Opioid substitution treatments through general practice in France: a french study based on reimbursement data

Tiphaine CANARELLI, French monitoring centre of drugs and drug addiction

EMCDDA meeting
European exchange on the practice and current issues in opioid substitution treatment (OST) in General Practioners’ settings

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Opioid substitution treatment in France:

Two opioid substitution treatments (OST) permitted:

- **High Dosage Buprenorphine (HDB):**
  - Subutex® (1996)

- **Methadone (MTD):**
  - Syrup (1995)
  - Capsule (2008)

**Prescription level:**

- **HDB predominant:** 80% of prescriptions
- **Recent recommendations aim at facilitating MTD use**

OST prescribed to over **130 000 opiate dependent people** in 2008
OST Prescription rules:

Strict guidelines for MTD:

- **Initial prescription restricted** (specialised care centres, hospitals, penal facilities). After stabilization, General Practitioners (GPs) liaising with structures are authorized to renew MTD

- **Strict patient compliance contract** (drinkable solution* of MTD, daily delivery at the centre, withdrawal of other opiates, urine tests, regular medical and psychological follow-up)

- Maximum daily dose 100 mg/day (60 mg recommended)

- Maximum of 14 days/prescription

More flexible framework for HDB:

- **Prescription by any physician** (GP or specialist, private or public structure)

- Maximum daily dose 16 mg/day (8 mg recommended)

- Maximum of 28 days/prescription

- No urine tests

*: MTD capsules are only allowed once patients are clinically stabilized (more than one year duration treatment)
Impact of OST for 15 years:

Clearly positive impact since they were introduced…

- **Broad access to treatment** (care facilities, antiretroviral treatments)
- **Reduction in the number of deaths due to heroin overdoses** (3500 lives saved)
- **Improved social integration**
- **Costs saving**

... But limits have appeared:

- **Heterogeneous access to treatment**
- **Misuse of the medication:**
  - Deaths due to MTD
  - Overdoses (MTD) and Buprenorphine-Benzodiazepine boosting
  - Injection and snorting of HDB
  - HDB black market and other substances black market (benzodiazepine, morphine sulphates…)

Monitoring of OST sales through reimbursement data
OST reimbursement data:

- Available through French National Health Insurance Organisation System (CNAM*)
- Regular collaborations CNAM / OFDT since 2002 dealing with:
  - **OST regional accessibility:**
    - In 5 French sites (2002) [1]
- New collaboration since 2008 dealing with:
  - **OST national accessibility:**
    - National representative patient sample in 2006 [3]
    - National representative patient sample in 2007 [3]
- Context of Health insurance organisation’s Plan to control the suspected misuse of OST started in 2004 and reinforced at the end of 2006

*: Caisse Nationale d’Assurance Maladie
Reimbursement trajectory of a national representative sample of 4,607 patients benefiting from the French general social security scheme who received at least one reimbursement of HDB and/or MTD between 1st January and 31st December 2007

Creation of several OST indicators per patient
- OST total dose dispensed during the year (HDB and/or MTD)
- Duration of treatment (HDB and/or MTD)
- Mean daily dose (MDD) received (HDB and/or MTD)
- Mean number and maximal number of health professionals met during the year (prescribers/pharmacies)
Definition of HDB misuse indicators
- HDB > 32 mg/Day
- 5 or more prescribers (lack of a fixed medical reference point)
- 5 or more pharmacies (lack of a fixed pharmacy point)

Thresholds beyond which HDB misuse is strongly suspected, particularly if they co-exist

Creation of potential HDB misuse regional indicator
(theoretical indicator of non therapeutic use of HDB)

Aims of the study:
- To describe the modalities of use of OST (levels of use, drug combinations)
- To describe misuses of OST especially for HDB
Patients results

- Characteristics of 2007 patients sample:
  - 80% (n=3711) received HDB vs 1 in 5 people MTD (n=896)
  - 78% Male / mean age 35 years old
  - 25% with Universal health care coverage (CMU)* (35% W/23% M)

- OST mean daily doses (MDD) in patients sample:
  - 8.9 mg/D HDB / 49.5 mg/D MTD
  - Beneficiaries of HDB: 87% MDD ≤ 16 mg/D / 11.2% [16;32]
  - Beneficiaries of MTD: 66% MDD [20;70] / 6% > 100 mg/D

- OST MDD among recipients of CMU:
  - 11.1 mg/D HDB / 52.9 mg/D MTD (more vulnerable population)

*: Special health insurance for people without income called “Couverture Maladie Universelle” (CMU)
Health professionals results

- Characteristics of physicians in private practice:
  - 97% of OST prescribers are GPs
  - Only 3% are specialists: Psychiatrists (55%) > gastroenterologists (8%) > gynaecologists (7%)
  - 90% of physicians prescribe HDB, 20% MTD, 10% both

- Characteristics of prescriptions in hospitals or specialised centres:
  - 27% patients concerned by such prescriptions (either exclusively hospital/centre treatment or in alternation -in case of relapse-)

- Characteristics of pharmacies:
  - 90% of pharmacies deliver HDB, 20% MTD, 10% both

In all, in 2007:
- patients have a mean number of 2 physicians
- number of physicians for HDB patients: [1;33] (vs [1;51] in 2006)
  for MTD patients: [1;8] (vs [1;7] in 2006)
- number of pharmacies for HDB patients: [1;42] (vs [1;67] in 2006)
  for MTD patients: [1;6] (as in 2006)
### Indicators of HDB misuse results

