage of inertia: 13% due to the x-axis and 8% due to the y-axis), with a graphical presentation in figure 1.

Two profiles are related to specific criteria of suspicion: a first profile linking suspect prescription form to the criteria stolen (STOLEN+), falsified (FALSIFIED+) and abnormal prescription (PRESCRIPTION+). They concerned specific prescription forms for scheduled drugs (SCHEDULE+) presented by men (M) aged <45 years (YOUNG and ADULT) in urban pharmacies (URBAN) and contained drugs for the nervous system (N+).

This first profile was opposed to a second profile based on the criteria of change on the prescription forms (CHANGE+). This category involved prescription forms presented by women (F) aged >45 years (EXPERIENCED and OLD) in rural pharmacies (RURAL), concerning cardiovascular (C+) and musculo-skeletal (M+) systems drugs. Two other profiles not associated with any criteria of suspicion were identified: prescription forms presented by men (M) aged <30 years (YOUNG), in urban pharmacies (URBAN), containing anti-infectives for systemic use (J+), drugs for alimentary tract and metabolism (A+), dermatologicals (D+), respiratory system (R+) and genito-urinary system drugs (G+). These prescriptions did not contain drugs for the nervous system (n-).

The final profile concerned prescription forms for nervous system drugs (N+) presented by women (F) aged >45 years (EXPERIENCED and OLD), in rural pharmacies (RURAL).

Profiles of Suspect Prescriptions Including Names of Drugs

The percentage of explained inertia was equal to 1.111 (percentage of inertia: 10% due to the x-axis and 6% due to the y-axis), with graphical results

Table II. List of drugs most frequently reported in suspicious prescriptions (more than ten reports for the entire 2001–4 period)

Name of drugs	2001 (n = 225)		2002 (n = 385)		2003 (n = 507)		2004 (n = 593)		Total (n = 1710)	
	nb	%	nb	%	nb	%	nb	%	nb	%
Flunitrazepam	44	19.6	60	15.6	55	10.8	35	5.9	194	11.3
Zolpidem	25	11.1	40	10.4	47	9.3	63	10.6	175	10.2
Buprenorphine	23	10.2	27	7.0	52	10.3	48	8.1	150	8.8
Bromazepam	16	7.1	22	5.7	17	3.4	46	7.8	101	5.9
Paracetamol (acetaminophen)	15	6.7	11	2.9	21	4.1	29	4.9	75	4.4
Zopiclone	9	4.0	13	3.4	22	4.3	26	4.4	70	4.1
Dipotassium clorazepate	7	3.1	14	3.6	16	3.2	21	3.5	58	3.4
Morphine	2	0.9	16	4.2	19	3.7	13	2.2	56	3.3
Paracetamol/cafeine/ dextropropoxyphene	10	4.4	7	1.8	15	3.0	20	3.4	52	3.0
Lorazepam	7	3.1	11	2.9	13	2.6	16	2.7	47	2.7
Paracetamol/codeine	4	1.8	3	0.8	12	2.4	24	4.0	43	2.5
Alprazolam	4	1.8	8	2.1	14	2.8	16	2.7	42	2.5
Clonazepam	4	1.8	4	1.0	15	3.0	13	2.2	36	2.1
Betamethasone	4	1.8	4	1.0	14	2.8	9	1.5	31	1.8
Fluoxetine	2	0.9	7	1.8	12	2.4	4	0.7	25	1.5
Oxazepam	3	1.3	3	0.8	5	1.0	13	2.2	24	1.4
Diazepam	2	0.9	3	0.8	8	1.6	10	1.7	23	1.3
Paracetamol/cafeine/opium	2	0.9	4	1.0	4	0.8	12	2.0	22	1.3
Levothyroxine sodium	2	0.9	4	1.0	3	0.6	8	1.3	20	1.2
Meprobamate/aceprometazine	1	0.4	2	0.5	4	0.8	9	1.5	20	1.2
Paroxetine	2	0.9	1	0.3	12	2.4	5	0.8	20	1.2
Lormetazepam	2	0.9	4	1.0	5	1.0	6	1.0	17	1.0
Salbutamol (albuterol)	2	0.9	4	1.0	4	0.8	7	1.2	17	1.0
Omeprazole	3	1.3	4	1.0	5	1.0	4	0.7	16	0.9
Tianeptine	0	0.0	3	0.8	5	1.0	8	1.3	16	0.9
Tramadol	2	0.9	2	0.5	4	0.8	7	1.2	15	0.9
Prednisolone	2	0.9	3	0.8	4	0.8	5	0.8	14	0.8
Cyamemazine	2	0.9	3	0.8	5	1.0	3	0.5	13	0.8
Diclofenac	2	0.9	0	0.0	5	1.0	6	1.0	13	0.8
Atorvastatin	0	0.0	2	0.5	8	1.6	2	0.3	12	0.7
Citalopram	2	0.9	4	1.0	2	0.4	4	0.7	12	0.7
Furosemide	0	0.0	2	0.5	6	1.2	4	0.7	12	0.7
Macrogol	0	0.0	3	0.8	6	1.2	4	0.7	12	0.7
Venlafaxine	2	0.9	3	0.8	3	0.6	4	0.7	12	0.7
Tetrazepam	0	0.0	6	1.6	4	0.8	1	0.2	11	0.6

