TRAJECTOIRES DOULOUREUSES

Karine Nouette-Gaulain

JARCA 2022

Le cadre

- 100 Millions de patients bénéficient d'une chirurgie tous les ans
  - 60% vont présenter une douleur modérée à sévères en postopératoire

Curr Med Res Opin 2014; 30:149–60

- DPO modérée à sévère en PO= Persistant PostSurgical Pain (PPSP)

Clin J Pain 2017; 33:588–94

- Définition International Classification of Disease 11
  - PPSP= Douleur supérieure à 3 mois après une chirurgie
  - 10 à 56% en fonction de la chirurgie

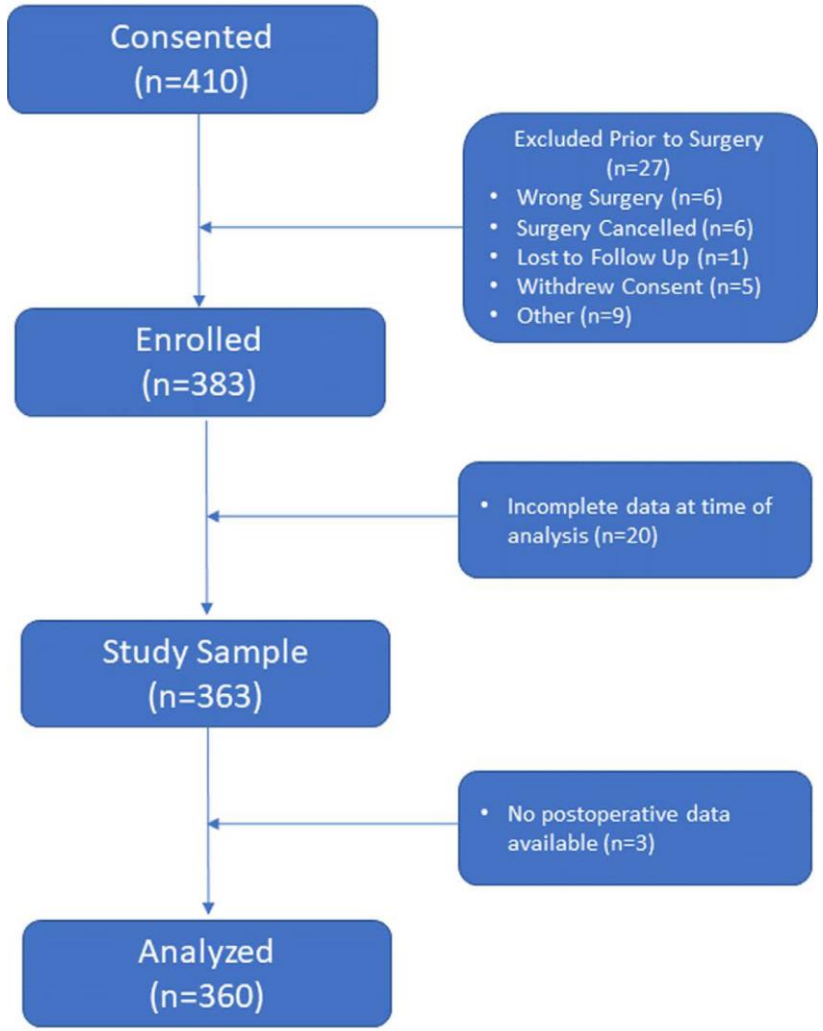
Pain 2015; 156:1003–7

??? L’énigme clinique ???

- **Faut-il être plus directif au sein des équipes et systématiser les protocoles de PEC de la DPO pour tous?**

- **Faut il privilégier des PEC de la DPO personnalisées selon les patients?**

DPO en 2022, où en sommes nous?



Chirurgie programmée majeure, orthopédique urologie, colorectal, pancreatic/biliary, thoracique, ou rachis

Douleur évaluée par the Brief Pain Inventory (BPI)
Moyenne, la pire et la plus légère/24H
PROMS.

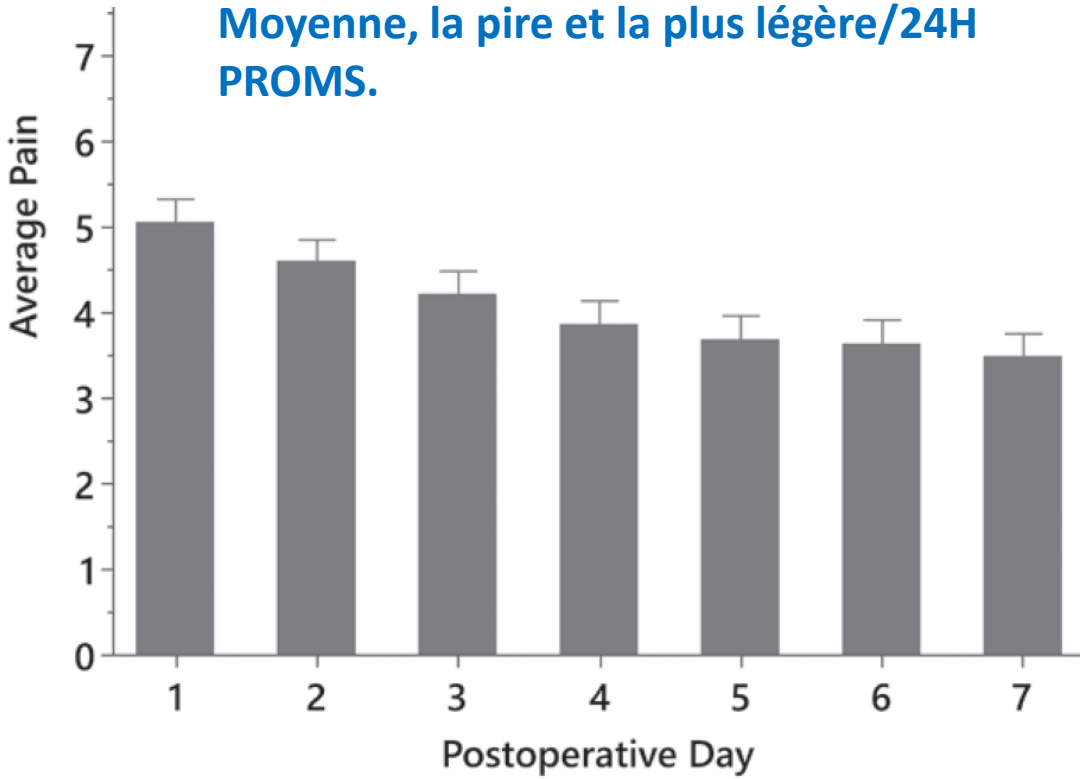
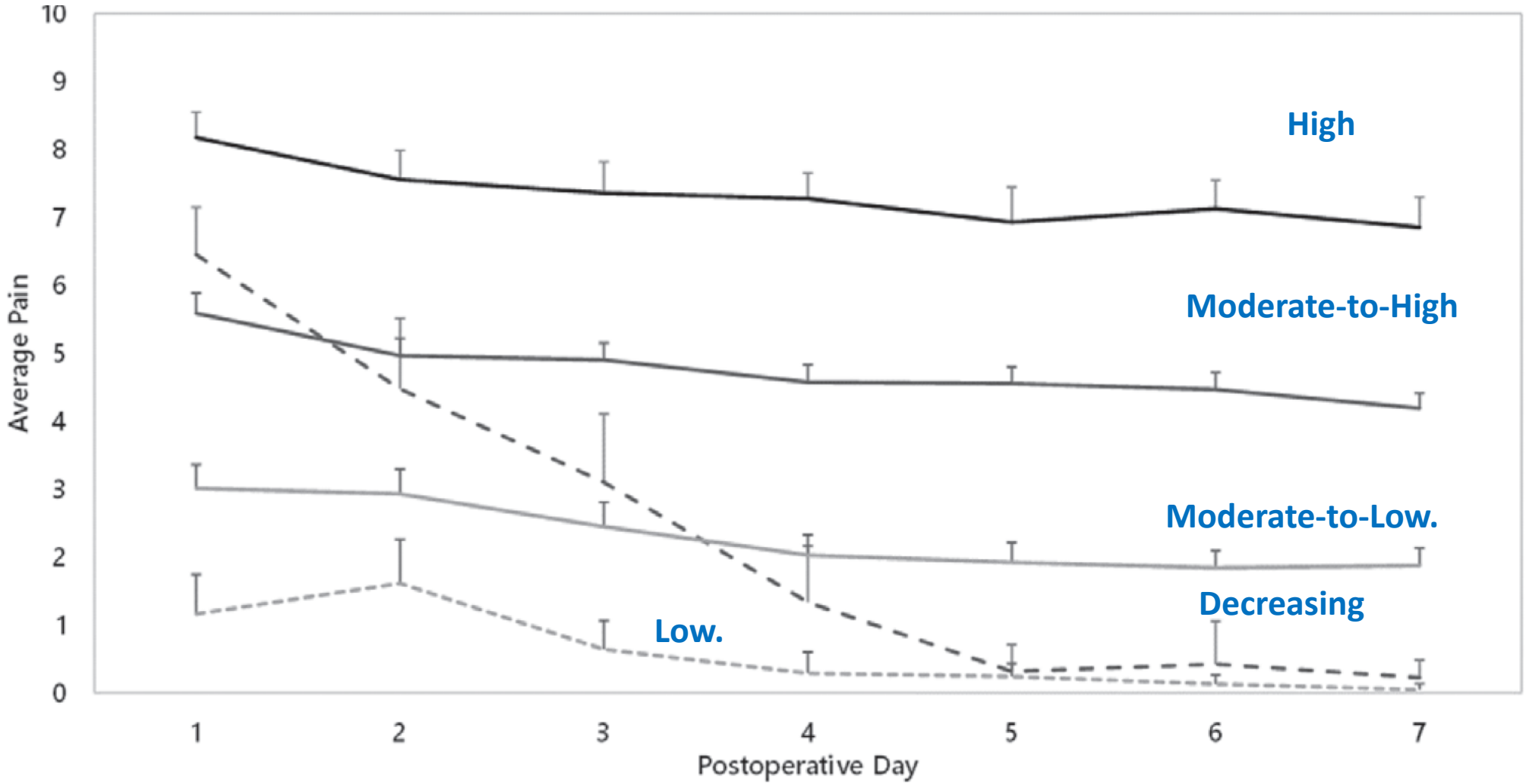


Fig. 2. Average daily pain across first 7 days after surgery, with overall trajectory for entire sample. *Error bars* indicate 95% CIs.

Vasilopoulos Anesthesiology 2021; 134:421–34

Modèle à 5 trajectoires



Vasilopoulos Anesthesiology 2021; 134:421–34

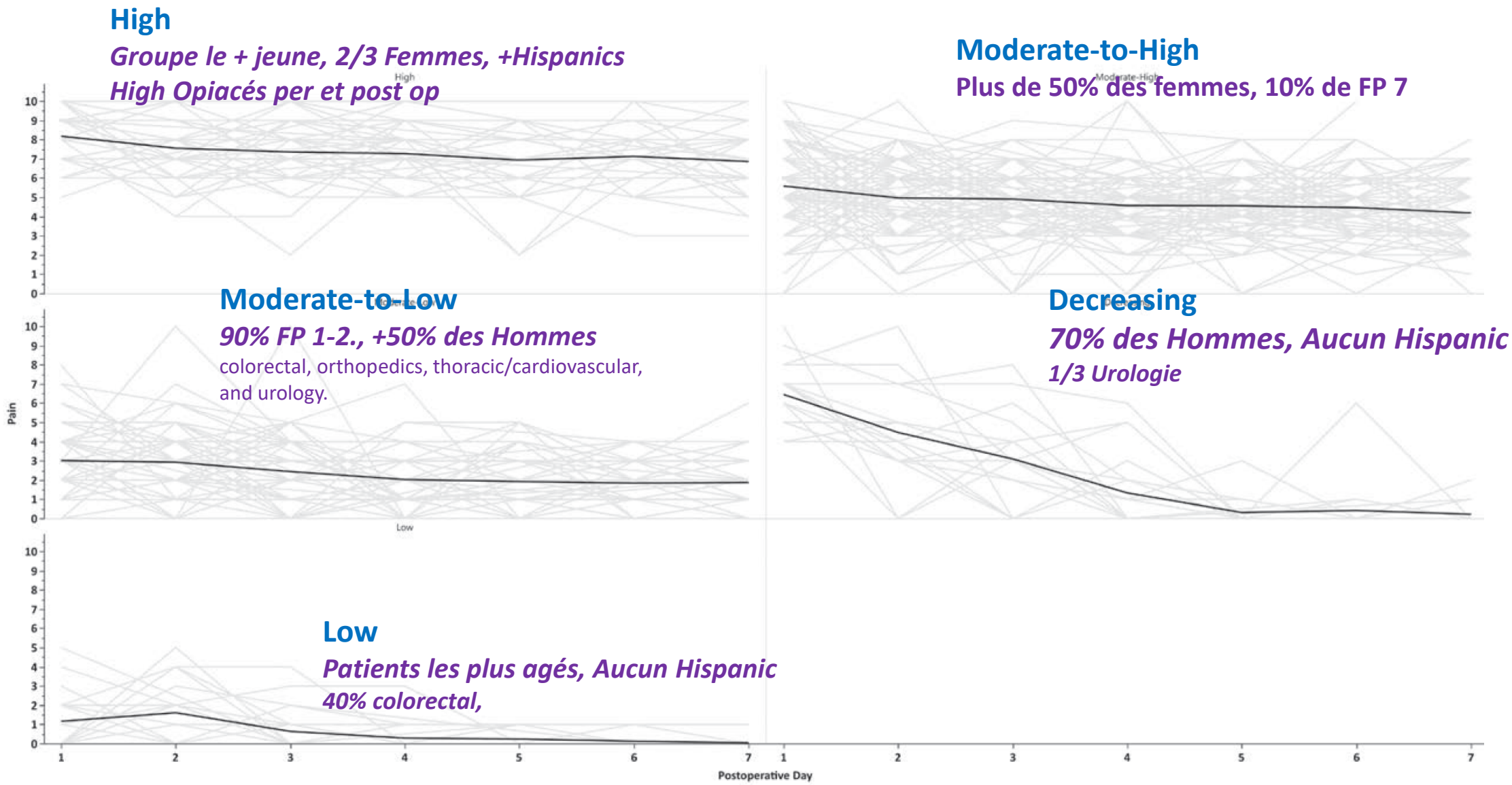
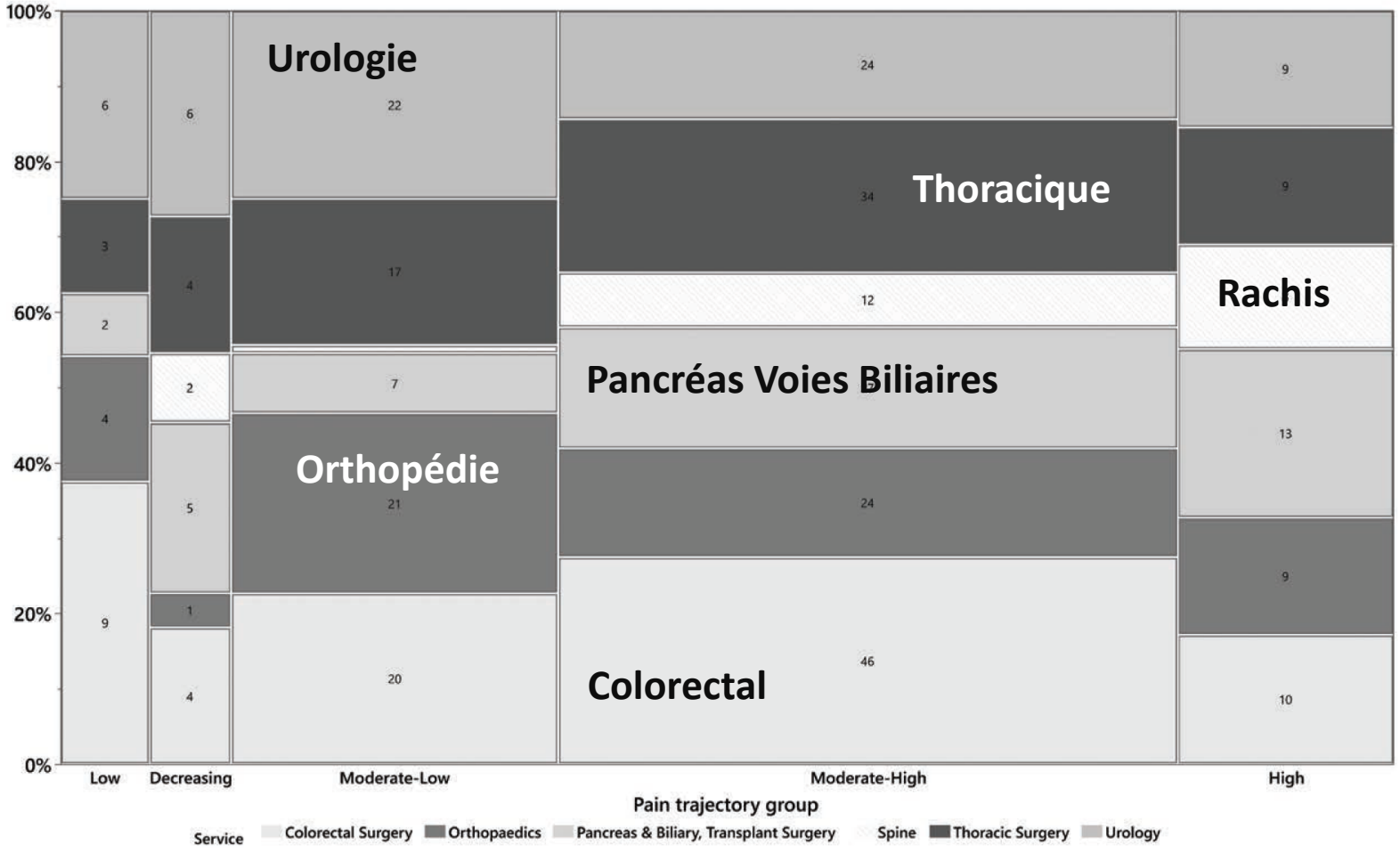