- **Significant fall of HDB > 32 mg/D doses:**
  - 1.6% in 2007 vs 2% in 2006 and 6% in 2002*  
  - Usual geographical localisation of HDB misuse in 3 regions: Ile-de-France, Provence-Alpes-Côte d’Azur (PACA) and Alsace

- Higher indicators among recipients of CMU (more vulnerable population)

- Regional indicator of HDB misuse (HDB doses potentially misused)
  - Ile-de-France (25%) > PACA (9%) > Alsace (7%)
  - In decrease compared to 2006: Ile-de-France (42%) > PACA (13%) > Alsace (11%)

*: MDD ≥ 32 and as many people (6%) ≥ 5 prescribers mostly in 3 sites (Paris, its northern suburbs and Marseilles)

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Geographical localisation of HDB misuse indicators:

- **Ile de France**
  - MDD > 32 mg/D (%)
  - ≥ 5 Prescribers (%)
  - ≥ 5 Pharmacies (%)

Maps showing the geographical distribution of HDB misuse indicators with color codes representing different percentages.
HDB > 32 mg/D patients profiles results (1)

- 1.6 % of the sample (n=61)
- 95 % Male / Higher mean age (38.6 years old)
- More frequently Universal care coverage beneficiaries (56 %)

Geographical localisation:
- In 14 regions: Ile de France (47 %) > PACA (14.7 %) > Alsace (9.8 %)
- Decrease of Ile de France HDB misuse predominancy (70 % in 2006)

Prescription and delivery modalities:
- Type of HDB > 32 mg/D prescription:
  - Princeps substance (Subutex®) in 50 %
  - Princeps/generic form in alternance in 50 %
- Type of HDB > 32 mg/D delivery:
  - Limited : all at once (30 %) or several times: 2 to 5 (50 %)

Health professional interactions:
- 67 % ≥ 5 prescribers / 70 % ≥ 5 pharmacies
Associated psychotropic drugs

Higher prescription rates of:

- **Most commonly used benzodiazepines, anxiolytics or hypnotics** used for therapeutic purpose and/or misuse
- **Other medicines:**
  - Indicators of misuse (**Fucidine®** local antibiotic used for skin abscesses potential marker of intravenous use)
  - Indicators of more global medicine traffic (**Cytotec®** gastric antisecretory agent exported as a pro-abortion substance)

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<td>Benzodiazepines prescription rate</td>
<td>40 %</td>
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<td>Fucidine® prescription rate</td>
<td>8 %</td>
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<td>Cytotec® prescription rate</td>
<td>0.4 %</td>
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*: Dipotassium Clorazepate (Tranxène®), Bromazepam (Lexomil®, Diazepam (Valium® 10 mg), Oxazepam (Séresta®), Clonazepam (Rivotril®), Flunitrazepam (Rohypnol®), Zolpidem (Stilnox®), Zopiclone (Imovane®)
Other data dealing with OST misuse/traffic

Qualitative data (TREND network system*):

- **HDB traffic organization**
  - HDB traffic growth until 2004 (beginning of health insurance control plan)
  - HDB traffic restructuring since 2006:
    - Local traffic decrease (HDB patients own resale)
    - International traffic expansion
      Dealers (Eastern Europe) collecting HDB through “mules” or patients and distributing HDB locally or in other countries** (Russia, Georgia)

- **HDB traffic targets**
  - Certain patients under OST treatment (MDD insufficient)
  - Other people: drug users (treatment and/or getting high), night clubbing or rave parties, week-end drug consumers among upper social classes
  - Other countries: global traffic (psychotropic drugs, Cytotec®…)

- **MTD traffic almost inexistent** (loaning between patients in case of MTD lacking)

*: Information system established in order to identify and describe changes in the trends and emerging phenomena related to illegal or misused substances

**: Subutex® 8 mg costs around 70 € per pill in these countries (versus 3 € through french black market)
Health organisation’s control plan to fight against HDB misuse

- Actions launched at regional level (health insurance offices) in 2004 and then reinforced at the end of 2006 aim at identifying OST traffickers or redefining treatment among rare patients (HDB daily dose > 32 mg, ≥ 5 prescribers and/or pharmacies)

- Types of actions (patients and/or health professionals):
  - Information letters for misusing patients *(HDB may not be reimbursed anymore if misuse persists) +/– for health professionals*
  - Patients convoking *(health insurance physician) in order to establish a medical protocol (involving patient, prescriber and regional health insurance physician)*
  - Registration of complaint against misusing patients
  - OST reimbursement fees suspension
  - Information letters for concerned physicians or pharmacists
  - Sanctions of medical or pharmaceutical associations
  - Registration of complaint against health professionals involved in traffic*

*: in 2007, 10 prescribers and 17 pharmacists indicted for their implication in HDB traffic
Conclusion of this study:

- New co-operation with CNAM has made it possible to carry out a national review of levels of OST use and HDB misuse:
  - Predominance of HDB utilization but recent recommendations aim at facilitating MTD prescription
  - Significant fall of HDB misuse indicators in comparison to previous studies:
    - HDB > 32 mg/D doses: 1.6 % (2007) vs 2 % (06) and 6 % (02)
    - 5 or more prescribers: 6.3 % in 2007 vs 9.7 % in 2006
- Effectiveness of the measures taken as part of the Health insurance organization's control plan
- Decree of 1st April 2008 aims at favoring links between patient/GP/pharmacist:
  - HDB prescription* involves inscription of the name of pharmacist on each prescription / regular contacts between health professionals / medical protocol in case of misuse

*: also for 3 other medicines: MTD, flunitrazepam, methylphenidate
References:


