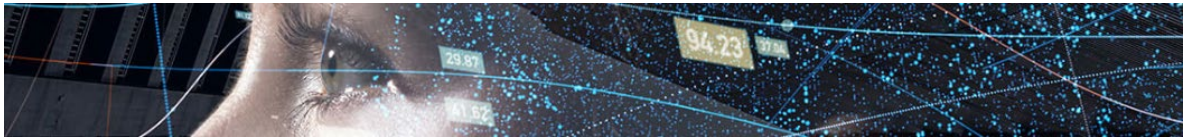

QSPainRelief Consortium

Pain Alliance Europe

24 June 2020

Elizabeth CM de Lange, PhD, PharmDhc, Coordinator QSPainRelief
Professor in Predictive Pharmacology,
Division of Systems Biomedicine & Pharmacology,
LACDR, Universiteit Leiden
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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 848068.

The Problem: Chronic Pain

Chronic pain has less to do with tissue injury and more with our Central Nervous System.

"It's like the volume button on the Pain System has been left tuned up!"

Current chronic treatment options for chronic pain are insufficient, indicated by 60% of the patient population that does not respond adequately to prescribed treatments, and suffer from significant side-effects.

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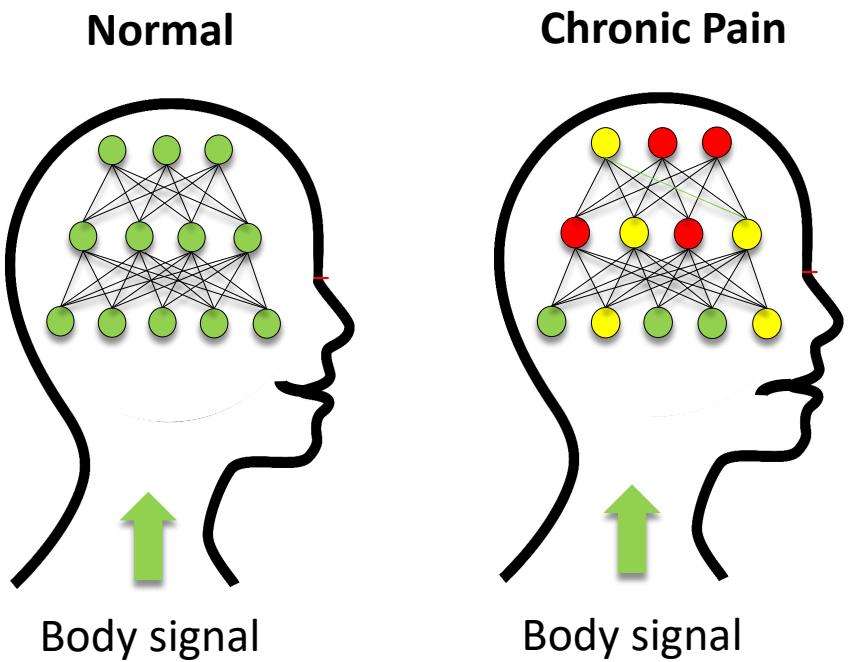
Chronic pain: The role of the Brain

The problem occurs when the brain starts to interpret normal nerve signals as danger.

When this happens people can feel pain when there is no danger present and this can lead to chronic pain.



Source: https://davidpapo.wordpress.com/2014/05/11/reconstructing-functional-brain-networks-have-we-got-the-basics-right/

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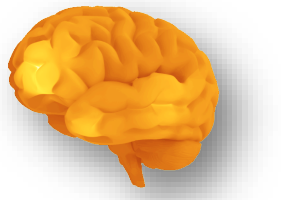
Chronic Pain: What can help?



- Help in understanding your pain
- Support by your surrounding in coping with pain
- Help by taking medicines

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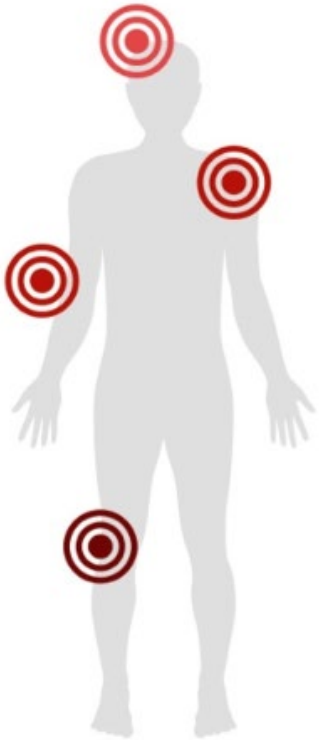
Chronic Pain Medicines: What can help?



- Non-opioid (e.g. gabapentin)
- Opioid (e.g. oxycodone)
- Combination of opioid and non-opioid

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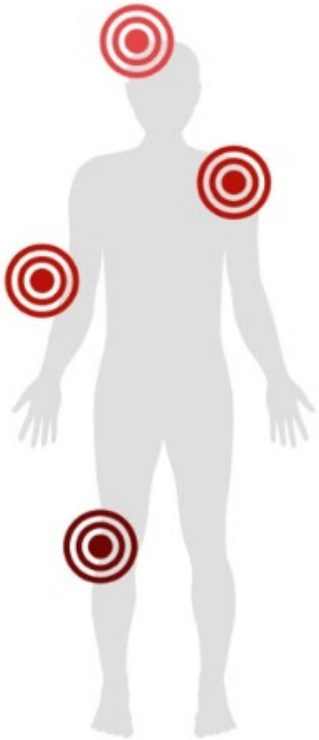
Chronic Pain Medicines: What can help?



- Non-opioid (e.g. gabapentin)
- Opioid (e.g. oxycodone)
- Combination of opioid and non-opioid

However …. in many cases not successful (enough)