Fig. 4. Spaghetti plots for individual trajectories within each pain trajectory group.

Vasilopoulos Anesthesiology 2021; 134:421–34



. 5. Mosaic plot for surgical service and pain trajectory groups. The *number* in each cell indicates the number of patients in that group. cular service (n = 1) was not included in this analysis.

Vasilopoulos Anesthesiology 2021; 134:421–34

Global burden of postoperative death

thelancet.com Vol 393 February 2, 2019

*Dmitri Nepogodiev, Janet Martin, Bruce Biccard, Alex Makupe, *Aneel Bhangu, on behalf of the National Institute for Health Research Global Health Research Unit on Global Surgery†*

Our analysis suggests that at least 4·2 million people worldwide die within 30 days of surgery each year, and half of these deaths occur in LMICs. This number of postoperative deaths accounts for 7·7% of all deaths globally,[4] making it the third greatest contributor to deaths, after ischaemic heart disease and stroke (figure). More people die within 30 days of surgery annually than from all causes related to HIV, malaria, and tuberculosis combined (2·97 million deaths).[4] We project that an expansion of surgical services to address unmet need would increase total global deaths to 6·1 million annually, of which 1·9 million deaths would be in LMICs.

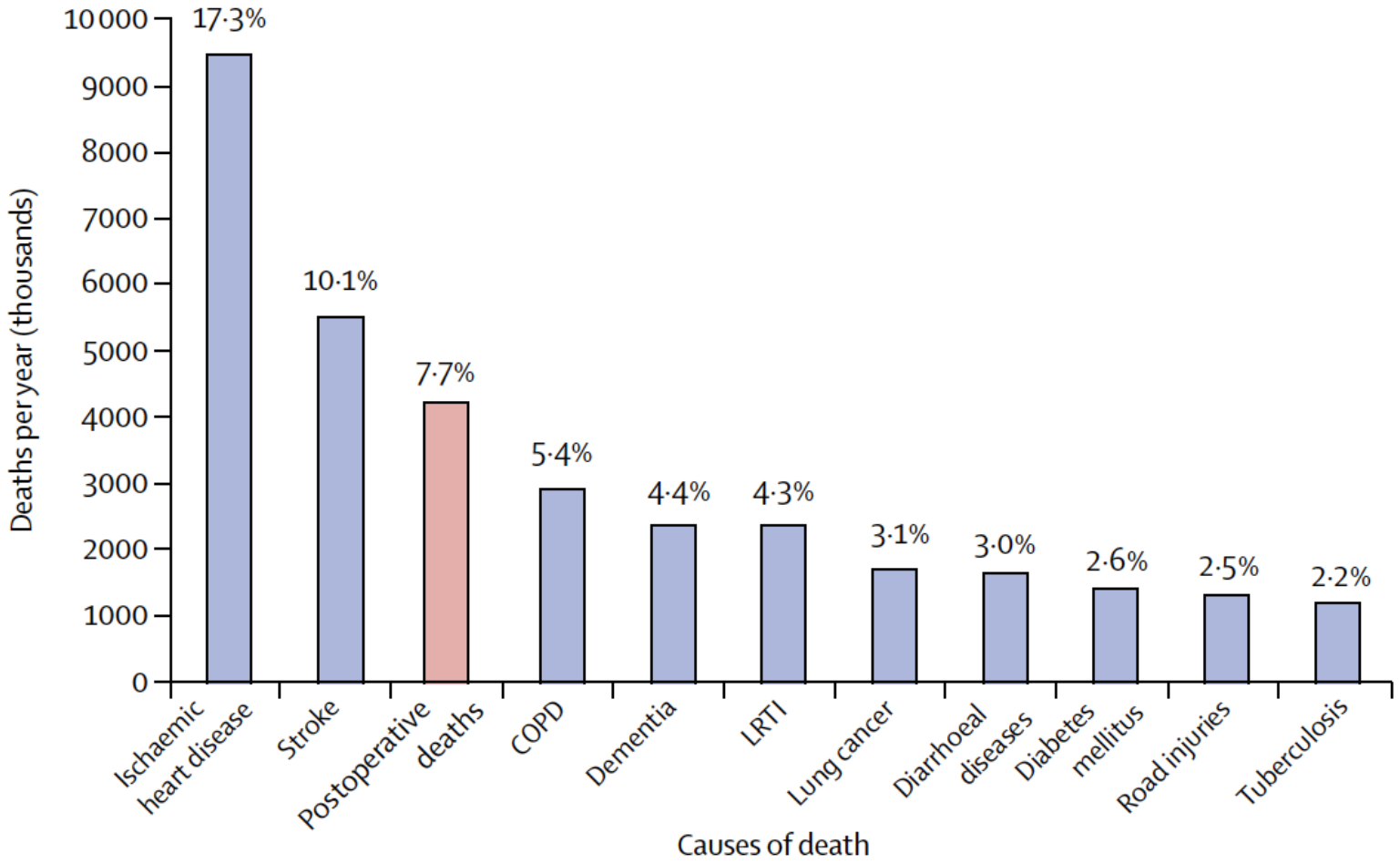


Figure: **Top ten global causes of death, 2016**

Mortality after surgery in Europe: a 7 day cohort study

Rupert M Pearse, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology*

Lancet 2012; 380: 1059–65

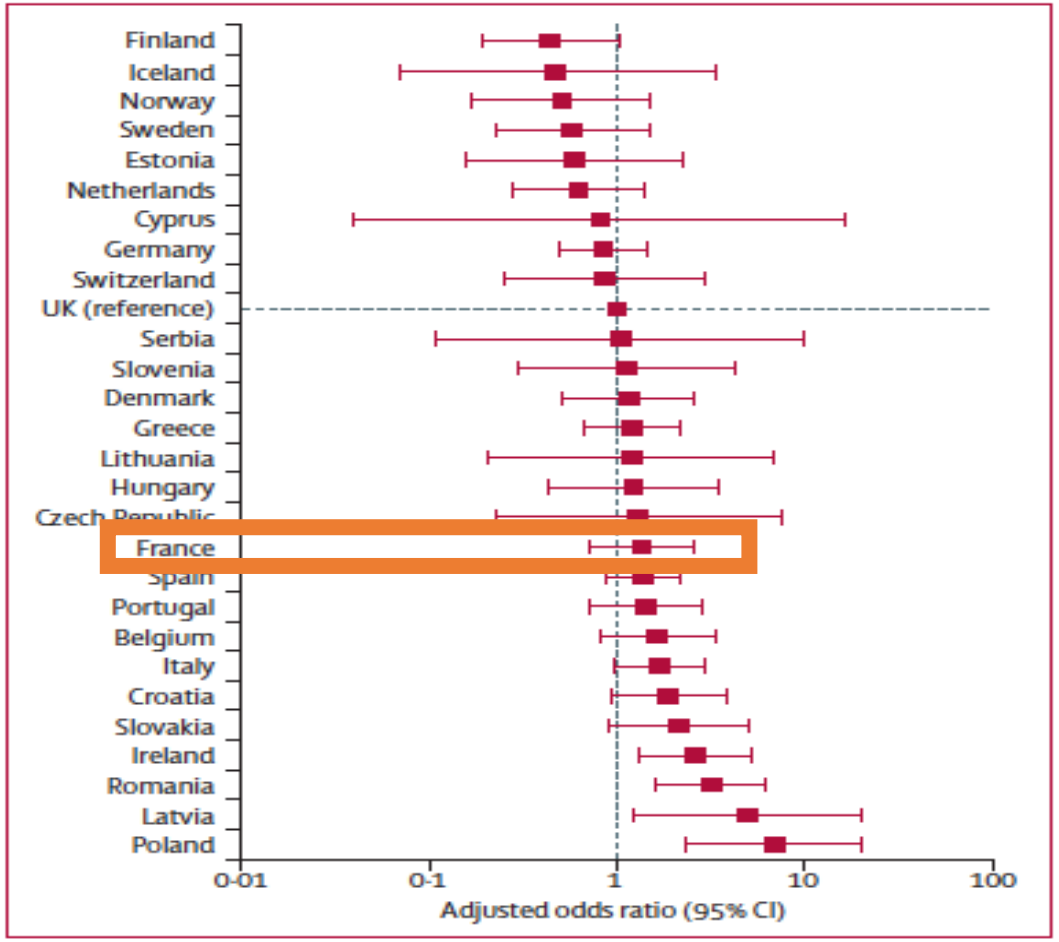


Figure 3: Adjusted odds ratio for death in hospital after surgery for each country

Findings We included 46 539 patients, of whom 1855 (4%) died before hospital discharge. 3599 (8%) patients were admitted to critical care after surgery with a median length of stay of 1·2 days (IQR 0·9–3·6). 1358 (73%) patients who died were not admitted to critical care at any stage after surgery. Crude mortality rates varied widely between countries (from 1·2% [95% CI 0·0–3·0] for Iceland to 21·5% [16·9–26·2] for Latvia). After adjustment for confounding variables, important differences remained between countries when compared with the UK, the country with the largest dataset (OR range from 0·44 [95% CI 0·19–1·05; p=0·06] for Finland to 6·92 [2·37–20·27; p=0·0004] for Poland).

!!! L’énigme clinique : sujet important !!!

- ~~**Faut-il être plus directif au sein des équipes et systématiser les protocoles de PEC de la DPO pour tous?**~~

- **Faut il privilégier des PEC de la DPO personnalisées selon les patients?**

Pourquoi?

Persistent Postsurgical Pain

ANESTHESIOLOGY 2018

Pathophysiology and Preventative Pharmacologic Considerations

Philippe Richebé, M.D., Ph.D., Xavier Capdevila, M.D., Ph.D., Cyril Rivat, Ph.D.

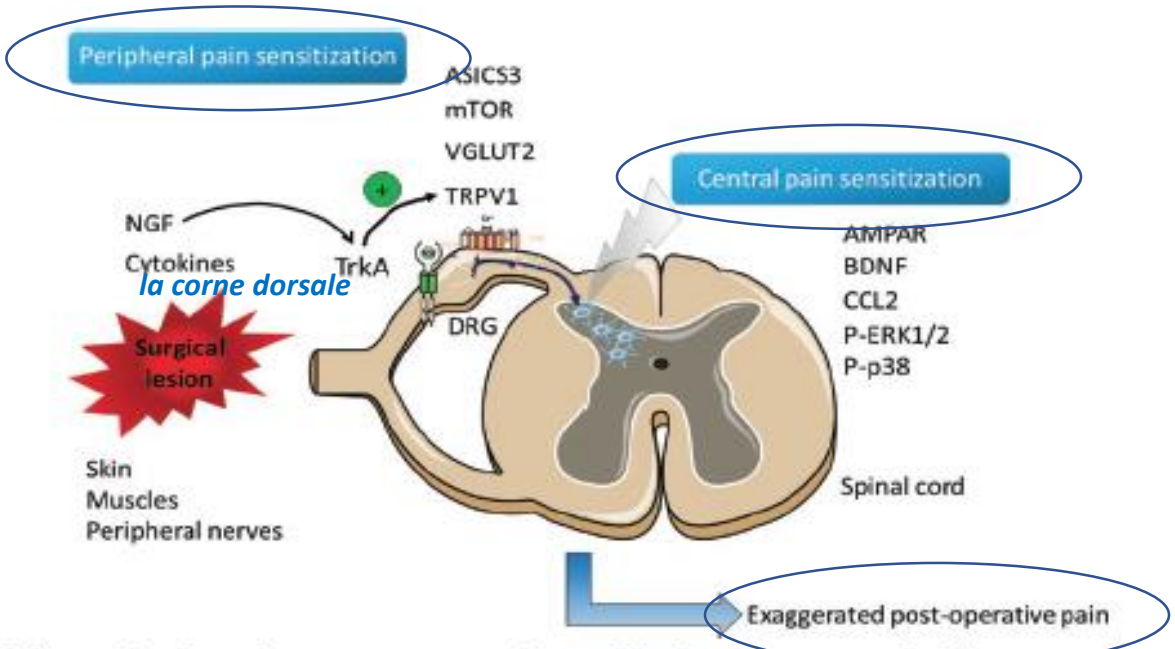


Fig. 1. Summary of the mechanisms that may support pain sensitization after surgery leading to persistent postsurgical pain. Nociceptive inputs due to surgery produce local molecular changes such as nerve growth factor (NGF) and cytokine release and in primary sensory neurons of the dorsal root ganglia (DRG) including increased expression of acid-sensing ion channels 3 (ASICS3), transient receptor potential cation channel subfamily V member 1 (TRPV1), and mechanistic target of rapamycin (mTOR). The latter controls vesicular glutamate transporter 2 (VGLUT2) expression that generates an increased glutamatergic activity in the spinal cord. These changes are responsible for peripheral pain sensitization that then influences spinal neuronal activity referred to as central pain sensitization. Central sensitization depends upon increased expression of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) and brain-derived neurotrophic factor (BDNF) release. Activation of AMPAR may account for extracellular signal–regulated kinase 1/2 activation (P-ERK1/2) leading to the development of sustained pain hypersensitivity. MAPK kinase p38 (P-p38) and chemokine ligand 2 (CCL2) also contribute to surgery-induced central pain sensitization. TrkA = tropomyosin receptor kinase A.

