

# Opioids prescriptions in pain therapy and risk of addiction: a one-year survey in Italy.

## Analysis of national opioids database

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### Abstract

**Background.** An “epidemic use” of legal opioids in the USA and other countries has been reported in the last 15 years. We have analysed the database of the Italian Ministry of Health regarding the prescription of opioids for pain management to verify the trend of opioids uses in Italy.

**Methods.** The amount of opioids prescribed for every single Italian patient in 2013 was anonymously recorded and transformed in daily MED (morphine equivalent dose). We considered every monthly percentage increase of MED during the entire period of chronic therapy for each patient.

**Results.** Classes of dosage increase for all patients in chronic therapy, distinguished between cancer and non-cancer ones, were created. We deduce that decreases or increases of small proportions prevailed in the observation period.

**Conclusions.** The opioids “plague” that is striking the USA is not registered in Italy during the observation period. The reasons might be due to the innovative and effective law 38/2010 and a health care system able to guarantee appropriate prescriptions for major analgesics.

### Key words

- influenza vaccine
- effectiveness
- Italy
- cohort study
- administrative data

## INTRODUCTION

### Overall situation

An “epidemic” in the use of opioids in the USA and other countries, including European ones, has been reported in the last 15 years [1-6]. Several scientific and governmental institutes bodies deal with this issue, including the Atlanta CDC (Center of Disease Control) that detected an increased number of deaths due to opioids use between 2014 and 2015 [7, 8]. One of the reasons is that patients, who begin to take opioids for pain therapy after surgery (postoperative analgesia), may develop an “addiction” when the treatment becomes chronic [9], i.e. when it lasts for more than three months [10]. American scientific and governmental bodies, that analysed this issue, agreed upon the need to set up national and supranational registers including prescription and consumption of opioids (which were difficult to establish in the USA) as well as the need for spe-

cific laws and guidelines regarding opioids prescriptions [11]. The main corrective actions were assisted by the ASIPP (American Society of Interventional Pain Physicians) through the establishment of a national register of prescriptions (NASPER – National All Schedules Prescription Electronic Reporting Act), however with limitations that relegated it to single states in the US and not to the whole country [12]. From a regulatory point of view, ASIPP established collaborations with the Atlanta CDC, the NIDA (National Institute on Drug Abuse) and the FDA (Food and Drug Administration) in order to guarantee appropriate prescription by physicians along with the promotion of a correct education in patients in treatment with opioids [13-15].

### Risk of addiction

Based on several surveys (principally carried out in the USA), the risk of addiction seems to develop when

prescribed doses exceed 40-50 mg MED (Morphine Equivalent Dose in milligrams) a day [11]. Another parameter as the average pro capita a year being 144 MED in Italy, is far below the average of 693 MED a year in the USA and other European and non-European countries (taking in consideration the six most common opioids) [11].

### **The aim of the study**

This study aims to assess if there is a risk of addiction for Italian patients suffering from chronic cancer and non-cancer pain, who undergo chronic pain therapy with opioids, based on a previous Italian study that defined which patients are to be considered chronic opioids users [16]. In that paper, Authors analysed a yearly Italian opioids prescription database with the aim to determine, with a specific algorithm, chronic cancer and non-cancer opioids users. With this in mind, we began analysing the same previous database of Italian Ministry of Health [16] regarding the prescription of opioids for pain management, to determine potentially addictive behaviours.

## **METHODS**

### **The population of the study**

All opioid prescriptions covered by the National Health System in 2013 were collected anonymously. Patients with at least one prescription of an opioid a month for three consecutive months and/or six non-consecutive months in the reporting period (from 1 January to 31 December) were considered chronic. Cancer patients were those who entitled to exemption code 048 ("malignant neoplastic disease") or the ones who were given ROOs (Rapid Onset Opioids; drugs that can only be prescribed to cancer patients in Italy).

### **Opioids requirements**

Analysing the encrypted identification codes of the patients, we examined the attitude of prescriptions for each cancer and non-cancer patient. The amount of required opiates for any patient was transformed into daily MED. The MED is calculated using a specific conversion tool to pass from any opioid prescribed to morphine equivalent dosage [17]. We excluded the first three months of therapy, as a period of dosage adjustment. Starting from the fourth month (our baseline), we considered every monthly percentage increase of MED during the entire period of chronic therapy.

### **Statistical analysis**

The patients were subdivided into classes of the percentage increase or decrease from the baseline value. We compared the results of cancer and non-cancer patients through two unpaired Student *t*-test samples. P values < 0.05 were considered significant.

## **RESULTS**

Based on previous study referring to the same database [16] in Italy 422 542 patients were found to be on chronic opioid therapy in 2013, of which 52 581 were cancer patients (with ticket exemption code number 048 – "malignant neoplastic disease"). The following

specific analysis of the database shows in *Table 1* the classes of mean dosage increase/decrease for all the patients considered as a unique cluster on chronic therapy and then distinguishes between cancer and non-cancer ones. *Figure 1* shows the numbers of total patients, cancer and non-cancer ones, in each incremental class. *Figure 2* represents the percentage increase in MED of opioids for all patients, cancer and non-cancer ones. Looking at both figures, we deduce that small proportions of decrease or increase prevailed in the reporting period. Cancer patients had a greater percentage of increases, although they were not statistically significant (*p*-value > 0.05). The mean MED for each patient is already described in a previous work [16].

