



Pain epidemiology in neonates and infant patients

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Epidemiology and pain

- Epidemiology can help in designing adequate pain management strategies
- Wide field : clinical or non-clinical studies, specific settings, retrospective, prospective or cross-sectional studies provide different information
- Epidemiological pain data is relevant if associated with an indication of pain severity
 - Since pain is subjective, determination of pain severity in infants is a challenge
- Pain epidemiological data : procedural, postoperative, disease related, cancer, trauma, different settings (NICU, emergency room...)
- Even healthy infants undergo about a dozen punctures during their first year of life: disease screening, immunizations

Painful events are very frequent in sick neonates

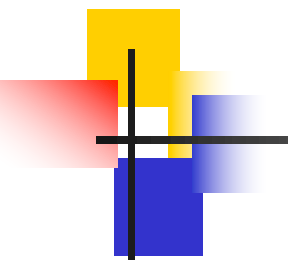
Intubation
Mechanical ventilation
Repetitive invasive procedures
Repetitive stressful procedures
Painful pathological conditions...



Nociception



Pain

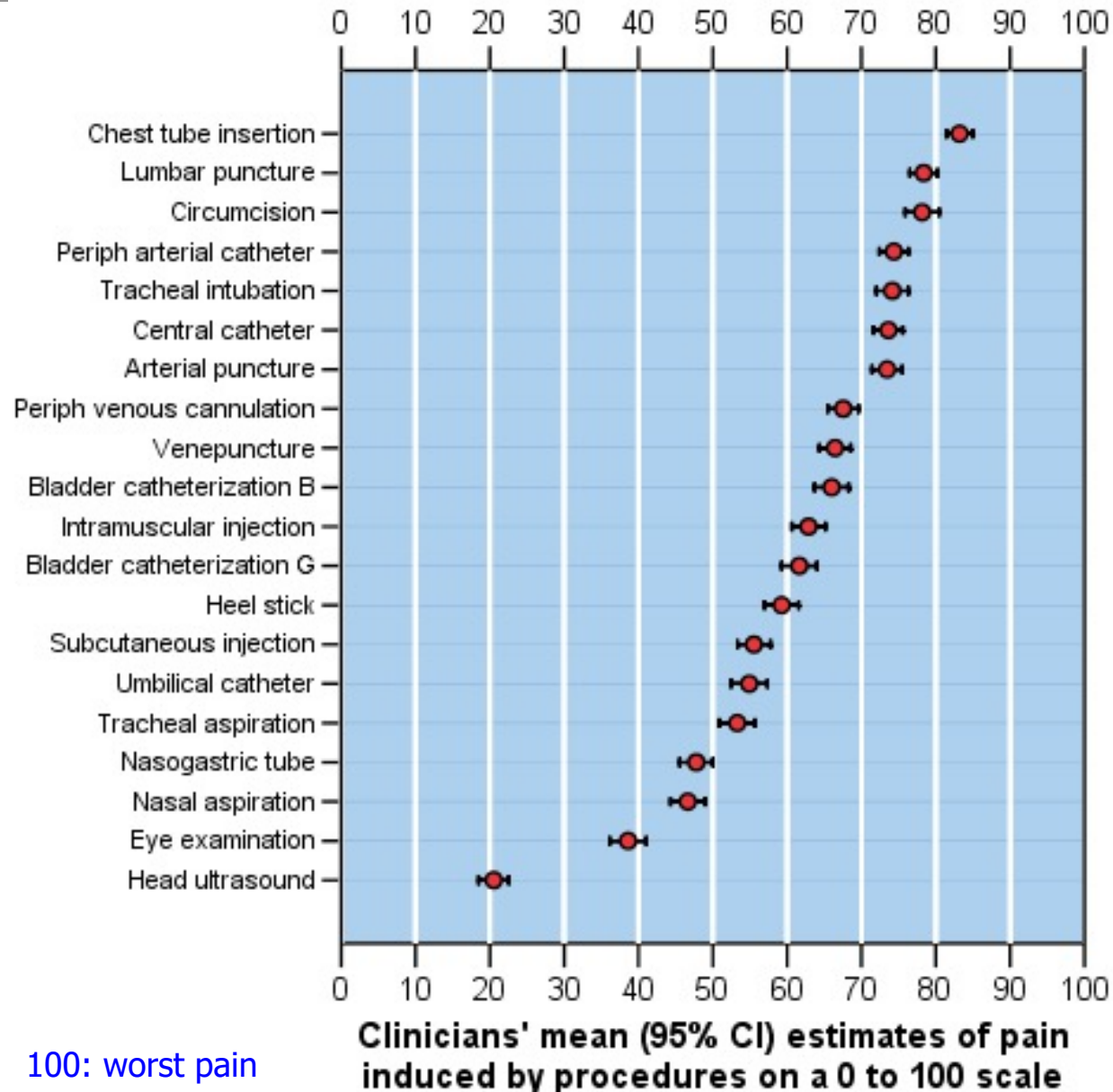


What's NICU staff's opinion about
pain induced by common
procedures?

