Pr Lynda ABED
Maitre de conférences « A »
Anesthésie réanimation
CHU Douera

Douleur transitionnelle :
De la douleur aigue à la douleur chronique il n'y a qu'un pas

Conflit d’intérêt

La petite histoire…

1846
Ether

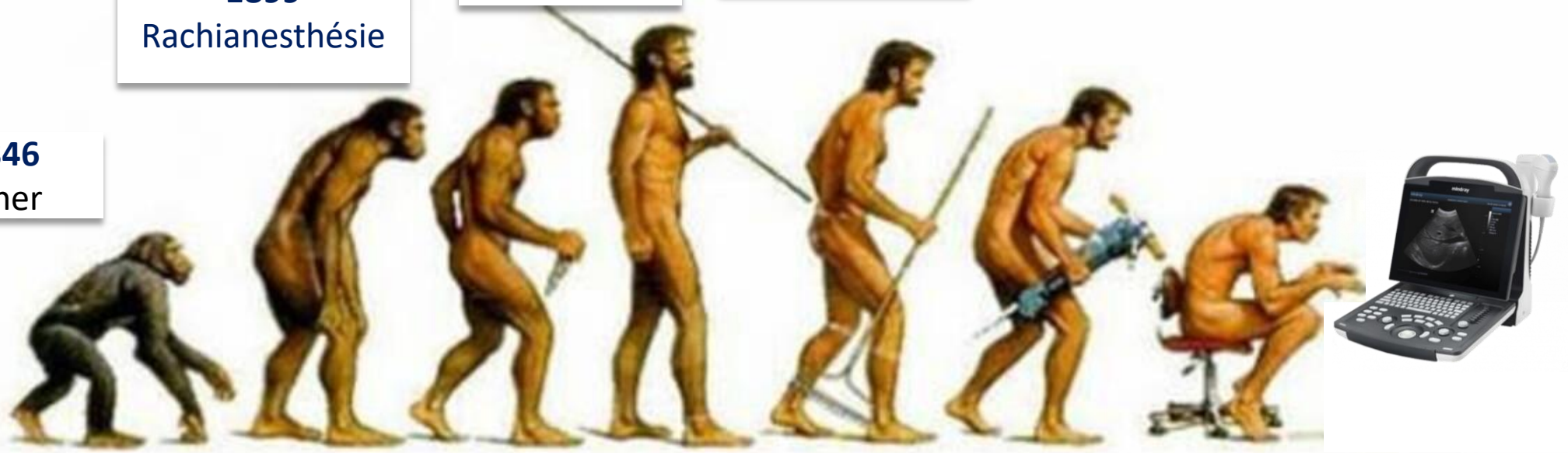
1899
Rachianesthésie

1901
Péridurale

1911
ALR plexus brachial

1962
Neurostim

1990
Echographie



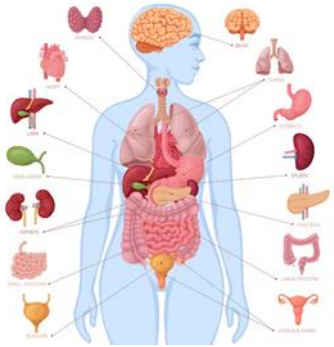
DOULEUR AIGUE → **DOULEUR CHRONIQUE**

- 80% douleur aigue post-opératoires
- Traumatisme tissulaire= inflammatoire
- Prévisible en chirurgie réglée
- Intensité variable
- Retentissement (cardio-vx, resp, réhabilitation,…)
- Facteurs de risque
- < 50% : analgésie adéquate
- Prise en charge multimodale

- **Prévalence 10,1% - 55,2%**
- **Douleur chronique sévère 11%**
- **Complexe et subjective**
- **Syndrome multidimentionnel**
- **Maladie à part entière**
- **Problème de santé publique**
- **Prise en charge difficile**
- **Retentissement économique**