## **DISCUSSION**

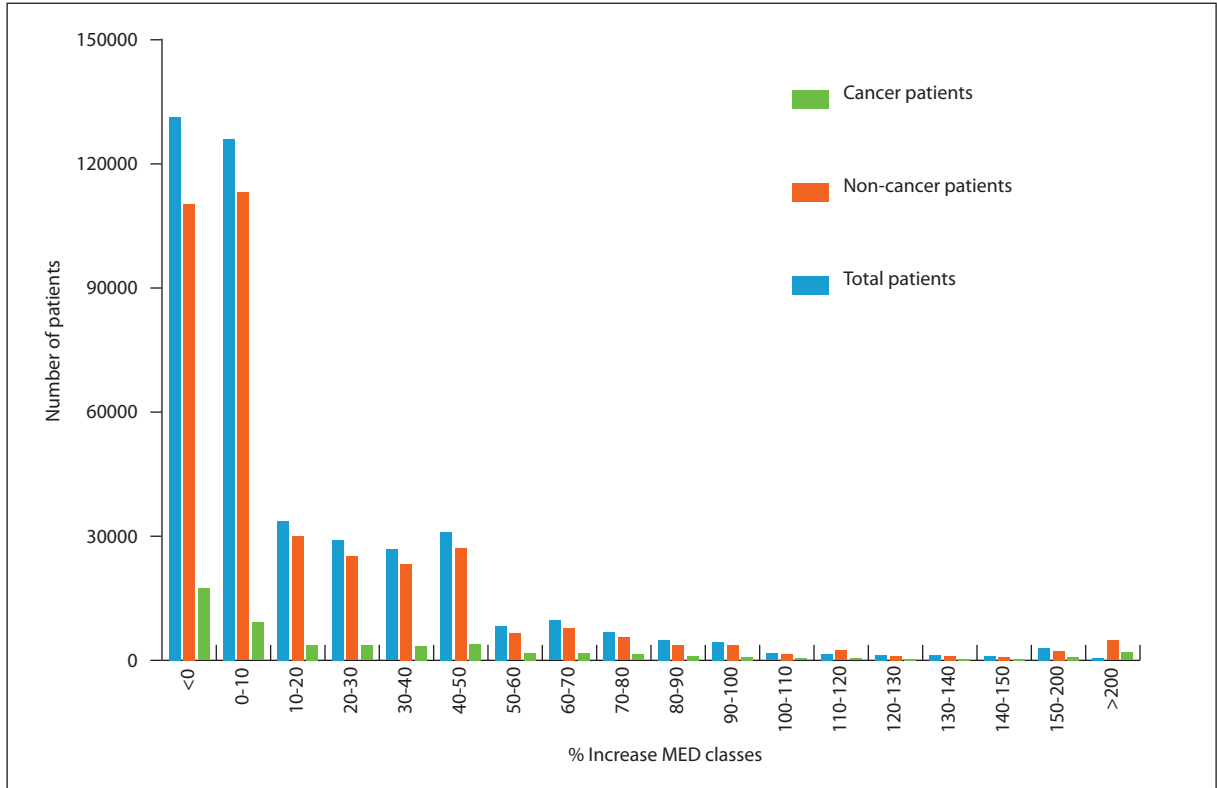
### **Opioids increase rate**

Our results did not show an excessive dosage increase in patients on chronic therapy with opioids in Italy during the observational period (patients mainly had a decrease or only a modest increase in their dosage). Despite not having an international database to compare to, this probably means that the American opioid epidemic did not involve Italy. This situation could be due to the Italian law 38/2010 [18] which, for the first time in Europe and one of the first times in the world, regulated the clinical practice regarding opioid therapy for patients suffering from chronic pain. In particular, it facilitates opioid prescription when necessary, meanwhile creating a culture of knowledge for healthcare professionals and instruments of control