Clinicians' estimates of pain induced by procedures: Survey of 510 physicians and nurses in NICUS

- 14 units level 2 and 3 in Lima-Peru
- Physicians 36.8%
Nurses 42.8%
Nurse assistants 20.4%
- Female 78.2%
- Estimation of pain induced by the procedure performed WITHOUT analgesia (0-100)

Carbajal R et al. Beliefs and Attitudes of Clinicians About Procedural Pain in Neonates in a Developing Country. Pediatric Academic Societies Meeting. Washington, May 2004.

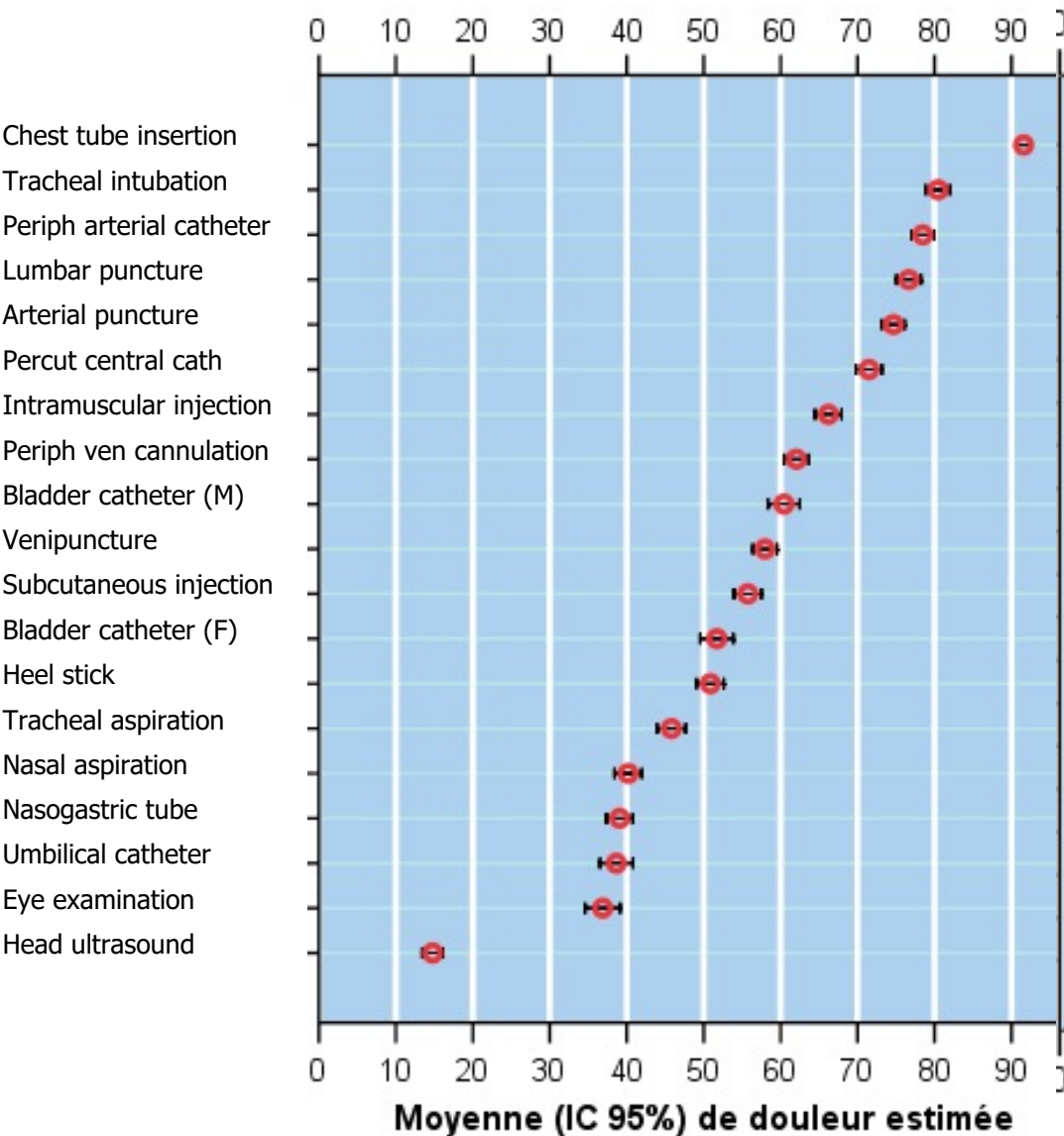


Same survey in 652 NICU staff members in France

France

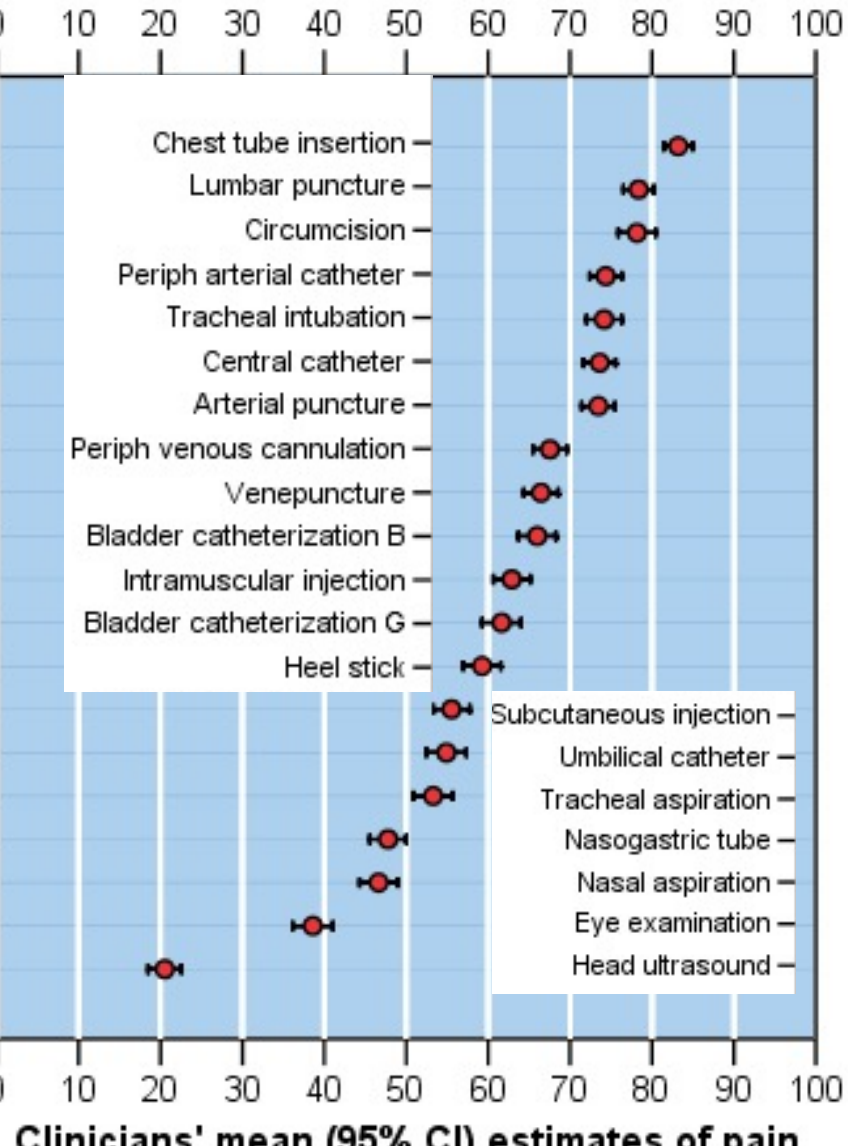


Peru



Moyenne (IC 95%) de douleur estimée

652 physicians, nurses and nurse assistants



Clinicians' mean (95% CI) estimates of pain induced by procedures on a 0 to 100 scale



The burden of neonatal pain

- Prematurity (<37 weeks' gestation) vary from 7 to 12%
- Between 2 to 3% of all neonates may be admitted to NICUs
- Painful and stressful procedures are very frequent in the NICU (Barker 1995), (Carbajal, *Jama* 2008;300: 60-70), (Simons, *Arch Pediatr Adolesc Med* 2003;157: 1058-1064)
- Pain is an inherent part of life-saving care in the NICU
- A minority of all painful procedures are treated preemptively with an analgesic (Carbajal, *Jama* 2008;300: 60-70)



Epidemiology and Treatment of Painful Procedures in Neonates in Intensive Care Units