Douleur chronique

Troubles sommeil



Répercussions locales et générales

Coût

635* billion $

Dépression

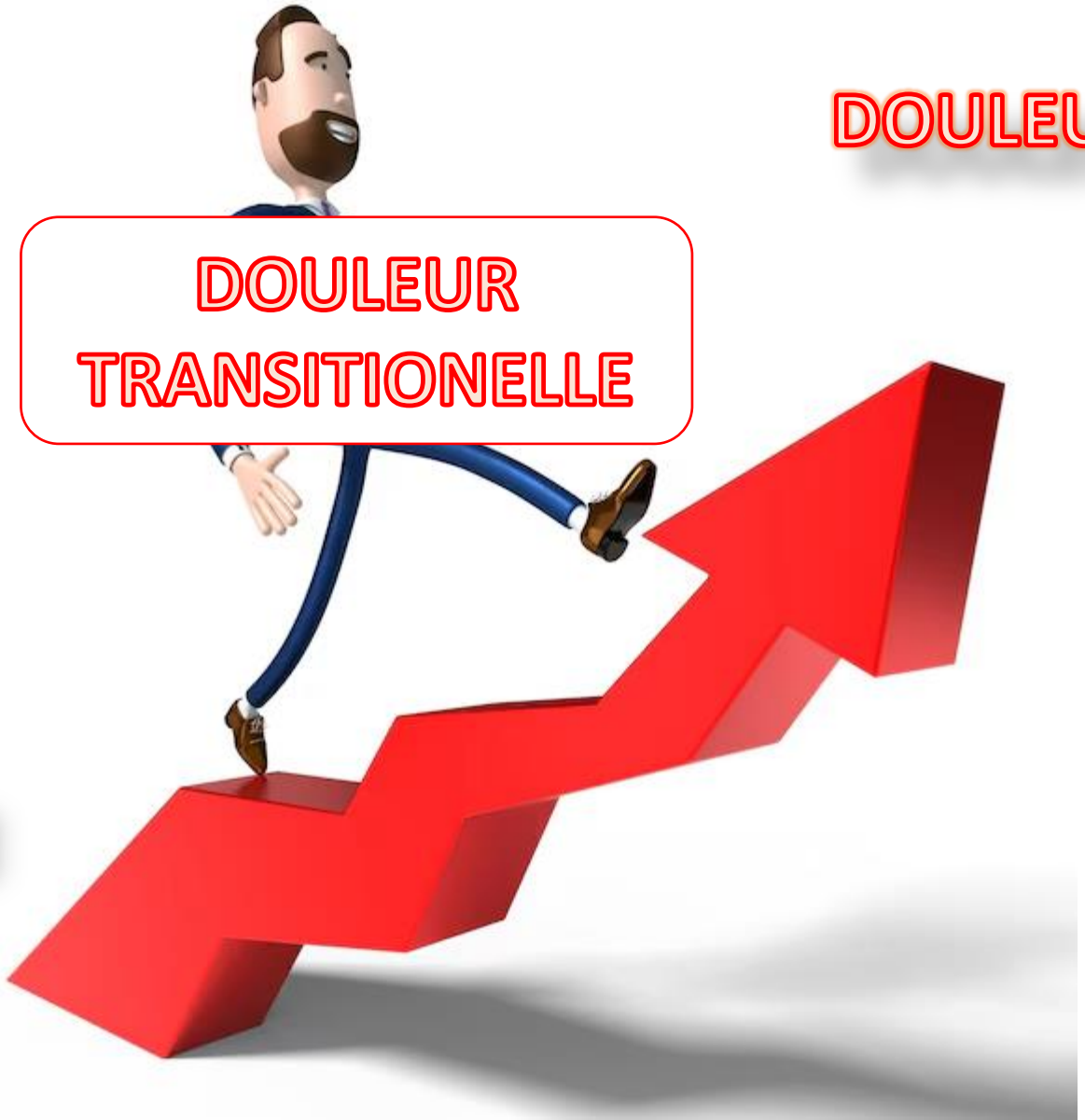
Problème de santé publique

https://www.sciencedaily.com/releases/2012/09/120911091100.htm

La douleur chronique: prévisible?

DOULEUR CHRONIQUE

DOULEUR TRANSITIONELLE

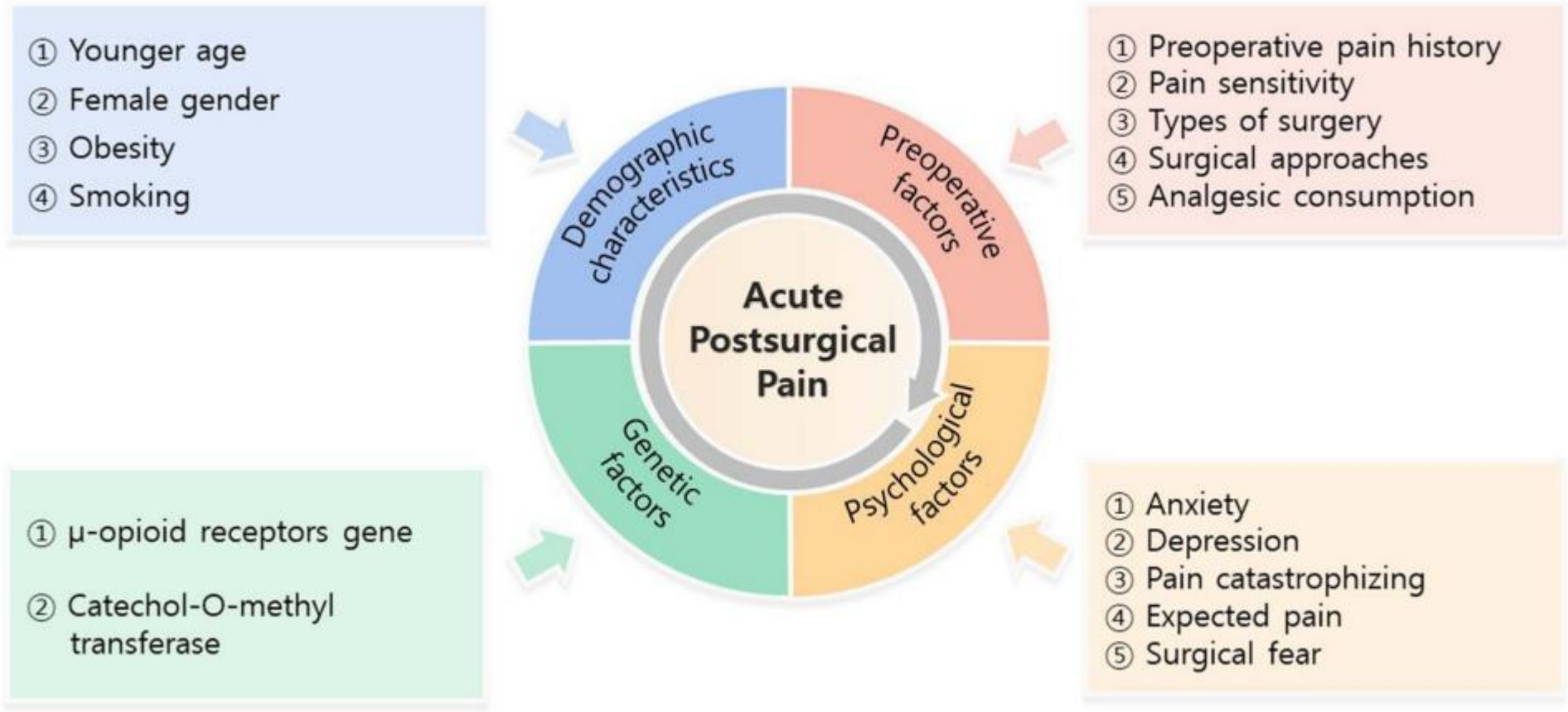


DOULEUR AIGUE

- **PPSP**
- **Douleur persistante après chirurgie**
- **30-50%**
- **2-10% sévère**
- **Retentissement sur l'activité quotidienne, qualité de vie**
- **Problème de santé public**
- **Cause majeure de douleur chronique**
- **Facteurs de risque**

Kalso E. Br J Anaesth 2013

Facteurs de risque de douleur post-opératoire



Journal of Pain Research 2024:17 1793–1804

Transition from acute to chronic pain after surgery

Paul Glare, Karin R Aubrey, Paul S Myles

Lancet 2019; 393: 1537–46

	Any intensity (%)	Moderate-severe intensity (%)	Prevalence (%); prevalence if restricted to a severe pain rating	Number of operations in US non-federal community hospitals* in 2014[7]
Amputation of limb	30–85%	5–10%	Up to 85%[8]	Not available
Arthroplasty, knee	13–44%	15%	44% (15%)[9]	723 086
Caesarean section	6–55%	5–10%	Up to 12%[10]	1 142 680
Cholecystectomy	3–50%[11]	Not reported	Not reported	300 245
Craniotomy	0–65%[12]	25%	12–16%[13]	Not available
Hip replacement	27%	6%	27% (15%)[9]	487 625
Inguinal hernia repair	5–63%	2–4%	6–29%[14]	Not available
Laminectomy and spinal fusion	10–40%	4–6[15]	5–36%[16,17]	564 911
Mastectomy	11–57%	5–10%	22%[18]	Not available
Coronary artery bypass graft	30–50%	5–10%	28% (4%)[19]	160 240
Thoracotomy	5–65%	10%	48%[20,21]	Not available

*Non-federal community hospitals account for 786 874 (87%) of 902 202 hospital beds in the USA.

Table 1: **Prevalence of chronic postsurgical pain in common surgeries in the USA[11,22–24]**

Sévérité et durée de la douleur post-opératoire

- 3 facteurs contributifs:

Patient

- Douleur préexistante
- Consommation chroniques d'opiodes
- Caractéristiques (Age,sexe,…)

Chirurgie

- Lésions cutanées
- Inflammation
- Lésions nerveuses

Sens. SNC

- Glutamate
- Substance P
- Gène de calcitonine

Eisenach and Brennan. Pain. 2018 June

Development and validation of a multivariable prediction model for early prediction of chronic postsurgical pain in adults: a prospective cohort study

BJA

Marjelle E. C. van Driel[1], Jacqueline F. M. van Dijk[1], Sara J. Baart[2], Winfried Meissner[3],

N= 150

Table 2 Final prediction models for chronic postsurgical pain. Results are presented as β coefficients and odds ratios (95% CI). CI, confidence interval; CPSP, chronic postsurgical pain; OR, odds ratio; POD, postoperative day; NRS, numerical rating scale.

Predictor	Model POD1			Model POD14		
	β coefficient	OR (95% CI)	P-value	β coefficient	OR (95% CI)	P-value
(Intercept)	−2.540	0.08 (0.04–0.17)	0.000	−2.540	0.08 (0.04–0.17)	0.000
Surgery type, bone surgery	0.785	2.19 (1.29–3.74)	0.004	0.696	2.01 (1.10–3.67)	0.024
Preoperative treatment with opioid	1.023	2.78 (1.60–4.85)	0.000	1.397	4.04 (2.13–7.70)	0.000
Worst pain score (NRS) on POD1	0.123	1.13 (1.02–1.25)	0.015	–	–	–
Presence of pruritus within the painful area on POD1	0.732	2.08 (1.08–4.02)	0.030	–	–	–
Pain score (NRS) on POD14	–	–	–	0.449	1.57 (1.34–1.83)	0.000
Presence of painful cold within the painful area on POD14	–	–	–	1.578	4.85 (1.85–12.68)	0.002

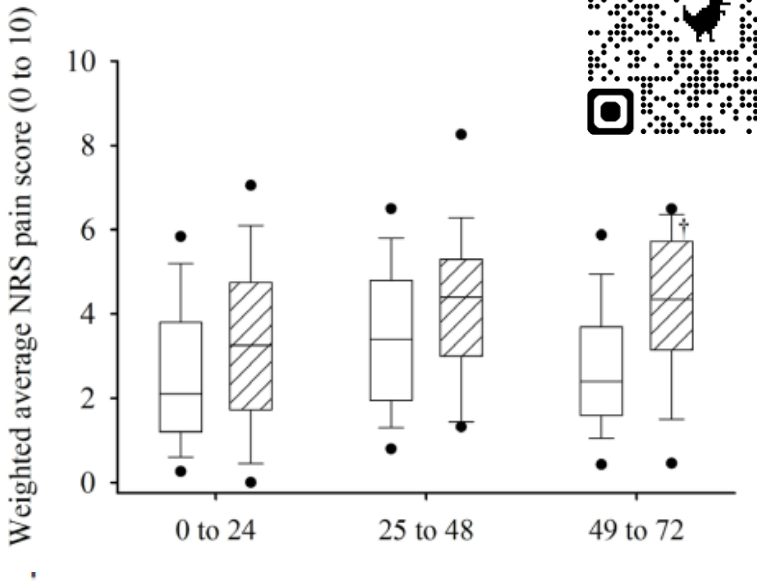
British Journal of Anaesthesia, 2022

Insuffisance d'analgésie post-opératoire

Original article

Acute postoperative pain is an independent predictor of chronic postsurgical pain following total knee arthroplasty at 6 months: a prospective cohort study

Results 245 cases were analyzed. The incidence of CPSP was 14% (95% CI 10% to 19%). Median APSP values were 4.2 (2.2–5.0) in the CPSP group and 2.8 (1.8–3.7) without CPSP, difference 1.4 (95% CI 0.1 to 1.8, p=0.005). The unadjusted odds for CPSP with an increase of 1 in APSP was 1.46 (95% CI 1.14 to 1.87, p=0.002)). After multivariable risk adjustment, the OR for CPSP for an increase of 1 in the APSP was 1.53 (95% CI 1.12 to 2.09, p=0.008).



Conclusions APSP is a risk factor for CPSP following TKA even after adjusting for confounding variables such as pain catastrophizing, anxiety, depression and functional status. Studies are needed to determine if APSP is a modifiable risk factor for the development of CPSP.