We need to understand how to get to better treatment

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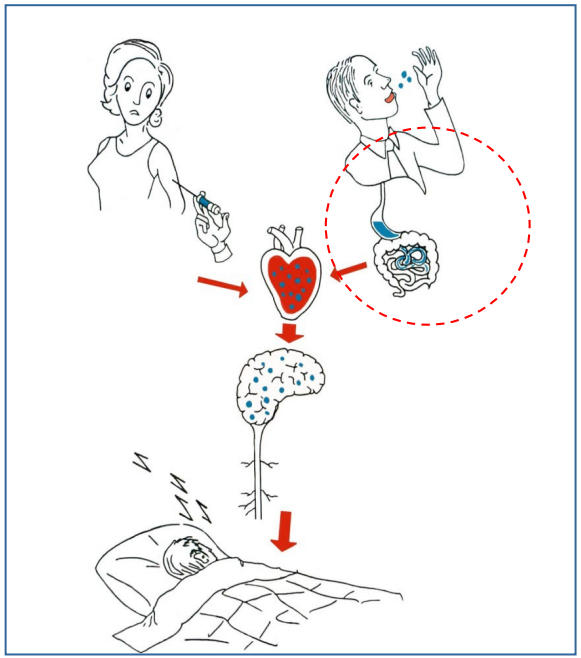
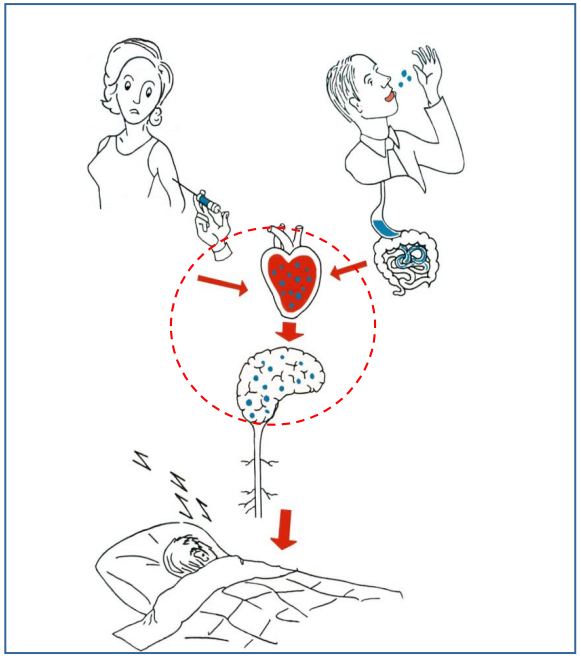
Pharmacokinetics - WHERE does the Medicine go?

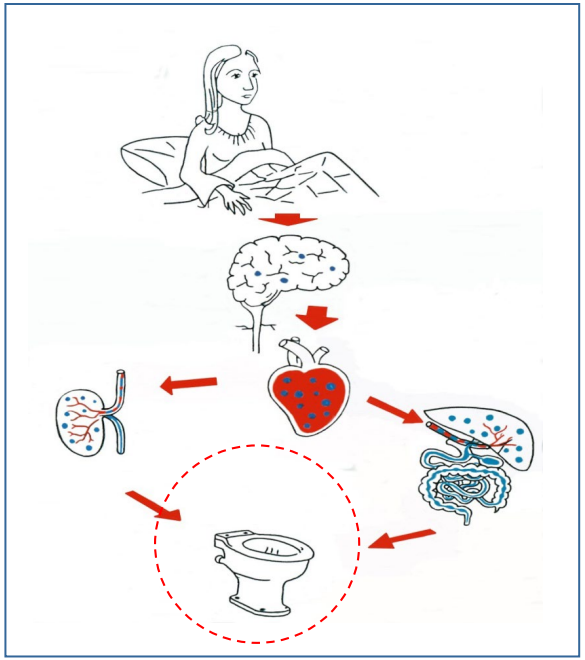
Absorption



Distribution



Elimination



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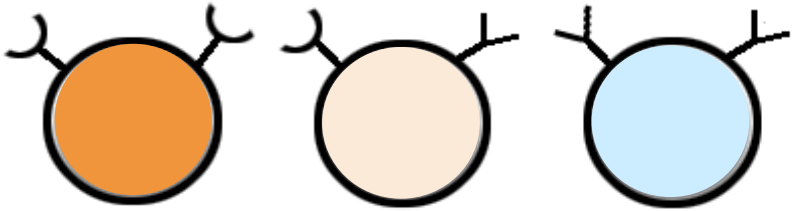
Pharmacodynamics – WHAT will the medicine do?

- The body has many cells



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Pharmacodynamics – WHAT will the medicine do?

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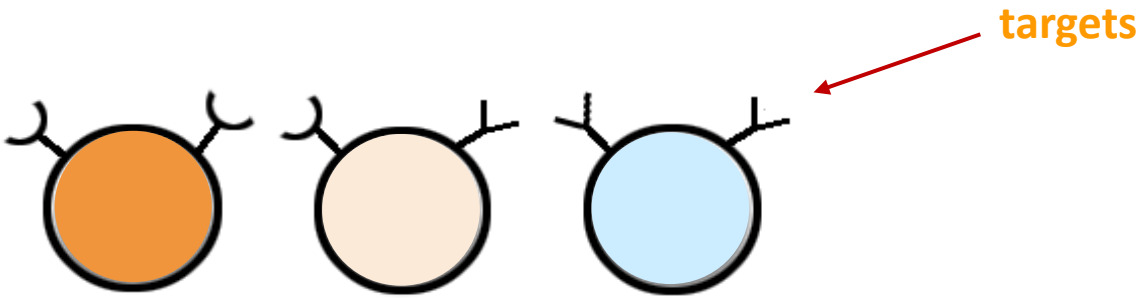

- Each cell has “sensors” (such as receptors)
- Pharmacologists call these sensors **targets**

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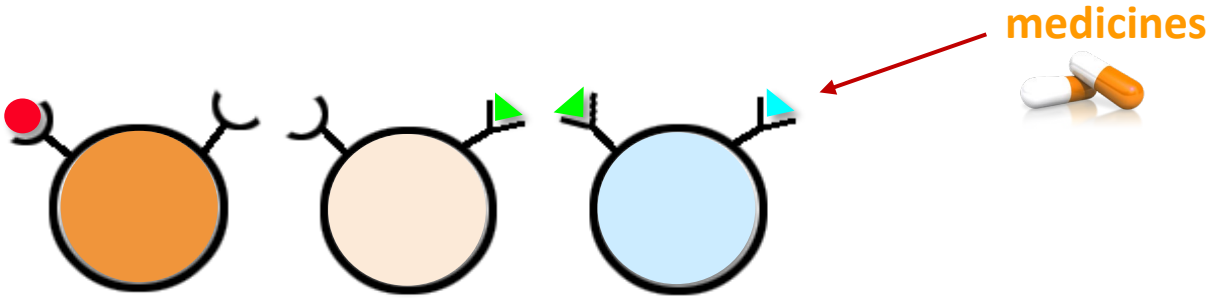
Pharmacodynamics – WHAT will the medicine do?

- The body has many cells



- Each cell has “sensors” (such as receptors)
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- Specific **medicines** can **bind to these targets**

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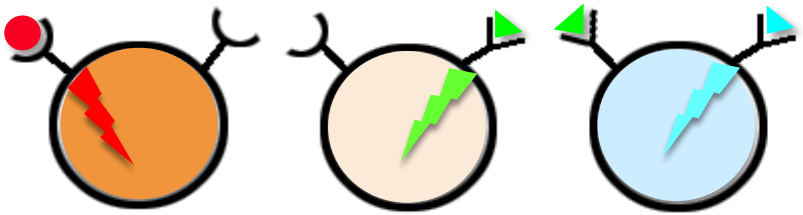
Pharmacodynamics – WHAT will the medicine do?