Ricardo Carbajal, MD, PhD

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Claude Danan, MD

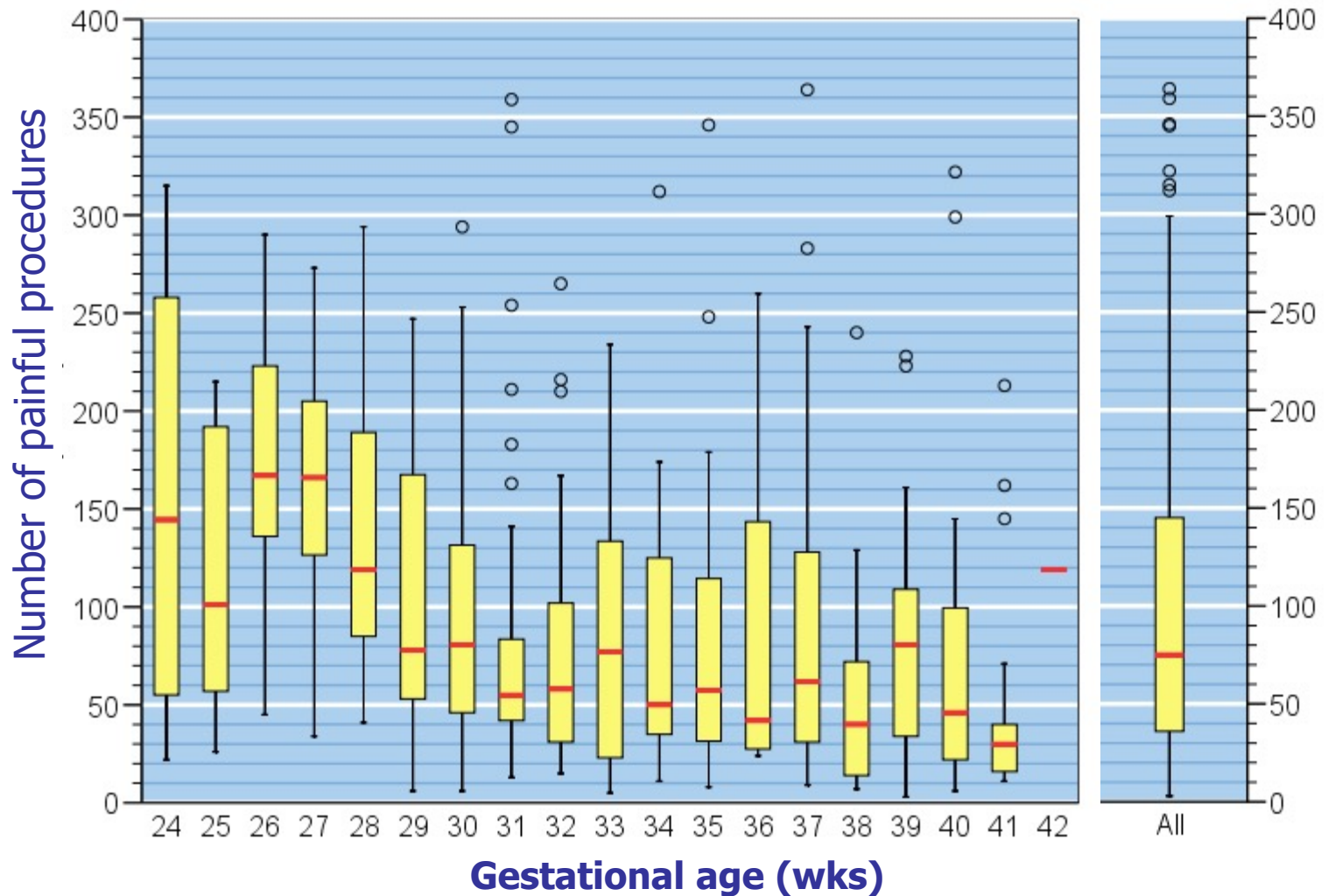
Context Effective strategies to improve pain management in neonates require a clear understanding of the epidemiology and management of procedural pain.

Objective To report epidemiological data on neonatal pain collected from a geographically defined region based on direct bedside observation of neonates.