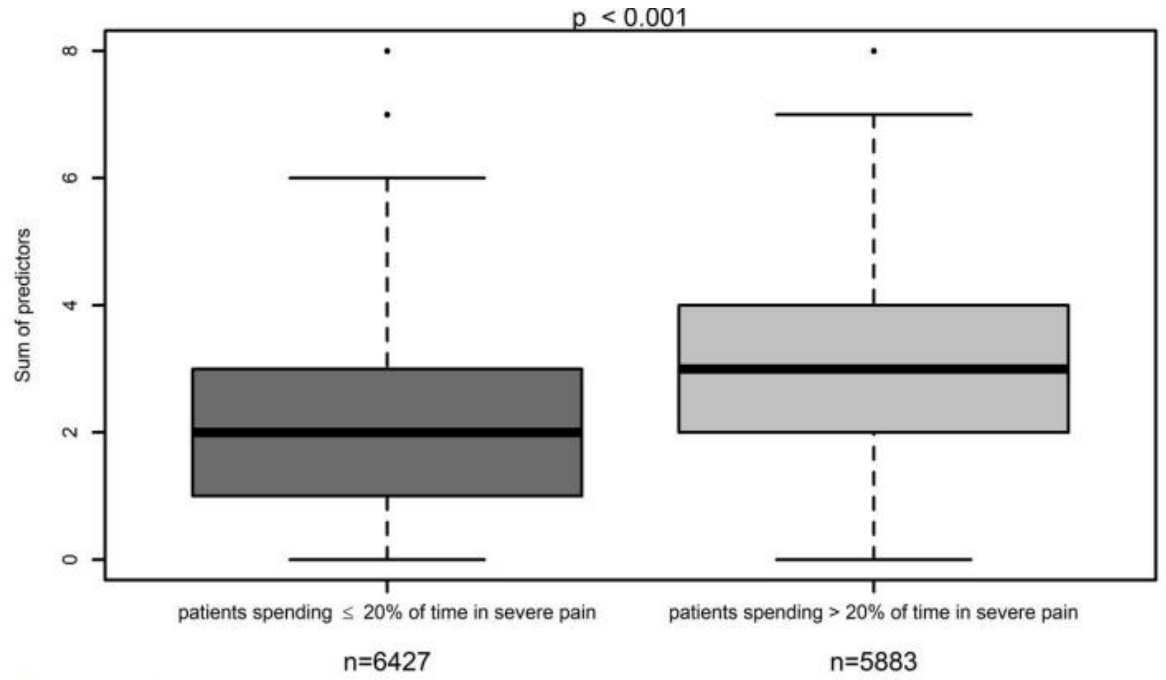
Buvanendran A, et al. Reg Anesth Pain Med 2019

Predicting poor postoperative acute pain outcome in adults: an international, multicentre database analysis of risk factors in 50,005 patients

Alexander Schnabel[a], Maryam Yahiaoui-Doktor[b], Winfried Meissner[c], Peter Konrad Zahn[d], Esther Miriam Pogatzki-Zahn[a,*]

PAIN REPORTS®

3 FDR= DPO ≥7 et +20% de temps avec DPO sévère



Comparison of the number of risk factors within the group of patients suffering from more than the 20% of time spending in severe pain in the last 24

- Younger age <54 years, (OR: 1.277)
- Preoperative chronic pain (OR: 1.195)
- Female sex (OR: 1.433)
- Duration of surgery >90 minutes (OR: 1.308)
- Preoperative opioid intake (OR: 1.250)
- Anxiety (OR: 1.239)
- Depression (OR: 1.198)

L'intensité de la DPO aigue, la composante neuropathique, le temps passé avec une DPO intense sont des FDR de DCPO

ORIGINAL ARTICLE

Development of a risk index for the prediction of chronic post-surgical pain

EJP
European Journal of Pain

A. Althaus[1], A. Hinrichs-Rocker[1], R. Chapman[2], O. Arránz Becker[3], R. Lefering[1], C. Simanski[4], F. Weber[5], K.-H. Moser[6], R. Joppich[7], S. Trojan[7], N. Gutzeit[1], E. Neugebauer[1]

Table 2 Items of the initial risk index version.

	P	Odds ratio
Please ask the patient before surgery: no/yes		
1. Have you suffered from preoperative pain in the part of the body operated on?	<0.001	4.80
2. Have you suffered from preoperative pain elsewhere (chronic headache, back pain etc.)?	<0.003	2.80
3. Have you felt hopelessness, sadness or depression lasting longer than two weeks in the past 6 months?	<0.166	1.61
4. Considering the last 6 months, have you felt extremely nervous and/or anxious?	<0.067	1.88
5. Have you suffered from capacity overload/overstrain in the past 6 months?	<0.006	2.61
6. Do you suffer from any of the following symptoms: Sleeping disorder, exhaustibility/exhaustion, frightening thoughts, dizziness, tachycardia, feeling of being misunderstood, trembling hands, or do you take any sleeping/sedation pills. (the item is assessed positive if the patient suffers from two ore more symptoms)	<0.001	3.40
7. How do you see your convalescence? Do you think you will be fit for work again or to do your daily activities within the next 6 months? (belief that no recovery/resumption is possible after months)	<0.096	2.70
Please assess:		
8. Does the surgery imply an increased risk of nerve injury (thoracotomy, mastectomy, hernia repair, abdominal surgery, etc.)?	<0.075	0.53
9. Does the patient undergo a removal/revision surgery or a primary surgery?	<0.699	1.17
10. Will a non-laparoscopic or minimally invasive surgery be performed?	<0.005	0.34
11. Will a mesh implantation be performed?	<0.089	0.32
12. Is it inpatient (or ambulatory) surgery?	<0.033	9.49
Please assess after surgery:		
13. Did any post-operative complications occur (e.g., infection, haemorrhage, organ rupture, compartment syndrome)?	0.310	0.32
14. Did the patient suffer from considerable post-operative acute pain (NRS ≥ 5)? (average pain intensity between the 1st until the 5th day after surgery = NRS ≥ 5)	<0.001	3.22

ORIGINAL ARTICLE

Development of a risk index for the prediction of chronic post-surgical pain

A. Althaus[1], A. Hinrichs-Rocker[1], R. Chapman[2], O. Arránz Becker[3], R. Lefering[1], C. Simanski[4], F. Weber[5], K.-H. Moser[6], R. Joppich[7], S. Trojan[7], N. Gutzeit[1], E. Neugebauer[1]

