SIP

Societal Impact of Pain

2017

Structured Cooperation between Health Care Systems tackling the societal impact of pain!

The Innovative Medicines Initiative (IMI) and pain research

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Innovative Medicines Initiative

Disclosure Statement of conflict of interest in the context of the subject of this presentation

Within the past 12 months, I or my spouse/partner have had following financial interest/arrangement(s) or affiliation(s)

• **Support for travel**	**NO**
• **Honoraria for lectures**	**NO**
• **Honoraria for advisory board activities**	**NO**
• **Participation in clinical trials**	**NO**
• **Research funding**	**NO**
• **Financial shares and options**	**NO**

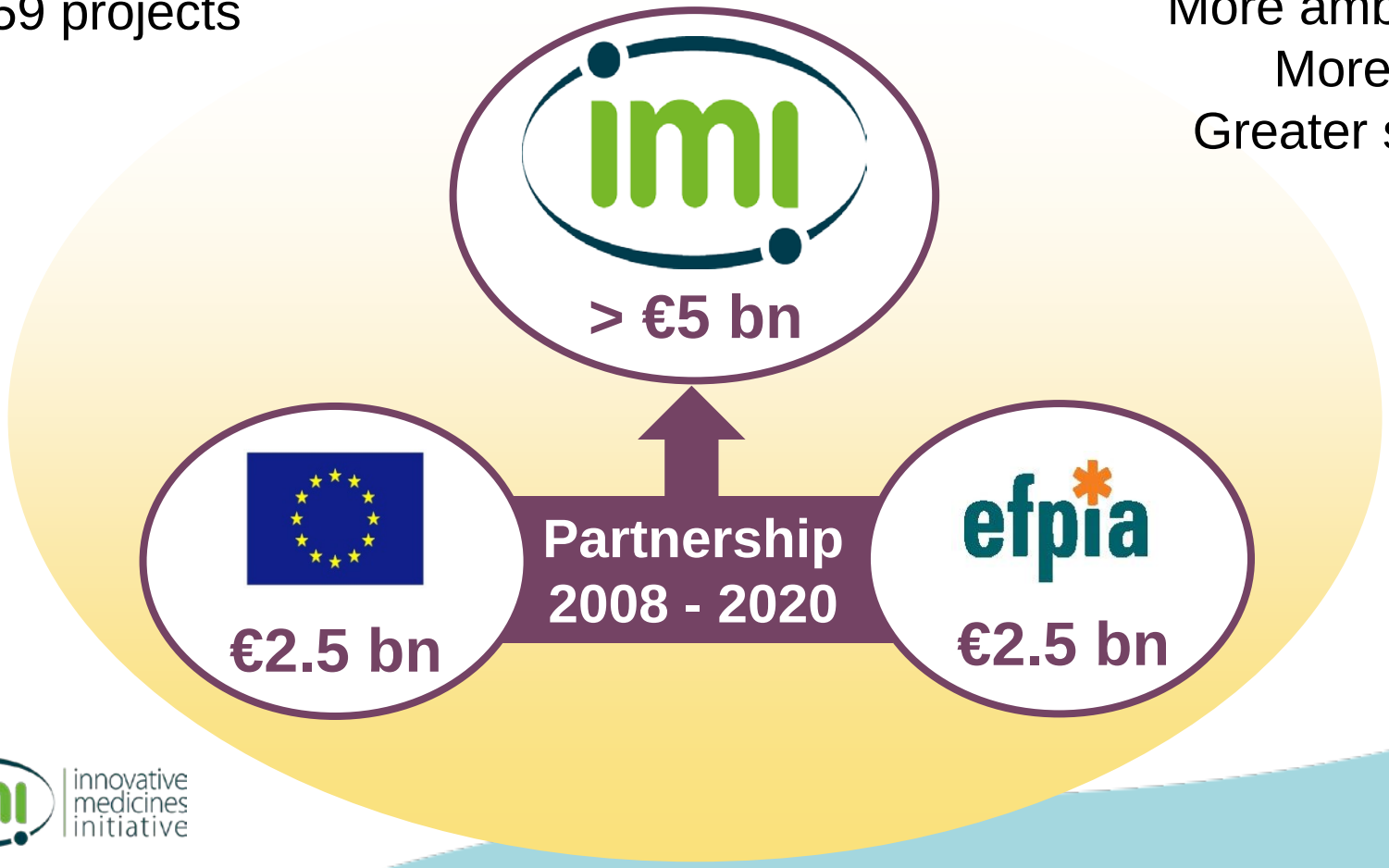
IMI – Europe's partnership for health

IMI1: 2008-2013

€2 bn budget
59 projects

IMI2: 2014-2020

€3.3 bn budget
More ambitious
More open
Greater scope



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IMI – Europe’s partnership for health

IMI mission

IMI facilitates open collaboration in research to advance the development of, and accelerate patient access to, personalised medicines for the health and wellbeing of all, especially in areas of unmet medical need.

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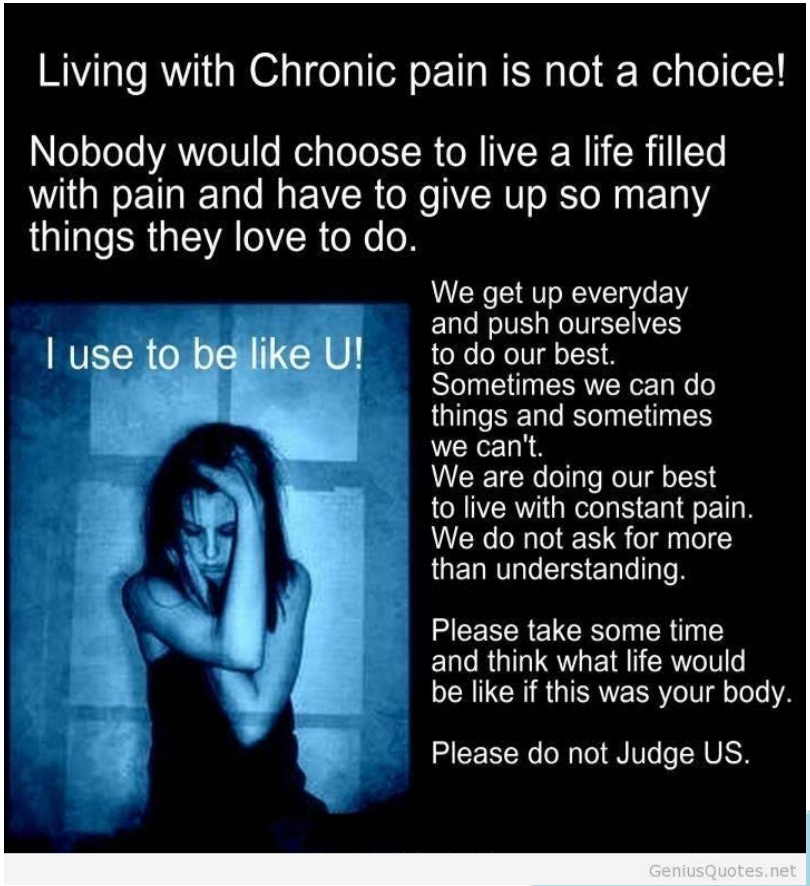
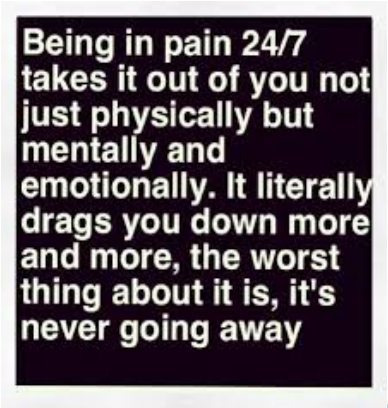
The Societal burden of chronic pain