JAMA®

JAMA. 2008;300(1):60-70

Number of painful procedures in NICUS*

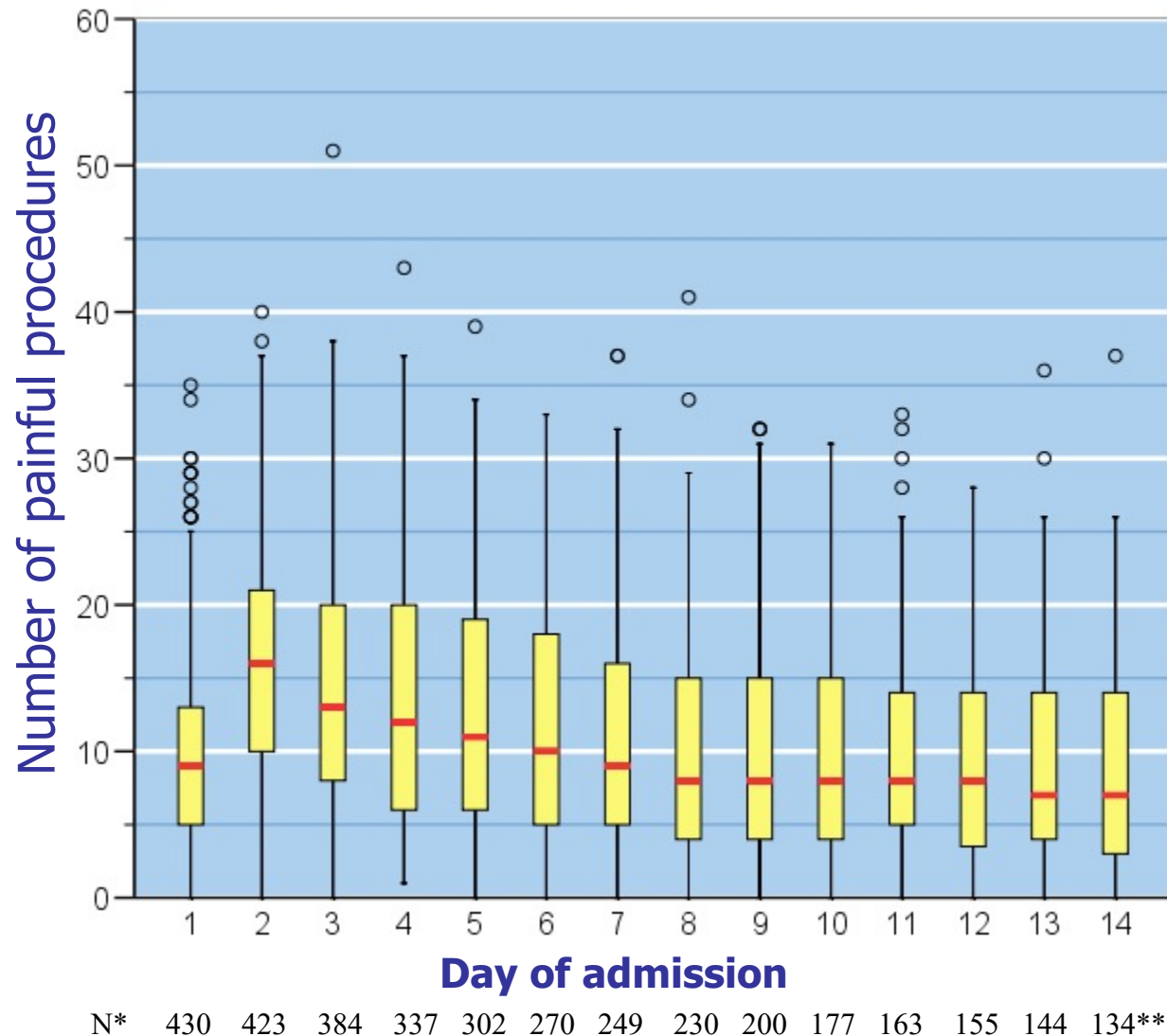


N° neonates 4 9 23 28 32 23 40 39 29 20 25 28 11 30 22 22 23 21 1 430

*during the first 14 days of admission to ICU

EIPPAIN STUDY: Carbajal *et al*, JAMA 2008;300:60-70

Painful procedures by day of admission



** 126 hospitalized >14 days

(Carbajal, *Jama* 2008;300: 60-70)



Skin-breaking procedures

- A total of 11031 skin-breaking procedures in 430 neonates during a mean stay of 8 days
- A mean of 25 skin-breaking procedures per neonate
 - Some procedures needed multiple attempts

Number of attempts to terminate some common painful procedures

	Number of attempts				Max of attempts
	1	2	3	≥ 4	
Tracheal aspiration n=9883	75.3%	21.2%	2.8%	0.8%	10
Heelstick n=8396	97.4%	2.3%	0.3%	0.0%	3
Venipuncture n=757	70.2%	18.5%	7.8%	3.6%	10
Arterial puncture n=755	62.1%	21.6%	9.9%	6.4%	10
Intravenous cannula n=576	45.9%	22.5%	13.1%	18.5%	14
PI central catheter n=240	40.3%	14.2%	15.4%	29.6%	12
Tracheal intubation n=101	72.3%	17.8%	7.9%	2.0%	15
Arterial catheter n=43	39.5%	27.9%	11.6%	21.0%	9
Lumbar puncture n=38	65.8%	26.3%	7.9%	0.0%	3



Factors Associated With Analgesia Use

- Analgesia use among centers:
4.8% to 49.6% for specific preprocedural
25.8% to 85.8% for “some form of analgesia”
- **Greater use of specific analgesia:** Prematurity, parental presence during procedures, neonates undergoing surgery, daytime performance (7 AM to 6 PM), and day of hospitalization (2-14 d) were associated with
- **Less frequent use of specific analgesia:** Mechanical ventilation, noninvasive ventilation, concurrent analgesia, and a higher CRIB score were associated with.