EJP
European Journal of Pain

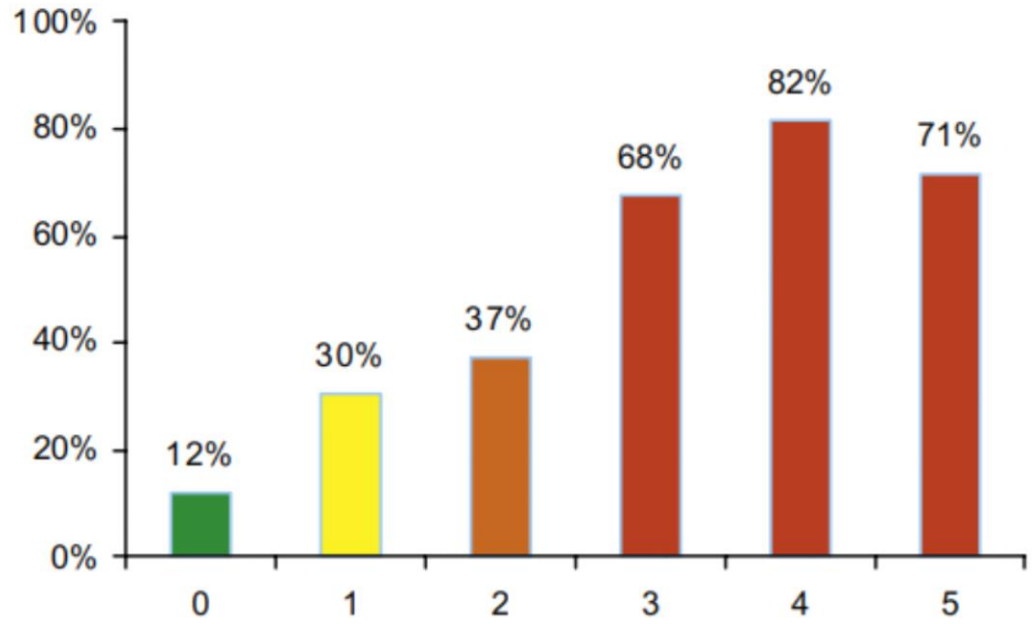
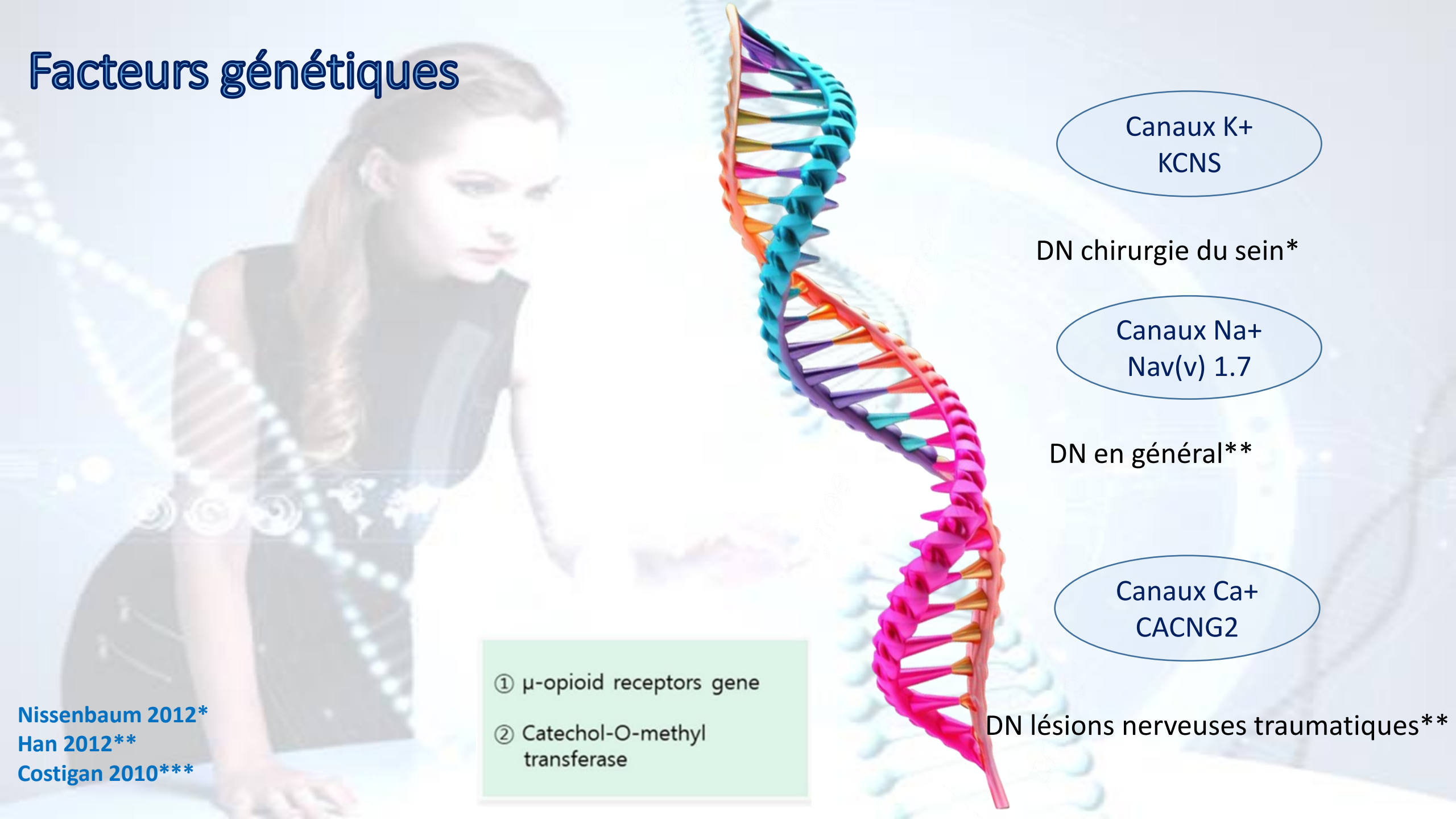


Figure 2 The proportions of patients presenting CPSP at 6 months follow-up as the empirical probability for developing CPSP depending on the particular scores of the risk index.

N= 150

Patients avec 3 à 5 FDR sont plus susceptibles de développer des CPSP que ceux avec 0 FDR (Sensibilité 74%, spécificté 65%)

Facteurs génétiques



Canaux K+
KCNS

DN chirurgie du sein*

Canaux Na+
Nav(v) 1.7

DN en général**

Canaux Ca+
CACNG2

DN lésions nerveuses traumatiques**

① μ-opioid receptors gene

② Catechol-O-methyl transferase

Nissenbaum 2012*
Han 2012**
Costigan 2010***

Facteurs génétiques

① μ-opioid receptors gene

② Catechol-O-methyl transferase

nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-017-02449-5 OPEN

Inhibition of Poly(A)-binding protein with a synthetic RNA mimic reduces pain sensitization in mice

Paulino Barragán-Iglesias[1], Tzu-Fang Lou[2], Vandita D. Bhat[2], Salim Megat[1], Michael D. Burton[1], Theodore J. Price[1] & Zachary T. Campbell[2]

Nociceptors rely on cap-dependent translation to rapidly induce protein synthesis in response to pro-inflammatory signals. Comparatively little is known regarding the role of the regulatory factors bound to the 3′ end of mRNA in nociceptor sensitization. Poly(A)-binding protein (PABP) stimulates translation initiation by bridging the Poly(A) tail to the eukaryotic initiation factor 4F complex associated with the mRNA cap. Here, we use unbiased assessment of PABP binding specificity to generate a chemically modified RNA-based competitive inhibitor of PABP. The resulting RNA mimic, which we designated as the Poly(A) SPOT-ON, is more stable than unmodified RNA and binds PABP with high affinity and selectivity in vitro. We show that injection of the Poly(A) SPOT-ON at the site of an injury can attenuate behavioral response to pain. Collectively, these results suggest that PABP is integral for nociceptive plasticity. The general strategy described here provides a broad new source of mechanism-based inhibitors for RNA-binding proteins and is applicable for in vivo studies.

