
First EFIC® Symposium - Societal Impact of Pain
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Therapeutic strategies for the treatment of pain

Paolo D. Siviero

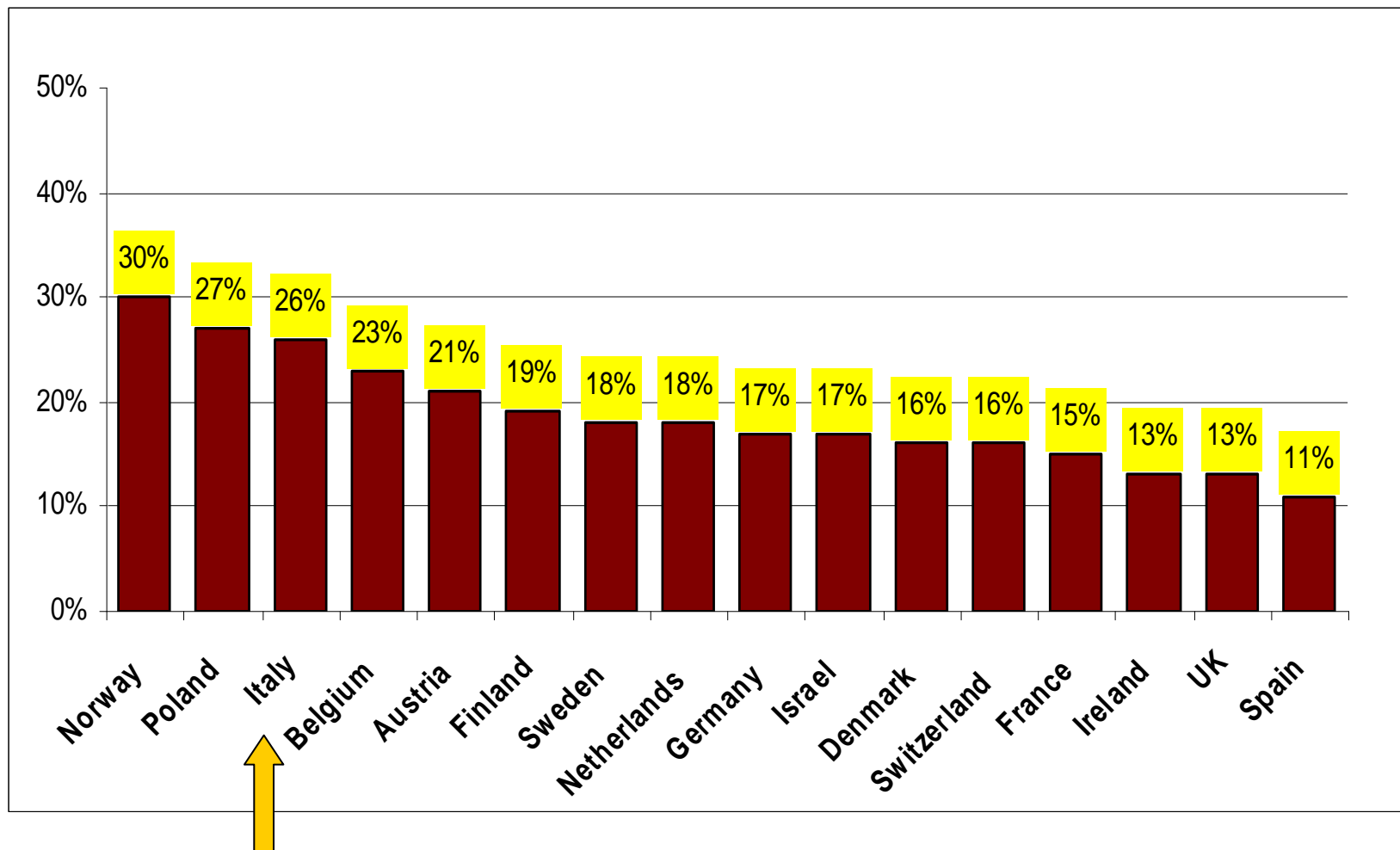
Economic Strategy and Pharmaceutical Policy Department