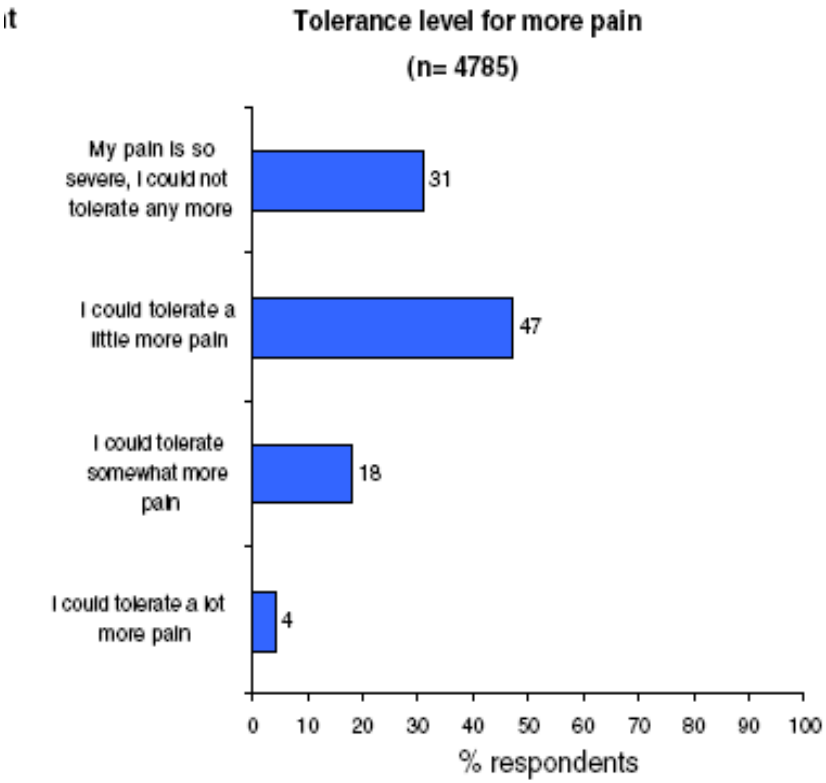
Chronic pain affects One in FIVE Europeans: in UK (2016) between **one-third and one-half** of the population, corresponding to just **under 28 million adults**: from 14.3% in 18–25 years old, to 62% in the over 75 age group, although the prevalence of chronic pain in young people (18–39 years old) may be as high as 30%



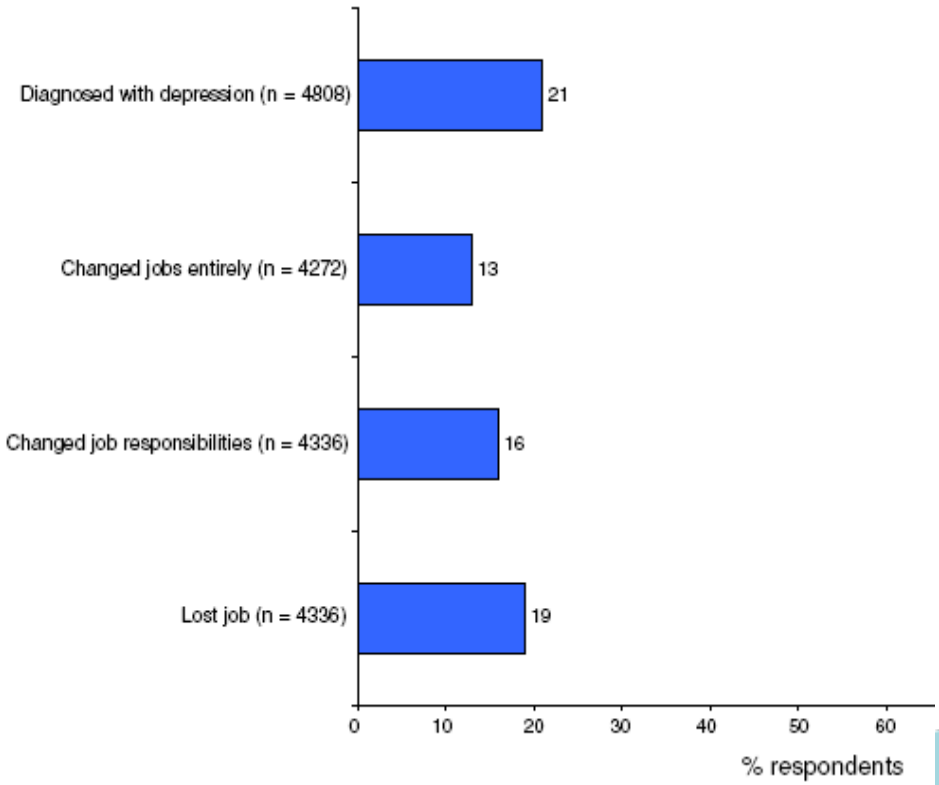


The Societal burden of chronic pain

In 31% of cases Chronic pain is defined as unbearable



Chronic pain influence job perspectives and may lead to depression



H. Breivik et al. / European Journal of Pain 10 (2006) 287–333

IMI 2 budget (2014 – 2020)

EU funding goes to:

Universities

SMEs

Mid-sized companies

Patient groups

etc…

€1.638 bn

€1.425 bn

EFPIA companies

receive no funding

contribute to projects 'in kind'

Other €213 m

Associated Partners e.g. charities, non-EFPIA companies

IMI 2 total budget €3.276 billion

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An international, cross-sector community

Over 9 000 researchers working for:

- open collaboration
- improved R&D productivity
- innovative approaches to unmet medical needs

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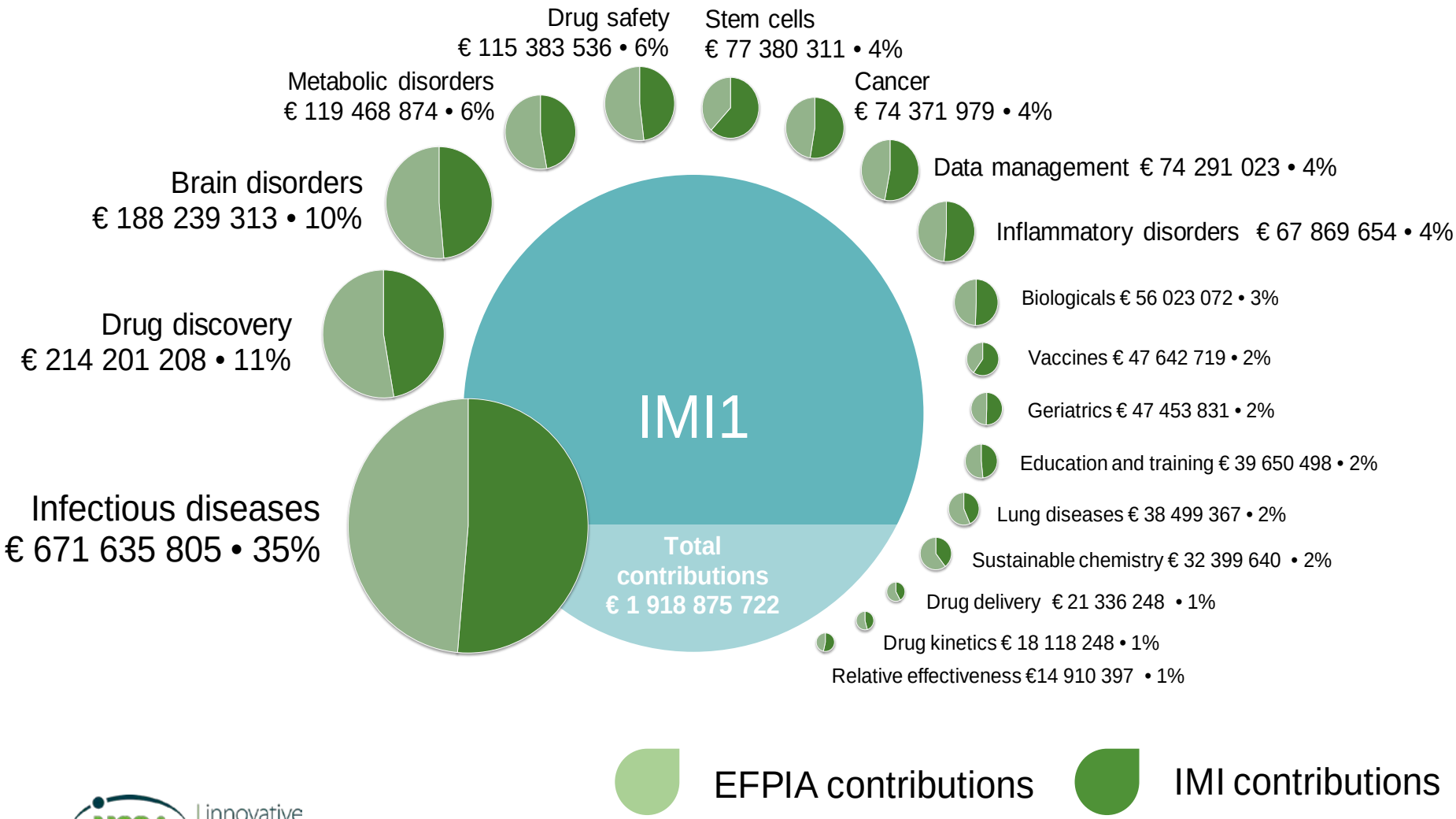
Figures from June 2016