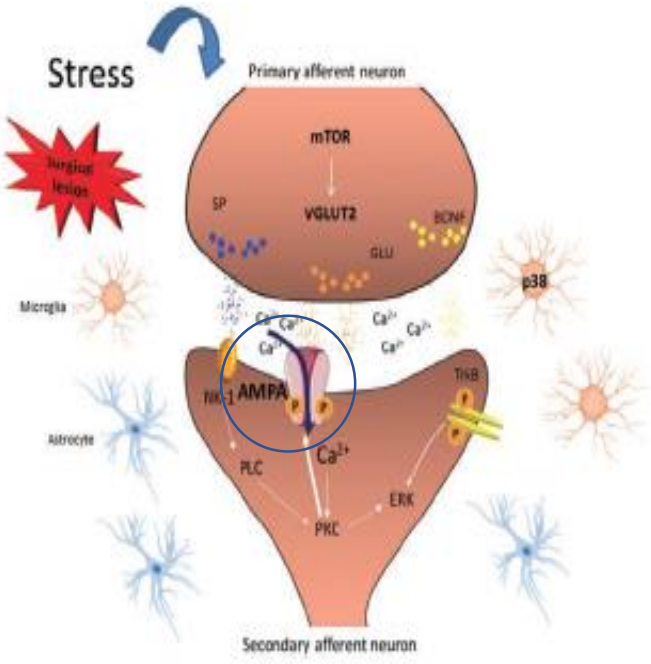
Anesthesiology 2018; 129:590-607)

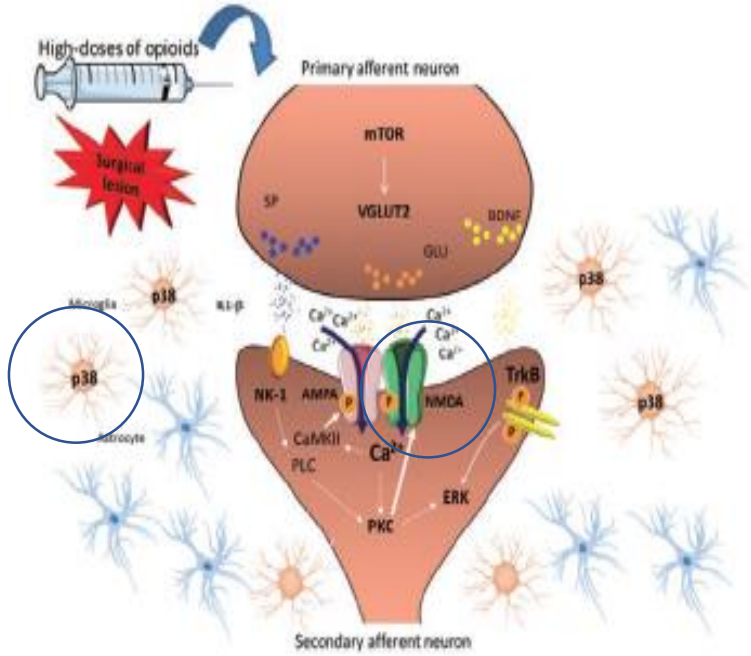
Persistent Postsurgical Pain

ANESTHESIOLOGY 2018

Pathophysiology and Preventative Pharmacologic Considerations

Philippe Richebé, M.D., Ph.D., Xavier Capdevila, M.D., Ph.D., Cyril Rivat, Ph.D.





Opiacés préop:
Activation p38microglie
ReLargage de IL1béta

Sensibilisation Centrale de la douleur par la chirurgie et opiacés
-Récepteur AMPA Calcium dépendant
-Récepteur NMDA
-Cellules gliales

Risque d'hyperexcitabilité neuronale prolongée
Besoins en morphiniques en postopératoires?

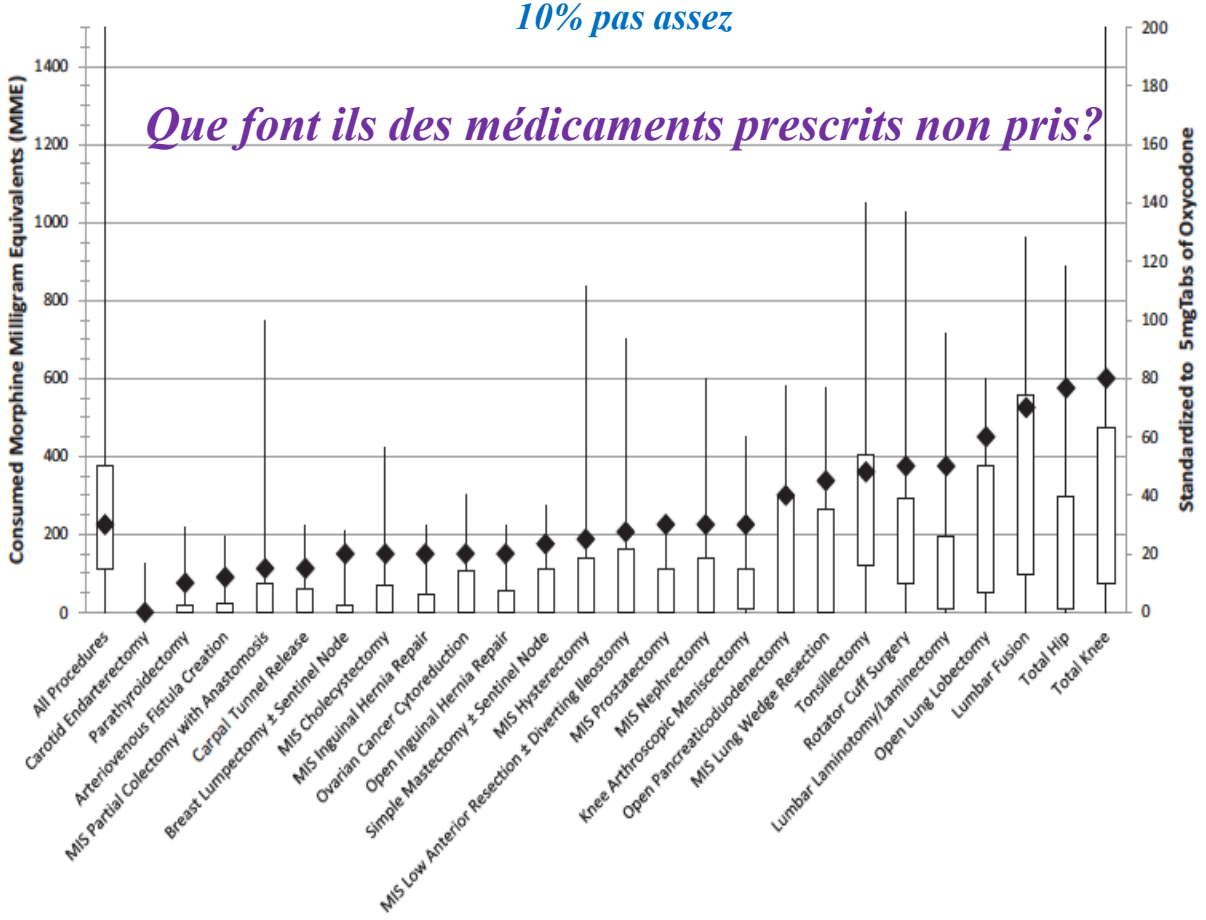
Results of a Prospective, Multicenter Initiative Aimed at Developing Opioid-prescribing Guidelines After Surgery

Cornelius A. Thiels, DO, MBA,† Daniel S. Ubl, MPH,†‡ Kathleen J. Yost, PhD,‡§ Sean C. Dowdy, MD,¶ Tad M. Mabry, MD,|| Halena M. Gazelka, MD,** Robert R. Cima, MD, MA, FACS, FASCRS,*† and Elizabeth B. Habermann, MPH, PhD*†‡*

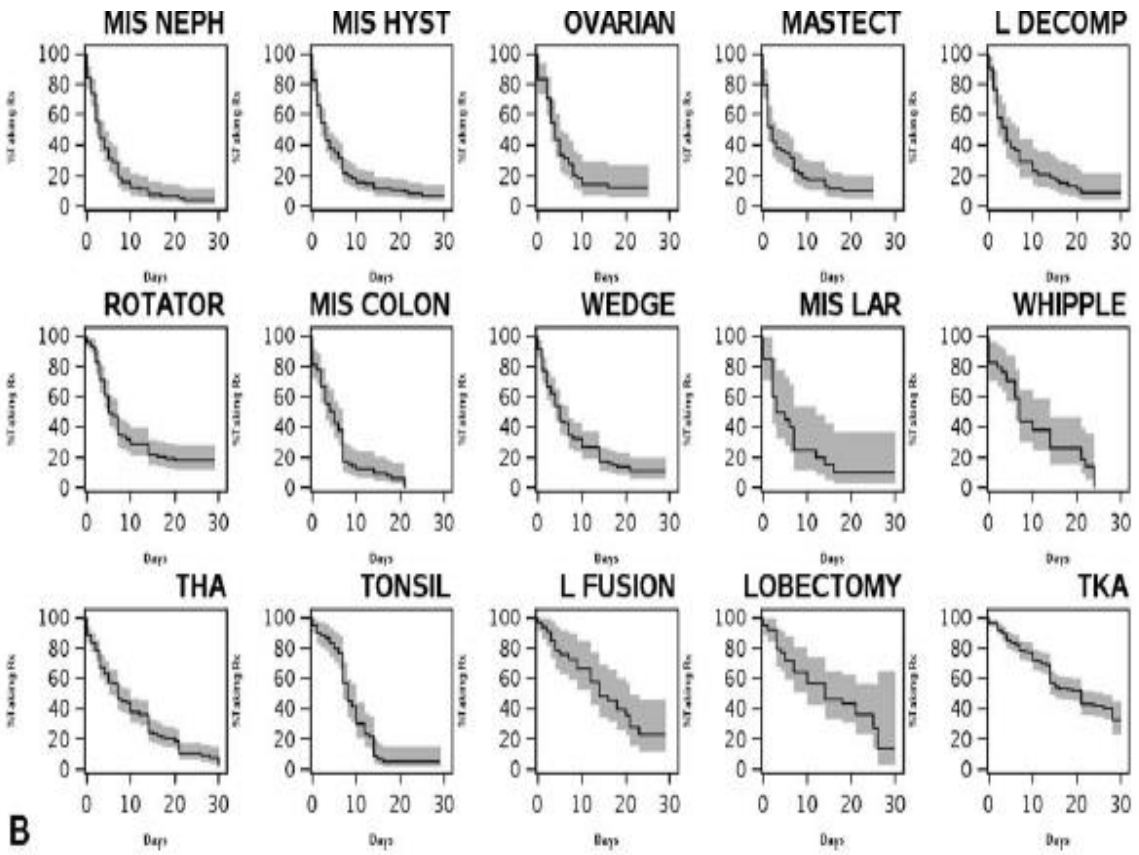
Ann Surg 2018;268:457–468

3412 Patients, 91.2% des patients naïfs reçoivent des opiacés,
28.3% prescription en excès
10% pas assez

Que font ils des médicaments prescrits non pris?



Stop à J3: 53.1%,; J5: 64.2%, and J7: 73.8%



Postsurgical Opioid Prescriptions and Risk of Long-term Use

An Observational Cohort Study Across the United States

Jessica C. Young, MSPH, ✉ Nabarun Dasgupta, MPH, PhD,† Brooke A. Chidgey, MD,‡ and Michele Jonsson Funk, PhD**

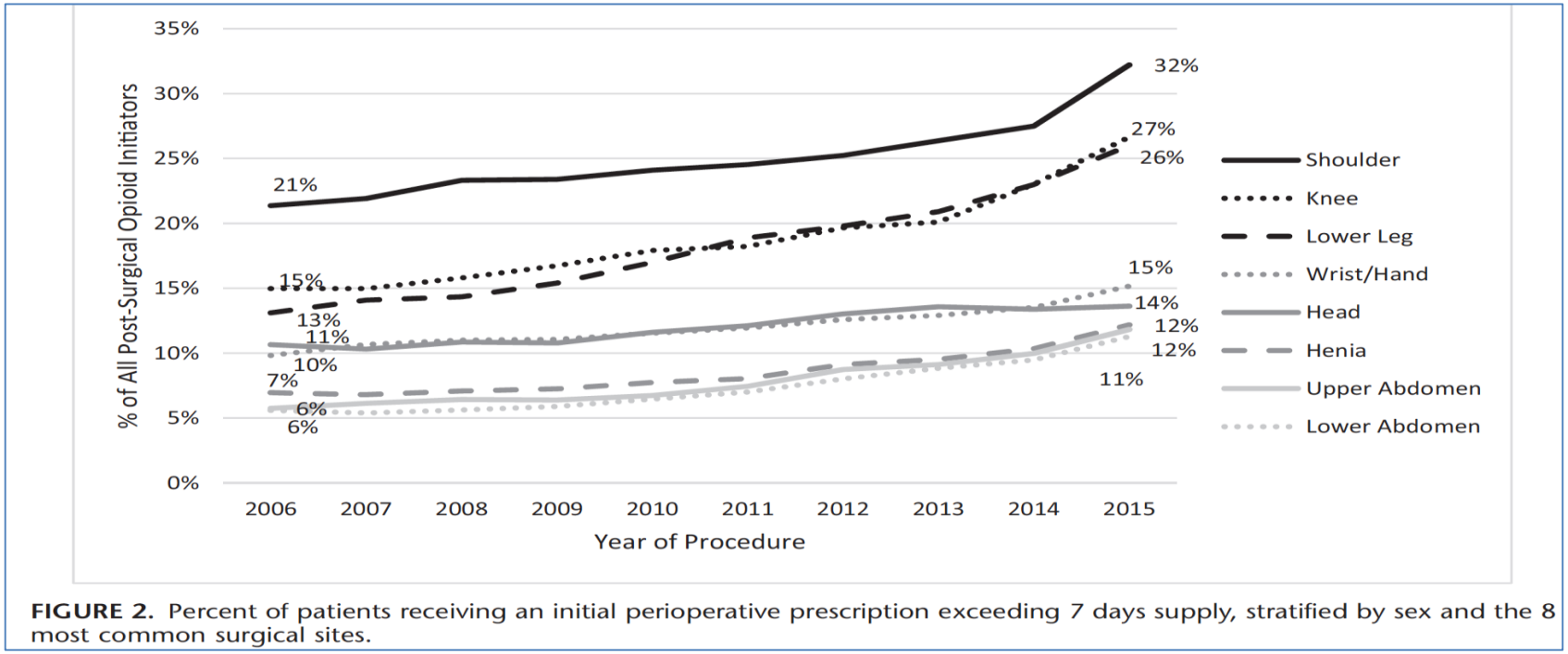


FIGURE 2. Percent of patients receiving an initial perioperative prescription exceeding 7 days supply, stratified by sex and the 8 most common surgical sites.