- The body has many cells



- Each cell has “sensors” (such as receptors)
- Pharmacologists call these sensors targets
- Specific medicines can bind to these targets
- **Binding** will **induce effects in the cell**

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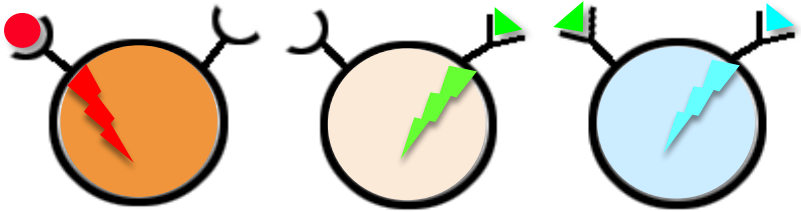
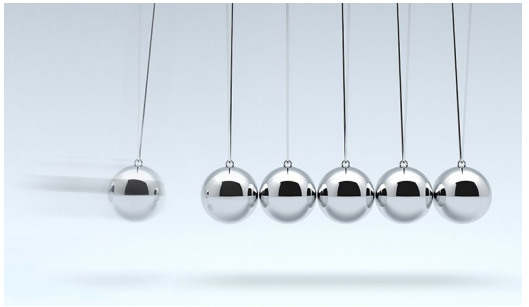
Pharmacodynamics – WHAT will the medicine do?

Cellular effects will bring about body effects





EFFECT

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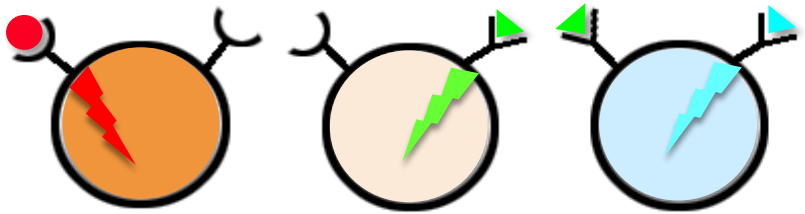
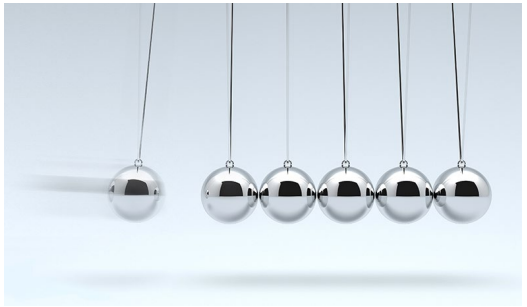
Pharmacodynamics – WHAT will the medicine do?

Cellular effects will bring about body (CNS) effects





EFFECT

The effect of medicines on the body depends on

- Where the medicine goes
- Medicine properties
- Target type
- Cell type

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Medicines used (single/combination) for Pain Relief

Category	Medicine
Opioids	Morphine, Oxycodone, Naloxone, Fentanyl, Hydrocodone, Codeine, Tramadol, Methadone, Hydromorphone, Meperidine, Buprenorphine, Alfentanil, Tapentadol, Sufentanil and Alfentanil
NSAIDS	Acetaminophen, Ibuprofen, Naproxen, Diclofenac, Celecoxib, Aspirin
CB1 analgesics	THC, Cannabigerol, Drinabant, Ibipinabant, Otenabant, Pregnenolone, Rimonabant, Rosonabant, Surinabant, Taranabant, Tetrahydrocannabivarin, Virodhamine
Benzodiazepines	Diazepam, Alprazolam, Clonazepam, Midazolam
Anti-epileptics	Gabapentin and Pregabalin
Antidepressants	SSRI's: Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline, Viibryd
	SNRI's: Desvenlafaxine, Duloxetine , Milnacipran , Venlafaxine
	MAO's: Isocarboxazid, Phenelzine, Tranylcypromine
	Tricyclic antidepressants: Amitriptyline, Amoxapine, Clomipramine, Desipramine, Doxepin, Imipramine, Maprotiline, Nortryptyline, Protriptyline, Trimipramine
	Miscellaneous: Bupropion, Buspirone, Maprotiline, Mirtazapine, Reboxetine, Trazodone, Vilazodone

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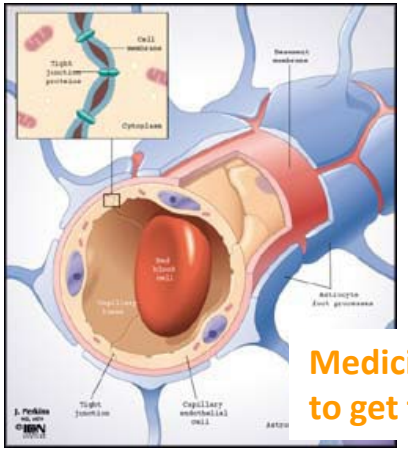
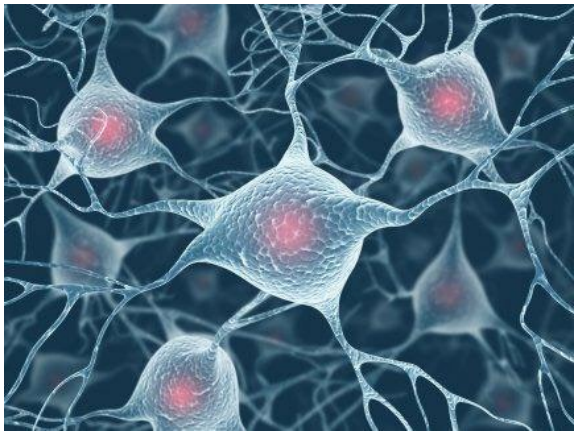
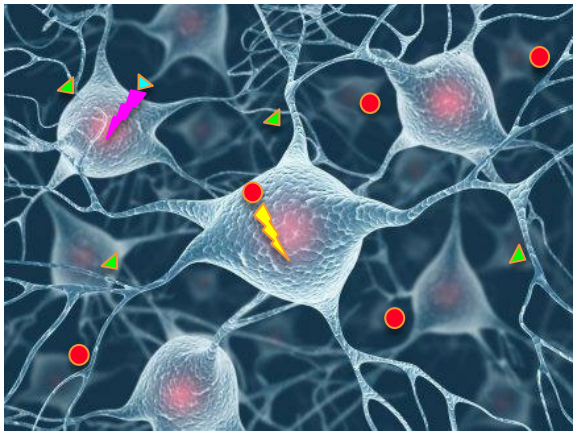
Right place, right time, right concentration ….