Office for Pharmaceutical Policy

Italian Medicines Agency

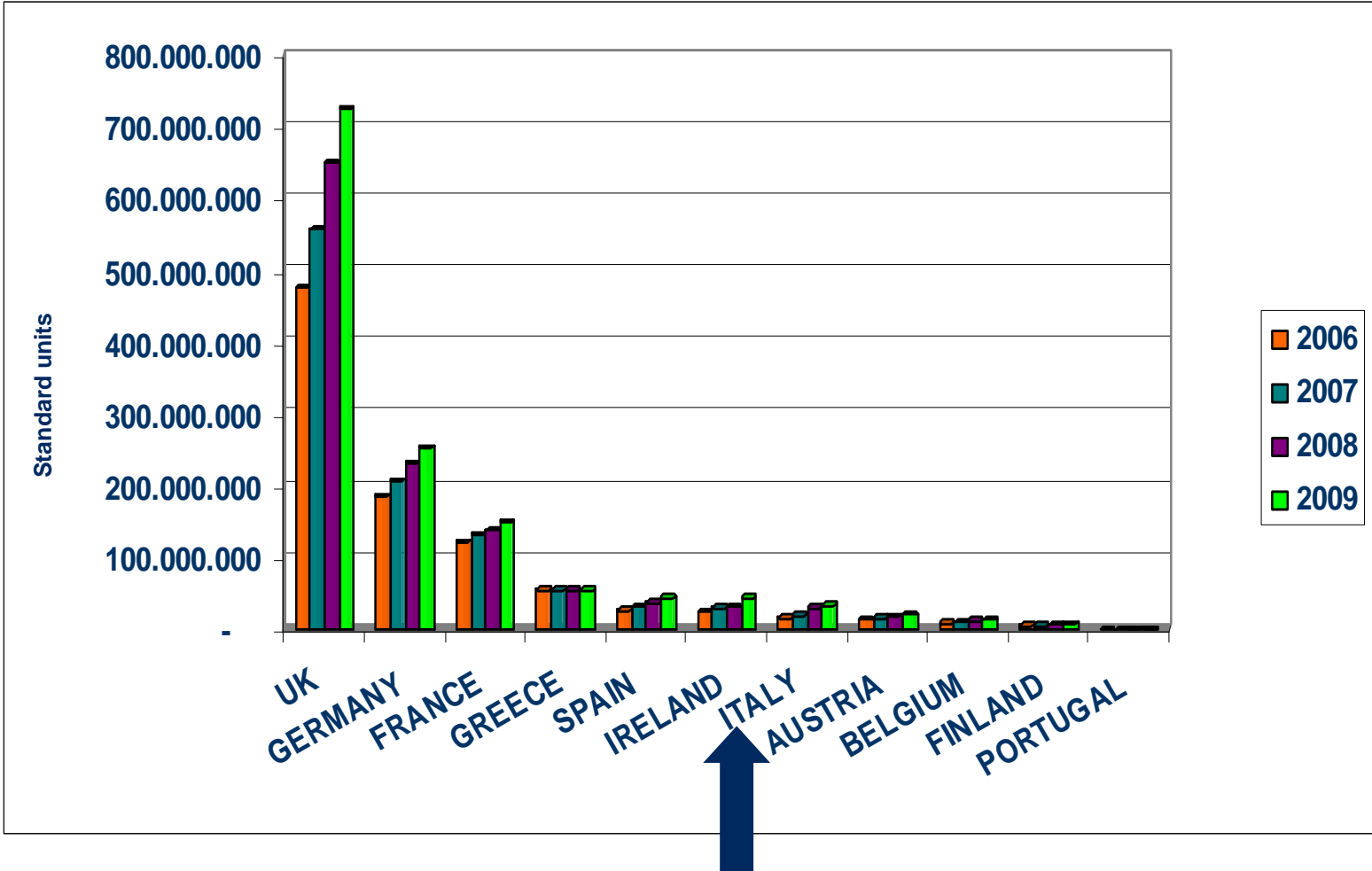
-AIFA-

Prevalence of chronic pain by country



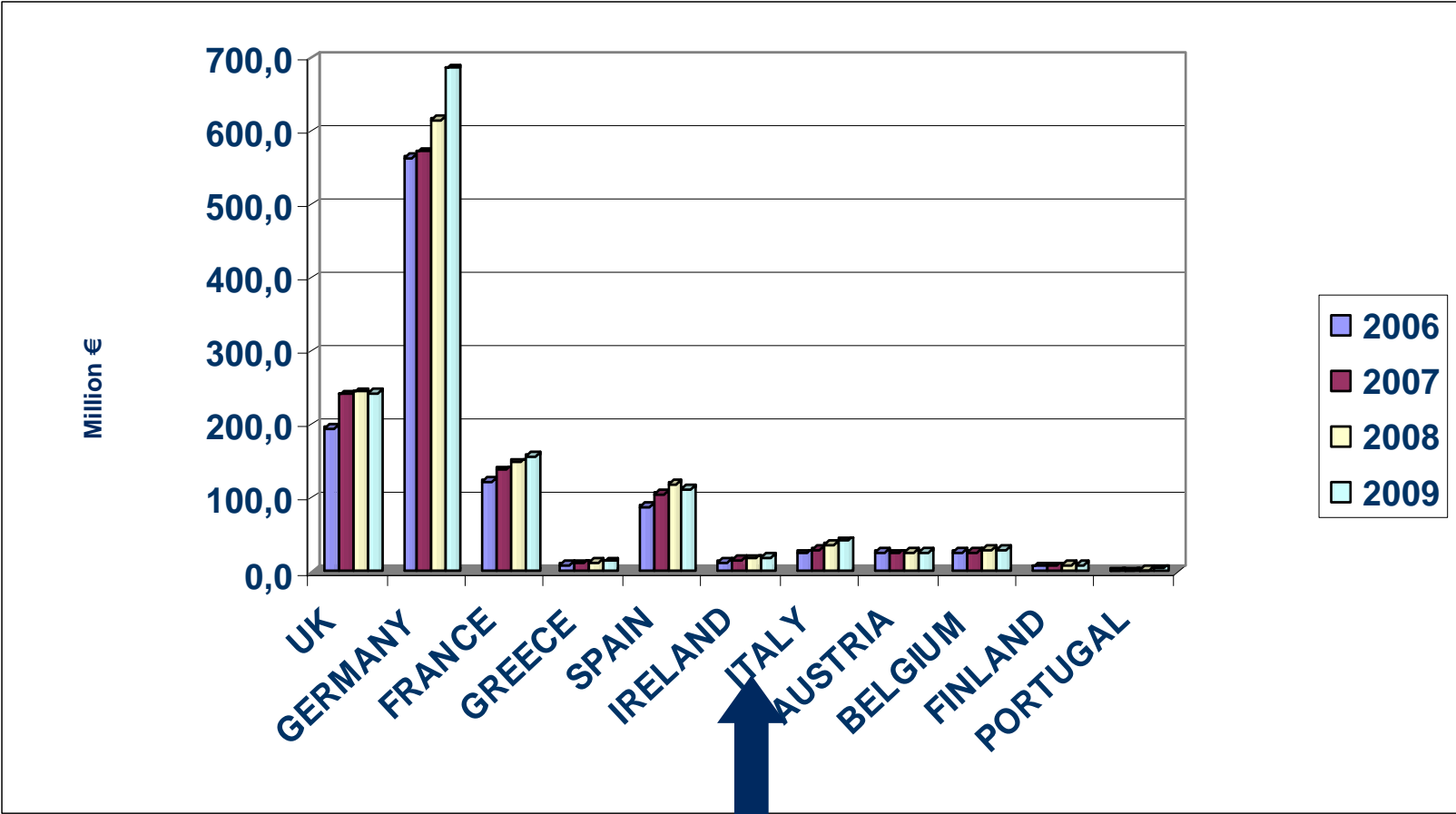
Source: Pain in Europe – A Report

Opioid medicines: consumption in Europe



Source: IMS Health data

Opioid medicines: expenditure in Europe



Source: IMS Health data

Laws for pain therapy in Italy

- **In Italy, in recent years, a series of rules have been approved to make the use of analgesic opioid medicines easier in pain therapy.**
- **The first step was taken with the law 12/2001.**
The main points of the law were:
 1. new prescription pad for opioid medicine in triplice copy;
 2. possibility of prescribing 2 opioid medicines or 2 different dosage of the same medicine for a therapy (maximum of 30 days);
 3. home delivery of medicines included in the Annex III bis.

Law n° 12/2001

Active substances included in the Annex III bis

Opioids	Cannabinoids *
<ul style="list-style-type: none">•Buprenorphine•Codeine•Dihydrocodeine•Phentanyl•Hydrocodone•Hydromorphone•Methadone•Morphine•Oxycodone•Oxymorphone	<ul style="list-style-type: none">•Delta(9)-tetrahydrocannabinol•Trans- Delta(9)-tetrahydrocannabinol <p>*This medicines are not commercially available in Italy. Physicians who want to use these cannabinoids for their patients must apply for their import to Central Narcotics office of the Ministry of Health.</p>

Ministerial Decree April 4th 2003

- **Simplification to the law 12/2001**
- prescription of active ingredients associations one of which included in the Annex III bis (atropine + morphine, paracetamol+ codeine; propyphenazone +codeine)
- Elimination of obligation by physician to:
 - write measures, dosages and route of administration on every copy
 - retain copy of prescription for six months

AIFA determination March 9th 2005

- **Abolition of *Note AIFA number 3* for the association codeine/paracetamol**
- **Only Tramadol was subject to *note AIFA number 3***

Tramadol prescription

- Since October 2009 the *note AIFA number 3* "medicines for the treatment of pain" was abolished.
- The medicines, subjected to *note 3*, are therefore reimbursed by the national health service, without the limitations provided by the note.

Tramadol



Variation date 27/10/2009			
Product data before changes		Product data after changes	
Type of price	Public retail price for mutual recognition. (LAW 449/97 ART.36) included VAT and abolition of regressive markup (FINANZ.2003)	Type of price	Public retail price for mutual recognition. (LAW 449/97 ART.36) included VAT and abolition of regressive markup (FINANZ.2003)
Class NHS	A	Class NHS	A
NHS system	Only for patient pathology affected	NHS system	Reimbursed
AIFA note	Note 3: Class A for pathology	AIFA note	
Type of prescription	RNR – NOT REPEAT PRESCRIPTION ART.89 D.L.VO 219/06	Type of prescription	RNR – NOT REPEAT PRESCRIPTION ART.89 D.L.VO 219/06

New law for pain therapy in Italy (1)

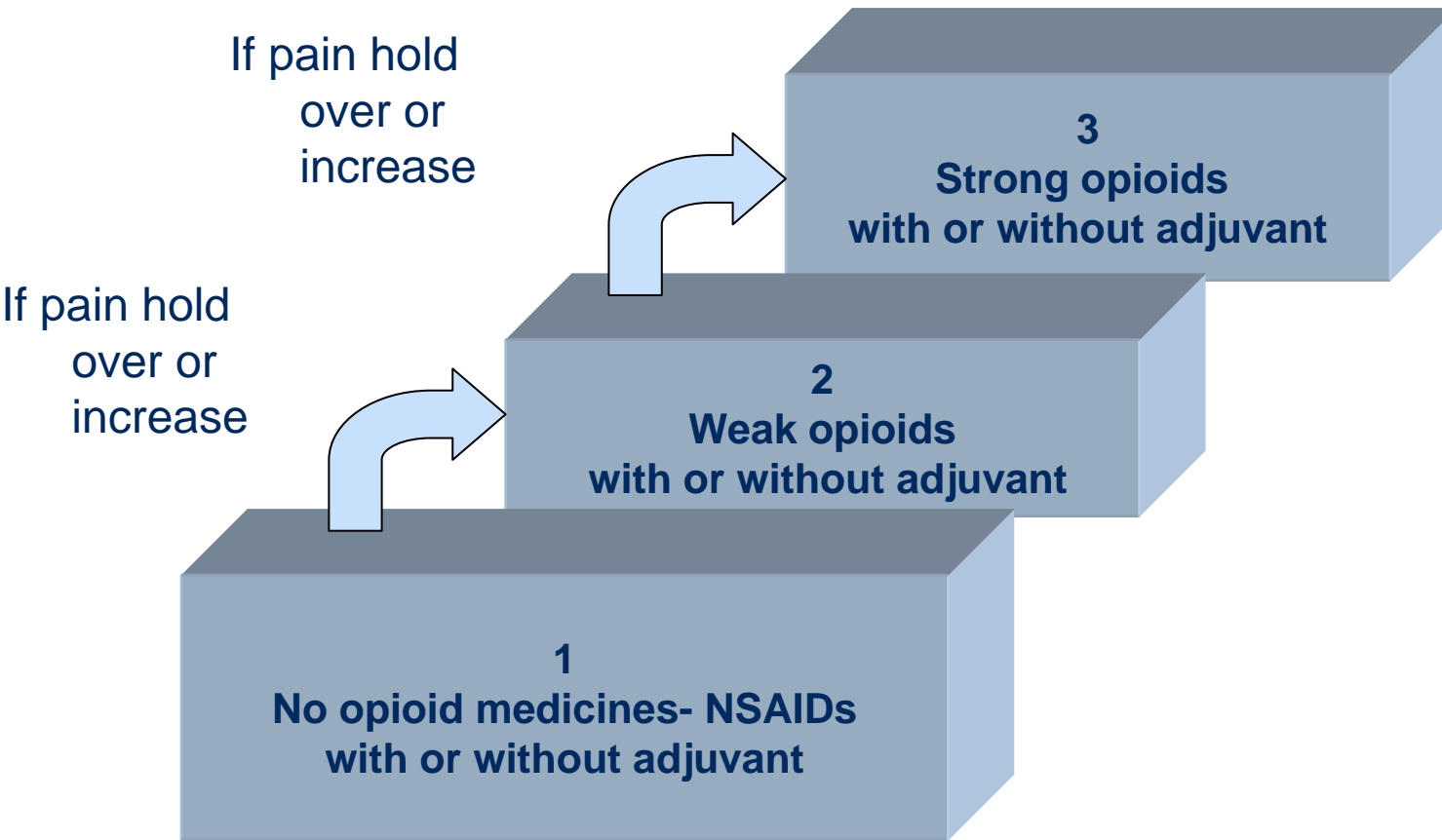
- A very important new law was adopted on March 9th 2010 in Italy,
- that considers **pain as an integral and indispensable patient's therapeutic pattern** and takes into consideration the **respect, the dignity and integrity" OF THE PERSON"** providing equal access to assistance and appropriateness to the specific needs of the sick.

New law for pain therapy in Italy (2)

Main points:

- Assessment of pain and use of medicines in case history;
- Creation of a network for pain treatment and palliative care on a regional basis. It will facilitate the access both to palliative care and pain treatment;
- Simplification of the prescription for non injectable opioids;
- No more prescriptions on special pad for opioids but use of the National Service prescription pad.