Effet Période d'étude et sociétal

Effet Durée de ttt >7j/7J

Effet Dose >400MME

Ann Surg 2019

We identified 5,148,485 opioid-naive surgical patients. Overall, **55.5%** received an opioid for postoperative pain, with median days ***supply 5 and median total MME 240.***

The proportion of patients receiving prescriptions ***above 7 DS increased from 11% in 2006 to 19% in 2015.***
Among those receiving postoperative opioids, 8% had long-term opioid use, and risk of long-term use was 1.16 times [95% confidence interval (CI), 1.10–1.25] higher among those receiving >7 days compared with those receiving 7 days.

Those receiving >400 total MME (15% of patients) were at 1.17 times (95% CI, 1.10–1.25) the risk of long-term use compared with those receiving 400 MME.

JAMA Network Open. 2019;2(3):e190168.

Factors Associated With Acute Pain Estimation, Postoperative Pain Resolution, Opioid Cessation, and Recovery

Secondary Analysis of a Randomized Clinical Trial

Jennifer M. Hah, MD, MS; Eric Cramer, BS; Heather Hilmoe, BS ; Peter Schmidt, MD; Rebecca McCue, BS ; Jodie Trafton, PhD; Debra Clay, BSN, RN; Yasamin Sharifzadeh, BS; Gabriela Ruchelli, BS; Stuart Goodman, MD, PhD; James Huddleston, MD; William J. Maloney, MD; Frederick M. Dirbas, MD; Joseph Shrager, MD; John G. Costouros, MD; Catherine Curtin, MD; Sean C. Mackey, MD, PhD; Ian Carroll, MD, MS

422 participants, chirurgie lourde

CJP:

1. Temps pour la résolution de la douleur

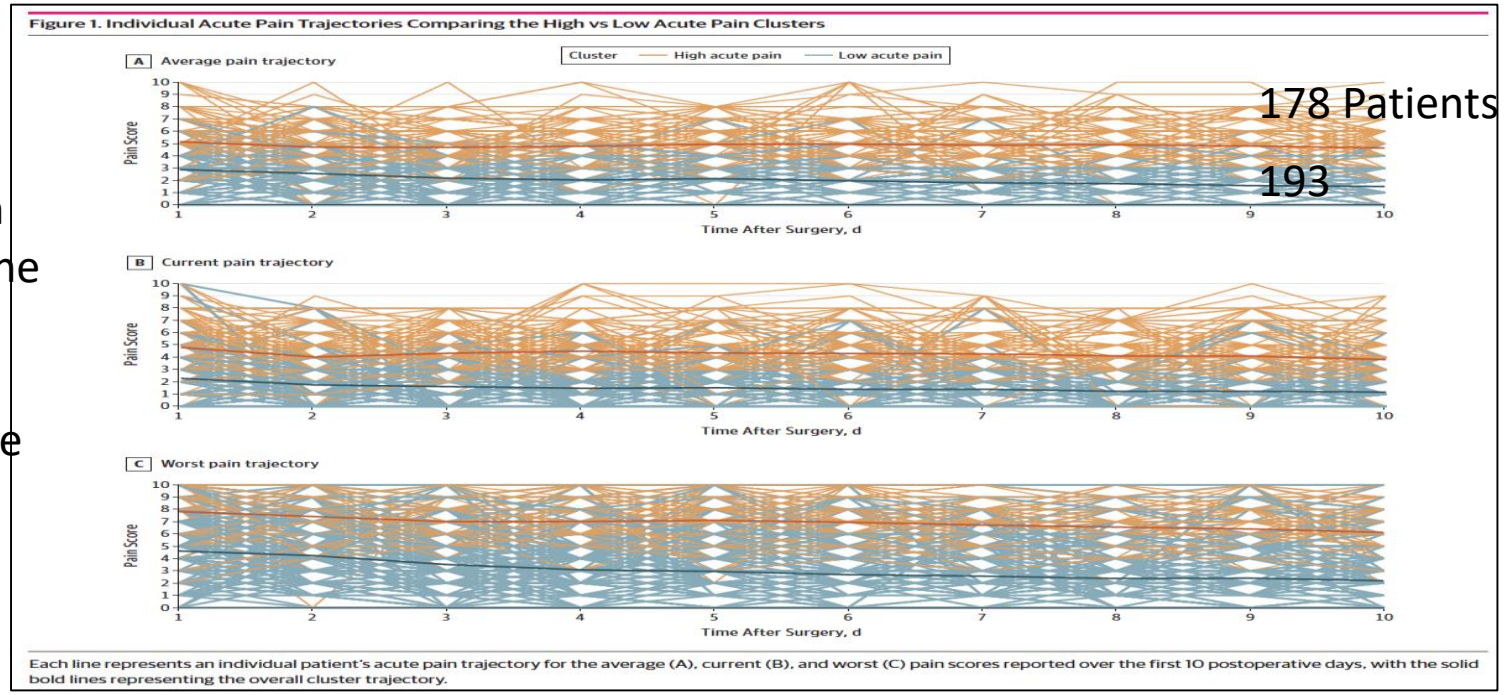
(5 consecutive reports of 0 of 10 average pain over the last 24 hours at the surgical site on the Numeric Pain Rating Scale),

2. Temps pour arrêt des opiacés

(5 consecutive reports of 0 opioid use over the past 24 hours),

3. récupération de l'état antérieur

(responding yes to the question, "Would you say that you are fully recovered from your surgery?").



178 Patients

193

Factors Associated With Acute Pain Estimation, Postoperative Pain Resolution, Opioid Cessation, and Recovery

Secondary Analysis of a Randomized Clinical Trial

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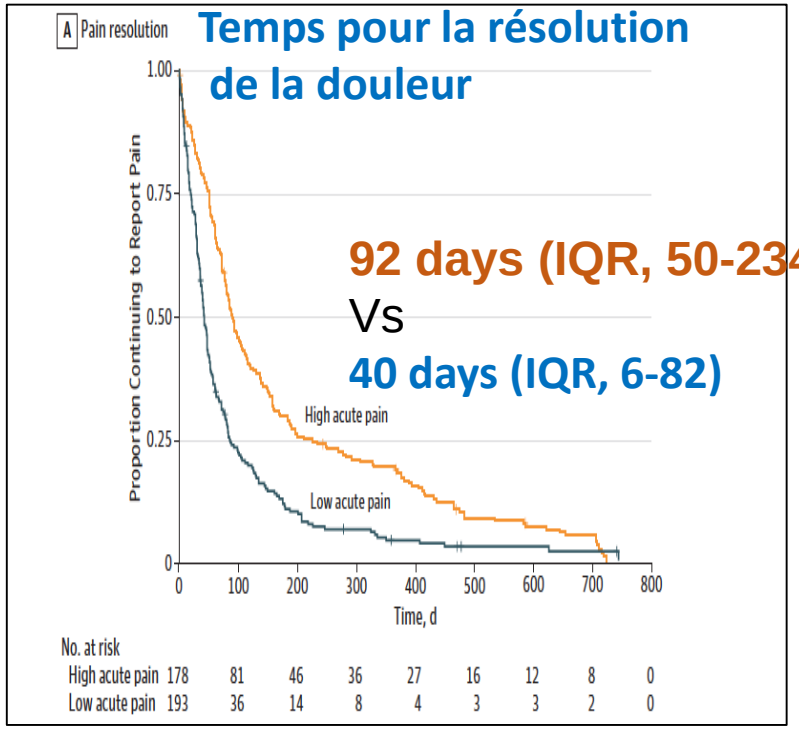
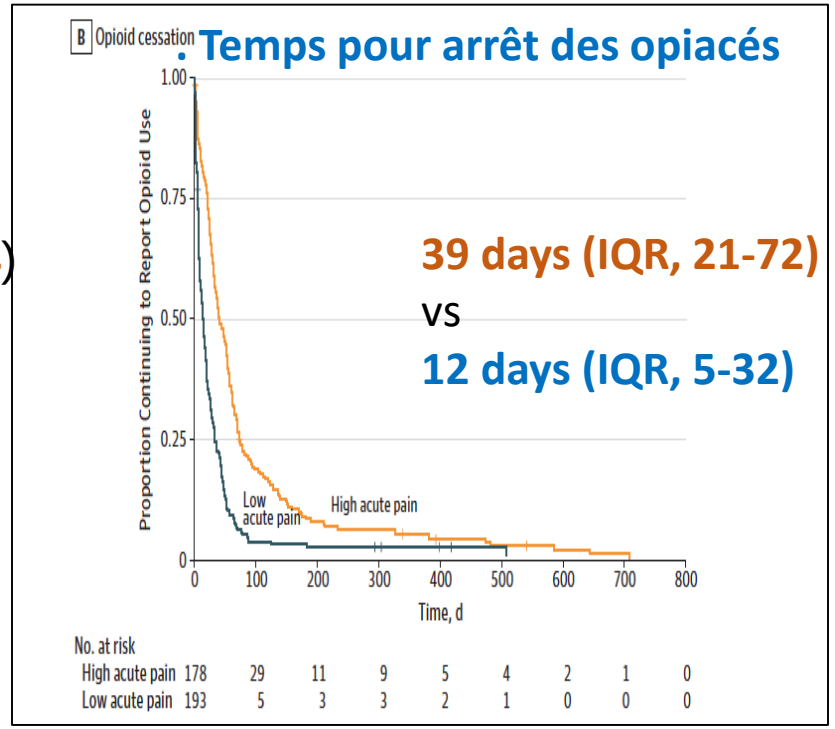
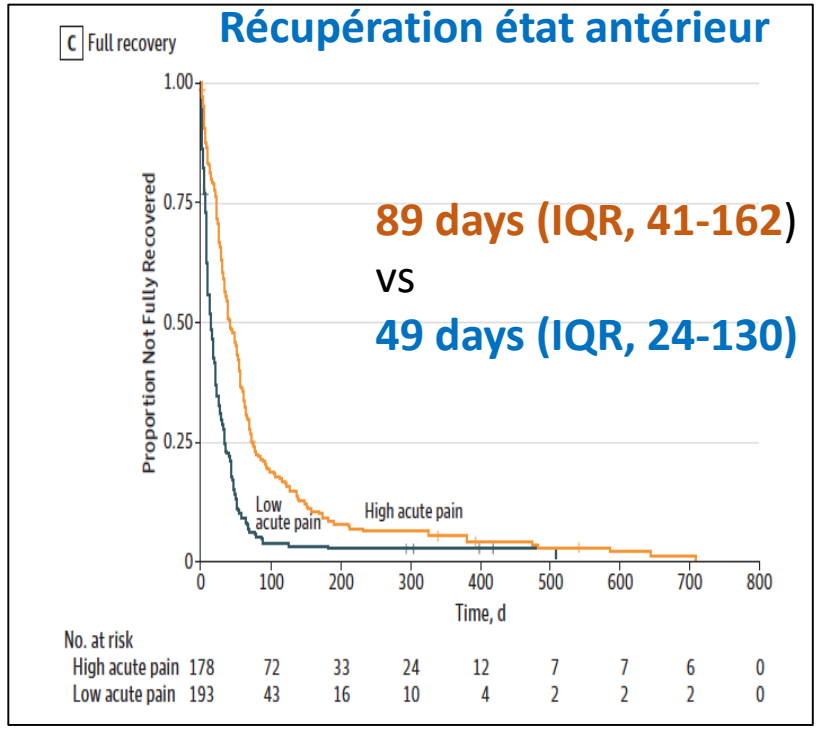
La pire douleur à 10 j est le meilleur Predicteur pour identifier la résolution de la douleur







Postoperative Pain Trajectories and Pain Chronification—an Empirical Typology of Pain Patients

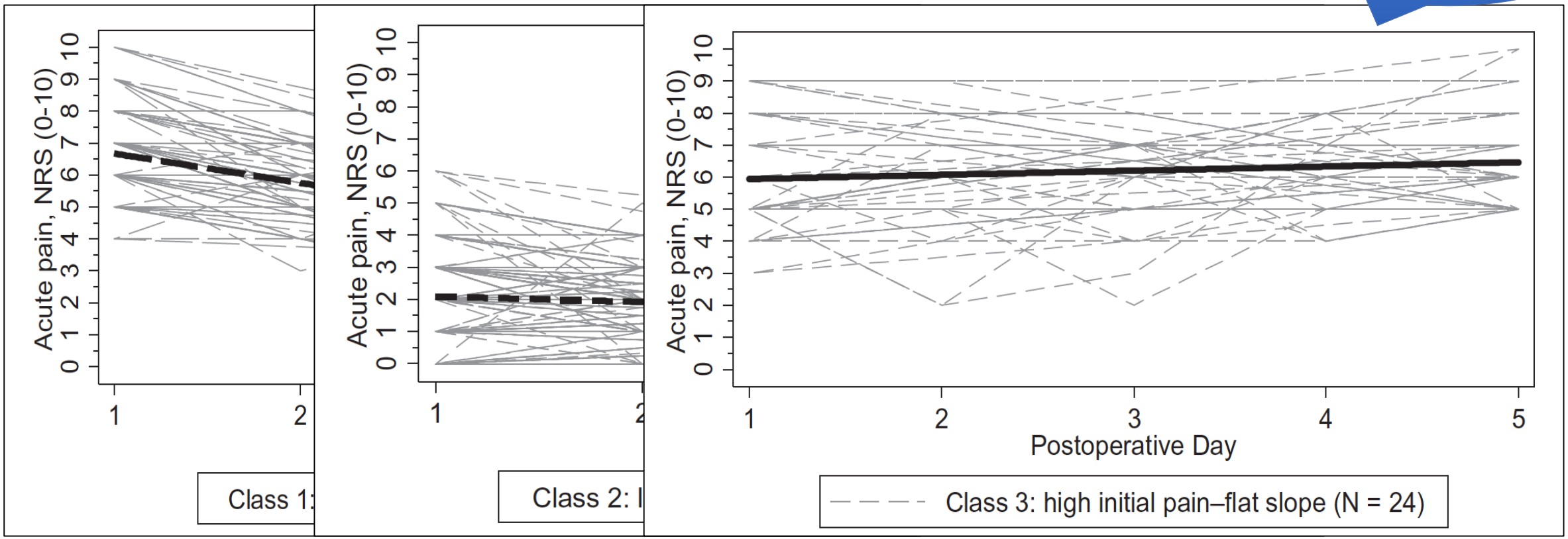
Astrid Althaus, PhD,* Oliver Arránz Becker, PhD,† Karl-Heinz Moser, MD,‡ Eberhard Albert Lux, MD,§ Friedrich Weber, MD,¶ Edmund Neugebauer, PhD,‖ and Christian Simanski, MD‖