Medicines need to get to the CNS target

- **at the right time**
- **at the right concentration**





+ medicines

Medicines need to pass the blood-brain barrier to get to their CNS target

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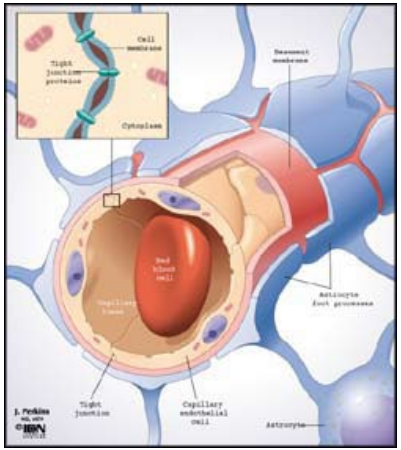
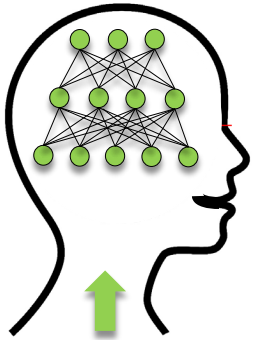
Right place, right time, right concentration ….



Medicines need to get to the CNS target

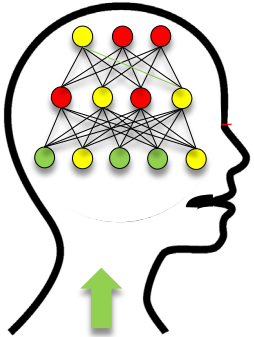
- **at the right time**
- **at the right concentration**

Normal



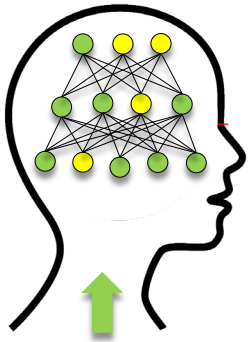
Body signal

Chronic Pain



Body signal

Chronic pain + medicine(s)



Body signal

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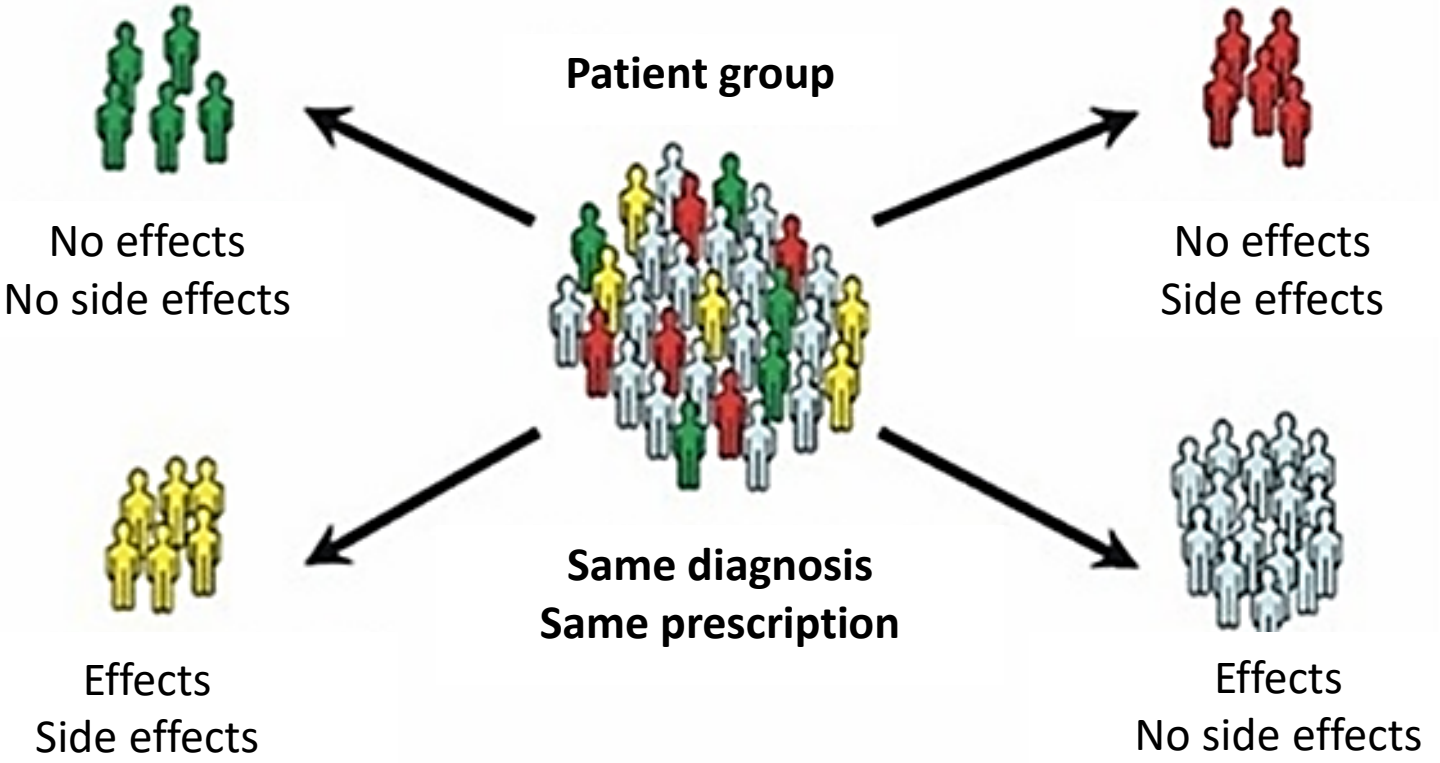
Variability