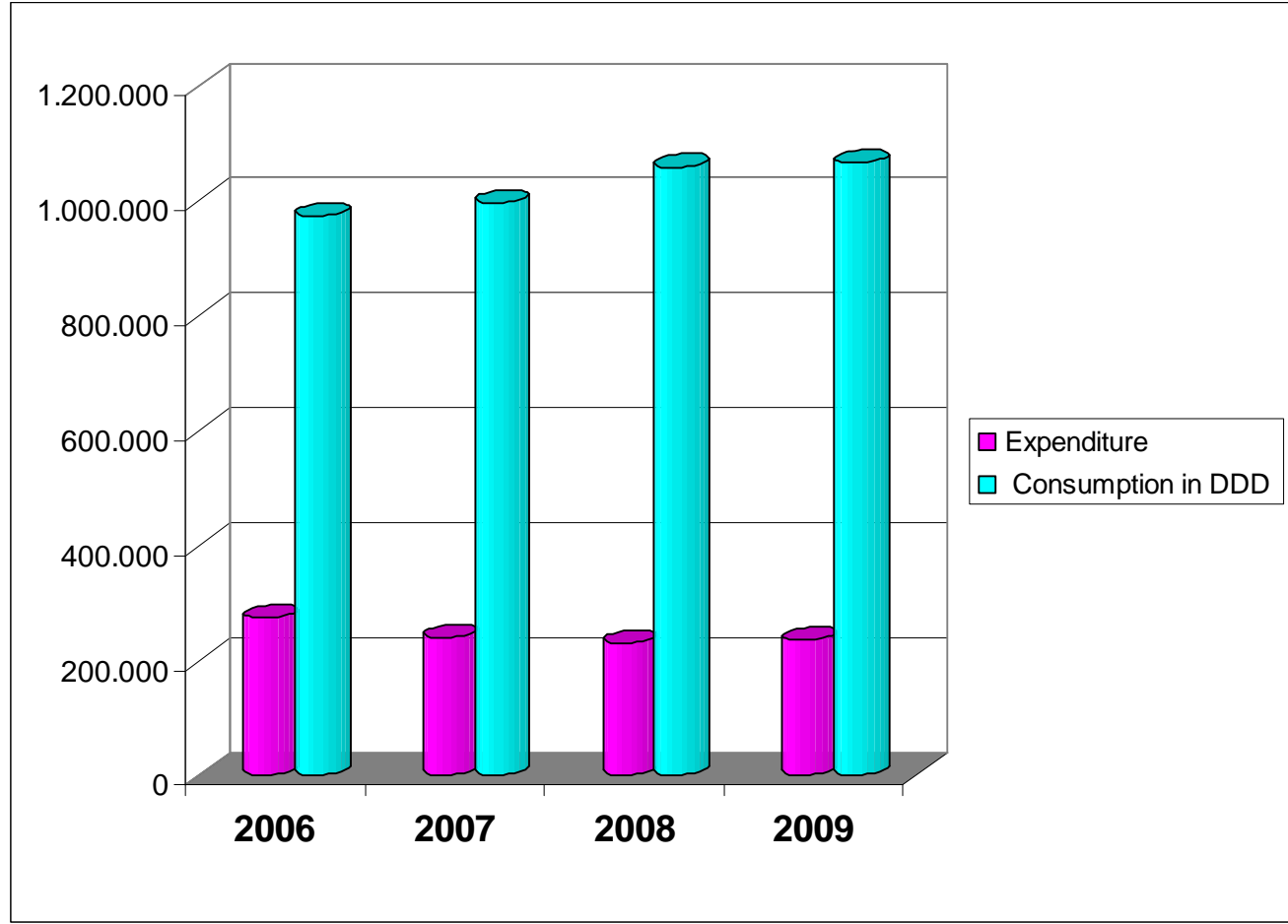
OMS Analgesic Scale



Total consumption and expenditure for pain therapy in Italy



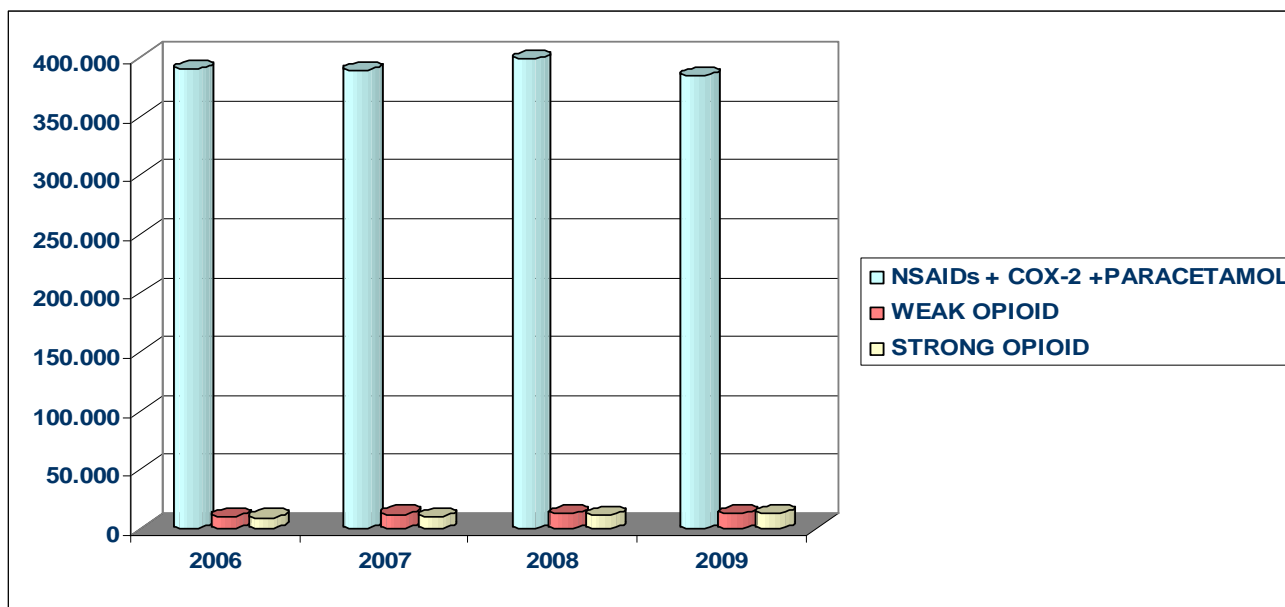
AGENZIA ITALIANA DEL FARMACO



Source: IMS Health data

Consumption according to OMS Analgesic Scale

	2006	2007	2008	2009
NSAIDs + COX-2 +PARACETAMOL	390.260	388.917	398.884	385.054
WEAK OPIOID	10.227	11.793	12.106	12.533
STRONG OPIOID	9.039	10.259	11.360	12.666



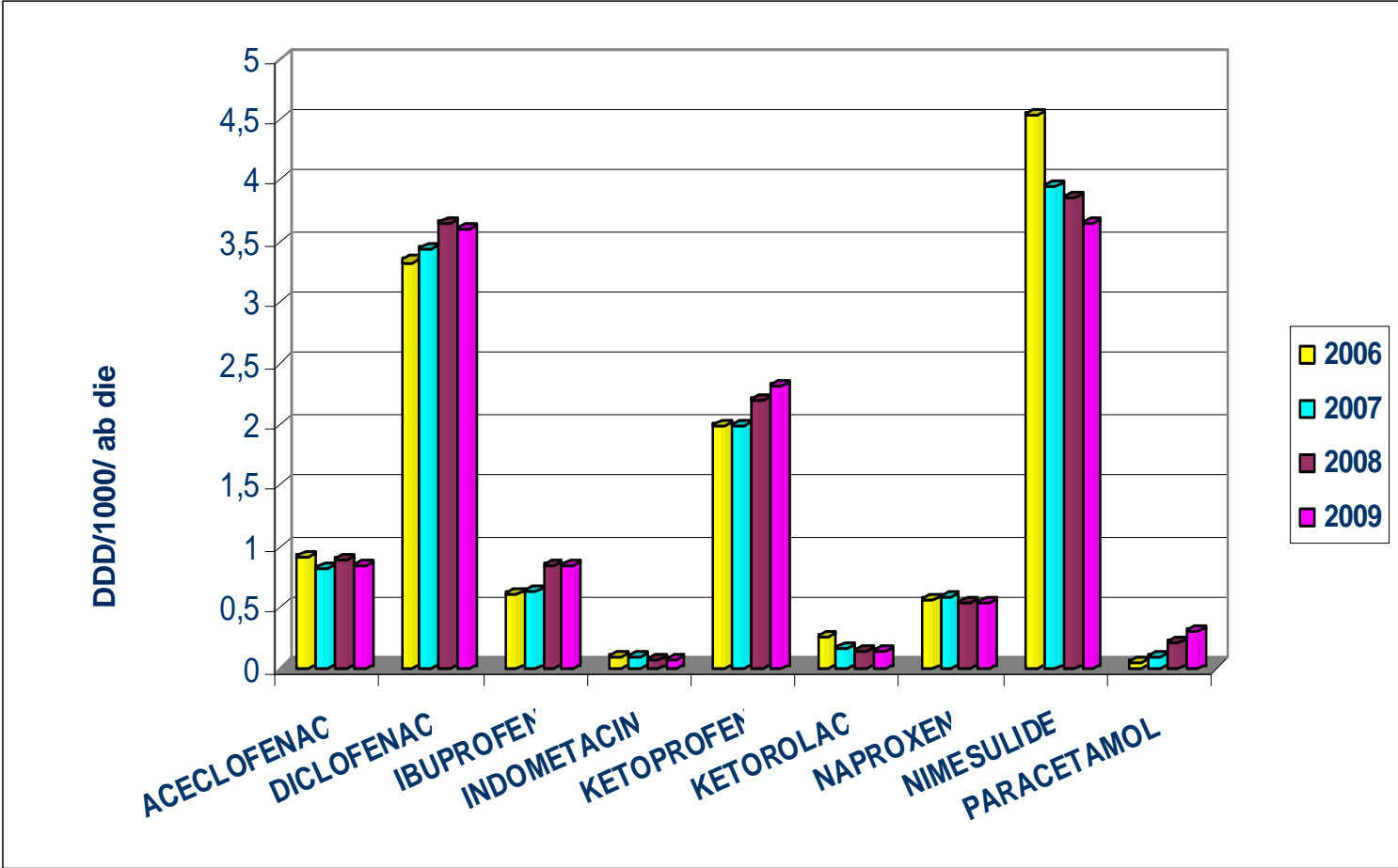
Source: IMS Health data

No opioids- NSAIDs with or without adjuvant: Consumption

MOLECULE	Consumption in DDD/1.000 Ab/ die for pain therapy			
	2006	2007	2008	2009
ACECLOFENAC	0,92	0,82	0,89	0,83
DICLOFENAC	3,33	3,44	3,65	3,60
IBUPROFEN	0,60	0,64	0,84	0,84
INDOMETACIN	0,10	0,09	0,08	0,06
KETOPROFEN	1,98	1,99	2,19	2,31
KETOROLAC	0,25	0,16	0,15	0,14
NAPROXEN	0,55	0,59	0,54	0,54
NIMESULIDE	4,54	3,96	3,85	3,64
PARACETAMOL	0,05	0,10	0,21	0,30
TOTAL	12,32	11,79	12,4	12,26