Pain Medicine 2018; 19: 2536–2545

174 patients et 3 groupes

2 FACTEURS ESSENTIELS: dOULEUR AU DÉPART ET niveau de résolutionde la douleur

Chronic Pain



Contents lists available at ScienceDirect

Anaesthesia Critical Care & Pain Medicine

journal homepage: www.elsevier.com

Original Article

Characterisation of pragmatic postoperative PAin Trajectories over seven days and their association with CHronicity after 3 months: a prospective, pilot cohort study (PATCH study)

Joël L'Hermite [a,*], M. Gabrielle Pagé [b,c], Thierry Chevallier [d], Bob Occean [d], Eric Viel [a], Olivier Bredeau [a], Jean-Yves Lefrant [a], Philippe Cuvillon [a]

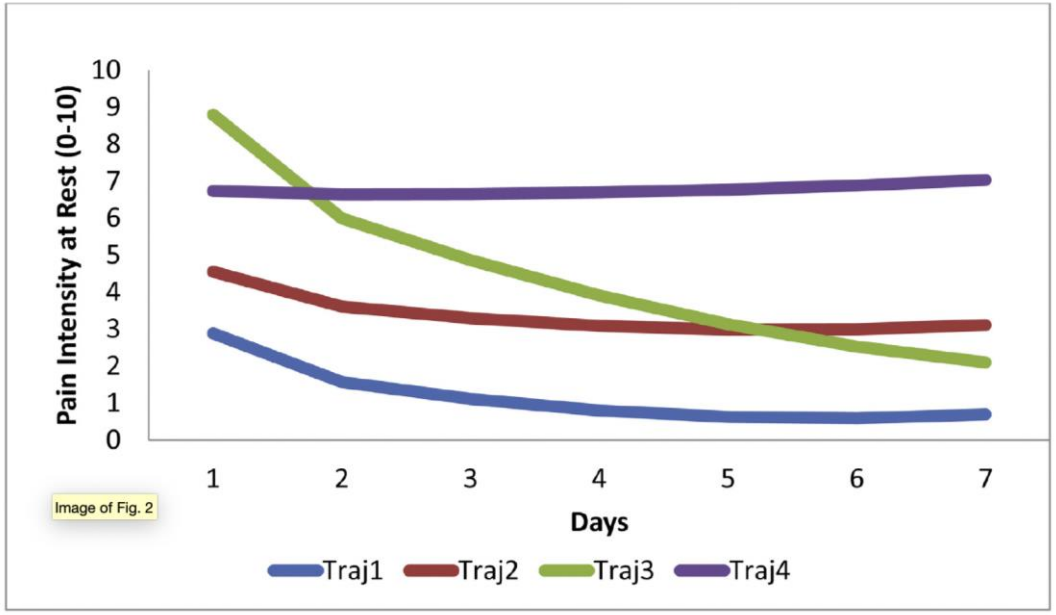


Image of Fig. 2

ain trajectories characterised with Growth Mixture Modeling (GMM).
rajectory 1; Traj 2: trajectory 2; Traj 3: trajectory 3; Traj 4: trajectory 4.

Table 4
Distribution of patients with PPSP according to the type of pain trajectories.

	Clinical definition of pain trajectories (n = 308)		Pain trajectories characterised with GMM (n = 344)	
	Ideal	Non-ideal	Traj 1	Traj 2 + Traj 3 + Traj 4
Number of patient	210	98	182	162
Missing data	19	9	19	19

210 x 280 mm

Spine

SPINE Volume 45, Number 21, pp E1421–E1430

EPIDEMIOLOGY

OPEN

Preoperative Factors Predict Postoperative Trajectories of Pain and Disability Following Surgery for Degenerative Lumbar Spinal Stenosis

Jeffrey J. Hébert, DC, PhD [a,b] Edward Abraham, MD, FRCSC [c,d,e] Niels Wedderkopp, MD, PhD [f,g]

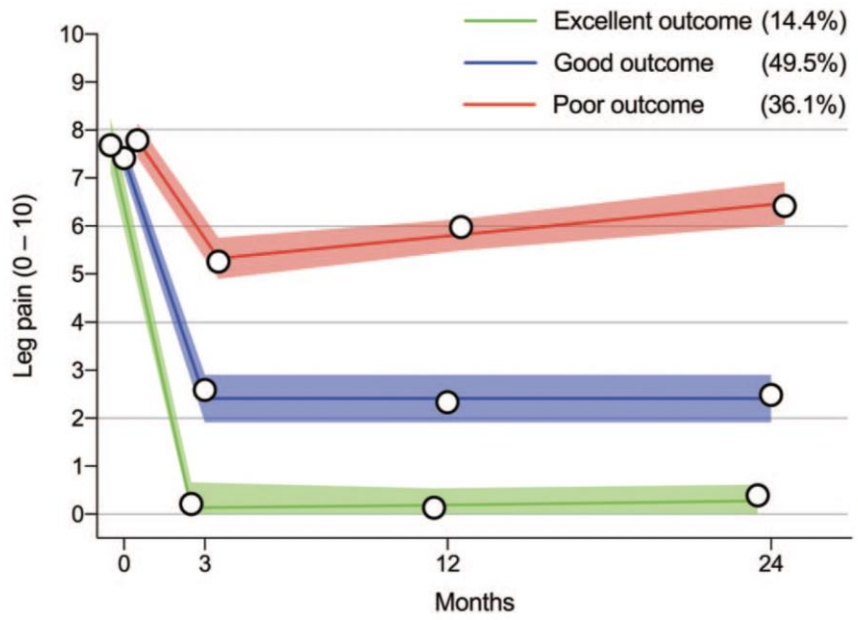


Figure 2. Clinical outcome trajectory groups for leg pain with prevalence estimates (N = 529). Point estimates are average outcome scores (0–10 numeric pain rating scale). Shaded areas represent 95% confidence intervals.

529 patients

36,1% douleur de jambe
27,9 % outcome péjoratif

Spine

SPINE Volume 45, Number 21, pp E1421–E1430

EPIDEMIOLOGY

OPEN

Preoperative Factors Predict Postoperative Trajectories of Pain and Disability Following Surgery for Degenerative Lumbar Spinal Stenosis

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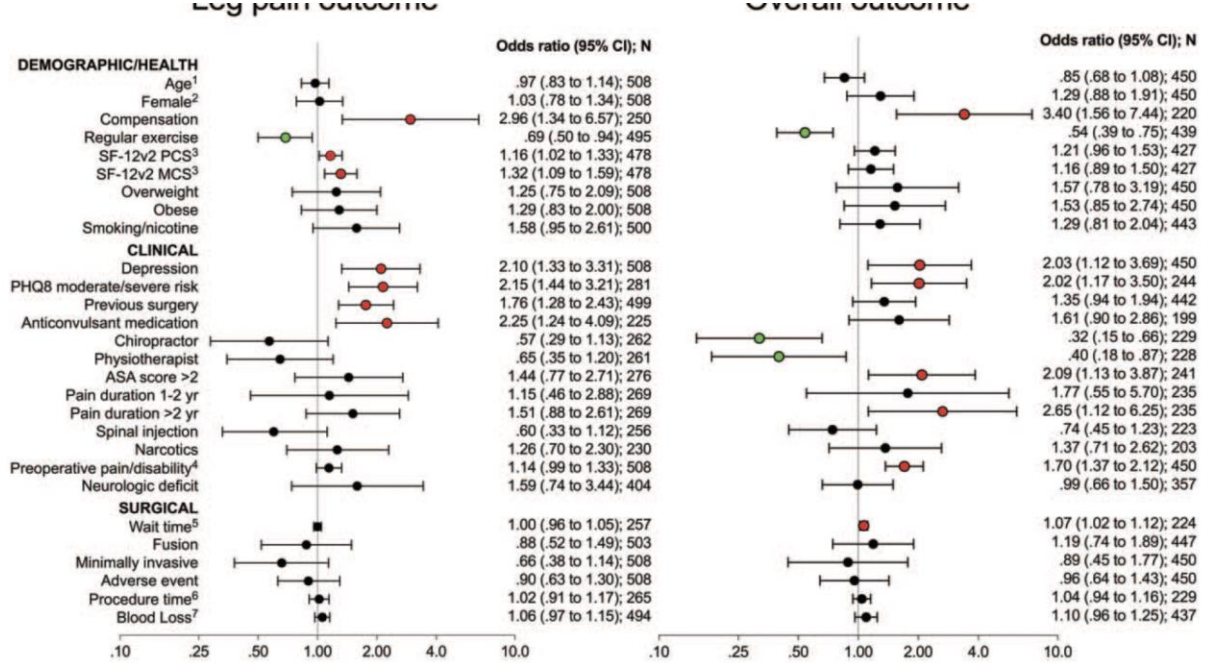


Coordinated Surgical Immune Signatures Contain Correlates of Clinical Recovery

Sci Transl Med. 2014

Brice Gaudilliere[1,2,*], **Gabriela K Fragiadakis**[2,3,*], **Robert V Bruggner**[2,4], **Monica Nicolau**[1], **Rachel Finck**[2,3], **Martha Tingle**[1], **Julian Silva**[1], **Edward A Ganio**[1], **Christine G Yeh**[1], **William J Maloney**[6], **James I Huddleston**[6], **Stuart B Goodman**[6], **Mark M Davis**[3], **Sean C Bendall**[2,3], **Wendy J Fantl**[2,3], **Martin S Angst**[1,†], and **Garry P Nolan**[2,†]

[1]Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, USA

- Traumatic injury initiates an intricate programmed immune response : **Hours after severe trauma, neutrophils and monocytes are rapidly activated and recruited to the periphery by damage response antigens, alarmins (for example, HMGB1), and increased levels of tumor necrosis factor–a (TNF-a), interleukin-1b (IL-1b), and IL-6** .
- This is followed by a **compensatory phase characterized** by decreased numbers of T cell subsets.
- Traumatic injury organized more than 80% of the leukocyte transcriptome according to cell type specific signaling pathways.

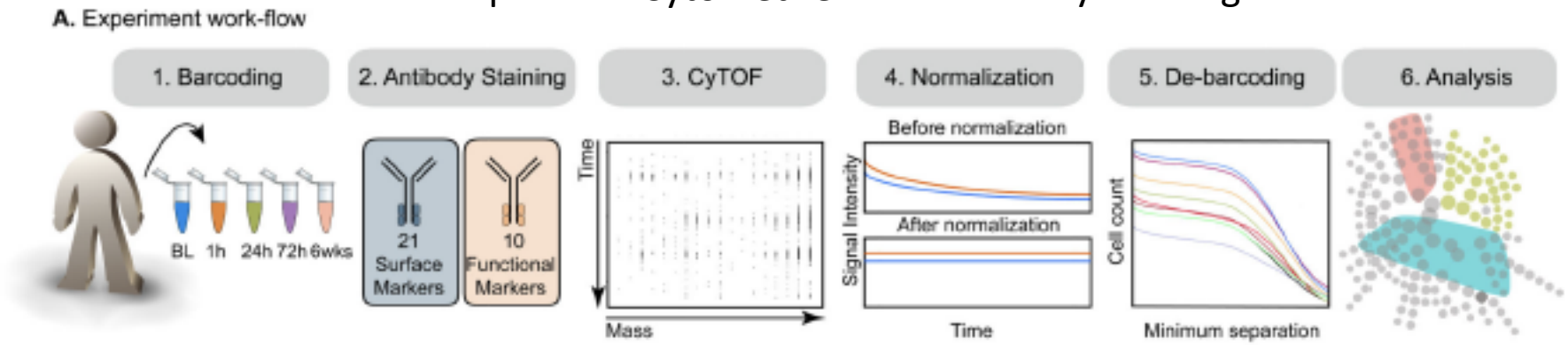
6 patients pour PTH

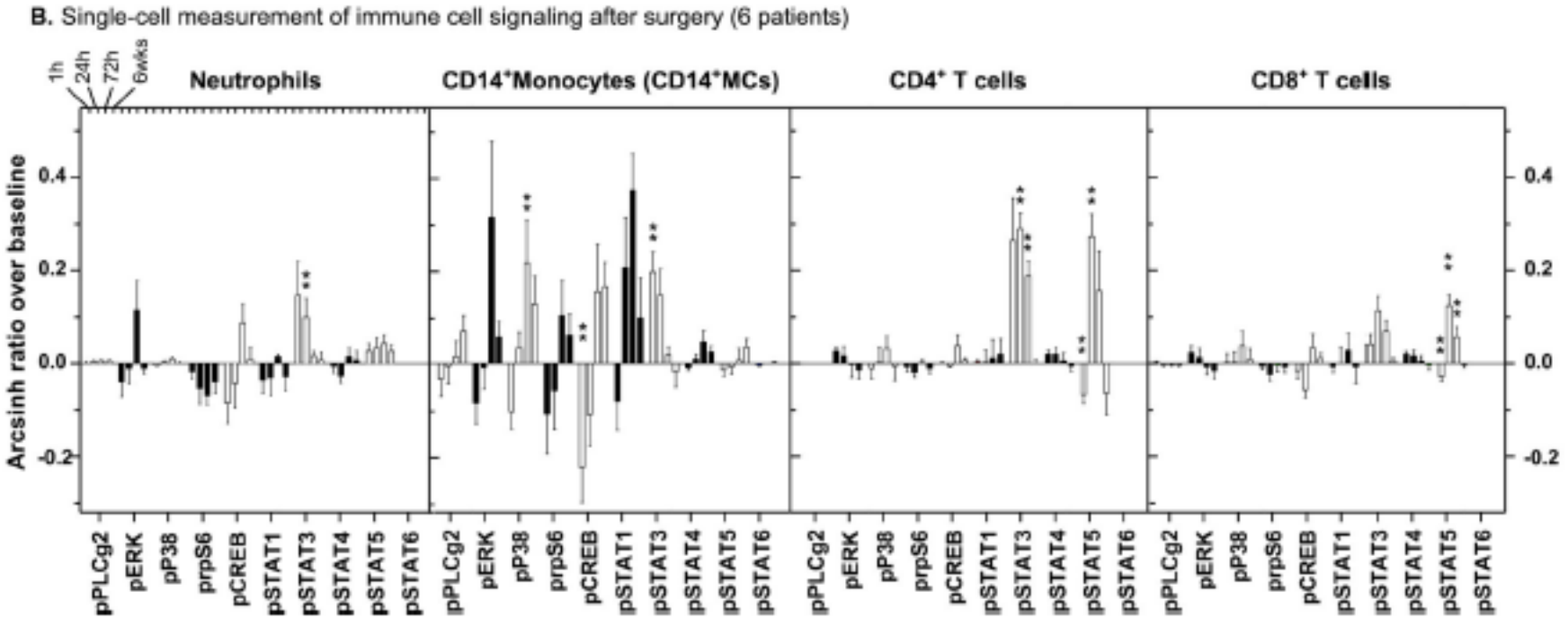
Prélèvements
à BL,1H, 24H, 72H et 6j
Après la chirurgie