Distribution of funding per scientific area – IMI1



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Why do we need IMI?

Because drug development is very…

complex

risky

inefficient

lengthy

expensive

Because…

- Biological mechanisms underlying disease are complex
- Clinical trial designs need to be adapted to scientific knowledge
- Regulatory pathways need be adapted in certain cases

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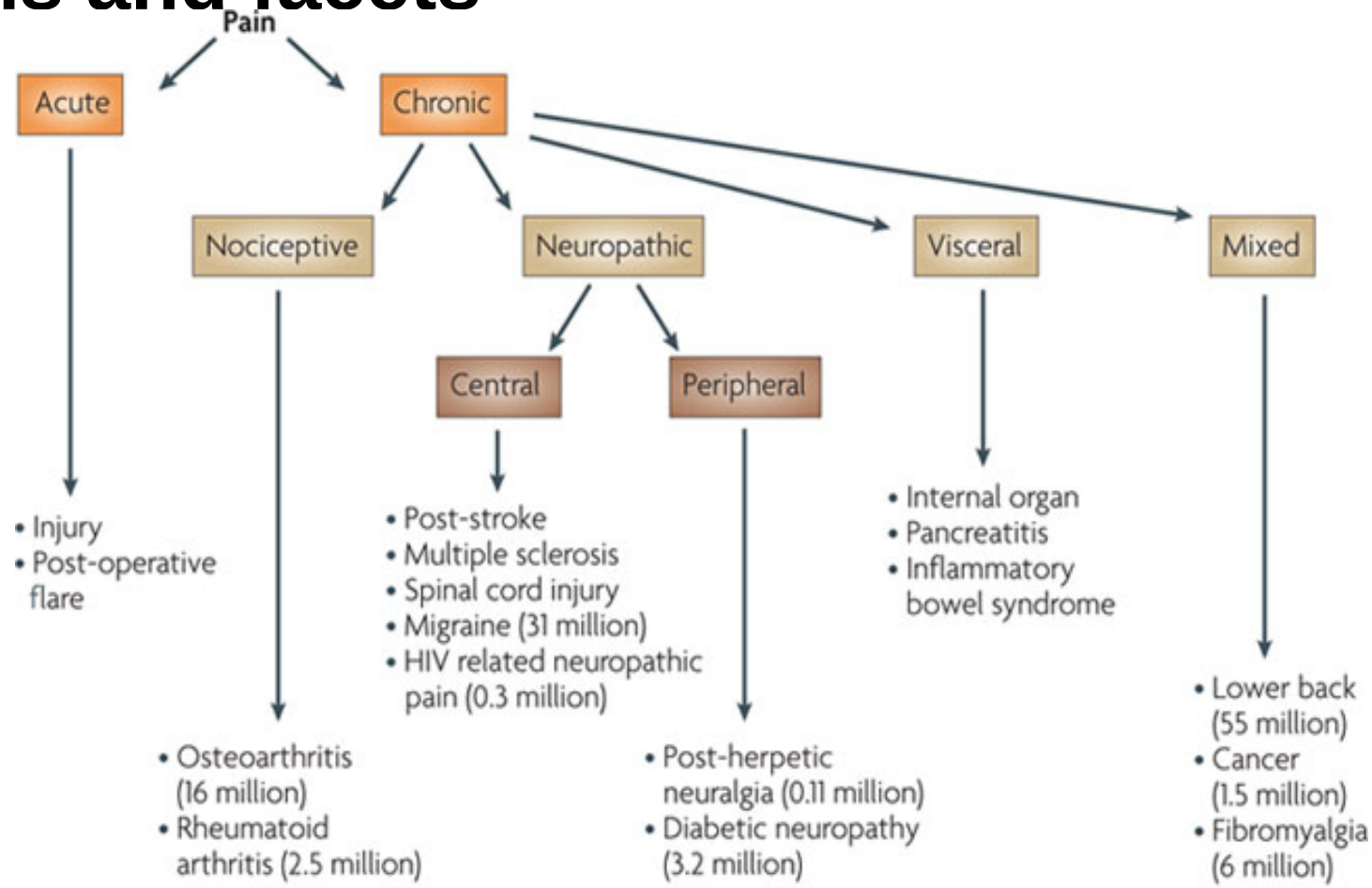
Pain is complex and comes in many forms and facets



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Nature Reviews | Drug Discovery

Treatments of Pain

Many of the drugs used 100 years ago remain the drugs we use today:

With available treatments only 1/3 of chronic pain patients obtain adequate pain relief

Finding new (chronic) pain drugs is difficult because:

- Unpredictability of cause effect relationship and many potential different underlying mechanisms.
- Challenge in defining the right patient segment for personalised health care
- The gap between animal behavioural models and humans has not been overcome
- The high complexity of pain biology hampers the identification of novel targets

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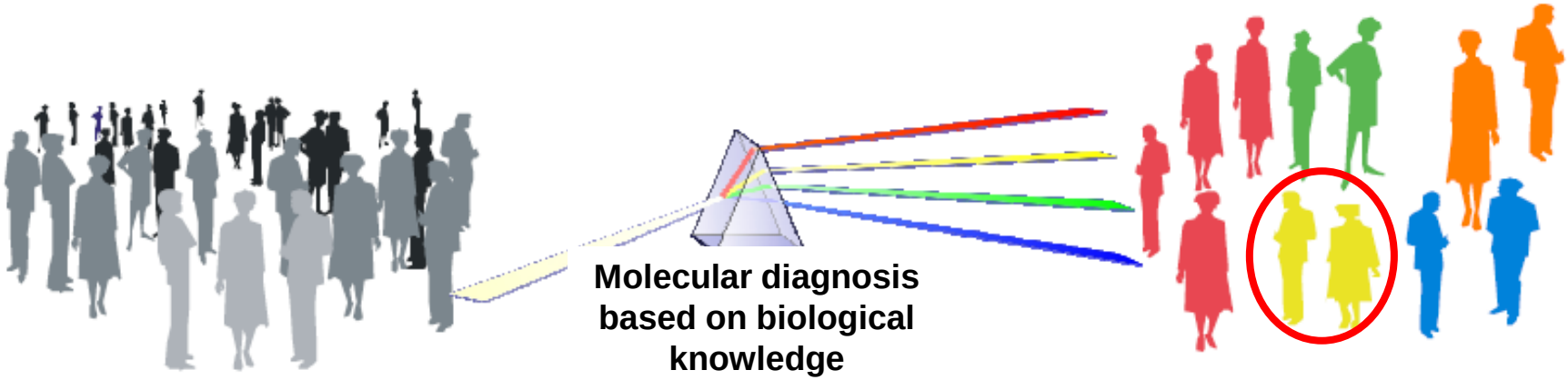
The Vision for IMI2, very relevant for Pain