Painful procedures in the NICU decrease over time : Comparison of EPIPAIN 1 (2005) vs. EPIPAIN 2 (2011)

	Epippain 1, n=430	Epippain 2, n=589	P value
	Median (IQ)	Median (IQ)	<i>Mann Whitney</i>
Procedures per day			
Painful procedures	10 (5-17)	8 (4-14)	<0.001
Stressful procedures	4 (2-8)	14 (9-19)	<0.001
Procedures during the study period			
Painful procedures	75 (36-145)	44 (24-95)	<0.001
Stressful procedures	22 (9-68)	78 (33-161)	<0.001
Analgesia for painful procedures, %	20 (8-35)	36 (17-59)	<0.001

Painful: invaded the neonate's bodily integrity, causing skin injury or mucosal injury from the introduction or removal of foreign material into airway or digestive or urinary tract. Other procedures that were considered painful by clinicians at the bedside were also registered.

Stressful: those that mainly caused physical uneasiness or annoyance, or disturbed the existent equilibrium between the neonate and its environment



Most frequent stressful procedures

N=62312 stressful procedures

Procedure	Procedures, No. (%)
Nursing care	22087 (35.4)
Oral aspiration	11347 (18.2)
Blood pressure measurement	11166 (17.9)
Physiologic parameters measure	7764 (12.5)
Infant weighing	3540 (5.7)
Eye cover for phototherapy	1386 (2.2)
X-rays	1104 (1.8)
Washing the neonate	1093 (1.8)
Nasal cannula insertion	974 (1.6)
External repositioning of tubes and catheters	555 (0.9)
Miscellaneous	1296 (2.0)
Total	62312 (100.0)

In Epippain 1, staff reported 18,556 stressful procedures

Analgesia for some painful procedures

Epippain 2 vs.
Epippain 1

Procedure	Specific pre procedural analgesia			Continuous analgesia (%)	All forms of analgesia (%)		
	Non pharm only (%)	Pharm only (%)	Non pharm and/or pharm (%)				
Tracheal aspiration	4.6	1.6	6.4	6.6	66.7	69.6	55.5
Heel stick	55.9	1.7	58.2	44.0	26.4	75.2	62.2
Veinipuncture	65.7	6.3	75.1	71.9	25.9	86.7	81.6
Arterial puncture	57.6	5.0	65.5	70.1	31.9	82.1	82.4
Tracheal intubation	0.0	40.9	42.3	42.6	41.6	68.6	59.4
Subcutaneous injection	72.3	5.4	83.0	88.4	29.5	90.2	92.8