10 marqueurs
dans 4 types cellulaires
(Neutrophiles, CD14 MCS,
CD4⁺ T et CD8⁺ T)

5 PhosphoProt changent
pSTAT1, pSTAT3, pSTAT5,
P38, pCREB

Isotope Cytométrie Analyse du signal





Sci Transl Med. 2014

Frequencies of neutrophiles, CD14+ monocytes (CD14+ MCs), and CD4+ and CD8+ T cells
Surgery induced a 1.2-fold (±0.06, q < 0.01) expansion of neutrophils 1 hour after surgery,
a 1.9-fold (±0.19, q < 0.01) expansion of CD14+ MCs at 24 hours, and a contraction of CD4+ and

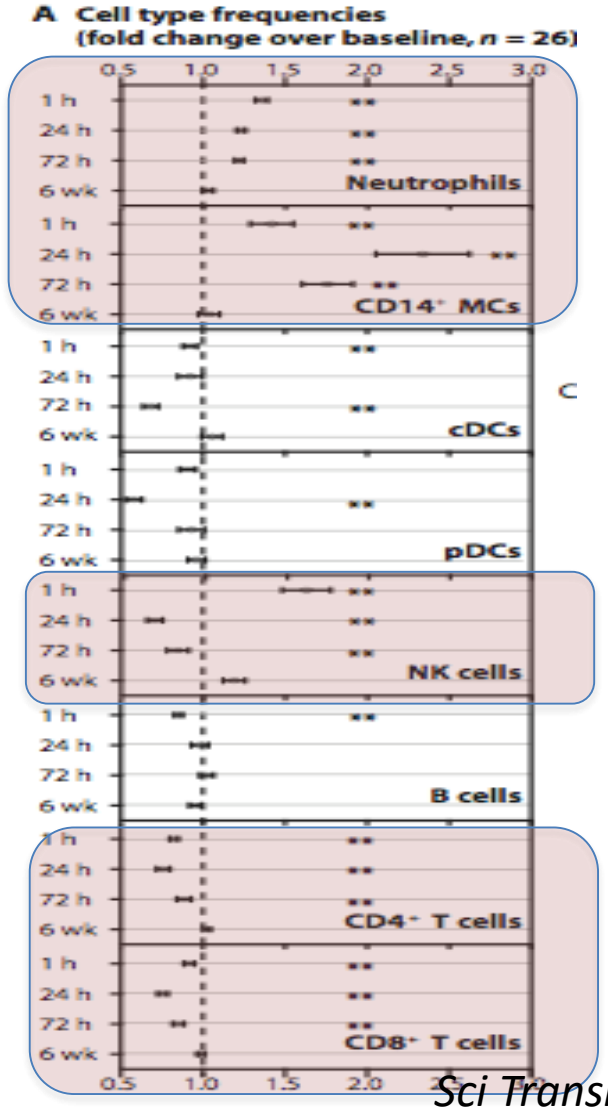
CD8+ T cells to 0.77-fold (±0.07, q < 0.01) and 0.71-fold (±0.07, q < 0.01), respectively, at 24 hours

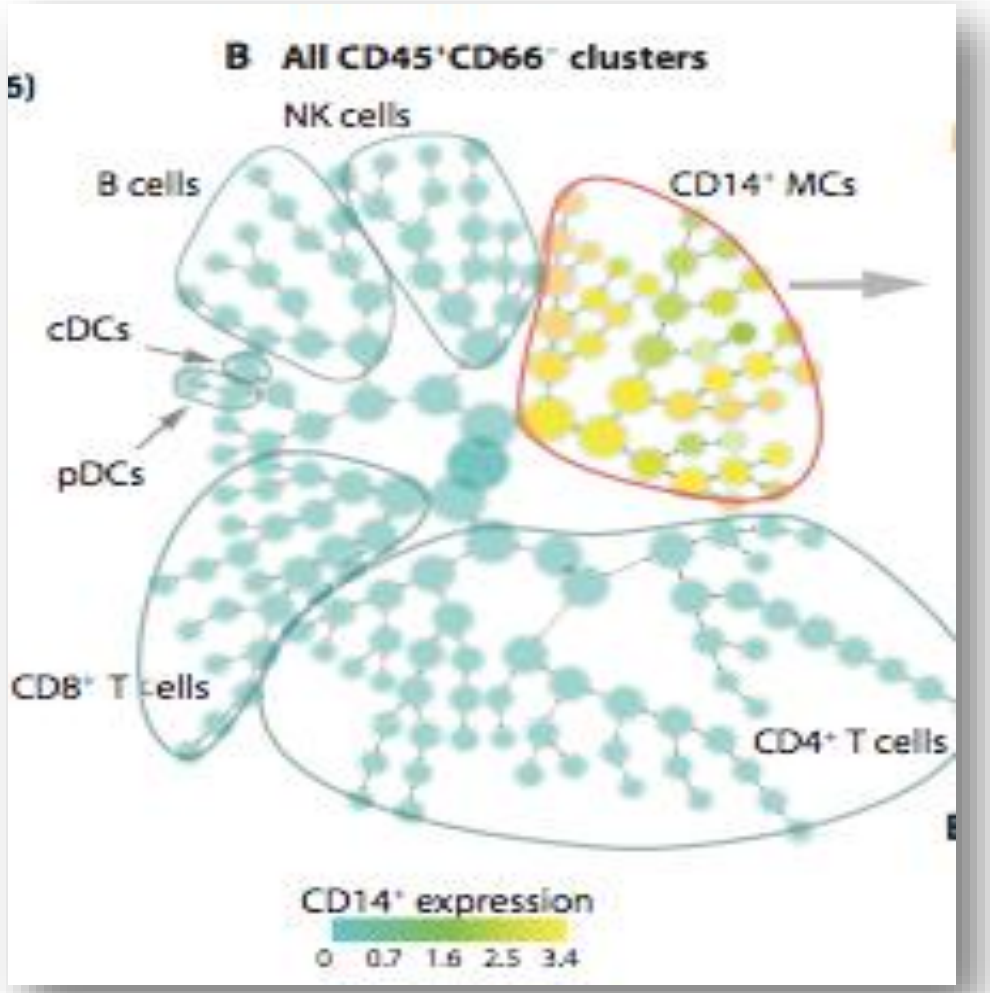
26 patients pour PTH

Prélèvements
à BL,1H, 24H, 72H et 6j
Après la chirurgie

5 types cellulaires
(Neutrophiles, CD14 MCS,
NK, CD4⁺ T et CD8⁺ T)

Hyper expression de CD14





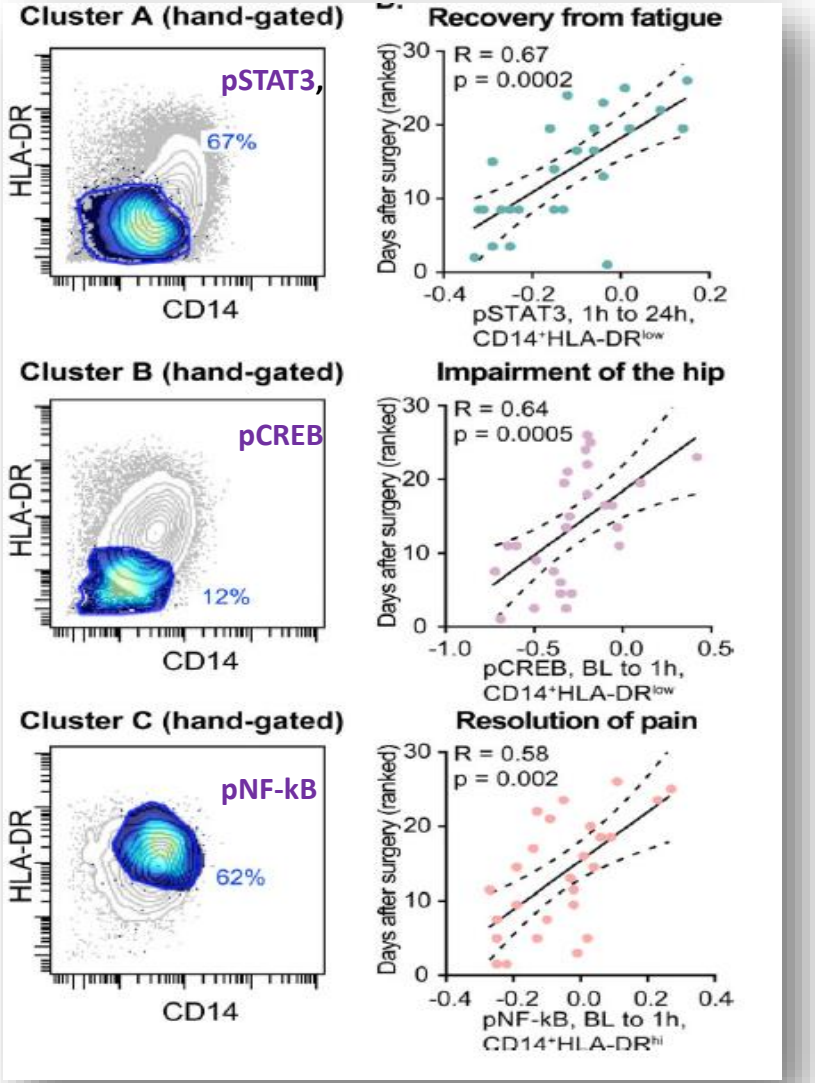
Sci Transl Med. 2014 September 24; 6(255): 255ra131.

STAT3, CREB, and NF-kB signaling in CD14+ MCs correlate with surgical recovery.

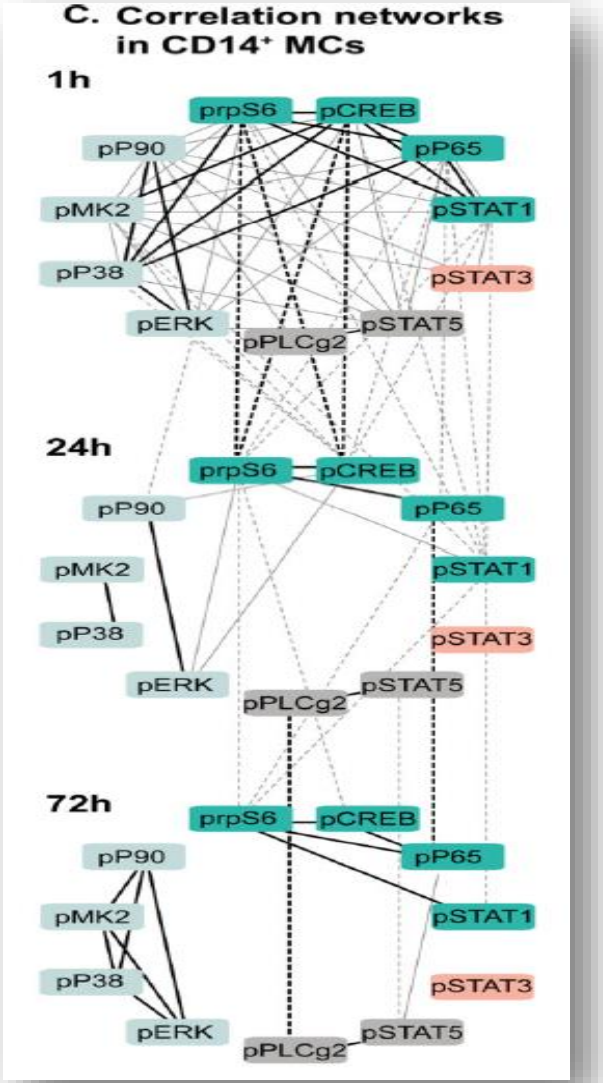
STAT3 and recovry
From fatigue

CREB and
Impairment of the Hip

NF-kB and
Resolution of pain



STAT3, CREB, and NF-κB signaling in CD14+MC subsets strongly correlate with surgical recovery



Surgery induces time-dependent and cell-type specific activation of immune signaling networks