Source: IMS Health data

No opioids- NSAIDs with or without adjuvant: Consumption



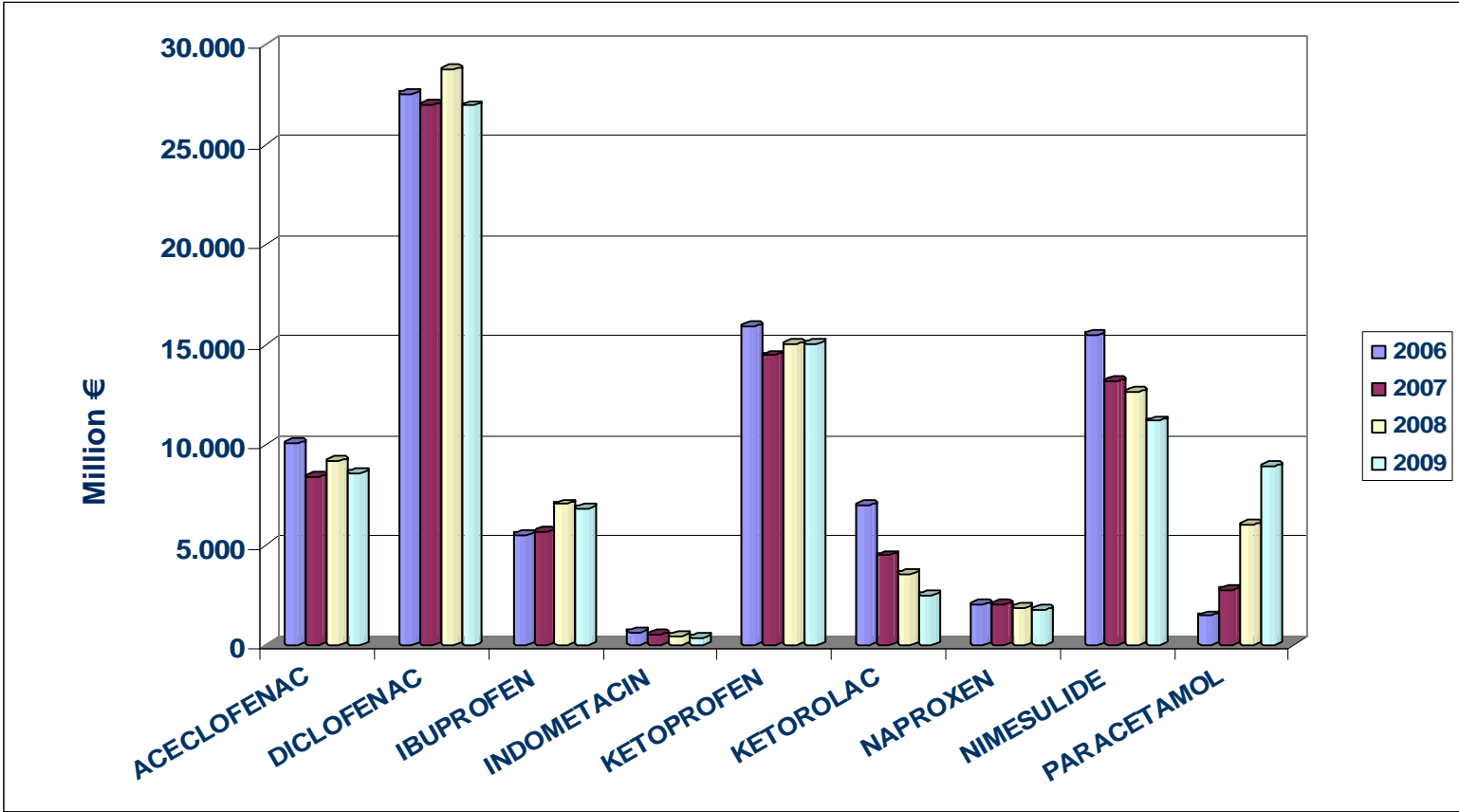
Source: IMS Health data

No opioids- NSAIDs with or without adjuvant: expenditure

MOLECULE	Reimbursed expenditure by NHS for pain therapy (€x 1.000)			
	2006	2007	2008	2009
ACECLOFENAC	10.086	8.373	9.169	8.609
DICLOFENAC	27.554	26.957	28.733	26.952
IBUPROFEN	5.506	5.629	7.043	6.824
INDOMETACIN	630	514	474	375
KETOPROFEN	15.913	14.473	15.018	15.075
KETOROLAC	6.977	4.468	3.542	2.499
NAPROXEN	2.027	2.013	1.859	1.740
NIMESULIDE	15.516	13.154	12.629	11.201
PARACETAMOL	1.454	2.770	6.006	8.916
TOTAL	85.662	78.350	84.473	82.191

Source: IMS Health data

No opioids- NSAIDs with or without adjuvant: expenditure



Source: IMS Health data

Weak opioids with or without adjuvant: consumption and expenditure



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	2006	2007	2008	2009
Expenditure				
Codeine	2.963	5.814	10.972	13.761
Tramadol	12.175	13.773	13.921	14.389
Total	15.138	19.587	24.893	28.150
Consumption*				
Codeine	0,45	0,38	0,4	0,29
Tramadol	10.226	11.793	12.106	12.533
DDD/1000 ab/die	0,48	0,55	0,56	0,57