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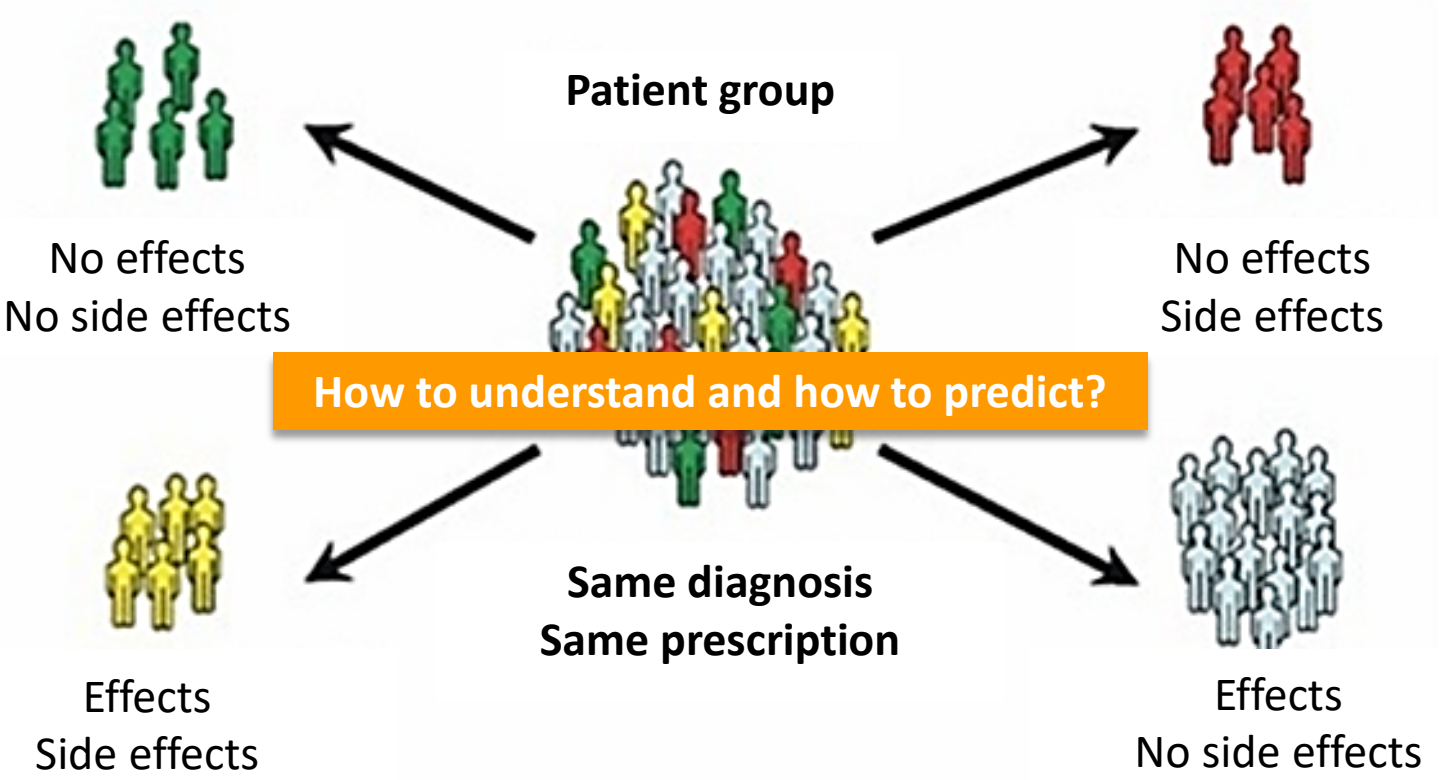

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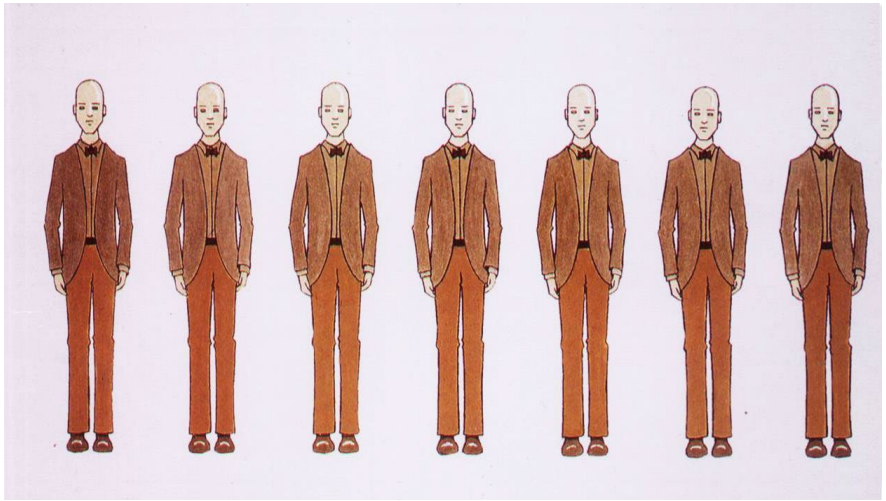

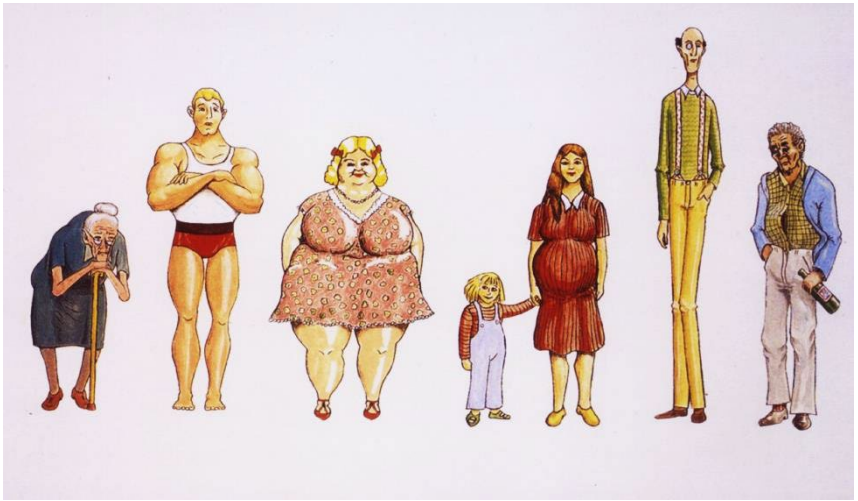

We **differ** in genetic background, gender, age, body weight, diet, but also in previous experiences (neuroplasticity), moods etc.