Science is driving the manner in which we view disease

Population ⟷ Individual



We "treat" a population.
Some respond and some don't

We "treat" a *targeted* population
They all respond

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IMI2 overall objectives, very relevant for Pain

- **improve the current drug development process** through development of tools, standards &approaches to assess **efficacy**, **safety** & **quality** of health products.
- **develop diagnostic & treatment biomarkers** for diseases clearly linked to clinical relevance & approved by regulators
- **reduce time to clinical proof of concept** (e.g. for cancer, immunological, respiratory, neurological/neurodegen. diseases)
- **increase success rate in clinical trials** of priority meds (WHO)
- **develop new therapies** for diseases with **high unmet need**, (e.g. Alzheimer's) & **limited market incentives** (e.g. AMR)
- **reduce failure rate of vaccine candidates** in phase III trials through new biomarkers for efficacy & safety checks

- IMI2 legislation, Article 2b

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How IMI generates its initiatives

Industrial partners align themselves around a real challenge for industry and agree to work together **and commit resources**

New ideas from public sector, universities, SMEs etc. are needed to address the challenge (OPEN CALLS to select beneficiaries)

Scale is a key to success and is provided through IMI funding

Outcomes should be transformative for the industry as well as having a clear “public” value, going beyond high impact publications

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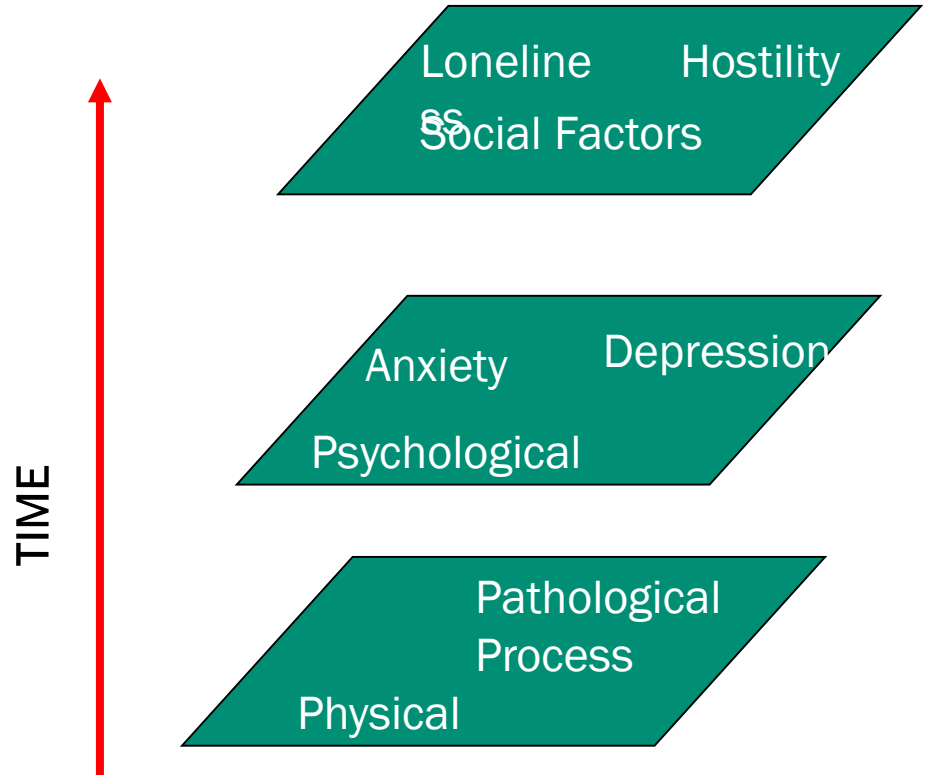
Chronic pain is multifactorial and multidimensional

- Psychologic factors – depression, anxiety, somatization
- Socioeconomic factors – cultural differences, urban
- poor, gender
- Spiritual factors – spiritual suffering, meaning of pain

- Physical factors – VERY complex neuroanatomy creating the pain sensation, from pain receptors to afferent nerves to spinothalamic tract, to thalamus to cortex with modulators all along the way



Need for a multi-disciplinary, multi-stakeholders approach!

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Europain – an IMI project

25 partners

EFPIA

AbbVie GmbH

Astellas

AstraZeneca Plc

Boehringer Ingelheim AG

Eli Lilly and Company Ltd

Esteve S.A.

Grünenthal GmbH

H Lundbeck A/S

Pfizer Ltd

Sanofi-Aventis R&D

UCB Pharma

EU contribution: 6.2M€
EFPIA contribution: 11.1M€
Project period:
Oct 1 2009 – Sept 30 2015