n = number of prescriptions reported during OSIAP each year; nb = number of cases reported each year; **OSIAP** = Ordonnances Suspectes Indicateur d'Abus et de Pharmacodépendance; % = percentage of prescriptions reported each year.

presented in figure 2. Two profiles were related to specific criteria of suspicion.

A first profile concerned the criteria stolen (STOLEN+), falsified (FALSIFIED+), abnormal prescriptions (PRESCRIPTION+) and specific prescription forms for scheduled drugs (SCHEDULE+)

presented by men (M) aged <45 years (YOUNG and ADULT), in urban pharmacies (URBAN). These prescriptions contained flunitrazepam (FLU+), buprenorphine (BUPRE+) or morphine (MOR+).

The second and opposed profile concerned suspicious prescriptions with the criteria of change on the

prescription forms (CHANGE+). They were presented by women (F) aged >45 years (EXPERIENCED and OLD) in rural pharmacies (RURAL), and did not concern prescription forms for scheduled drugs (schedule-).

Two other profiles not related to any criterion were found: the first profile concerned prescription forms that were not for scheduled drugs (schedule-) presented by patients (M and F) aged <31 years (YOUNG), in urban pharmacies (URBAN) and containing paracetamol/codeine (COPARA+), or benzodiazepines (zolpidem [ZOLP+], alprazolam [ALPRA+], bromazepam [BROMA+], dipotassium clorazepate [CLORA+]).

Finally, the last profile corresponded to specific prescription forms for scheduled drugs (SCHEDULE+) containing morphine (MOR+), lorazepam (LORA+) and paracetamol (PARA+).

Discussion

The diversion of prescription-controlled drugs or medication in general into illicit channels are a public health and safety issue.^[16] Despite the fact that preclinical and clinical behavioural studies in animals and humans (i.e. self-administration, discrimination, appetite studies) could suggest which medications could be abused, these methods have limited validity when the drug is available in the 'real-life' context. To assess the magnitude of medi-

cation abuse in France, a national system of drug abuse and dependence monitoring was set up in the early 1990s. The collection of data concerning prescription forgeries was chosen from among the different epidemiological tools. This system, called OSIAP, is an efficient tool for identifying abuse of medicines, for generating alerts and for describing profiles of forged medical prescriptions.^[3,10,11]

The aim of this study was to investigate profiles of suspicious prescriptions to help the pharmacists to identify abnormal prescriptions. The main limitation of the study was the difficulty in achieving exhaustive detection of falsified prescriptions, since there is no gold standard. For example, some falsified prescription forms can escape detection due to variations in the pharmacist's vigilance at different times of the day. In contrast, some prescriptions identified as suspect by pharmacists could be genuine medical prescriptions. This could lead to an underestimation of our results. The other problem concerns the representativeness of our sample of pharmacies, since only volunteer pharmacies took part in the survey. However, since the aim of OSIAP is to identify and to generate trends concerning the most diverted drugs, this skew is not important. The OSIAP system detects drugs already known for their addictive potential but also those not suspected of abuse. However, it is not possible to know why