As a result **pharmacokinetics** (fate of the medicine in the body) and **pharmacodynamics** (the effects of a medicine) **may differ**

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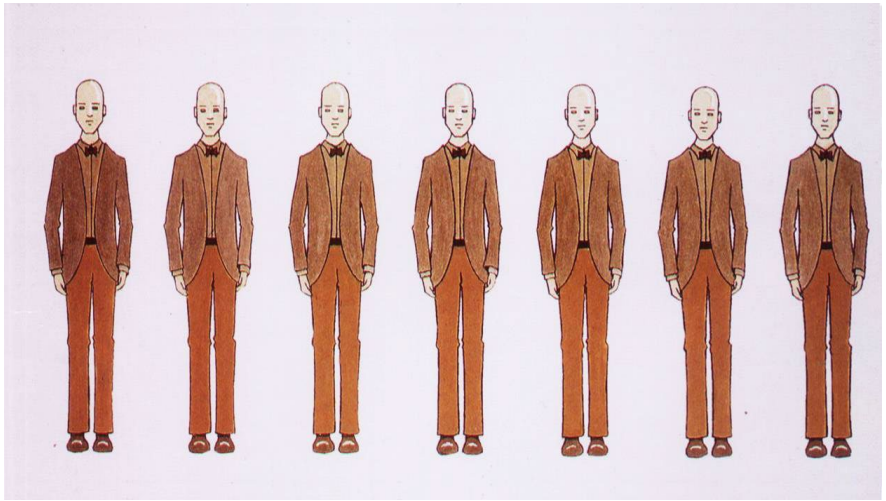
Variability



Need for personalised treatment

We **differ** in genetic background, gender, age, body weight, diet, but also in previous experiences (neuroplasticity), moods etc.

As a result **pharmacokinetics** (fate of the medicine in the body) and **pharmacodynamics** (the effects of a medicine) **may differ**

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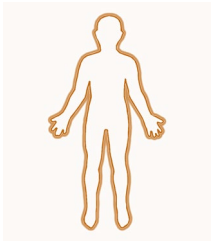
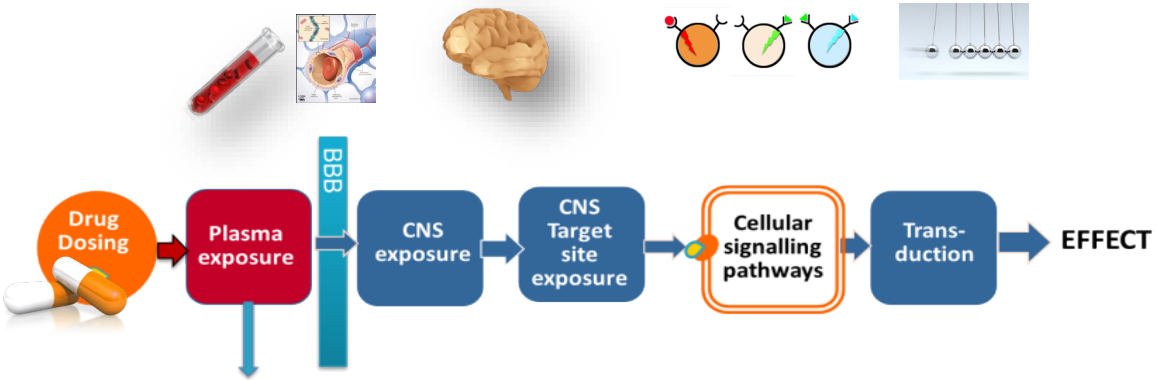
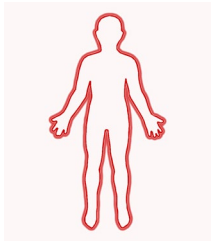
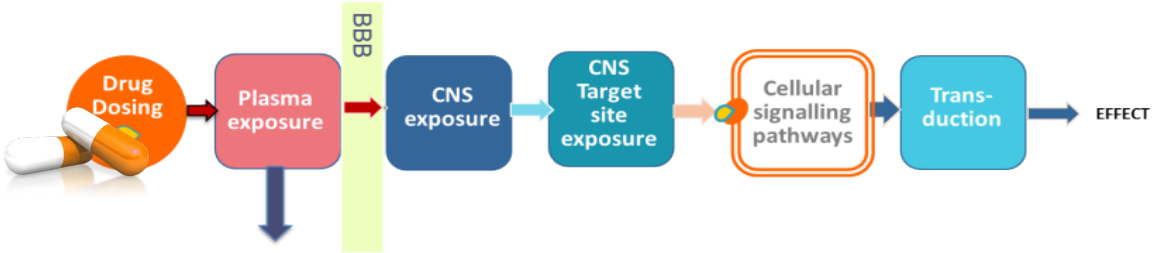
Right place, right time, right concentration for the RIGHT PERSON





Personal variation in each process between dose and effect





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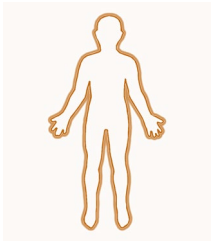
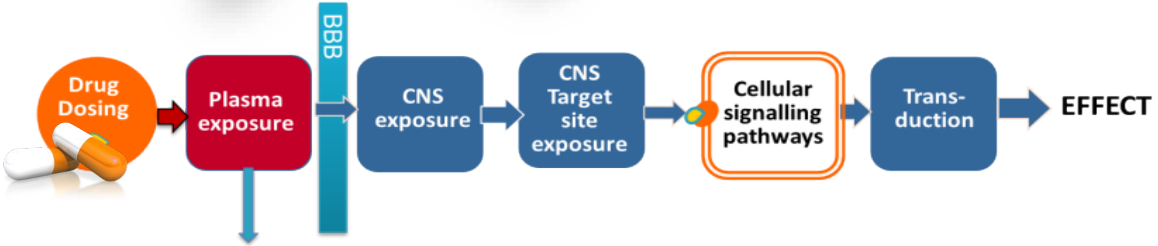
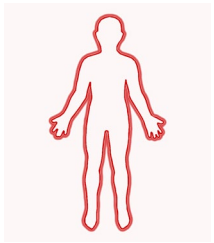
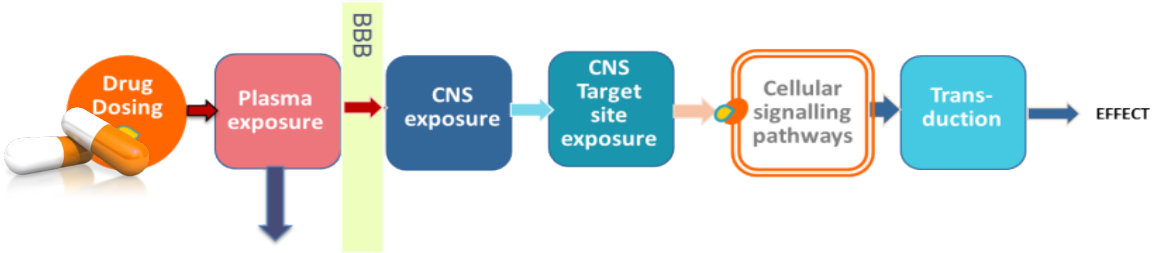




We need to take personal aspects into account





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QSPainRelief Consortium Partners