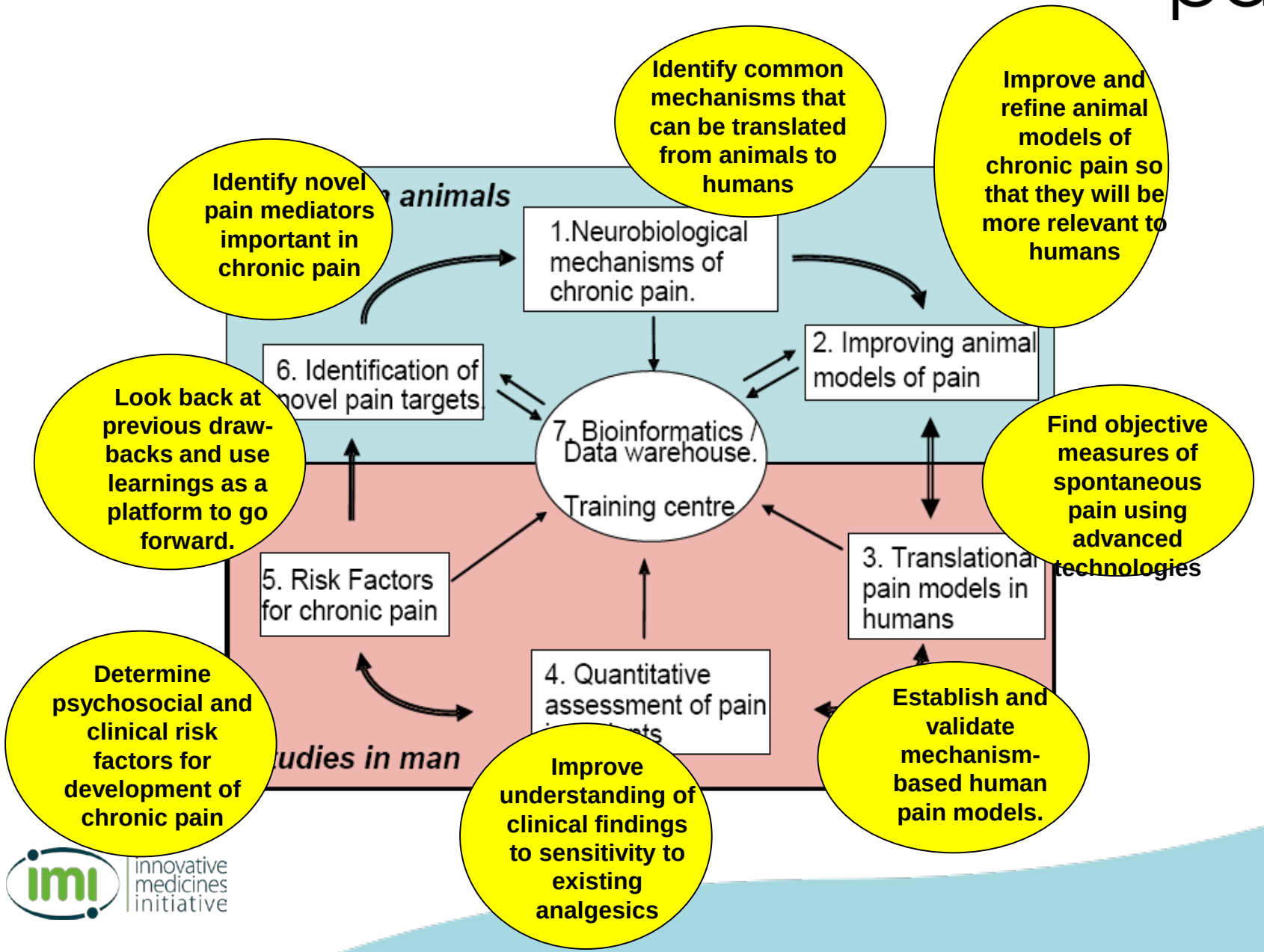
Academia

- King's College London
- University College London
- University of Oxford
- Imperial College London
- Christian-Albrechts-Universitaet zu Kiel
- Ruprecht-Karls Universitaet Heidelberg
- Technische Universitaet Muenchen
- BG Universitätsklinkum Bergmannsheil GmbH
- Klinikum der Johann Wolfgang Goethe-Universitaet
- Aarhus University Hospital
- Region Hovedstaden
- University of Southern Denmark

SME

- Neurosciences Technologies S.L.
- Neuroscience Technologies Ltd

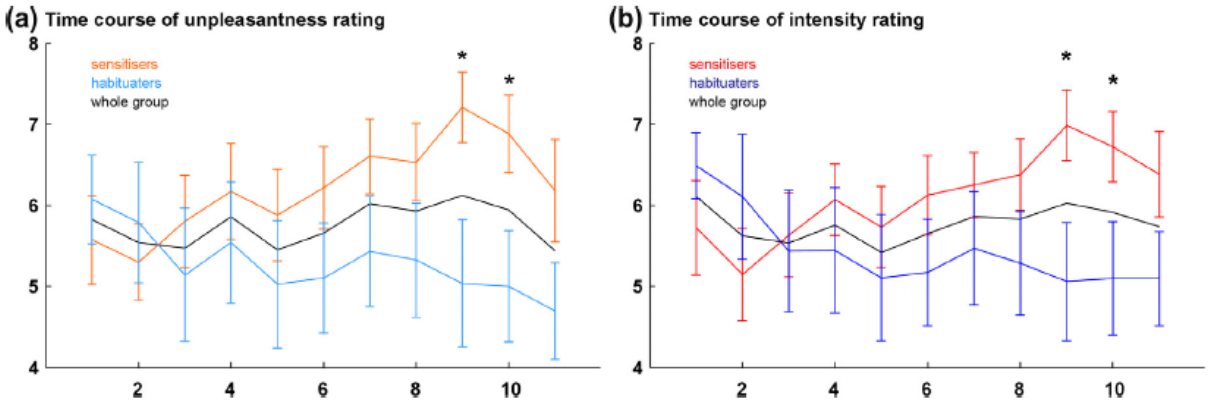
The EuroPain Project objectives



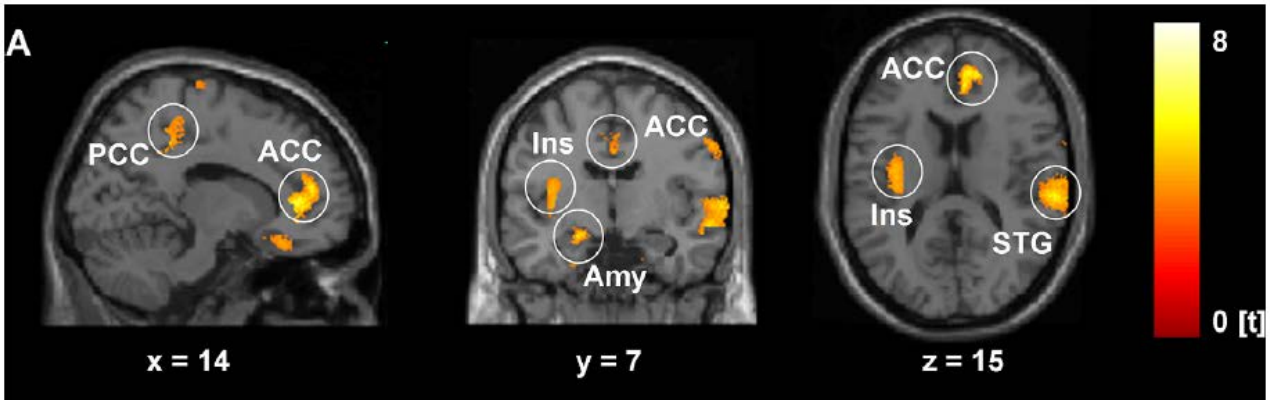
Achievements in chronic pain

- Leading **international consensus** on conducting preclinical trials
- Identified and translationally validated novel drug targets
- Conducting clinical trials to improve **patient stratification**
- Developing **tools to predict** which patients will respond to treatments
- Understanding the **placebo effect** to reduce clinical trial failures
- Initiated **EMA interactions** to frame regulatory landscape

Pain leads to structural changes in the brain



Control individuals are either pain sensitizers or not



(A) Pain sensitisers show grey matter decrease after repetitive painful stimulation in regions contributing to the processing of pain

Stankewitz et al, Pain 2013

Patients with different pain sensory phenotype respond differently to drugs

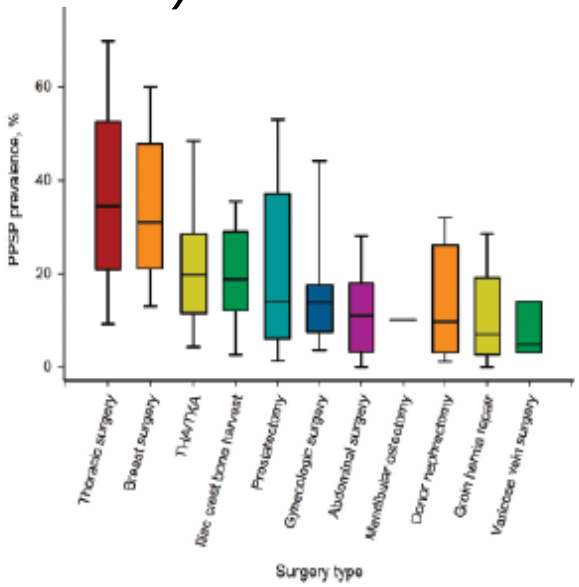
Table 4. Response on oxcarbazepine in patients with peripheral neuropathic pain with irritable and non-irritable nociceptor phenotype.