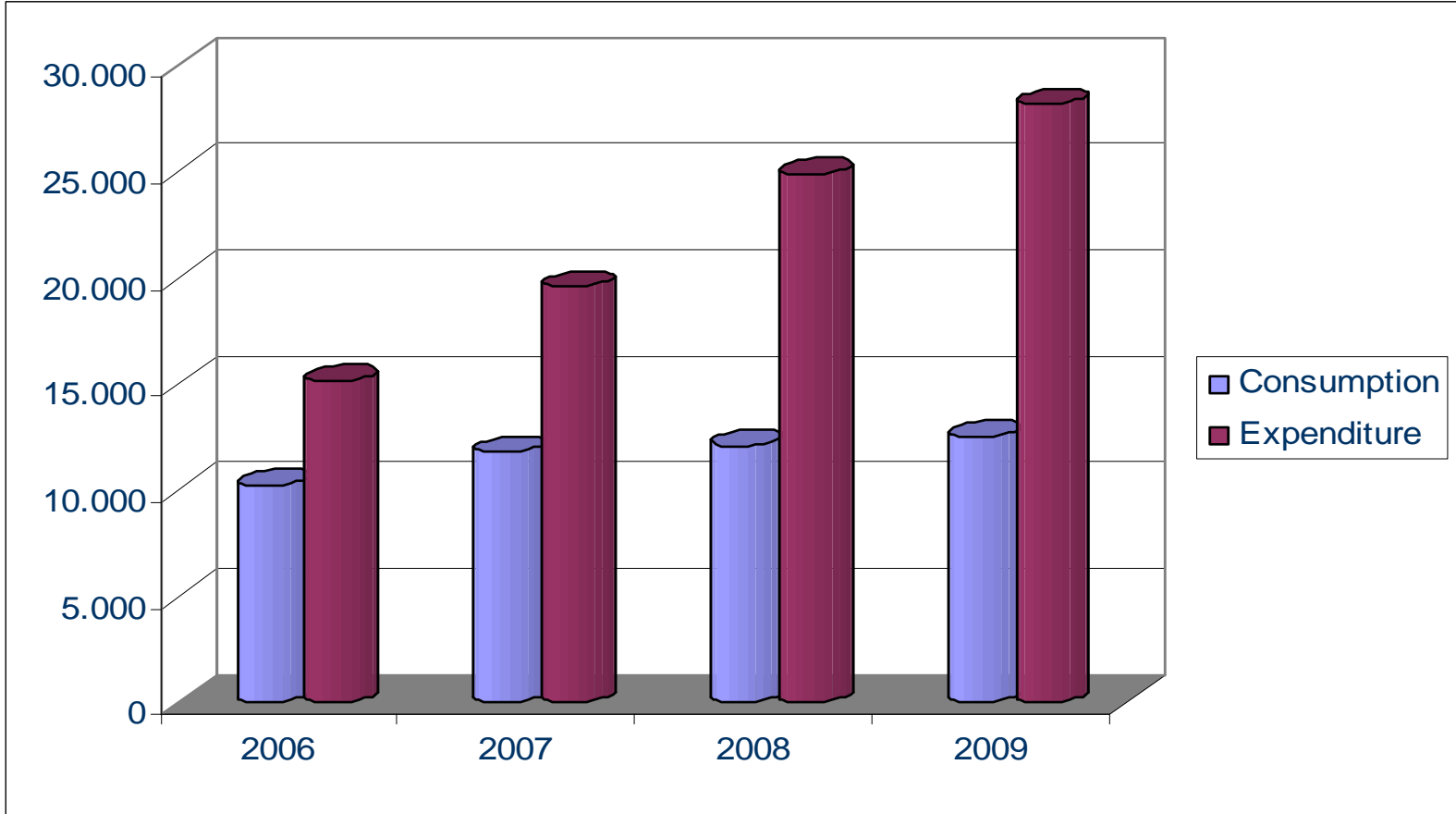
* Consumption is expressed in DDD

Source: IMSHealth data

Weak opioids with or without adjuvant: consumption and expenditure



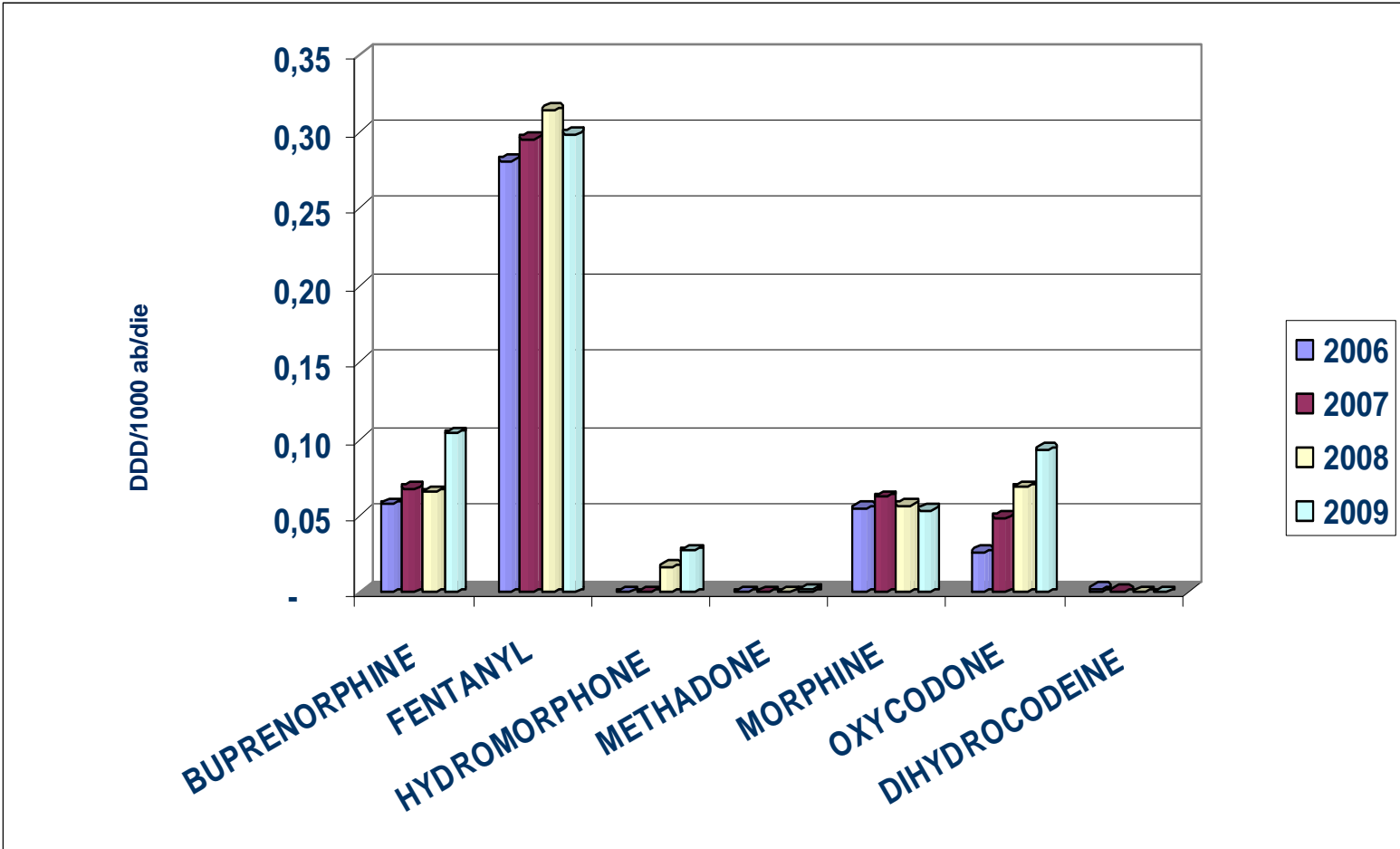
AGENZIA ITALIANA DEL FARMACO



* Consumption is expressed in DDD

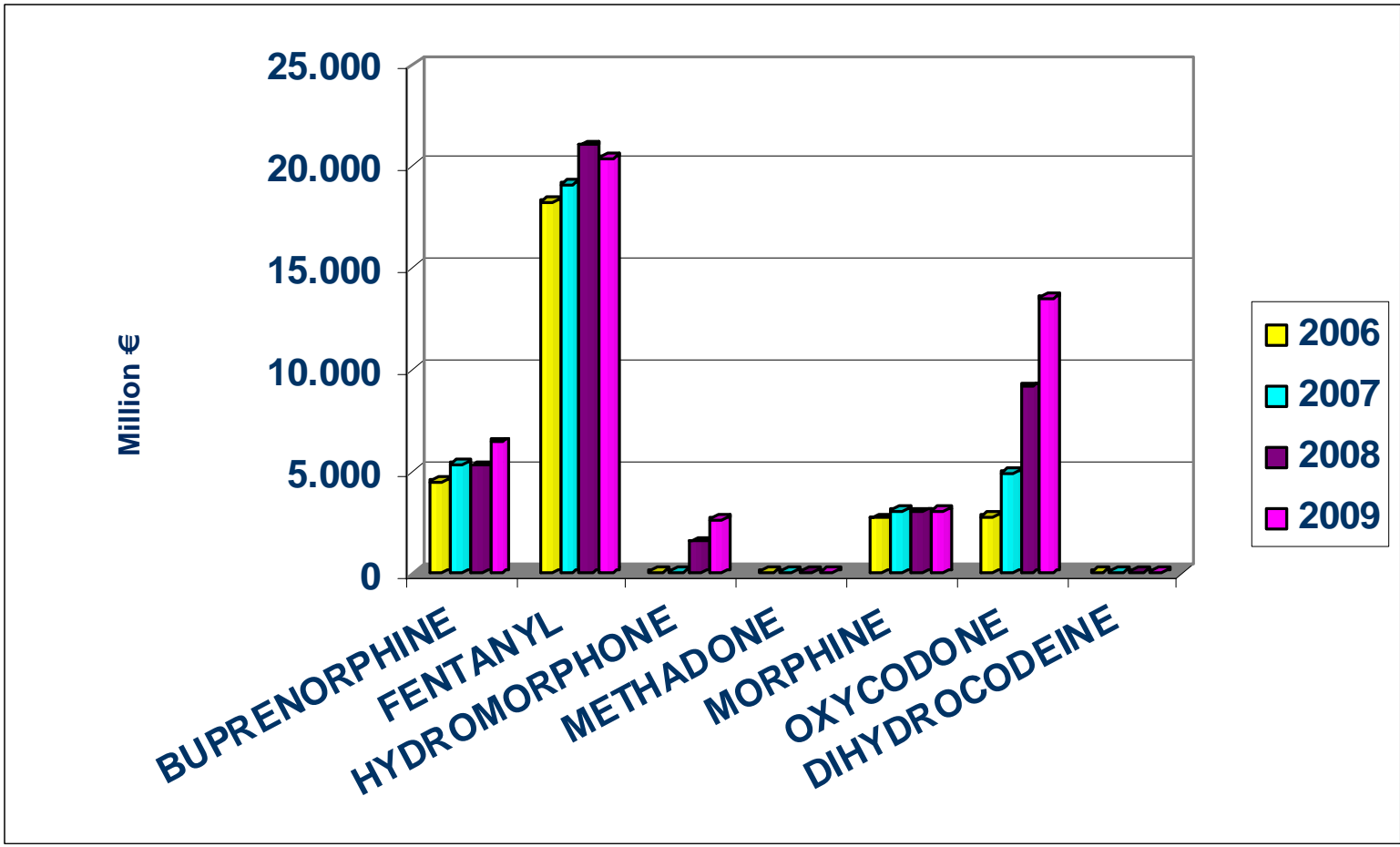
Source: IMSHealth data

Strong opioids with or without adjuvant: consumption



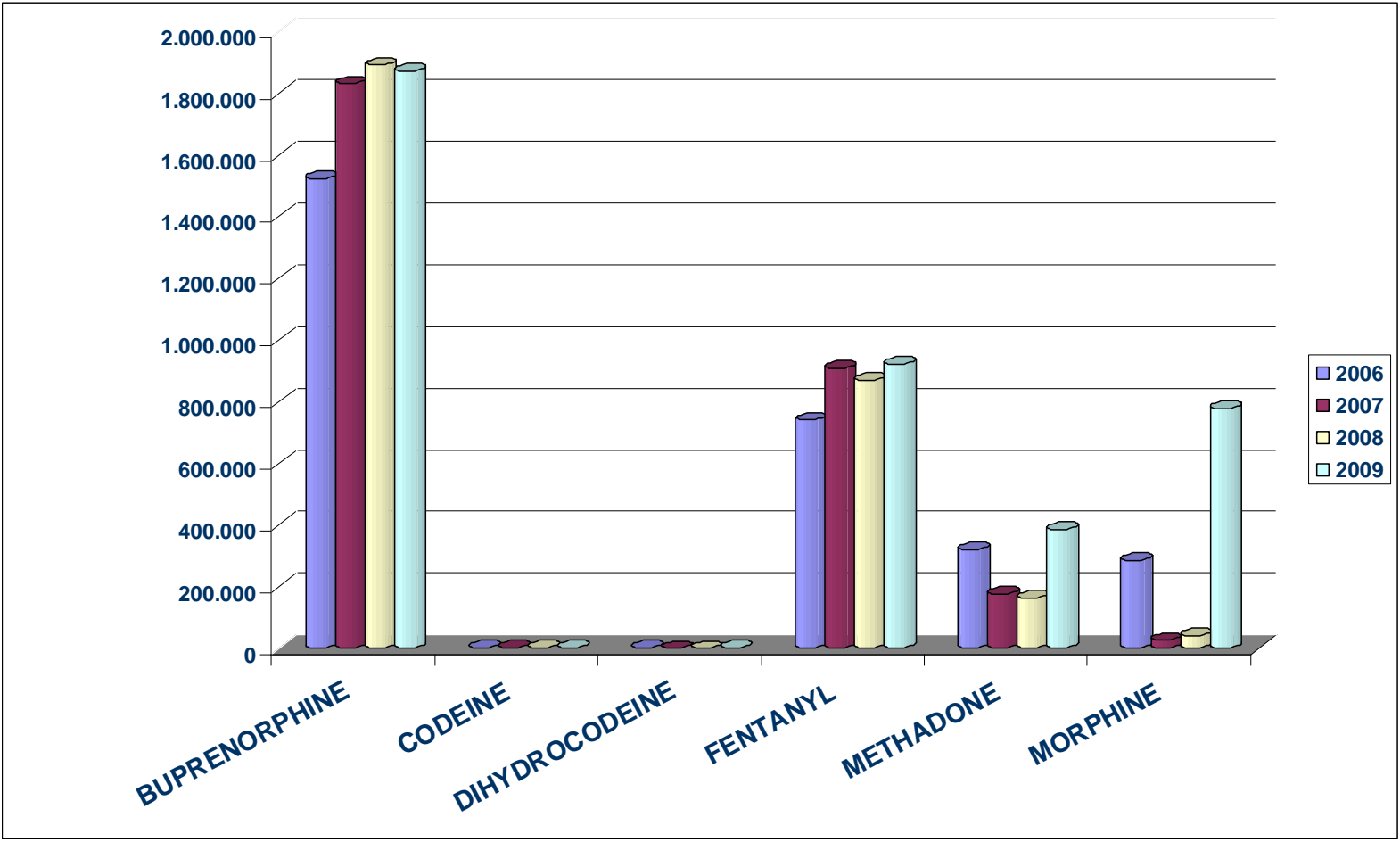
Source: IMS Health data