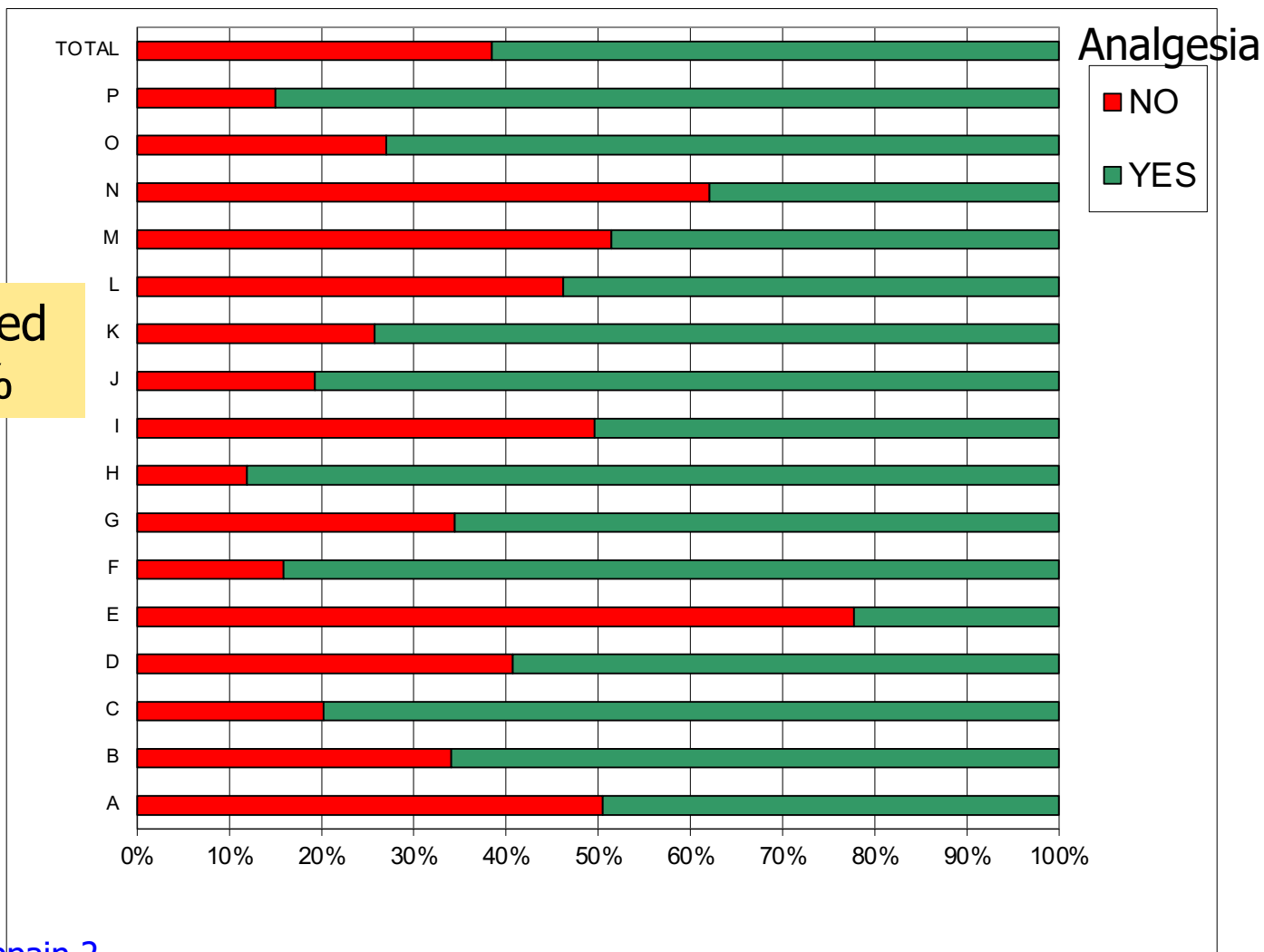
Epippain 1

WIDE variability in the use of analgesia

16 NICUS in the region of Paris, 589 neonates

Specific Analgesia for skin breaking procedures
(venipuncture, arterial puncture, heel stick)

Analgesia use varied
from 88% to 22 %



SYSTEMATIC REVIEW

Epidemiology of painful procedures performed in neonates: A systematic review of observational studies

M.D. Cruz^{1,3}, A.M. Fernandes^{2,3}, C.R. Oliveira^{4,5}

Study	Country	Study type	Participants		Outcome measures
			Units	Neonates	
Barker and Rutter, 1995	UK	Prospective	1	54	Nature and frequency of invasive procedures.
Johnston et al., 1997	Canada	Cross-sectional	14	239	Frequency and type of procedures and analgesia administration for all neonates in each NICU.
Stevens et al., 2003	Canada	Retrospective Cohort study	2	194	Nature, frequency and prevalence of painful procedures, analgesics and sedatives, and the relationship between painful procedures and analgesia for neonates at risk for

Conclusions: Painful procedures were performed frequently and often with inadequate pain management. Unlike neonate clinical factors, organizational factors may be modified to promote a context of care more favorable to pain management

Nóbrega et al., 2007	Brazil	Prospective	1	52	preventive and therapeutic measures. Painful procedures and relieving measures in newborns admitted to the NICU.
Carbajal et al., 2008	France	Prospective	13	430	Number of procedures considered painful or stressful by health personnel and corresponding analgesic therapy.

Procedural pain is common everywhere in NICUS

Table 1
Epidemiology of procedural pain in infants in intensive care

No. of Painful Procedures	Period of Time	Total Percentage that Were Needle Punctures	
60.8 per patient	Total stay	70%	Barker & Rutter, ⁴ 1995
2–10 per day	First 7 d	90%	Johnston et al, ⁵ 1997
14 per day	First 14 d	15.6%	Simons et al, ⁶ 2003
12–16 per day	First 14 d	25.6%	Carbajal et al, ² 2008
0.8 per day	7 d	94%	Johnston et al, ¹ 2011
4.3 per day	Total stay	66%	Kyololo et al, ⁷ 2014
7.5 per patient per day	First 14 d	19.8%	Jeong et al, ⁸ 2014
11.4 per patient per day	First 14 d	14%	Roofthoof et al, ⁹ 2014
6.6 per patient per day	Total stay	52.3%	Sposito et al, ¹⁰ 2017