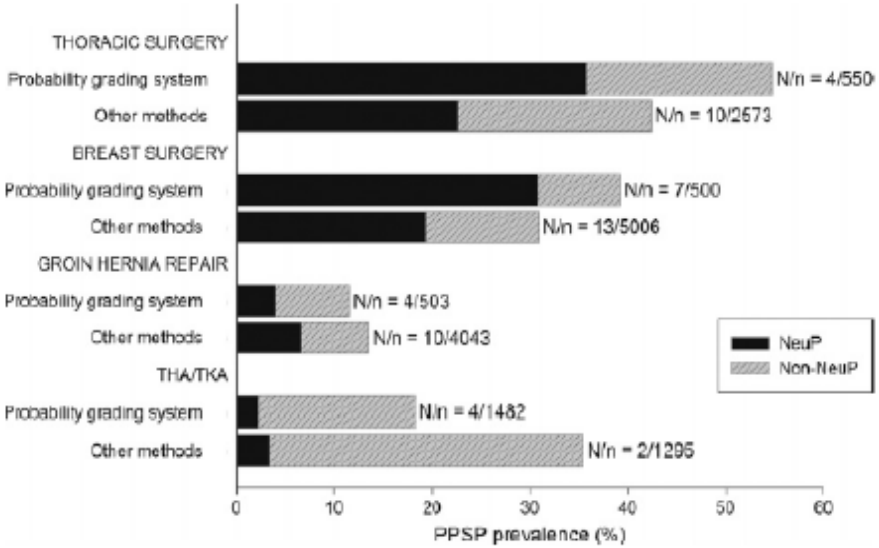
	Total	Irritable nociceptor	Non-irritable nociceptor
More than 50% reduction in pain	N = 83	N = 31	N = 52
Oxcarbazepine	16	9	7
Placebo	4	1	3
Change to better (placebo → oxcarbazepine)	15	9	6
[a]p	<0.01	<0.01	0.145
NNT (95% CI)	7 (4.2-22)	3.9 (2.3-12)	13 (5.2-∞)
A least moderate [b]pain relief	N = 62	N = 29	N = 33
Oxcarbazepine	29	12	17
Placebo	6	1	5
Change to better (placebo → oxcarbazepine)	25	11	14
[a]p	<0.001	<0.01	<0.01

In the future, prevention of post surgical chronic pain may be possible

- Improved surgical techniques
- Identifying and treating high risk patients (catastrophizing trait is a predictor for chronic pain and can be treated).

The prevalence of neuropathic pain in postsurgical pain is high following thoracotomy and breast surgery but low after hernia repair and hip/knee artroplasty

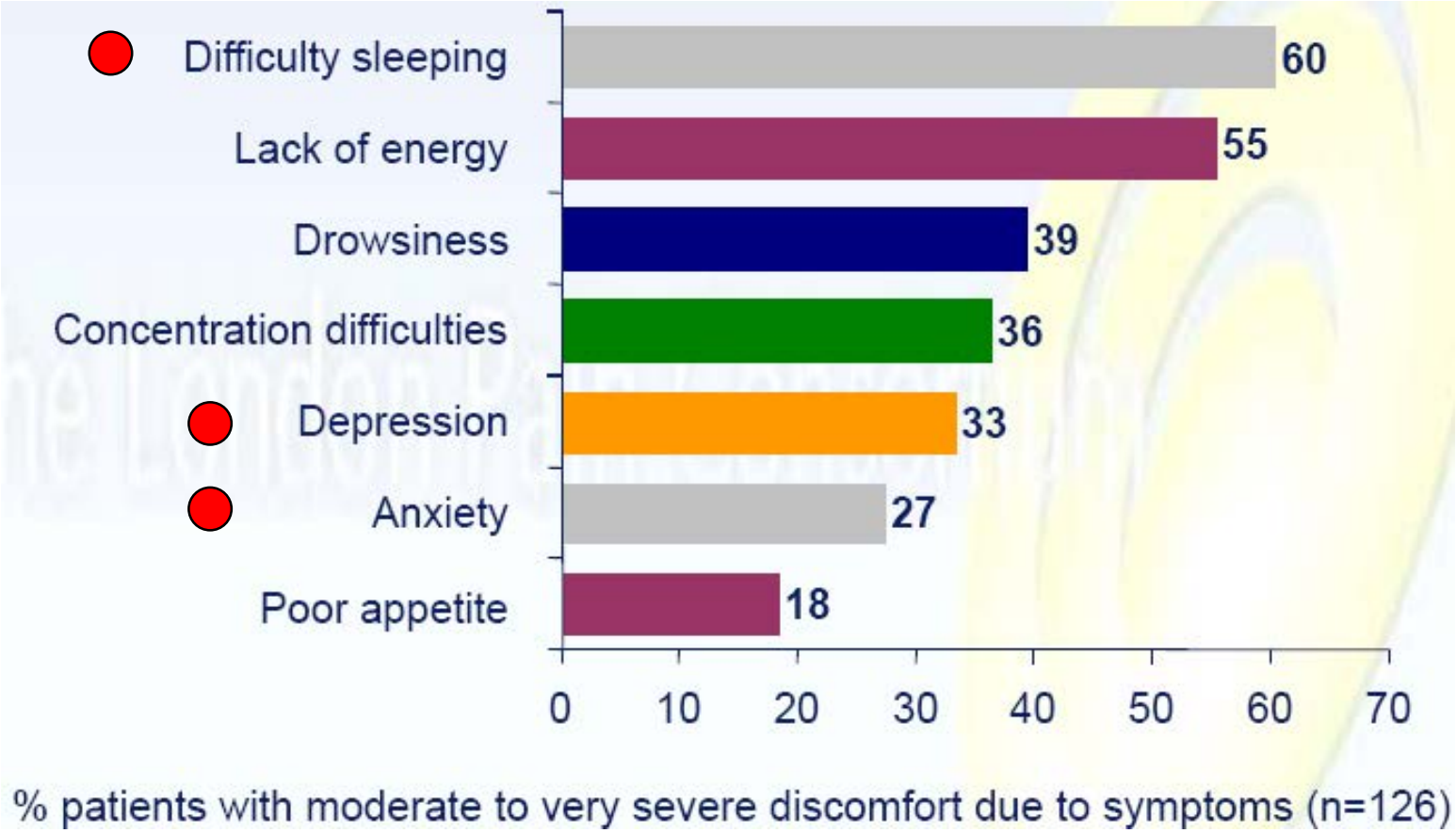




Conclusion: High probability of iatrogenic nerve damage during surgery following breast operation and thoracotomy