Strong opioids with or without adjuvant: expenditure



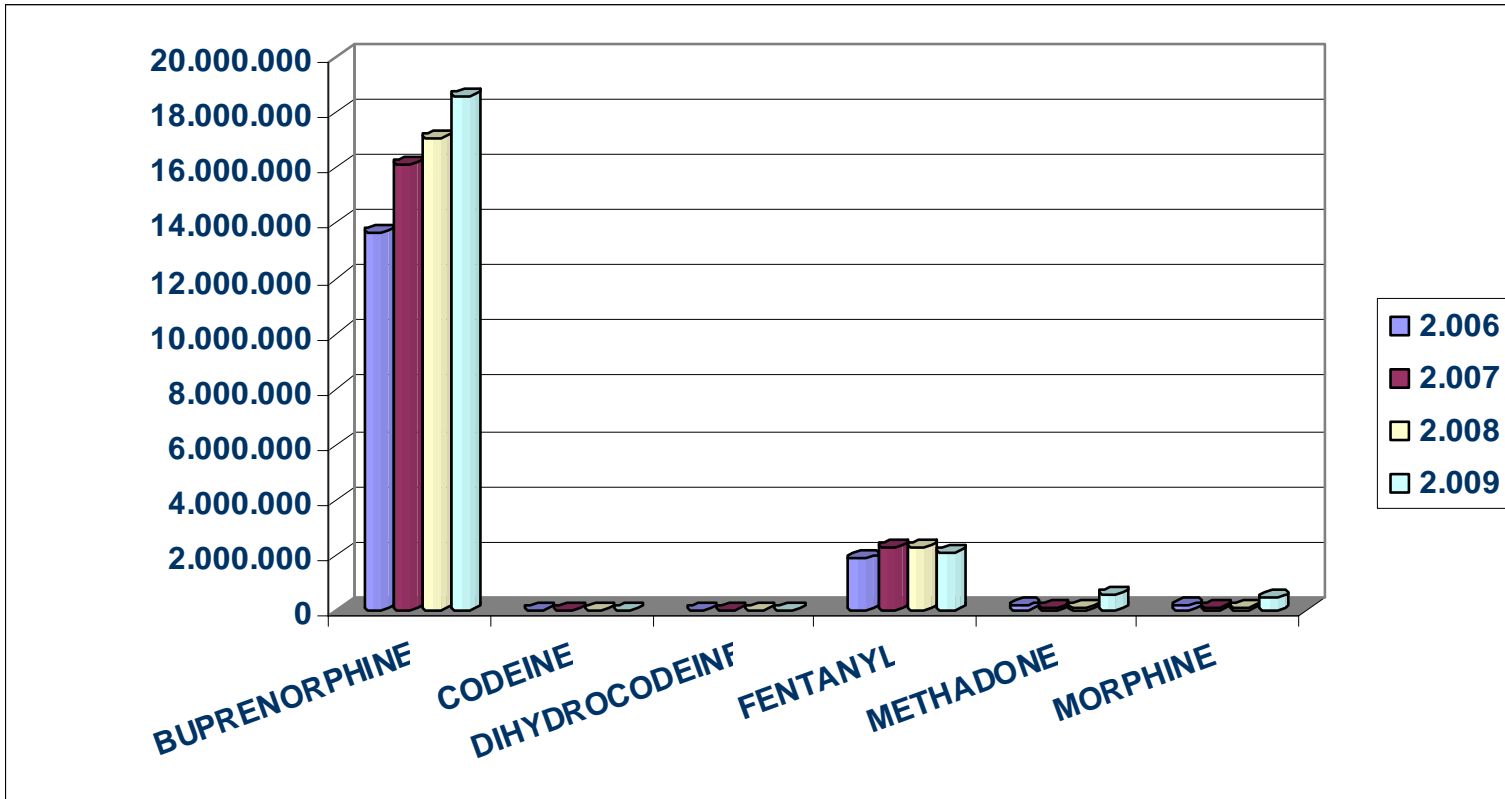
Source: IMS Health data

Opioid medicines: hospital consumption



Source: Traceability hospital data

Opioid medicines: hospital expenditure

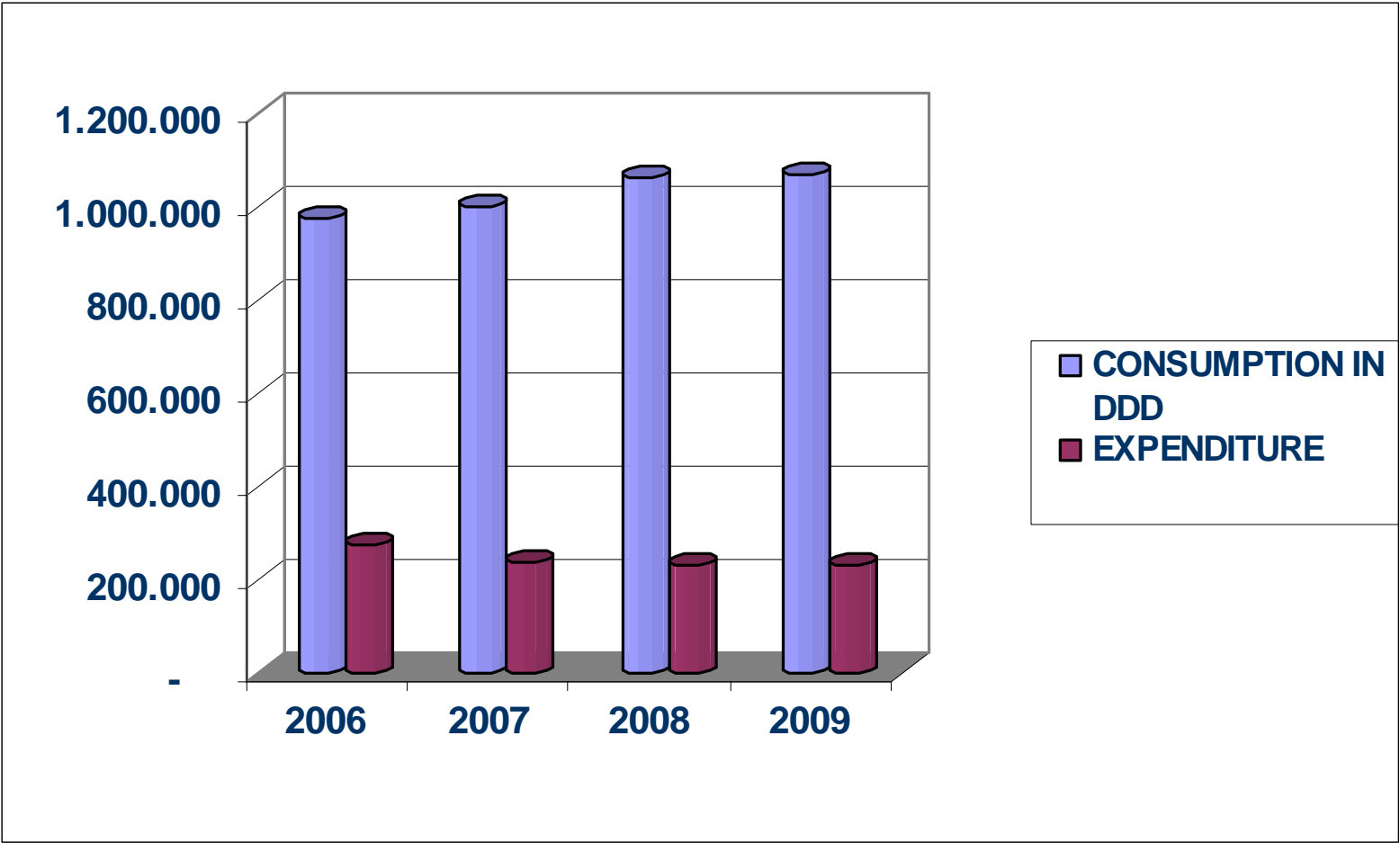


Source: Traceability hospital data

Adjuvant medicines: consumption and expenditure

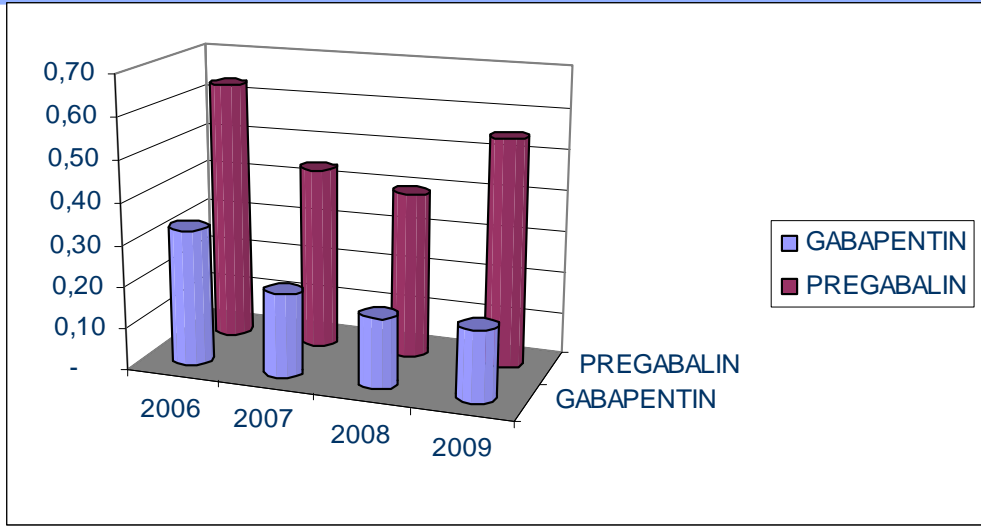


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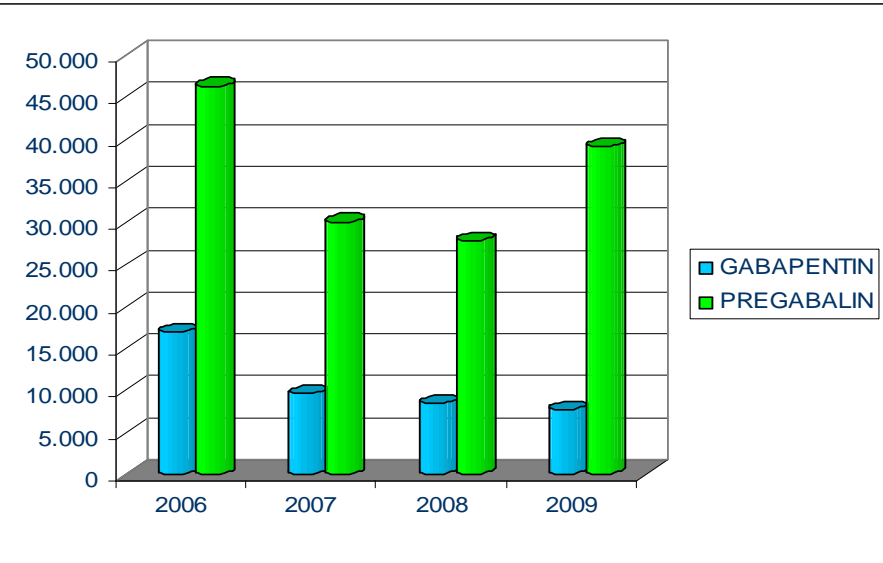