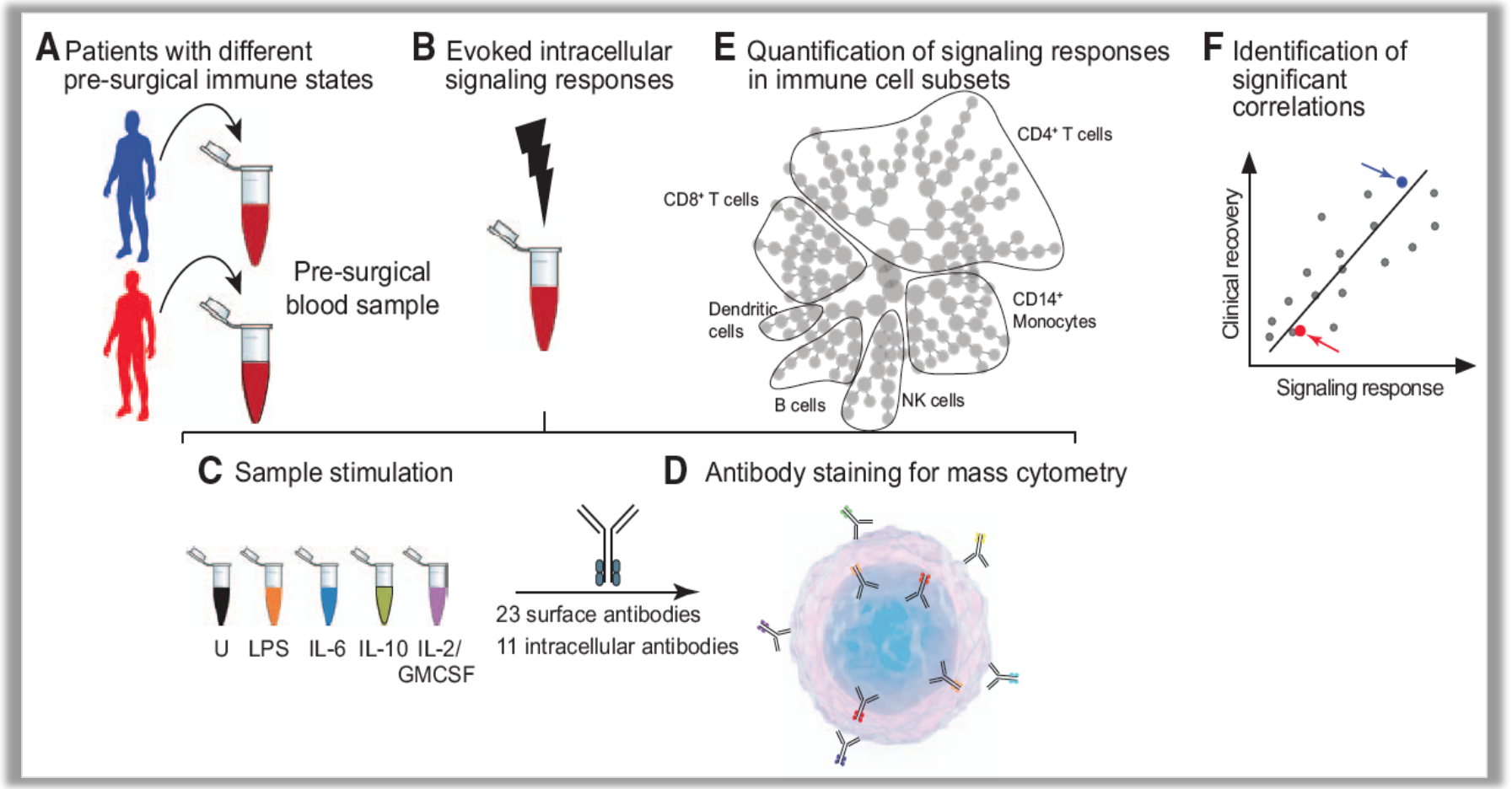
PERIOPERATIVE MEDICINE

Patient-specific Immune States before Surgery Are Strong Correlates of Surgical Recovery

Gabriela K. Fragiadakis, B.A., Brice Gaudillière, M.D., Ph.D., Edward A. Ganio, Ph.D., Nima Aghaeepour, Ph.D., Martha Tingle, R.N., Garry P. Nolan, Ph.D., Martin S. Angst, M.D.

- Importance de l'état immunitaire pré opératoire
  - Influence la réponse immunitaire à la chirurgie
  - Influence la récupération
- Modèle PTH
- Test ex vivo préopératoire
- Patients opérés de PTH et évaluation
  - Fatigue
  - Fonction
  - Douleur
- Influence de l'état préopératoire?

Anesthesiology 2015: 1241-53



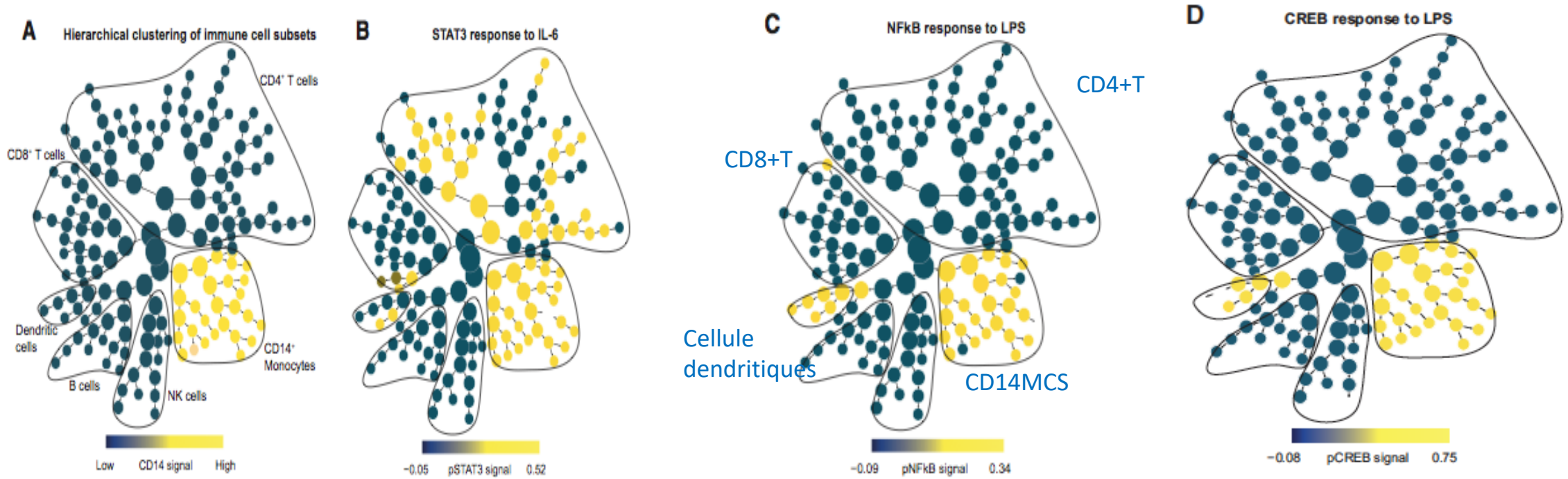
Whole blood was obtained 1h before surgery
(A). Separate whole-blood aliquots were stimulated ex vivo with extracellular ligands (B) (lipo-polysaccharide [LPS], interleukin [IL]-6, IL-10, or a combination of IL-2 and granulocyte monocyte colony-stimulating factor [GMCSF]) or left untreated (U) (C). Using mass cytometry, the expression of 23 cell surface markers and the phosphorylation states of 11 intracellular signaling proteins were measured in single cells from blood samples (D). Unsupervised hierarchical clustering and manual gating strategies were applied to visualize and quantify patient-specific signaling responses in immune cell subsets spanning the entire immune system. Shown is a visual representation of a cluster hierarchy plot (E). Signaling responses that correlated significantly with clinical recovery parameters were identified by significance analysis of microarrays (F)

Anesthesiology 2015: 1241-53

Fatigue

Douleur

Fonction

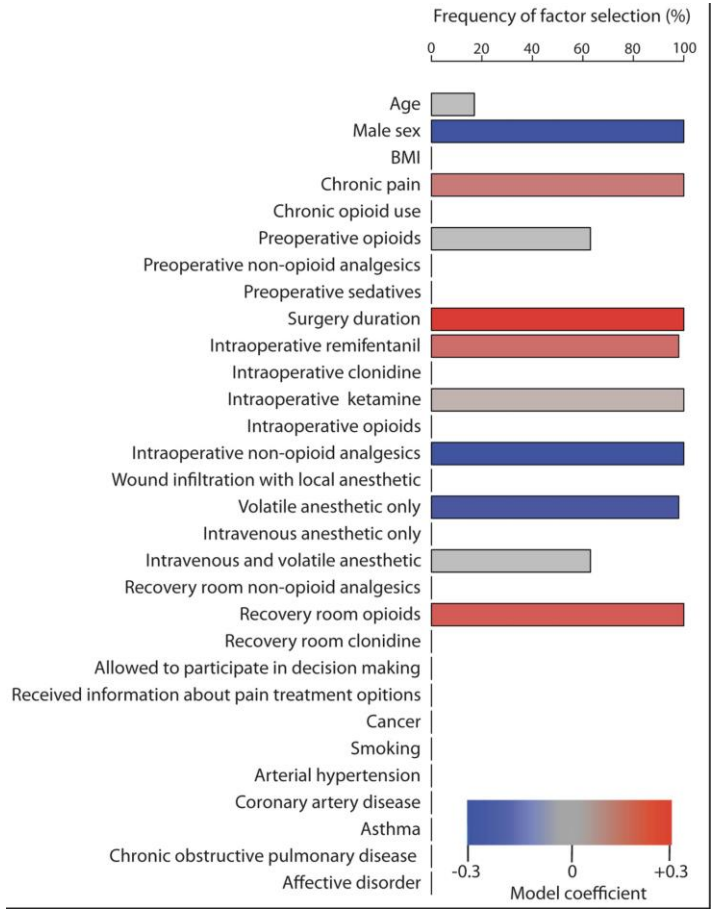


Evoked signaling responses in presurgical whole-blood samples

Anesthesiology 2015: 1241-53

Revenons aux sources de cette chaine…

Predicting Acute Pain After Surgery *A Multivariate Analysis*



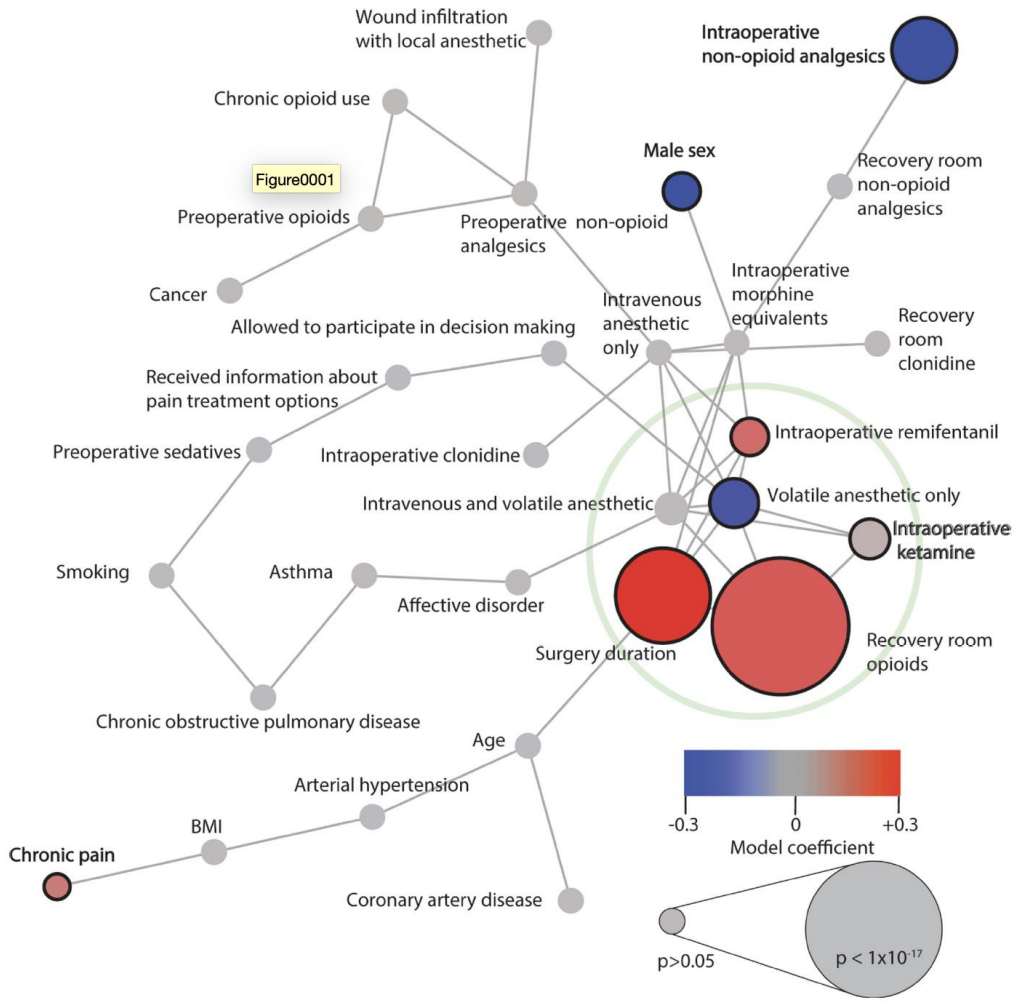


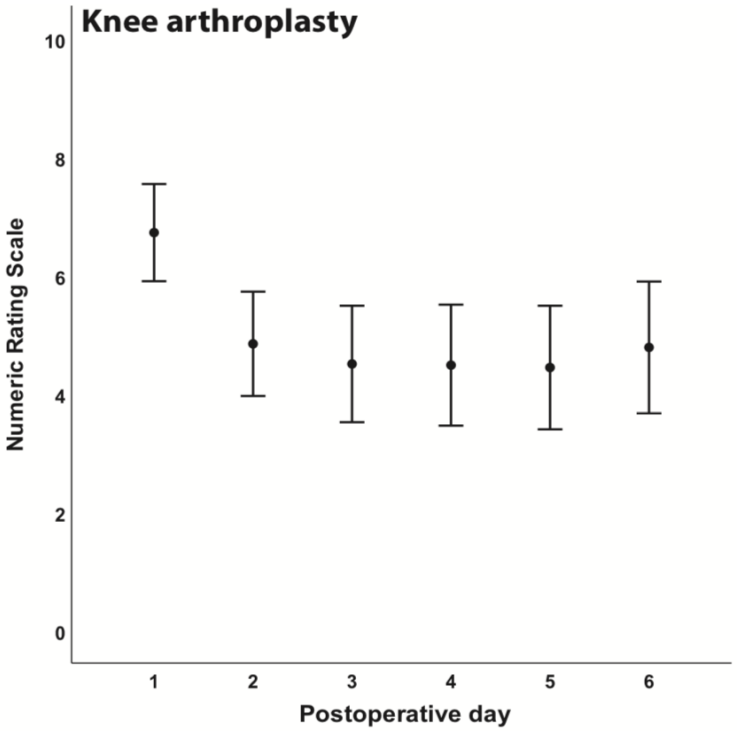
FIGURE 1.
Elastic net model. All clinical and pharmacological parameters collected by the PAIN OUT

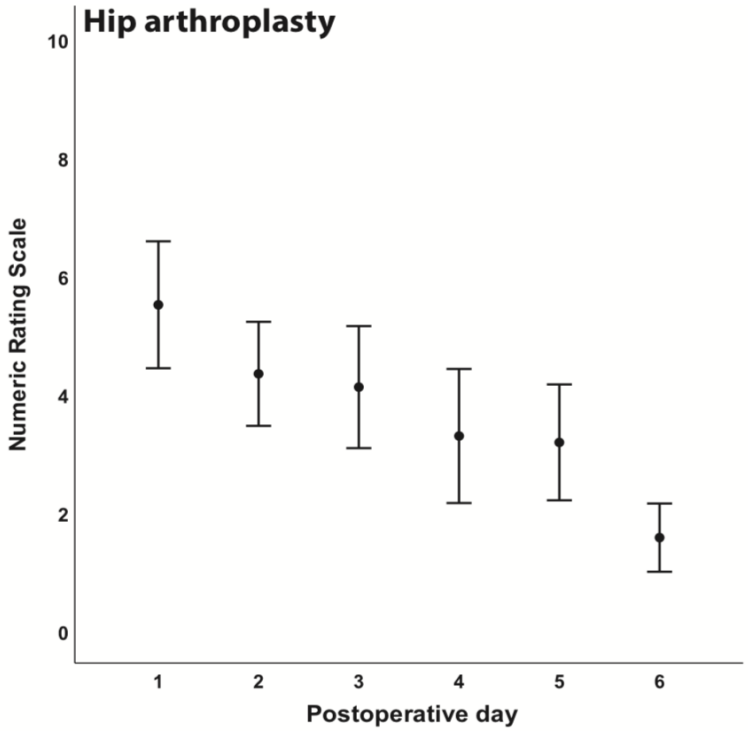
Ann Surg. 2021 February 01; 273(2): 289–298