A promising strategy, which could be used during surgery, is to interfere with the messenger RNA mediated cascade of pain-induced protein synthesis that occurs following injury. This is achieved by injecting a highly stable decoy RNA-binding protein into the site of injury at the time of injury. This strategy has been tested in a variety of mouse models of inflammatory sensitisation, and the decoy RNA-binding protein reduced the behavioural correlates of central sensitisation and increased the rate of recovery from sensitisation in the hours and days

Facteurs biologiques

N=60

RESEARCH ARTICLE Open Access

Cytokine and neuropeptide levels are associated with pain relief in patients with chronically painful total knee arthroplasty: a pilot study

Musculoskeletal Disorders (2017)

Jasvinder A. Singh[1,2,3,4*], Siamak Noorbaloochi[6,7] and Keith L. Knutson[5]

Marqueurs inflammatoires étudiés:

- CRP
- IL-6
- IL-12
- TNFα

2 mois après PTG:

- ↓ SP
- ↑cytokines IL-10 et IL-12

Table 2 Association of change in serum cytokine and neurotransmitter levels from baseline to 2-months with pain responder status on WOMAC pain at 2-month post-injection in painful TKA

	WOMAC Pain Responder*	N	Mean Change (FU-Baseline)	Std. Deviation	Std. Error Mean	*P*-value
Interleukin (IL)-7	No	23	0.084	0.91	0.19	**0.01**
	Yes	12	1.07	1.17	0.34	
IL-10	No	23	8.51	20.90	4.36	**0.01**
	Yes	12	27.72	21.56	6.22	
IL-12 p70	No	23	3.36	8.17	1.70	**0.004**
	Yes	12	12.91	9.60	2.77	
Eotaxin	No	23	−2.03	13.92	2.90	**0.046**
	Yes	12	7.85	12.28	3.54	
Interferon gamma (IFN-γ)	No	23	−1.24	23.18	4.83	**0.03**
	Yes	12	15.61	13.35	3.85	
Tumor necrosis factor-alpha (TNF-α)	No	23	4.46	21.32	4.44	**0.03**
	Yes	12	22.22	24.65	7.12	
IL-4	No	23	−0.02	0.16	0.03	0.12
	Yes	12	0.06	0.12	0.03	
IL-6	No	23	−15.90	275.66	57.48	0.09
	Yes	12	137.35	182.09	52.56	
IL-13	No	23	4.90	13.25	2.76	0.15
	Yes	12	12.18	14.87	4.29	
IL-15	No	23	0.31	11.87	2.47	0.09
	Yes	12	7.36	10.52	3.038	
Macrophage Inflammatory Protein-1 beta (mip1b)	No	23	5.55	91.43	19.06	0.16
	Yes	12	53.35	96.39	27.82	
Substance P	No	14	0.08	1.11	0.298	0.32
	Yes	5	−0.46	0.61	0.273	

Only those associations that either had a significant *p*-value or a *p*-value <0.33 are listed; The levels of other cytokine did not differ significantly between pain responders and pain non-responders (IL-1 beta, IL-1 alpha, IL-2, IL-5, IL-8, IL-9, IL-17, Basic FGF, G-CSF, GM-CSF, IP-10, MCP-1, MIP-1 alpha, PDGF, RANTES, and VEGF). Significant *p*-values <0.05 are in bold

Positive changes mean that at the 2-month follow-up time, the levels were higher than the baseline and a negative sign means follow-up levels were lower

WOMAC Pain Responder* is defined as reduction in WOMAC pain subscale of 20 or more 0–100 scale

Douleur chronique: prévention?

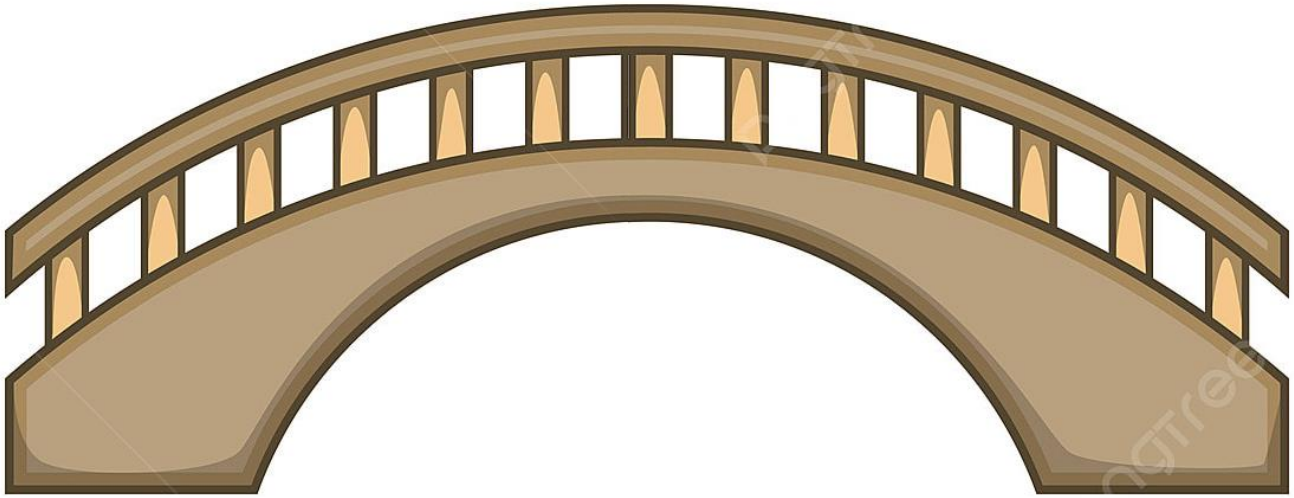
PREVENIR

VAUT MIEUX QUE

GUERIR ?