No	Partner name	Short name	Country
1	Universiteit Leiden	ULEI	NL
2	In Silico Biosciences, Inc	ISB	USA
3	PD-value BV	PD-value	NL
4	Concentris Research Management GmbH	concentris	DE
5	Universidad Autonoma de Barcelona	UAB	SP
6	Universidad Pompeu Fabra	UPF	SP
7	Alma mater Studiorium- Universita di Bologna	UNIBO	IT
8	Universite Cahtolique de Louvain	UCL	BE
9	Stichting Centre for Human Drug Research	CHDR	NL
10	Clinique Universitaires Saint-Luc	CUSL	BE

QSPainRelief - Aim

QSPainRelief aims to discover **novel effective combination treatments** in chronic pain patients, using **existing medicines**, to:

Improve

- **Analgesia**

Reduce

- Sedation
- Cognitive impairment
- Abuse liability

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QSPainRelief - Methods

QSPainRelief will assemble **existing and new computational models** into a **QSPainRelief model platform.**

It will use **existing and newly produced data** from

- Cellular systems
- Animals
- Healthy human subjects
- Real world *postoperative* pain disabled patients

These data will be used for calibration and validation, for QSPainRelief to **discover new combinational treatments to treat chronic pain.**

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QSPainRelief- Expected Impact

Personalised and maximized pain relief for individuals suffering from chronic pain

Creating **direct benefits** for chronic pain patients by

- Development and implementation of **novel combinational treatment strategies** in clinical practice
- **Higher treatment efficacy** due to personalised medicine and effective patient stratification
- **Improved acceptance of combinational therapies** in the clinical setting
- **Reduced stigmatisation of chronic pain** as a health condition through improved and clear communication to and with the general public

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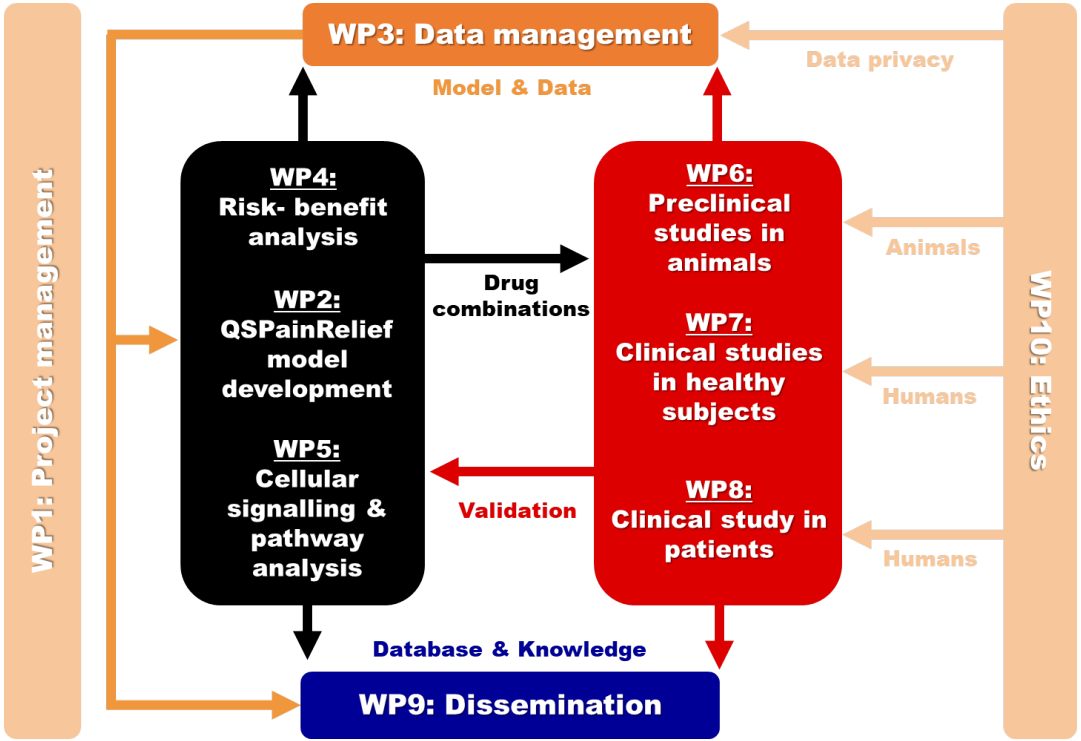
QSPainRelief – Work Packages



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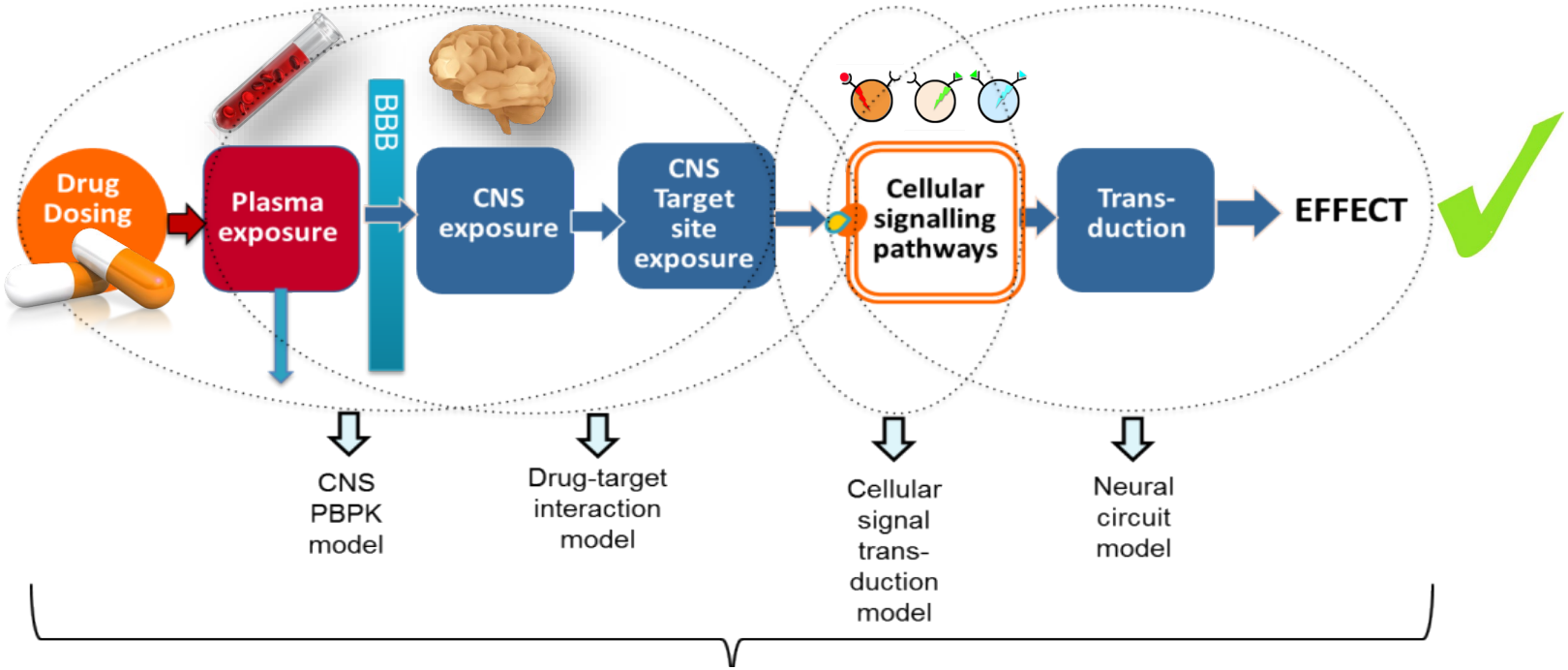