Using postoperative pain trajectories to define the role of regional analgesia in personalised pain medicine

Anaesthesia 2020

E. R. Mariano,[1,2] **K. El-Boghdadly**[3,4] and **B. M. Ilfeld**[5,6]





pain. Although we cannot extrapolate these data to every surgical population, we can conclude than any single-injection regional analgesic for total knee arthroplasty in all likelihood does not last long enough. As expectations grow

Avantages: titration, Limites: durée

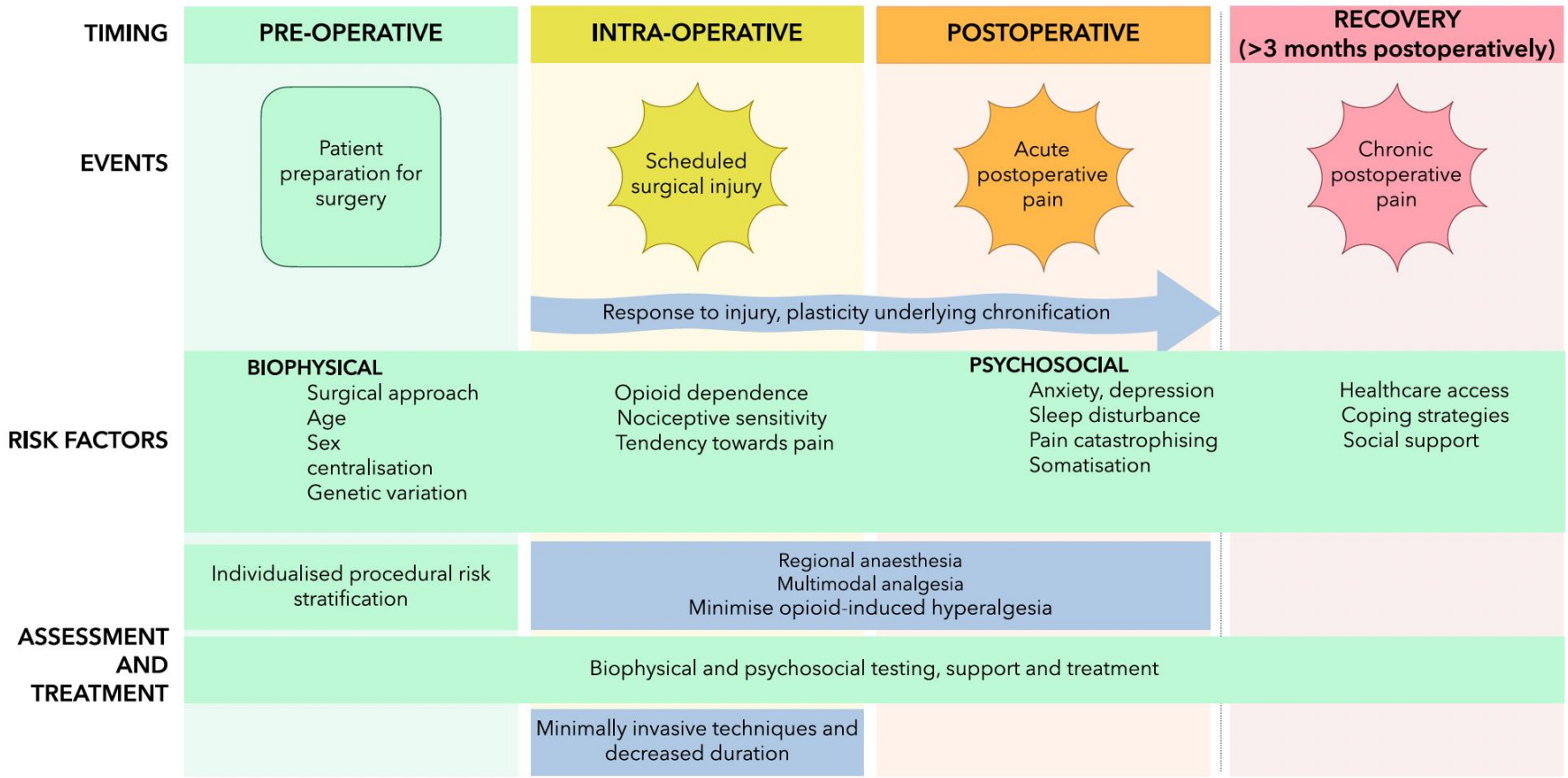
Continuous peripheral nerve block is the only technique currently available that enables titration of local anaesthetic solutions to a peripheral nerve or fascial plane [29]. Using an electronic infusion pump with an external reservoir, the infusion duration is typically limited by the amount of local anaesthetic a patient is able to carry, and single-use elastomeric pumps with an internal reservoir for local anaesthetic rarely last beyond 3 days without replacement [29], which may not be long enough for certain surgical procedures like knee arthroplasty. Based on one systematic review and meta-analysis, patients who receive continuous peripheral nerve block: report lower maximal pain scores during infusion; experience less nausea; have decreased opioid dose requirements; sleep better; and are more satisfied with pain management for the first 2 days after surgery, when compared with single-injection blocks [30].

Anaesthesia 2021, 76 (Suppl. 1), 8–17 doi:10.1111/anae.15256

Review Article

The role of regional anaesthesia and multimodal analgesia in the prevention of chronic postoperative pain: a narrative review

Y.-Y. K. Chen,[1] **K. A. Boden**[2] and **K. L. Schreiber**[3]



Personalised perioperative care by e-health after intermediate-grade abdominal surgery: a multicentre, single-blind, randomised, placebo-controlled trial

Eva van der Meij, Johannes R Anema, Wouter K G Leclercq, Marlies Y Bongers, Esther C J Consten, Steven E Schraffordt Koops, Peter M van de Ven, Caroline B Terwee, Johanna M van Dongen, Frederieke G Schaafsma, Wilhelmus J H J Meijerink, Hendrik J Bonjer, Judith A F Huirne

PATIENTS ADULTES

CHIRURGIE ABDOMINALE

(Hernie Inguinale, cholecystectomie..)

Suivi 6 mois

Retour à l'activité initiale

Douleur postopératoire

2 GROUPES:

Contrôle: Site web placebo, instructions générales)
26 days (95%CI 20–32)

E-Santé personnalisé: Site web personnalisé, interaction
21 days (95% CI 17–25)

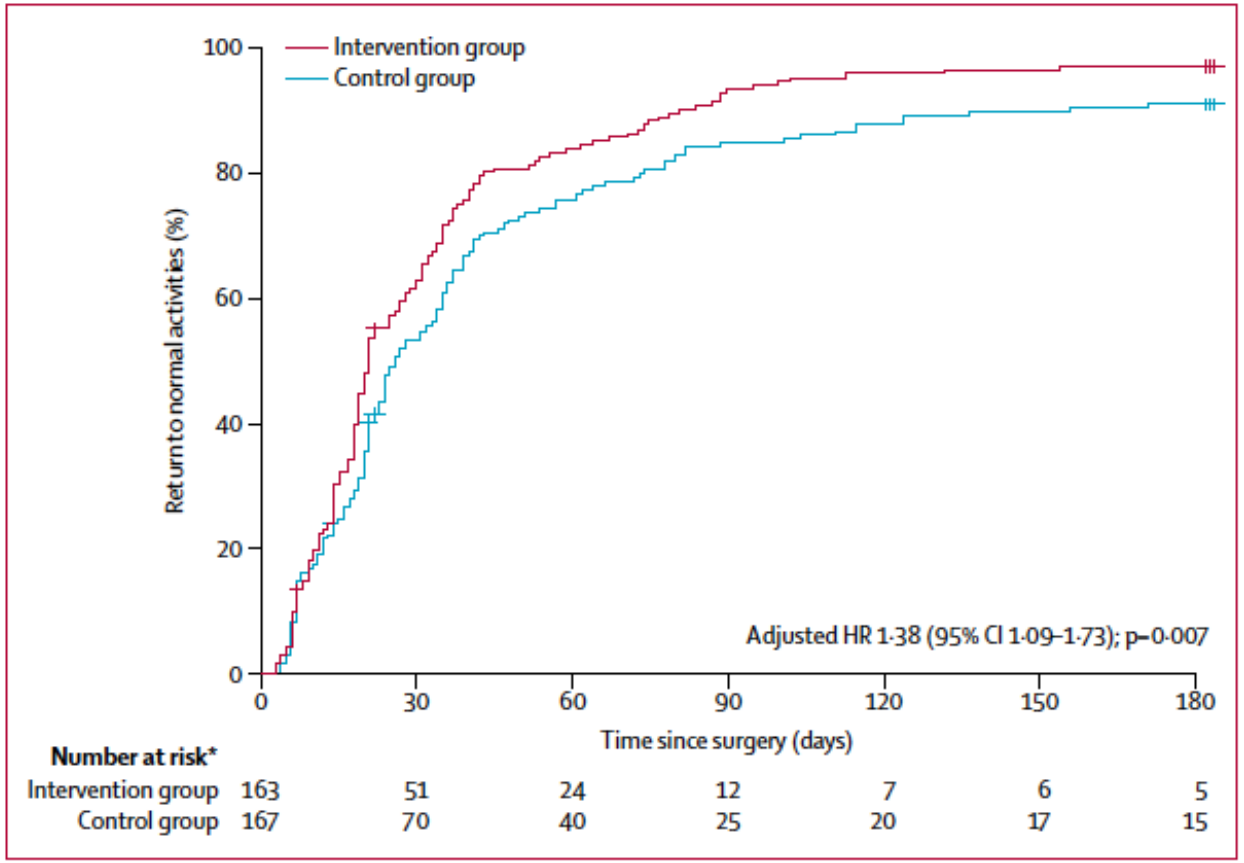
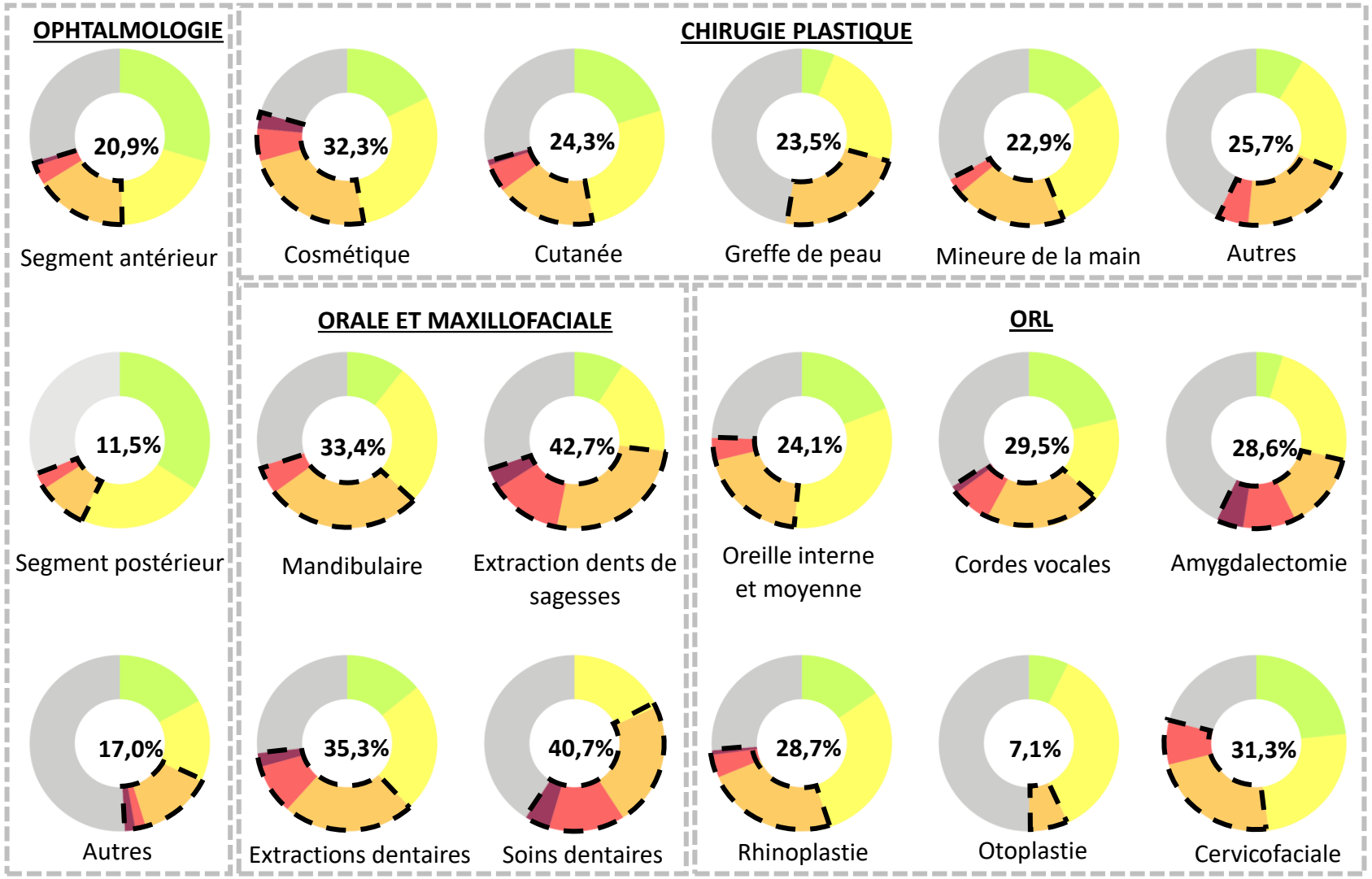


Figure 3: **Time to return to normal activities after surgery**
HR=hazard ratio. *Number at risk is the number of participants allocated to the group, minus the number who dropped out, minus the number who already reached the outcome event (return to normal activities).

Lancet. 2018 Jul 7;392(10141):51-59

Télé Santé: Web App Satelia
La réponse des 1691 patients est parfois surprenante



Douleurs à J7

- Pas de douleur
- Douleur faible
- Douleur modérée
- Douleur sévère
- Douleur très sévère
- Données manquantes

Douleurs modérées à très sévères : 29,1%

Carlier ACCPM 2021

#AnesthDoncRea mais surtout MPO en mode 2.0

- Personnaliser la PEC de la DPO:
  - Facteur d'influence très complexes et nombreux
- Patient acteur de son parcours
- Evaluer la douleur à J7-J10
- S'évaluer pour s'améliorer
- Intérêt de la Télémédecine et de la e-Santé à évaluer plus largement