Break the bridge

TRANSITION



ACUTE PAIN

CHRONIC PAIN

Transitional pain service

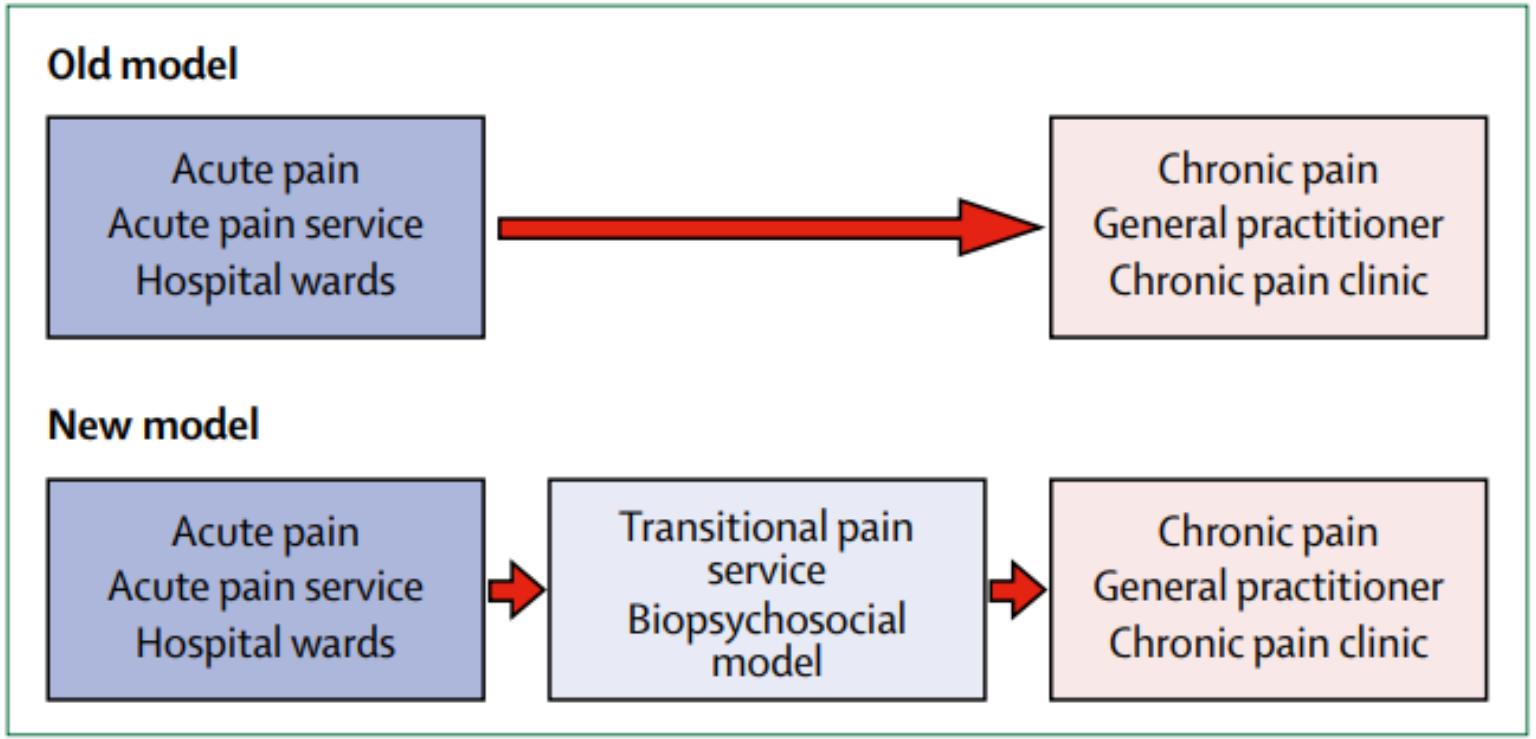
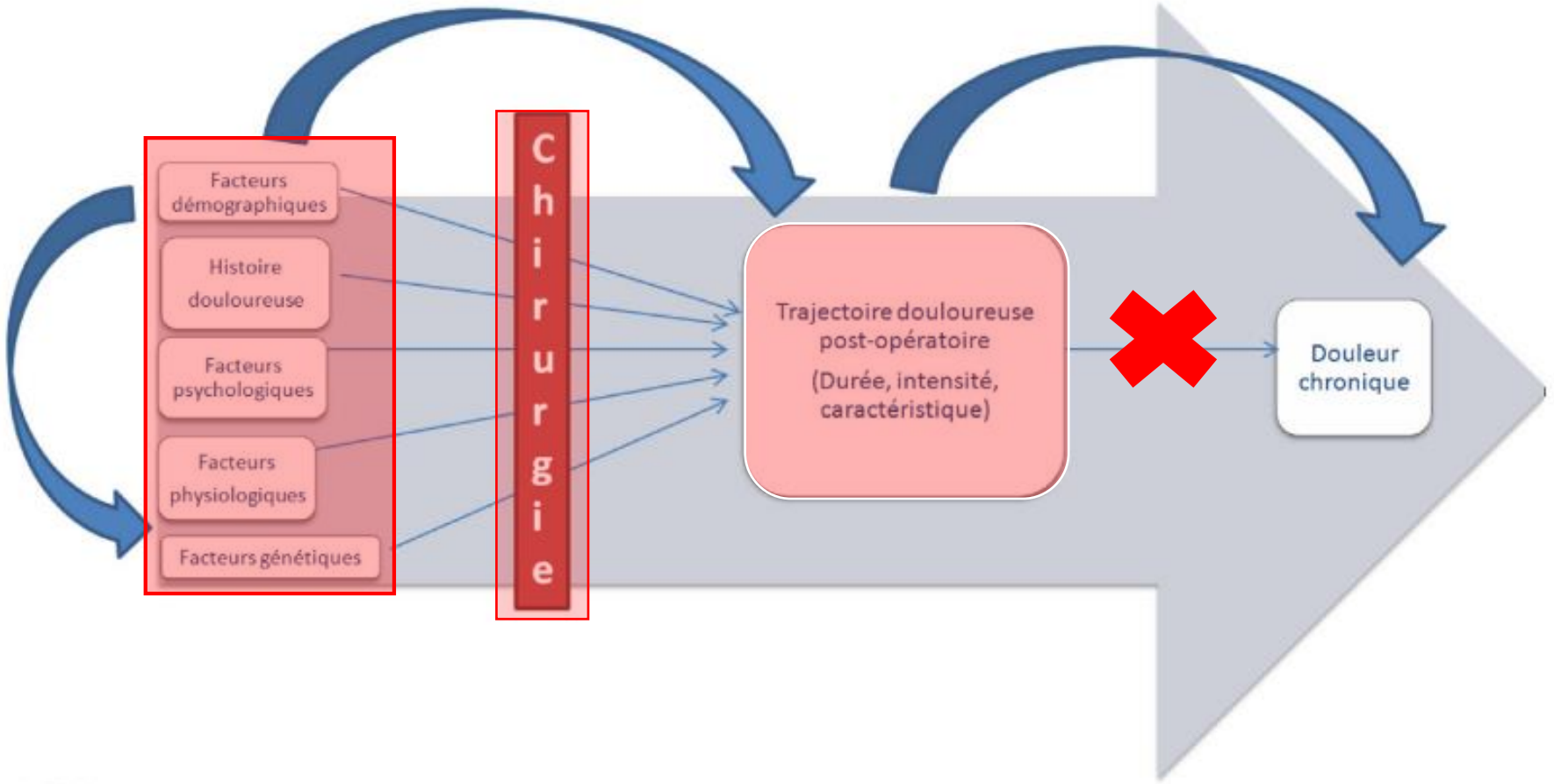