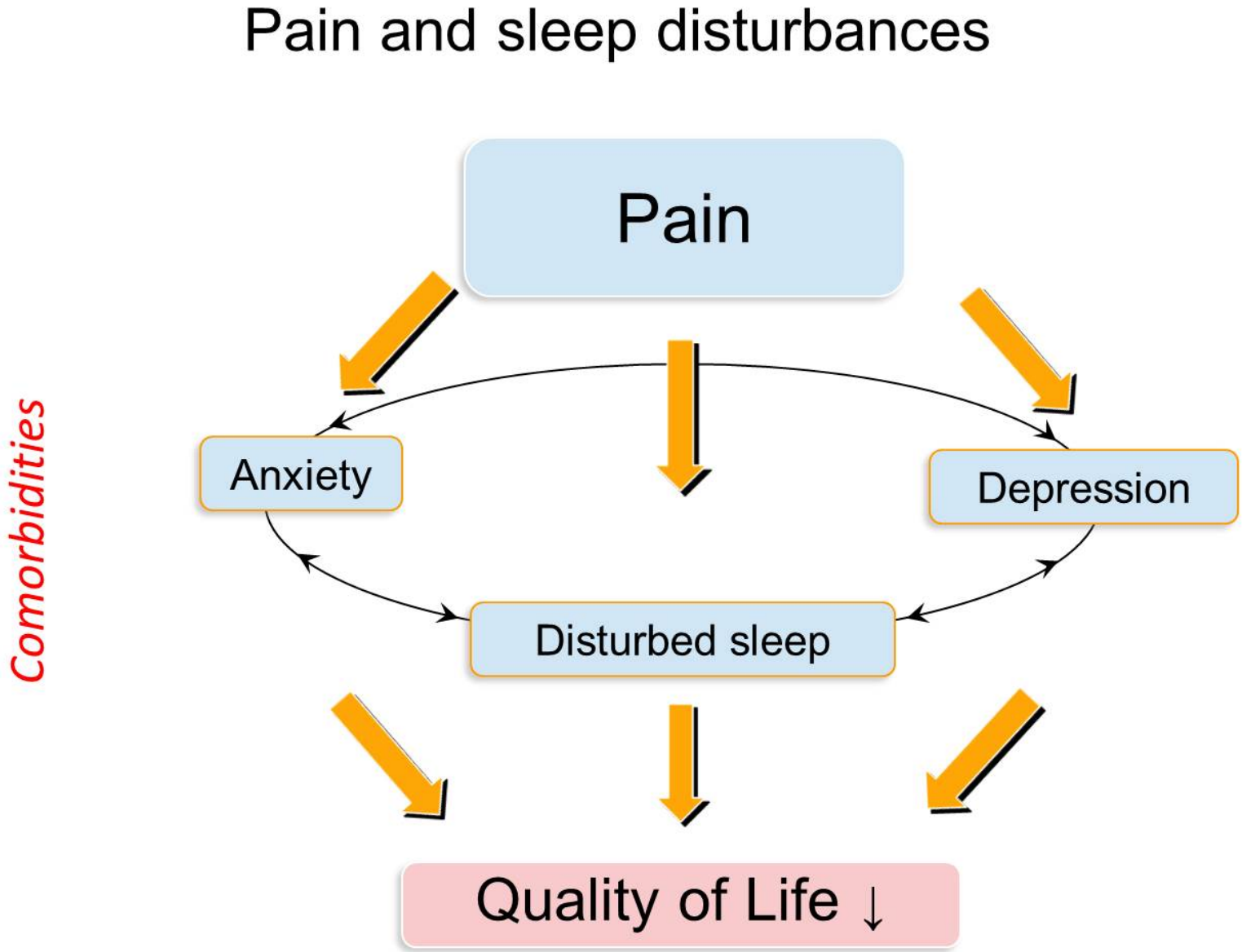
Haroutounian SH et al. Pain 2013

Co-morbidities associated with peripheral neuropathic pain



Meyer-Rosberg K et al. Eur J Pain 2001; 5: 379–389.

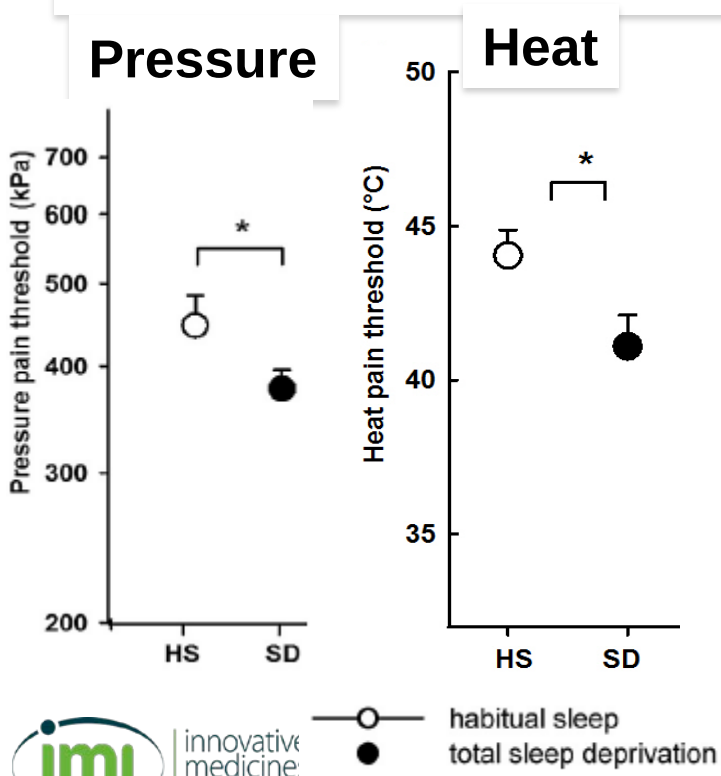
Sleep disturbance is an important co-factor in pain

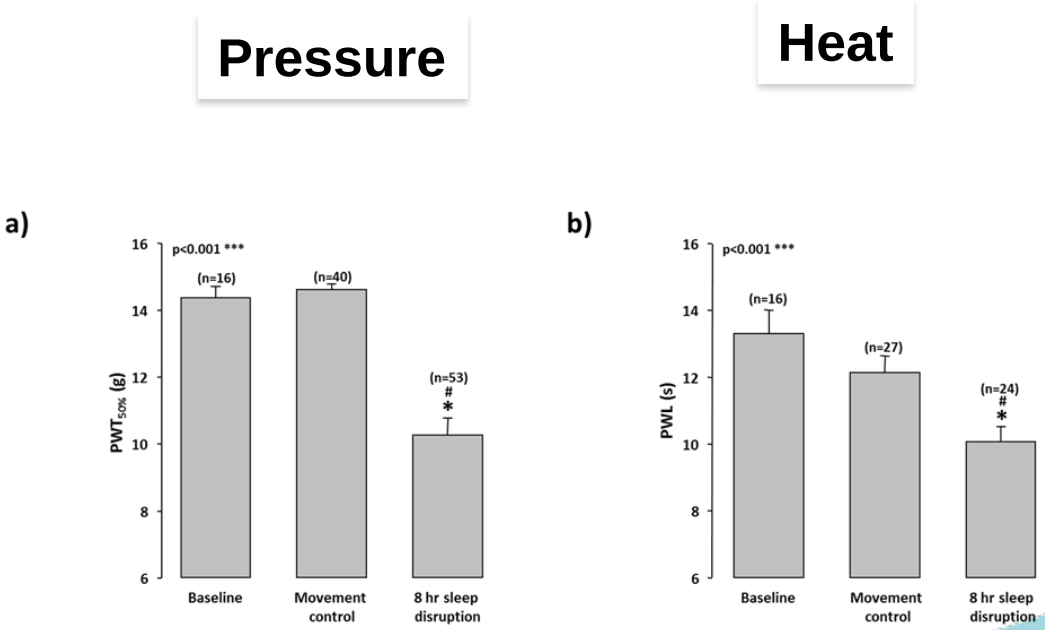


Development of experimental models to study the effect of sleep disturbances on pain

Sleep deprivation causes hyperalgesia in man....

.....And rats....





The EuroPain project: impact on regulatory science

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Clinical development of medicinal products intended for the treatment of pain

Email Print Help Share

Current version	**Adopted guideline** Date coming into effect - 01/07/2017
Reference number	EMA/CHMP/970057/2011
Published	22/01/2016
Effective from	01/07/2017
Keywords	Pain, neuropathic, nociceptive, chronic, acute, analgesia
Description	This guideline is intended to provide guidance on the clinical development of new medicinal products for the treatment of pain. It replaces and updates the separate guidelines on neuropathic and nociceptive pain (superseeded documents below).

