Belgian Association for Paediatric Anaesthesiology
Section of the Belgian Society for Anaesthesia and Reanimation

KINDER ZIEKENHUIS UZ LEUVEN

Pediatrisch Pijnsymposium 2018

De weg naar minder pediatrische pijn

Zaterdag 28 april 2018

appliedVR™

Air Liquide HEALTHCARE

Oncomfort™ With you in mind

puramed

eurocept pharmaceuticals

janssen

#dewegnaarminderpijn2018

pijnbestrijding bij de zuigeling: wat zijn de opties?

SAFE PEDRUG

Erasmus MC Rotterdam, the Netherlands

KU Leuven, Belgium

karel allegaert

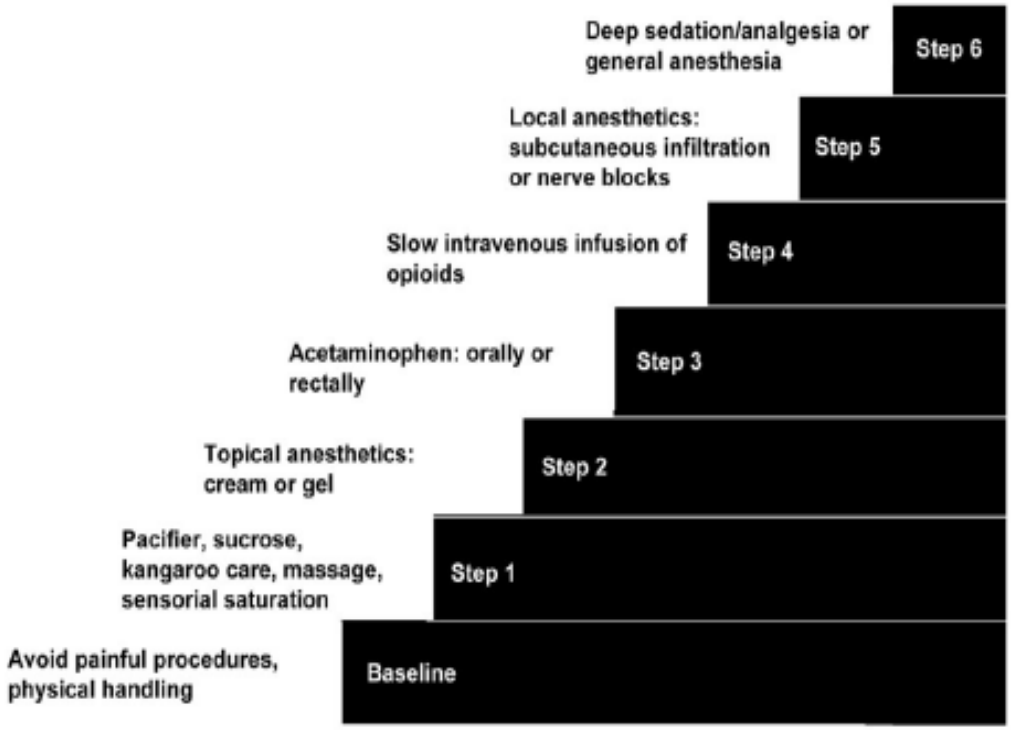


Figure 1. Stepwise approach to neonatal analgesia.

SUGGESTIE 1

Pain in babies may cause later harm

Photodisc file

Study in newborn rats suggests early trauma rewires nervous system

Debate has been raging in the medical community over how newborns experience pain and the impact later on.

REUTERS

July 27 — Newborns who have painful, but often life-saving, medical procedures in the early weeks of life may have a lower pain threshold in later years, according to a new animal study released Thursday.

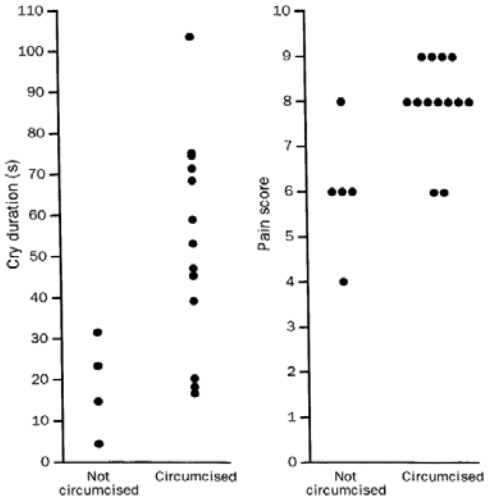
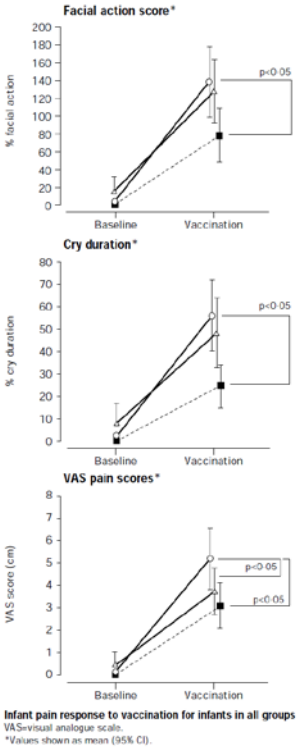


Figure: **Pain response during HIB injection in circumcised and uncircumcised boys**
Data not available for cry on 1 infant. p=0·02 for cry, p=0·01 for behavioural pain score.