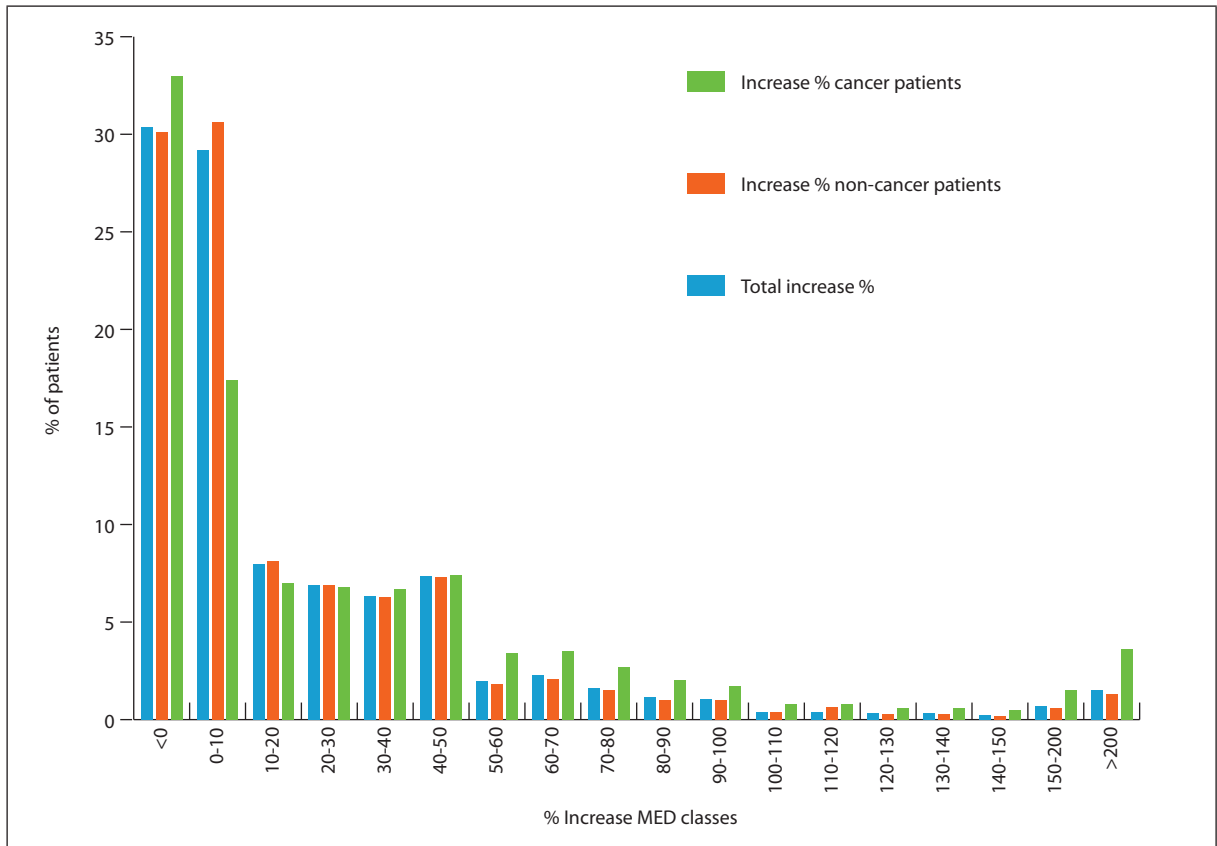
**Table 1**

Opioids morphine equivalent dose (MED) increase rate in chronic pain patients

Classes of MED increase (%)	Total patients	Non-cancer patients	Cancer patients
<0	131 316	112 358	18 958
0-10	125 055	115 108	9947
10-20	33 718	29 996	3722
20-30	29 070	25 127	3943
30-40	26 789	24 307	2482
40-50	31 014	27 077	3937
50-60	8366	6459	1907
60-70	9633	7769	1864
70-80	6802	5549	1253
80-90	4943	3699	1244
90-100	4436	3699	737
100-110	1690	1479	211
110-120	1521	1349	172
120-130	1309	1109	200
130-140	1309	1109	200
140-150	1014	739	275
150-200	2915	2219	696
>200	1642	809	833
Total	422 542	369 961	52 581



**Figure 1**  
Number of patients in each class of percent increase in daily MED of opioids.



**Figure 2**  
Percentage of patients in each incremental class of daily MED of opioids.

in order to ensure a constant appropriate prescription. This seems to prevent the development of the phenomenon of addiction in chronic patients. Other preliminary studies [16] proved that daily MED prescribed to non-cancer patients (30,13 mg) are lower than the baseline values of 40-50 mg/day that are considered to cause addiction by the American scientific society [11]. A recent analysis published on Pain [9] indicated how the starting dosage for patients who would receive chronic therapy in some American analgesic treatment centres (55 mg/day that would increase to 83 mg/day) was higher than the average dosage observed in Italy. This difference may primarily be due to the Italian law 38/2010 that created a “hub & spoke” organisation for the control and management of opioids, and secondly due to where the analysis took place in consideration that in the USA the analysis was done in specific analgesic treatment centres.

### **Situation in Italy**

In Italy all the prescriptions we considered, including those from general practitioners who might tend to start with lower doses due to lack of experience in the field of pain care. Recently we also considered cancer patients with long survival as patients potentially subject to addiction on the heels of the American “plague”. The average dosage in daily MED in Italian patients (79.47 mg) was coherent with an other international analysis that reported an average of 80 mg/day [19] in cancer patients.

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### **Risk of addiction**

Our analysis showed that neither a risk of addiction nor an indication to limit opioid therapy in these patients seems to exist, being in accordance with recent publications [20].

## **CONCLUSIONS**

The opioids “plague” that is striking the USA has not struck Italy. The reasons might be due to the innovative and effective law 38/2010 together with a health care system able to guarantee appropriate prescriptions for major analgesics. Nevertheless, it might be useful to continue the ministerial monitoring carried out in 2013, with the aim to identify any aberration in opioid prescriptions.

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### **Author contributions**

The authors contributed equally in study design, data analysis and interpretation and paper drafting.

### **Conflict of interest statement**

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