Source: IMS Health data

Neuropathic pain: consumption and expenditure



Expenditure in million €



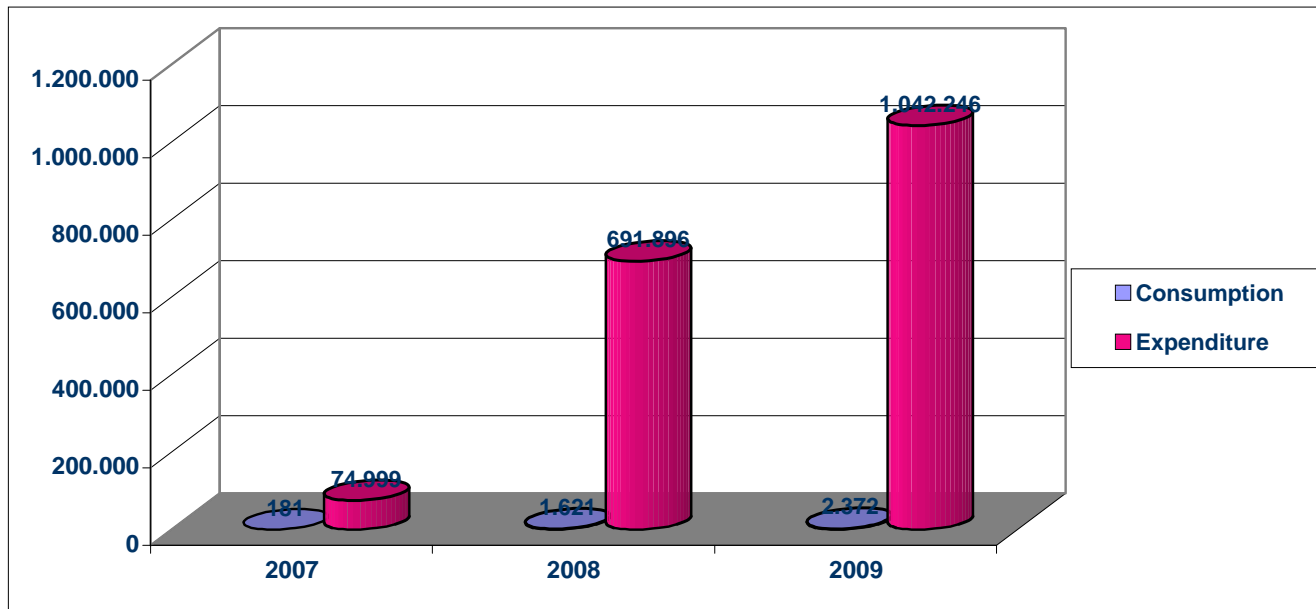
PRIALT: an orphan drug for pain therapy (1)

- **PRIALT** is indicated to manage severe chronic pain in patients for whom intrathecal (IT) therapy is warranted, and who are intolerant of or refractory to other treatments, such as systemic analgesics, adjunctive therapies, or IT morphine.
- Since the number of patients that required intrathecal therapy was very low, the disease was considered "rare", and Prialt in July, 2001 was designated an "orphan medicine"

PRIALT: an orphan drug for pain therapy (2)

- On 21 February 2005 the European Commission granted authorization to Marketing for Prialt, which is valid throughout the European Union
- This authorization was renewed for 5 more years
- In Italy Prialt granted authorization (AIFA 7/5/2007) and was on sale since 9/7/2007

Prialt: consumption and expenditure

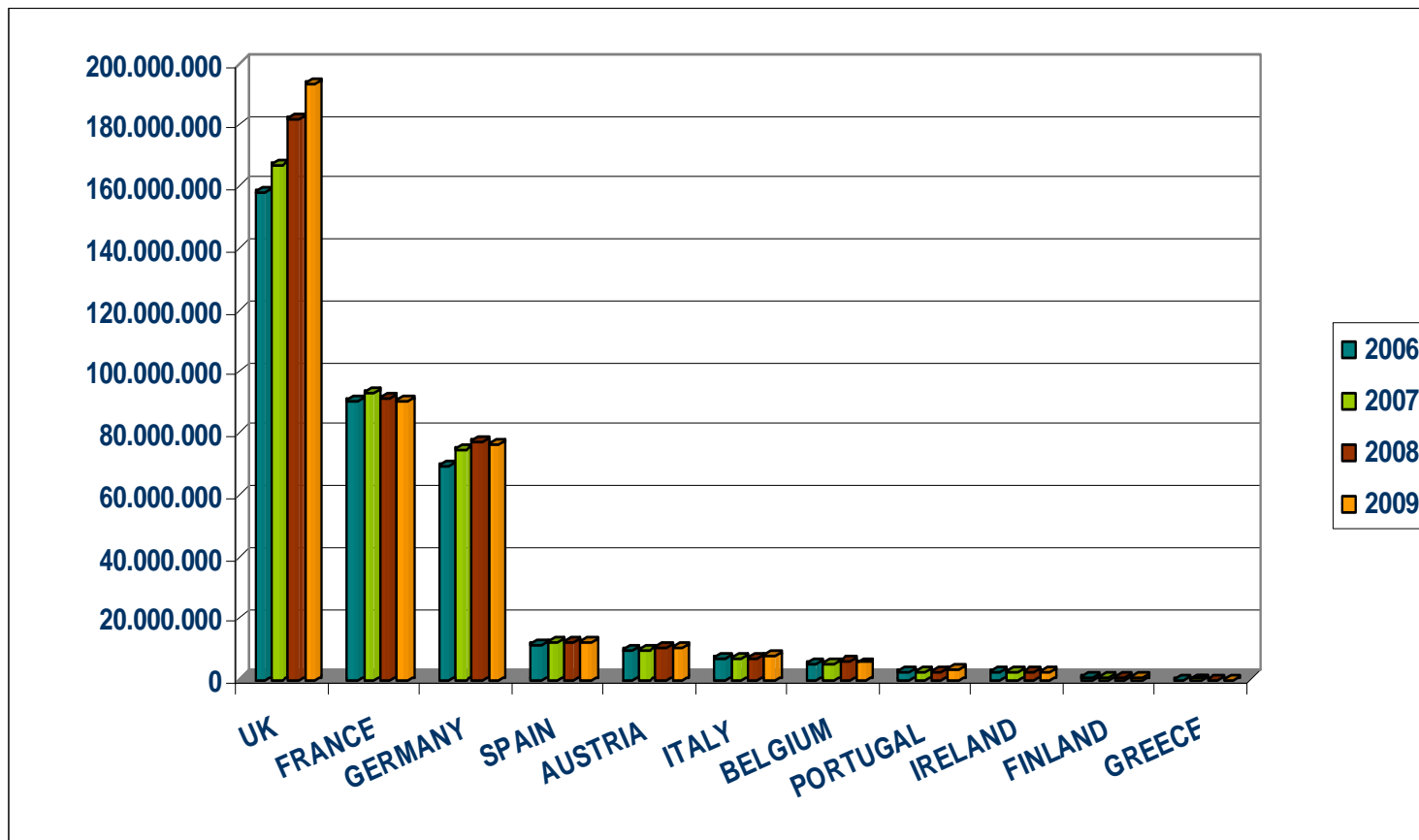


Source: Traceability hospital data

Prescription of strong opioids in EU

- **Oral morphine** remains the drug of choice for moderate or severe cancer pain and an important indicator of progress in cancer pain management, according to international guidelines
- We analyzed the trend in morphine and other strong opioids consumption in Europe