Table III. Criteria of suspicion reported by pharmacists in OSIAP between 2001 and 2004 as percentage of reported suspected prescriptions each year

Criteria of suspicion	2001 (n = 225) ^a	2002 (n = 385) ^a	2003 (n = 507) ^a	2004 (n = 593) ^a	Total (n = 1 710) ^a
Modification	29.8	28.5	42.0	42.2	37.4
Suspect writing	20.4	22.9	22.1	16.4	20.1
Writing over	17.3	16.4	16.4	19.2	17.5
Abnormal prescribed dose	15.6	20.0	12.6	7.4	12.9
Not obeying prescription rules	14.7	14.3	8.3	7.9	10.4
Photocopy/copy	5.3	4.7	9.3	12.0	8.7
Stolen form	5.3	8.3	7.9	7.9	7.7
Overlapping	3.6	1.6	6.7	7.2	5.3
Spelling mistake	1.8	4.4	6.5	5.2	5.0
Inconsistency	0.9	3.1	3.9	3.9	3.3
Other criteria of suspicion	15.1	8.3	9.1	0.0	6.6

a Sum of columns may exceed 100%, since some prescriptions could include more than one criterion.

OSIAP = Ordonnances Suspectes Indicateur d'Abus et de Pharmacodépendance.

Table IV. Coding of the variables included in the multiple correspondence analysis (MCA)

Variables	Coding in MCA (figures 1 and 2)
Sex	
men	M
women	F
Age (years)	
<31	YOUNG
31–44	ADULT
45–60	EXPERIENCED
>60	OLD
Type of the prescription form	
specific prescription form for scheduled drugs	SCHEDULE+
not a specific prescription form for scheduled drugs	schedule–
Location of the pharmacy	
<2000 inhabitants	RURAL
2000–99 999 inhabitants	URBAN
≥100 000 inhabitants	UNIT-URBAN
Criteria of suspicion	
stolen prescription form	STOLEN+/stolen–
photo or copy of prescription form	FALSIFIED+/falsified–
modification, suspect writing or writing over the prescription	CHANGE+/change–
overlapping or non-rational prescription	PRESCRIPTION+/prescription–
Anatomic Therapeutic Chemical classes of drugs	
alimentary tract and metabolism	A+/a–
cardiovascular system	C+/c–
dermatologicals	D+/d–
genito-urinary system	G+/g–
anti-infectives for systemic use	J+/j–
musculo-skeletal system	M+/m–
nervous system	N+/n–
respiratory system	R+/r–
Names of drugs	
flunitrazepam	FLU+/flu–
zolpidem	ZOLP+/zolg–
morphine	MOR+/mor–
buprenorphine	BUPRE+/bupre–
bromazepam	BROMA+/broma–
lorazepam	LORA+/ lora–
paracetamol (acetaminophen)	PARA+/para–
alprazolam	ALPRA+/alpra–
paracetamol/codeine	COPARA+/copara–
zopiclone	ZOPIC+/zopic–
betamethasone	BETH+/beth–
dipotassium clorazepate	CLORA+/clora–
paracetamol/dextropropoxyphene	DEXPARA+/dexpara–
methylphenidate	METHYL+/methyl–