McNair *et al.* Clin Perinatol 46 (2019) 709–730



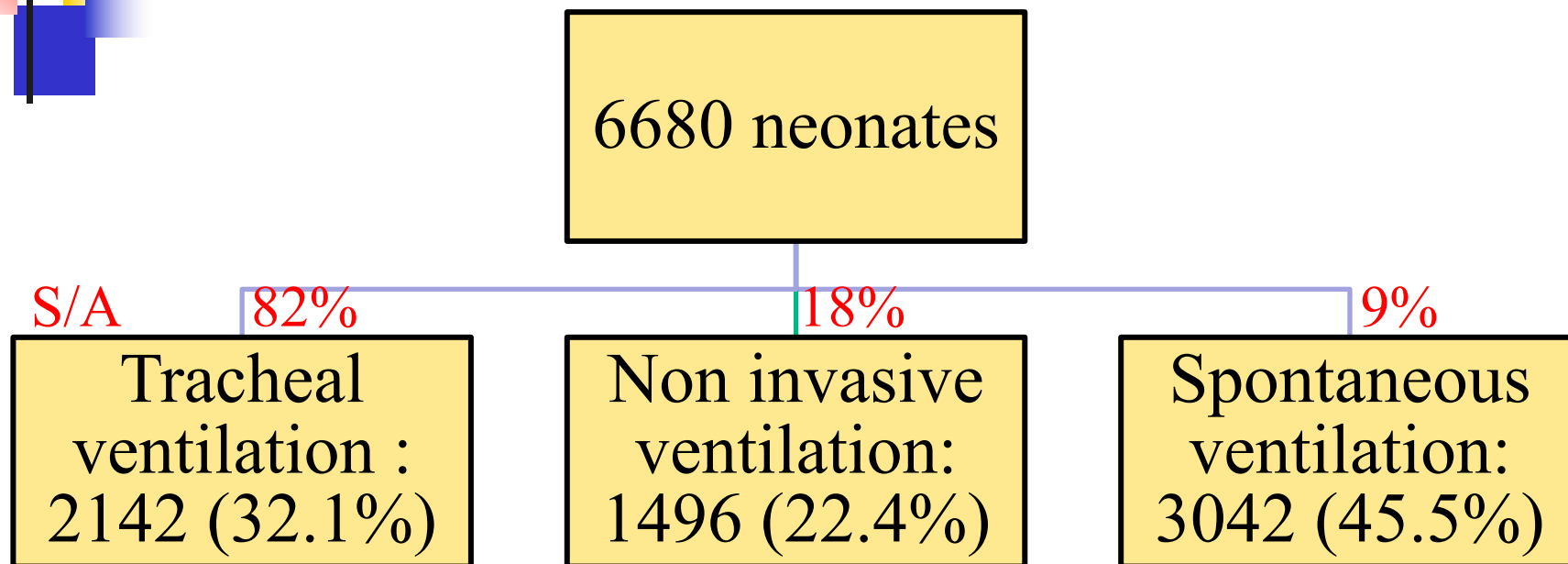
Sedation and analgesia practices in neonatal intensive care units (EUROPAIN): results from a prospective cohort study

*Ricardo Carbajal, Mats Eriksson, Emilie Courtois, Elaine Boyle, Alejandro Avila-Alvarez, Randi Dovland Andersen, Kosmas Sarafidis, Tarja Polkki, Cristina Matos, Paola Lago, Thalia Papadouri, Simon Attard Montalto, Mari-Liis Ilmoja, Sinno Simons, Rasa Tameliene, Bart van Overmeire, Angelika Berger, Anna Dobrzanska, Michael Schroth, Lena Bergqvist, Hugo Lagercrantz, Kanwaljeet J S Anand, on behalf of the EUROPAIN Survey Working Group**

*Lancet Respir Med 2015;
3: 796–812*

- Prospective cohort: sedation and analgesia in patients in NICUs
- All neonates admitted to NICUs during 1 month
- Data gathered during the first 28 days of admission
- From Oct 2012, to June 2013, 6680 neonates were enrolled in 243 NICUs in 18 European countries
- 74% of neonates were given opioids and a quarter were given midazolam
- Morphine (53%) and fentanyl (36%) are the most frequently drugs used in S/A intubated neonates
- Wide variations between centers and countries (0-100 %)

Population distribution according to the highest level of ventilation



Tracheal ventilation: tracheal ventilation of any duration

Non invasive ventilation: non invasive ventilation of any duration without tracheal ventilation

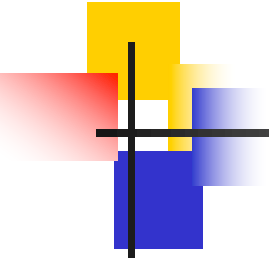
Spontaneous ventilation: no tracheal nor non invasive ventilation at any time

- 2294 (34%) received **Sedation/Analgesia** by continuous infusion or bolus or both: 82% in the TV group, 18% in the NIV group, and 9% in the SV group ($p < 0.0001$)



Procedural and disease related pain

- Procedural pain: most frequent source of pain in neonates and infants
- Beyond the neonatal period: procedural pain is still frequent. Immunizations or disease related venipunctures
- Disease related pain in young children: otitis, stomatitis, abdominal pain, headache
- Trauma pain at all ages
- Epidemiological data on the above conditions are scarce and vary according to the setting



Thank you for your
attention