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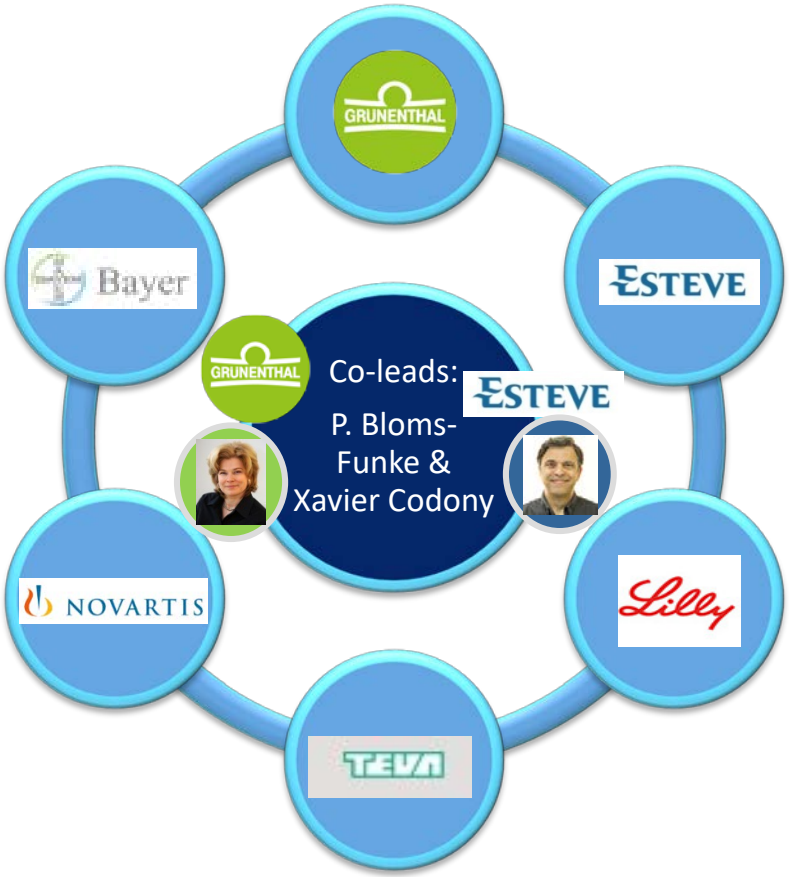
The IMI2 Pain Group – to drive solutions in pain

- the Pain Group is a satellite to the IMI2 Strategic Governance Group Neurodegeneration.
- The Pain Group unites European pharmaceutical companies dedicated to better understand, treat and manage pain.
- It is co-led by Petra Bloms-Funke (Grünenthal) and Xavier Codony (Esteve); other EFPIA members are Bayer, Novartis, Lilly and TEVA.



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Building a portfolio of Pain projects

- The Pain Group selects pre-competitive pain research areas of particular strategic societal value.
- It enables a portfolio of concrete pain projects which address a broad spectrum of challenges in the pre-competitive space (not asset related) ranging from pain target identification to real world clinical evidence of efficacy.
- Solutions are sought in partnership with consortia of partners selected via open competitive calls

NGN_PET: Modelling Neuron-Glia Networks into a drug discovery platform for Pain Efficacious Treatments

NGN-PET

Academia

NMI schafft Ergebnisse

KING'S College LONDON

Industry

AXAM INNOVATES, ENABLES, PERFORMS

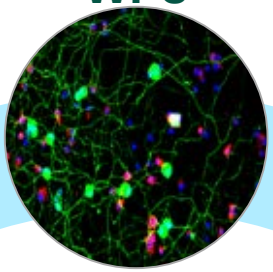
life&brain

GRÜNENTHAL

ESTEVE

Total budget: 3,328,000 €, duration 36 M

WP3



STUDY OF NEURON-GLIA CROSS-TALK AND DEV. OF RODENT NOCICEPTIVE TISSUE SCREENING ASSAYS

WP2

IN DEPTH ANALYSIS OF *IN VIVO* MODELS OF CHEMOTHERAPY- AND SNL-INDUCED NP

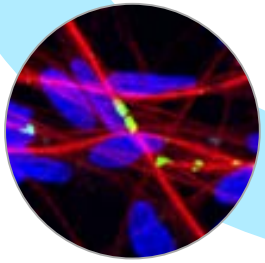
WP4

IDENTIFICATION OF BIOMARKERS FOR THE ANALYSIS OF NEURON-GLIA CROSS TALK IN RATS AND HUMANS

WP1

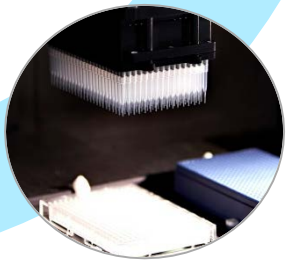
PROJECT MANAGEMENT
DISSEMINATION
EXPLOITATION

WP5



GENERATION OF hiPSCs DERIVED NEURON-GLIA CO-CULTURES

WP6



HCS ASSAYS BASED ON hiPSCs DERIVED NEURON-GLIA CULTURES

TRANSLATION

IMI2 Call 10 future project : Improving the care of patients suffering from acute or chronic pain

The future project will build an innovative pain platform covering and integrating three key areas in Pain:

- The use of Patient Reported Outcome Measures to improve the management of acute and chronic pain.
- The improvement of translatability of pharmacodynamic biomarkers in pain pathways of healthy subjects and preclinical species.
- The improvement of translation in chronic pelvic pain.

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IMI2 potential future ideas in the Pain area

- Identification and validation of novel pain targets/pathways with disease-modifying potential:
- Validation and standardisation of methods to measure neuronal activity in pain
- Clinical endpoints in headache medicine

IMI – Ecosystem for innovative collaborations

- Allow engagment in a cross-sector and disciplinary consortium at the forefront of cutting-edge research;
- Provide the necessary scale by combination of funding, expertise, knowlegde, skills and resources;
- Build a trustful collaboration upon a creative spirit, innovative and critical thinking;
- Gain from each others (new knowledge, skills, ways of working)
- Be transformative to make a difference in drug development and ultimately patients' life.

IMI is a **neutral platform** where **all involved** in drug development can engage in **open collaboration** on **shared challenges**.

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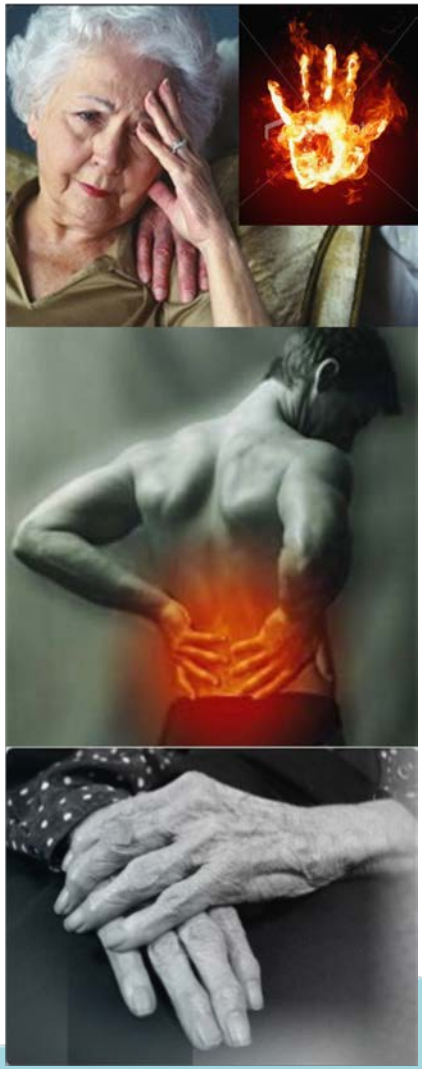
IMI initiatives in pain : the benefit for Europe

- Better pain treatment will reduce the socio-economic burden for patients and society

- Improved success rate in drug development will give industry better possibility to contribute to economic growth in Europe.



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Thank you

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