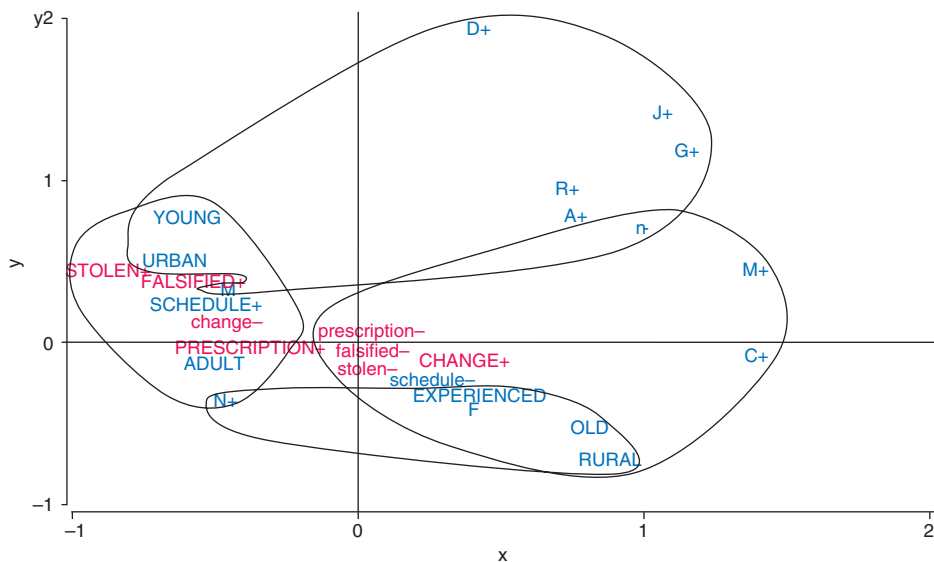
patients modify prescriptions and to what use the drugs are put if and when thus obtained.

MCA was developed in the early 1970s.^[13–15] MCA is a descriptive, exploratory technique de-

signed to analyse multi-way contingency tables containing some measure of correspondence between the rows and columns. The results provide information, similar in nature to that produced by factor analysis techniques and explore the structure of categorical variables included in the table. This method

uses the distributive principle of χ^2 to establish profiles. MCA gives a good idea of association between variables.

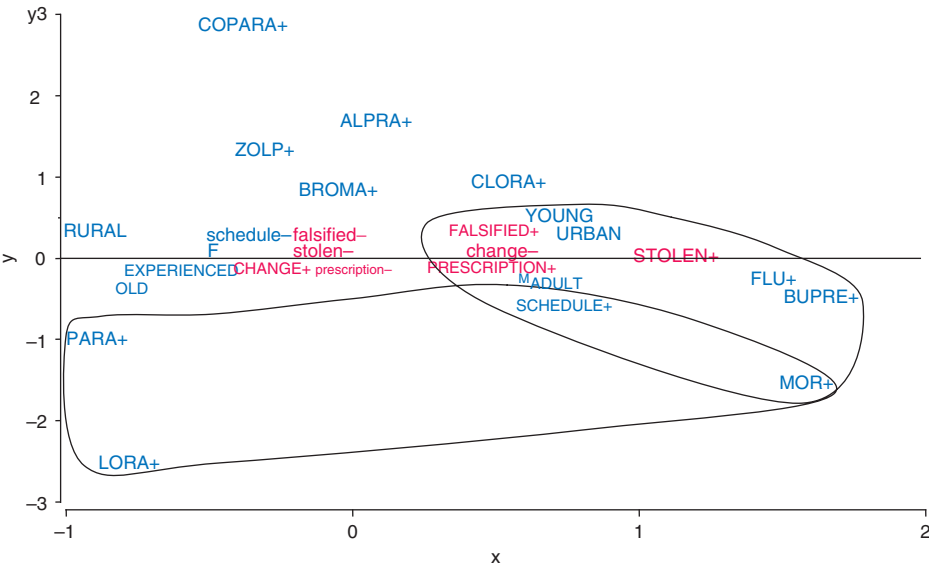
Among the suspicious prescriptions, we obtained two opposite profiles: one profile was associated with the criteria of ‘modification, suspect writing or



Summary of variables contributing on the axis in the MCA

Variables contributing on the x-axis		Variables contributing on the y-axis	
negative contribution	positive contribution	negative contribution	positive contribution
<div>Profile 1</div> <div>ADULT (3.8%) YOUNG (4.9%) M (5.0%) URBAN (7.3%) SCHEDULE+ (4.7%) N+ (7.6%) STOLEN+ PRESCRIPTION+ FALSIFIED+ Change-</div>	<div>Profile 2</div> <div>OLD (8.2%) EXPERIENCED (1.8%) F (4.1%) RURAL (3.8%) n- (16.4%) C+ (10.2%) M+ (5.9%) Stolen- Prescription- Falsified- CHANGE+</div>	<div>Profile 3</div> <div>YOUNG (11.9%) M (4.5%) URBAN (7.0%) n- (13.4%) A+ (5.8%) R+ (4.9%) G+ (6.1%) D+ (13.9%) J+ (3.8%)</div>	<div>Profile 4</div> <div>OLD (5.2%) F (3.7%) RURAL (4.0%) N+ (6.2%)</div>