Figure 2: **A transitional pain clinic model**
Care in hospital and after discharge pathways.

Stratégie


Facteurs démographiques
Histoire douloureuse
Facteurs psychologiques
Facteurs physiologiques
Facteurs génétiques
Chirurgie
Trajectoire douloureuse post-opératoire
(Durée, intensité, caractéristique)
Douleur chronique

Facteurs de risque

***Panel 1:* Risk factors for chronic postsurgical pain**

Demographics and lifestyle

- Age
- Gender
- Marital status or living arrangements
- Education level
- Employment status
- Compensation status
- Obesity
- Smoking

Genetic

- Candidate gene mutations associated with increased pain (eg, *COMT*,*OPRM1*, and *GCH1*)

Clinical

- Surgical factors, including surgical technique (open *vs* laparoscopic), duration of surgery, type of anaesthesia (general *vs* regional), and perioperative
- Analgesic regimen (systemic *vs* spinal and pre-emptive); surgical complications and re-operating
- Medical comorbidities
- Previous disability or pain interference

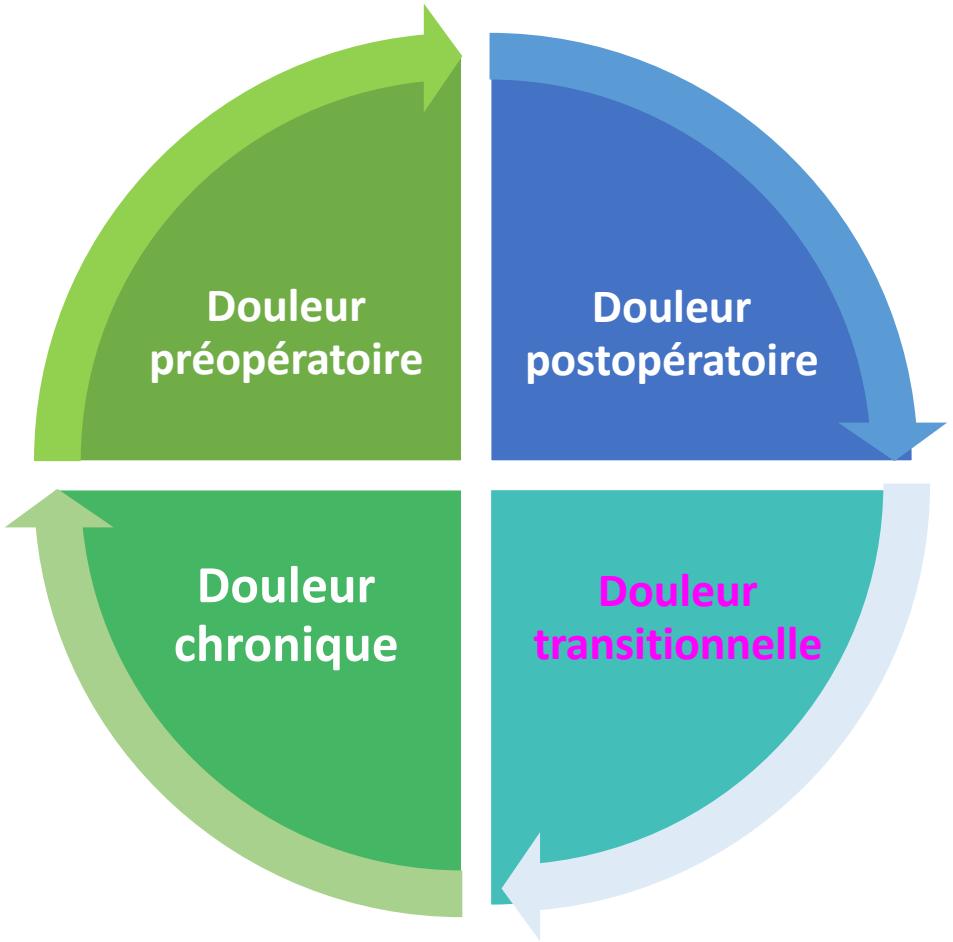
Preoperative pain (area of operation or elsewhere)

Postoperative pain (intensity and duration)

Psychological

- Fear or anxiety
- Depression
- Pain catastrophising
- Other psychological issues (eg, vulnerability factors)

ANTICIPER


Douleur préopératoire
Douleur postopératoire
Douleur chronique
Douleur transitionnelle

- Différents facteurs peuvent contribuer aux développement de douleurs chroniques
- Il est peu probable qu'un seul traitement soit efficace et approprié pour tous les patients
- Screening patients
- FDR souvent intriqués (pas indépendants)
- FDR prévisibles et modifiables
- Traitement personnalisé des sujets à risque
- Création de service de douleur transitionnelle

PAIN FREE

LIFE

Let's keep in touch!

Lynda Abed

Lyndouche Grey

abedlynda@gmail.com

MAPAP


NOT SURE IF THEY'RE CLAPPING FOR MY PRESENTATION
OR BECAUSE ITS FINISHED

MERCI