Morphine prescription in Europe

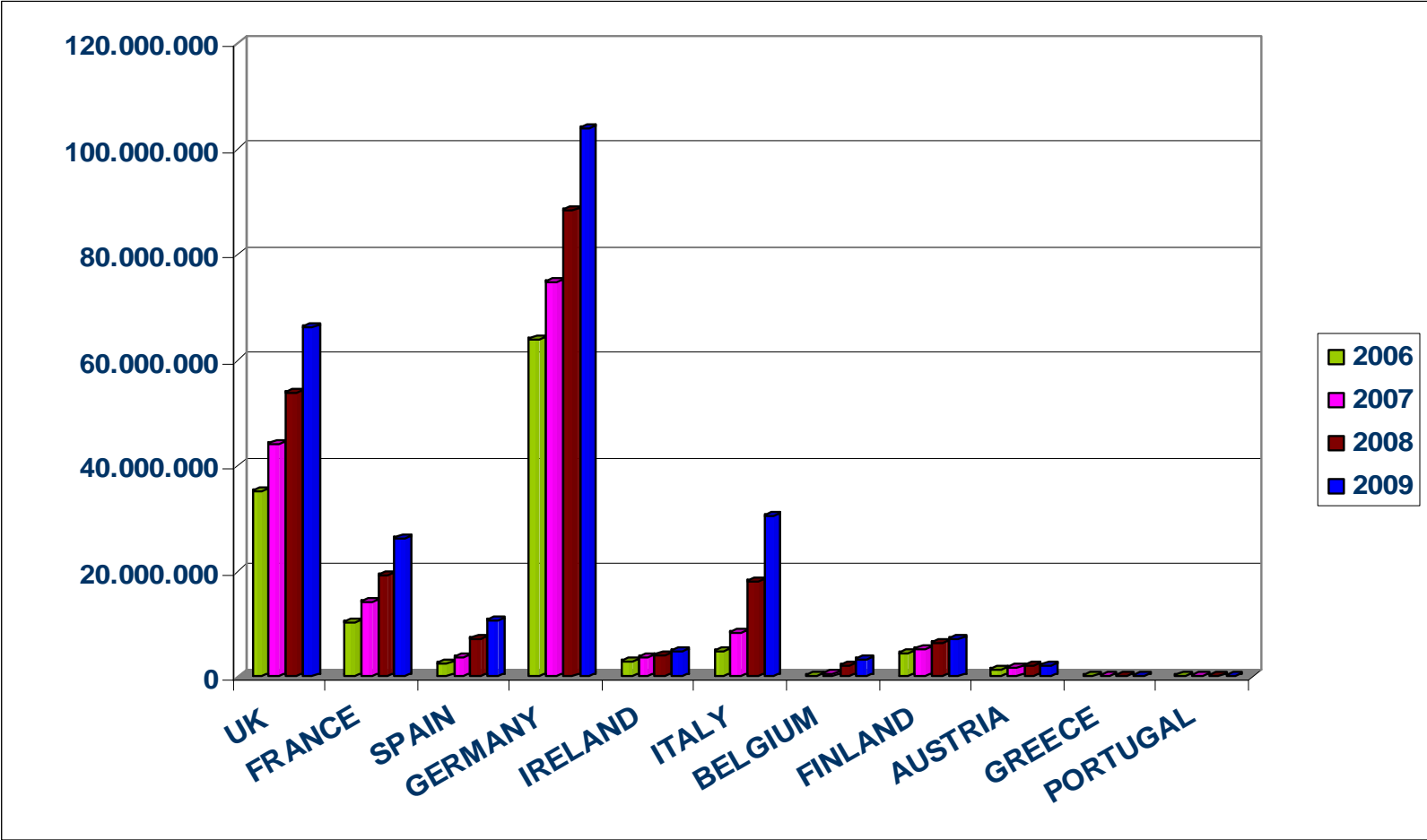


Source: IMS Health data

Oxycodone prescription in Europe



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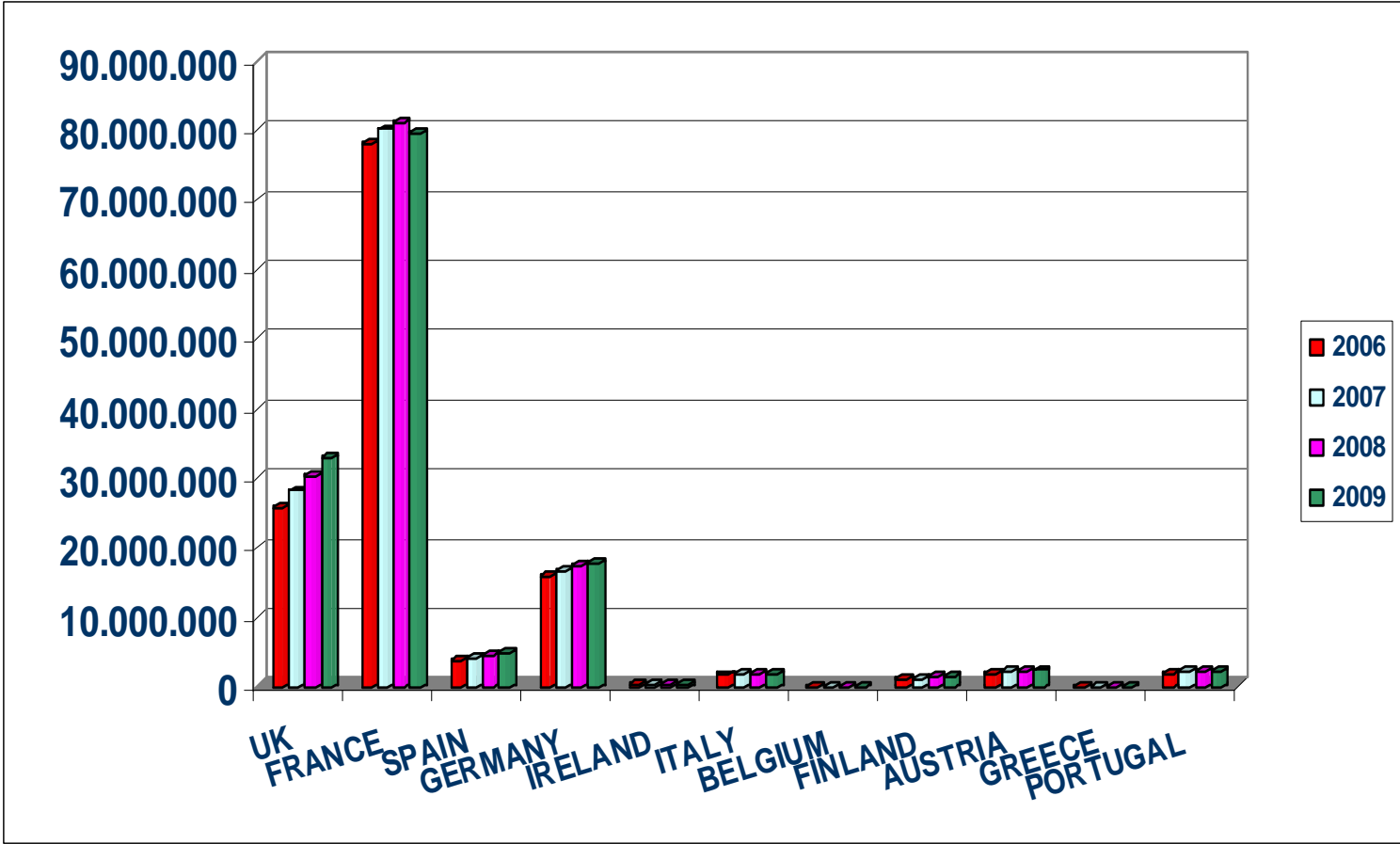


Source: IMS Health data

Buprenorphine prescription in Europe



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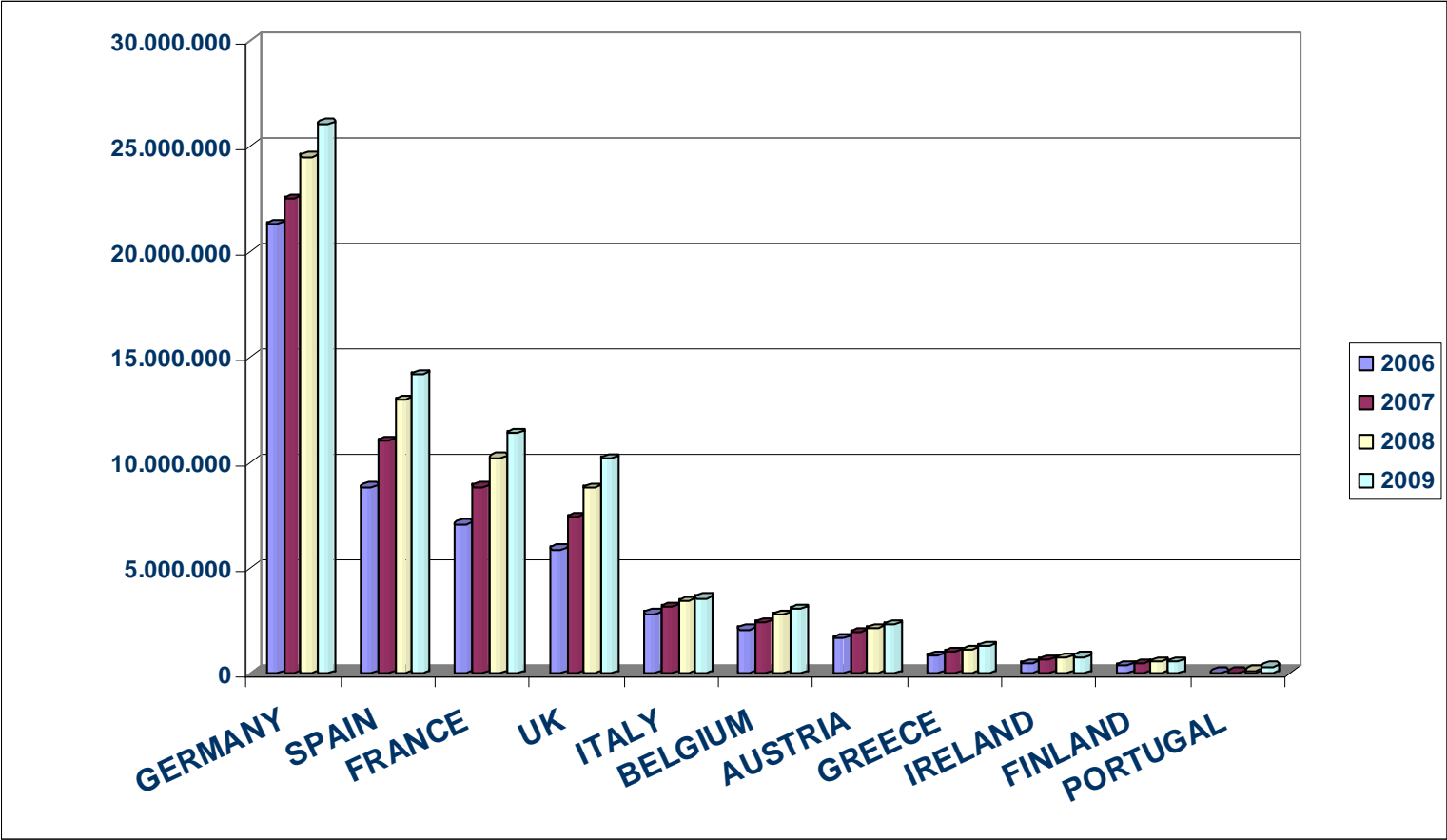


Source: IMS Health data

Fentanyl prescription in Europe



AGENZIA ITALIANA DEL FARMACO



Source: IMS Health data

What is next?

- Only one (opioid) product intended for submission this year to the EMA for the treatment of chronic pain.
- There were two scientific advice requests in 2009 on products for the treatment of chronic pain and two in 2008.
- However, these do not appear to have been translated into eligibility / rapporteurship requests for the centralised procedure yet.

Discussion

- In Europe the trend in morphine consumption increased significantly only in UK, whereas remained steady in other countries;
- After the launch into the market of new molecules, such as oxycodone, buprenorphine and fentanyl, we show in all European countries an increase in consumption, especially for oxycodone.
- **It is unclear if this is appropriate but is definitely not in accordance with international guidelines.**

Social Impact of Pain

- Absenteeism from work due to pain causes losses of 34 billion euros per year to the European economy;
- Most available studies present in literature, show that chronic pain such as arthritis has a significant impact on occupational performance in the workplace and contributes to decrease productivity, reduce rates of employment, personal and societal economic cost;

Social Impact of Pain

- Despite the extensive utilization of narcotic analgesics, pain is often uncontrolled;
- Inappropriate use of narcotic analgesics leads to uncontrolled pain management, dependence, and may lead to patient deaths, creating a tremendous cost burden on the health care system.
- The impact of opioid dependence on employers, managed care, and society is significant;

The Italian perspective: cost related to pain

- In Italy, pain therapy pharmaceutical expenditure is estimated to cost more than 200 million euros;
- Annual pharmaceutical expenditure for opioid medicine is over 50 million euros of which over 30 million euros is hospital expenditure;
- Cost-benefit analysis comparing the cost data resulting from absence from work and the need for medical care leads to the conclusion that treated patients cost to the society much less than the untreated patients.

The Italian perspective: open questions

- The difference between acute and chronic pain is recognised in Italy;
- In Italy the use of analgesic medicine for the treatment of pain is lower than in other EU countries but there is a desire to bring Italy in line with the rest of the world;
- Often it may be thought that the prolonged somministration of opioid medicines can cause opiate addiction as drug habit.

Conclusion

- **Italian NHS has begun a process for the simplification of procedures to facilitate the access to medicines for the treatment of pain.**
- **AIFA may reassess the distinction between acute and chronic pain, and the class of reimbursement for such medicines.**

Thank you!

psiviero@aifa.gov.it