Fig. 1. Graphical representation of the four different profiles of suspicious prescriptions including anatomic therapeutic chemical (ATC) classes of drugs, according to the results of the multiple correspondence analysis (MCA). **ADULT** = 31–44 years old; **A+** = alimentary tract and metabolism drugs; **CHANGE+/CHANGE-** = changes on prescriptions; **C+** = cardiovascular system drugs; **D+** = dermatologicals; **EXPERIENCED** = 45–60 years old; **F** = women; **FALSIFIED+/falsified-** = falsified prescriptions; **G+** = genito-urinary system drugs; **J+** = anti-infectives for systemic use; **M** = men; **M+** = musculo-skeletal system drugs; **N+/n-** = nervous system drugs; **OLD** = >60 years old; **PRESCRIPTION+/prescription-** = abnormal prescriptions; **R+** = respiratory system drugs; **RURAL** = rural pharmacies; **SCHEDULE+/schedule-** = prescription forms for scheduled drugs; **STOLEN+/stolen-** = stolen prescription forms; **URBAN** = urban pharmacies; **YOUNG** = <31 years old.



Summary of variables contributing on the axis in the MCA

Variables contributing on the x-axis		Variables contributing on the y-axis	
negative contribution	positive contribution	negative contribution	positive contribution
<div>Profile 1</div> <div>OLD (7.8%) EXPERIENCED (3.6%) F (6.4%) RURAL (4.6%) Schedule- (4.0%) Stolen- Falsified- CHANGE+ Prescription-</div>	<div>Profile 2</div> <div>ADULT (4.8%) YOUNG (5.9%) M (7.8%) URBAN (10.7%) SCHEDULE+ (8.4%) FLU+ (11.1%) MOR+ (4.2%) BUPRE+ (10.6%) STOLEN+ PRESCRIPTION+ FALSIFIED+ Change-</div>	<div>Profile 3</div> <div>YOUNG (6.5%) URBAN (4.5%) Schedule- (2.7%) ZOLP+ (13.7%) BROMA+ (3.6%) CLORA+ (2.6%) COPARA+ (17.0%) ALPRA+ (6.5%)</div>	<div>Profile 4</div> <div>SCHEDULE+ (5.6%) PARA+ (3.4%) MOR+ (6.3%) LORA+ (12.8%)</div>

Fig. 2. Graphical representation of the four different profiles of suspicious prescriptions including names of drugs, according to the results of the multiple correspondence analysis (MCA). **ADULT** = 31–44 years old; **ALPRA+** = alprazolam; **BROMA+** = bromazepam; **BUPRE+** = buprenorphine; **CHANGE+/CHANGE-** = changes on prescriptions; **CLORA+** = clorazepate; **COPARA+** = codeine-paracetamol; **EXPERIENCED** = 45–60 years old; **F** = women; **FALSIFIED+/falsified-** = falsified prescriptions; **FLU+** = flunitrazepam; **LORA+** = lorazepam; **M** = men; **MOR+** = morphine; **OLD** = >60 years old; **PARA+** = paracetamol; **PRESCRIPTION+/prescription-** = abnormal prescriptions; **RURAL** = rural pharmacies; **SCHEDULE+/schedule-** = prescription forms for scheduled drugs; **STOLEN+/stolen-** = stolen prescription forms; **URBAN** = urban pharmacies; **YOUNG** = <31 years old; **ZOLP+** = zolpidem.