The QSPainRelief model platform

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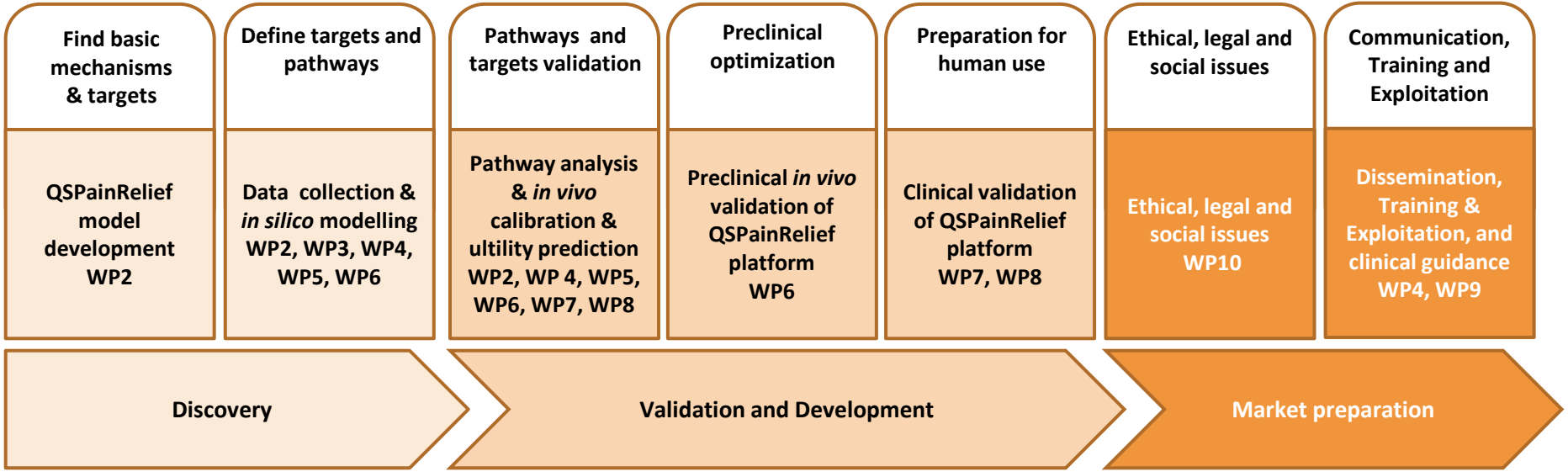
QSPainRelief – From Discovery to Market



QSPainRelief – The Team

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QSPainRelief – Scientific & Ethical Advisory Board

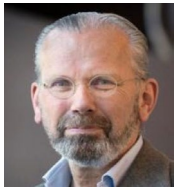
Joop van Griensven
President at Pain Alliance Europe (PAE)

Dr. Jan Freijer
Scientist

Prof. Dr. Albert Dahan
Professor of Anaesthesiology at Leiden University Medical Center

Prof. Dr. Frank Huygen
Professor of Anaesthesiology at Erasmus MC

Dr. med. vet. Caroline Johner
Animal Welfare Officer at the University Medical Center Freiburg



Dr Erwin Kompanje
Assoc prof Clinical Ethics &Clinical Researcher, Dept Intensive Care at Erasmus MC

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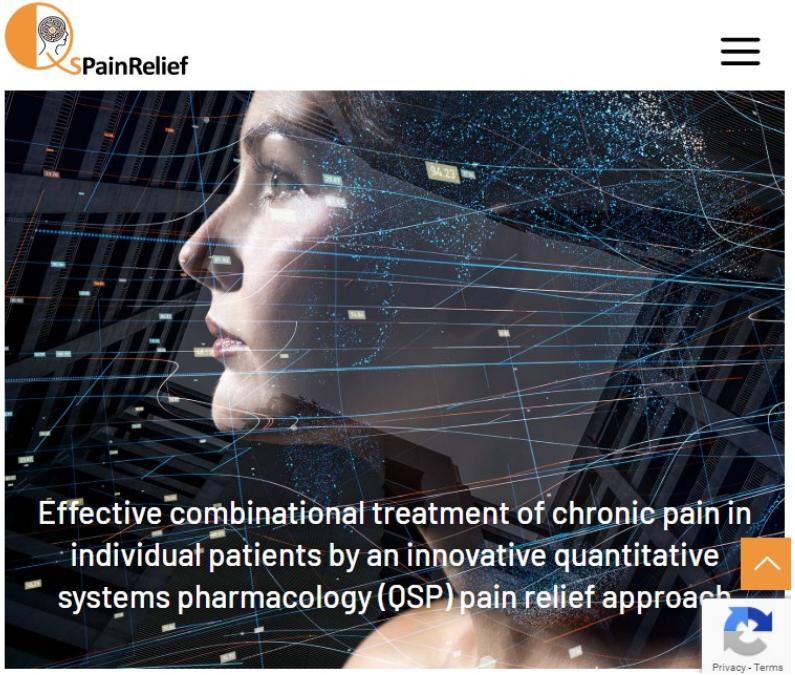
QSPainRelief – More Information on Website

https://qspainrelief.eu/



START DATE	01 January 2020
DURATION	60 months (5 years)
MEMBERS	10 institutions from 6 European countries and the USA
HORIZON 2020 FUNDING	6.24 million € (6,239,539 €)

QSPainRelief – Social Media & Newsletter

https://www.linkedin.com/company/qspainrelief

https://twitter.com/QSPainRelief

QSPainRelief – Social Media & Newsletter & Survey

https://www.linkedin.com/company/qspainrelief

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May we ask you to participate in our patients survey

https://twitter.com/QSPainRelief