over-writing on the prescription’. We observed that these criteria concerned prescriptions presented by women aged >45 years, in rural pharmacies, which were not on specific forms for scheduled drugs. These prescriptions were modified in order to obtain cardiovascular or muscular-skeletal system drugs (e.g. diuretics or benzodiazepines used for muscular contractions). A second profile was associated with the criteria of ‘stolen’, ‘falsified’ and ‘overlapping or non-rational prescription’. These criteria concerned prescriptions for scheduled drugs presented by men aged <45 years in urban pharmacies. They

are symptomatic of dubious behaviour because the individuals steal, copy or scan a prescription form in order to obtain nervous system drugs.^[17]

According to the literature, two profiles of a particular population could be defined. The first profile where modifications are made afterwards on a true medical prescription tends to be associated with behaviour patterns of self-medication, re-funding or because of a preferential or ignored pharmacodependence on a drug. This pharmacodependence could occur following several medical prescriptions with increasing doses over time. The second profile with stolen or falsified prescriptions, prescriptions not conforming to regulations and overlapping of prescriptions represents behaviour patterns observed among drug addicts who could divert nervous system drugs to modulate the consumption of other substances. Some of the drugs obtained by these prescriptions could also be sold on the street (e.g. buprenorphine in France).^[18,19]

Drugs identified on the diverted prescription forms were more frequently benzodiazepines, particularly flunitrazepam.^[19,20] A recent study about patterns of prescription of opiate maintenance drugs in Southern France found that flunitrazepam and zolpidem were most frequently used by patients who misuse buprenorphine.^[21] This pattern was related to multiple prescriptions and visits to physicians and pharmacists in the area in order to obtain high quantities of drugs. Because buprenorphine must be prescribed on a specific form for scheduled drugs, patients who abused it modified original prescriptions or robbed prescription forms to obtain the drug.^[5,18,22] Clonazepam, which was increasingly identified in the OSIAP survey, is a benzodiazepine marketed in France as an adjunctive treatment of epilepsy.^[23] Information obtained from the OSIAP system (complemented by other sources of information such as OPPIDUM [Observation des Produits Psychotropes illicites ou Détournés de leur Utilisation Médicamenteuse]) led to some modifications of prescription rules in France. During these last years, the French Medicine Agency has taken different measures to limit the misuse of drugs, such as with-

drawal of amineptine and scheduling of zipeprol. Since 2001, flunitrazepam has been limited to 14 days of prescription, without overlapping, and must be prescribed on specific prescription forms for scheduled substances. These rules explain the decreasing number of cases reported from 2001 to 2004, and the profile of suspicious prescriptions involving this drug. However, difficulties in diverting this drug led users to seek out another substance such as clonazepam^[23] or clorazepate^[19] (the higher dosage [50mg] was withdrawn from the French market in 2005).

Several drugs were found in diverted prescriptions even if they are not known for their addictive potential. We suspect that these medications may be sold on the black market: omeprazole, atorvastatin (found in stolen forms). Some drugs could be diverted for other purposes: thyroid hormones or diuretics could be used for weight loss. We also suspect an 'unrecognised pharmacodependence', for example paracetamol combined with caffeine and dextropropoxyphene, which is largely found in cases of drug-induced headache.

A new version of specific prescription forms for scheduled drugs was set up in 1999 in France. This modification took place as part of a general plan to improve pain management in the country. Thus, the aim of this unfalsifiable prescription form (with watermark) was to replace the counterfoil book,^[2] considered to be a barrier to the development of the prescription of major analgesics. In the OSIAP survey, these unfalsifiable forms accounted for 25% of all prescriptions. These categories of prescription forms represented 25% of all drugs implicated in the suspicious prescriptions, and were more frequently stolen than other prescriptions forms. By contrast, only 55% of drugs submitted to special rules of prescription were presented on accurate unfalsifiable prescription forms.

Conclusion

In conclusion, analysis of data collected from community pharmacies in the OSIAP survey gives information about patterns of diversion of medication in France. This system is able to evaluate the

impact of measures implemented in order to decrease the misuse of drugs and able to identify new patterns of drug diversion. Identification of profiles of suspicious 'prescription forms' could help pharmacists to better identify abnormal prescriptions. A European project has recently been implemented to extend this kind of survey to other countries in Europe.

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