Infant pain response to vaccination for infants in all groups
VAS=visual analogue scale.
*Values shown as mean (95% CI).

Anand *et al.* New Engl J Med 1987
Taddio *et al.* JAMA 2002
Taddio *et al.* Lancet 1995 and 1997

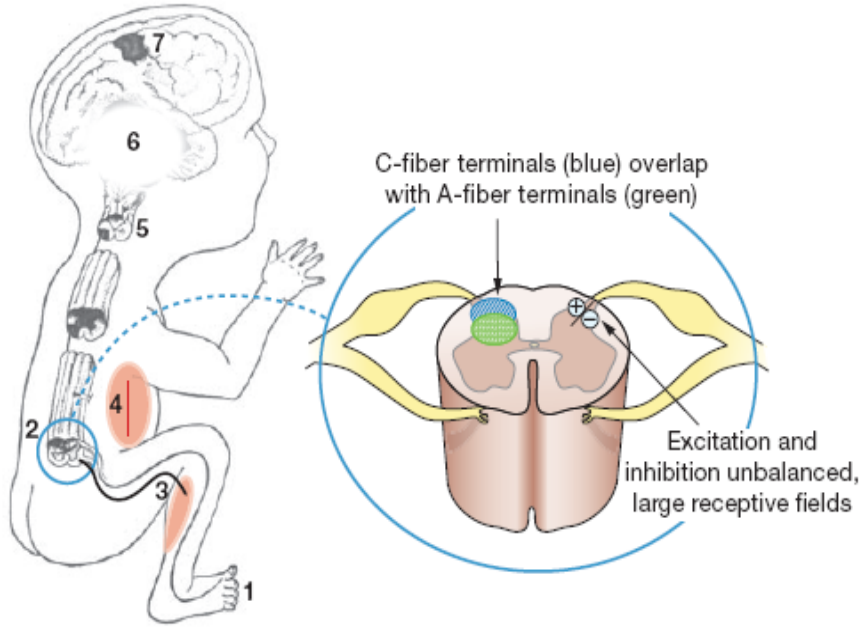
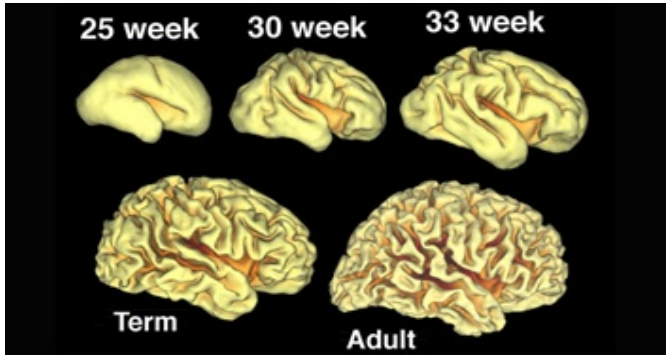


Figure 1 Key sites of developmental transition in infant pain pathways. The areas of the nervous system are indicated where developmental changes and plasticity impact pain detection and treatment in this group. (**1**) Peripheral innervation is vulnerable and sensitive to tissue injury. (**2**) Dorsal horn sensory pathways undergo considerable postnatal reorganization. (**3**) Nociceptive reflex pathways are diffuse and poorly tuned. (**4**) Primary hyperalgesia develops before secondary hyperalgesia. (**5**) Endogenous descending controls via the brainstem are unbalanced. (**6**) Extensive cortical development begins postnatally, but little is known of the development of intracortical network connections in infancy. (**7**) The somatosensory cortex is activated by noxious stimulation from an early age, but little is known of activation in other cortical regions.



SUGGESTIE 2

Venipuncture Is More Effective and Less Painful Than Heel Lancing for Blood Tests in Neonates

Björn A. Larsson, MD*; Gunnilla Tannfeldt, RN*; Hugo Lagercrantz, MD, PhD‡; and Gunnar L. Olsson, MD, PhD*

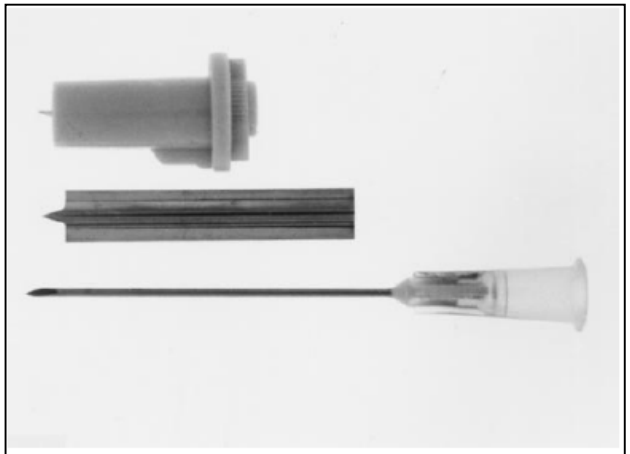


Fig 1. Three devices used for the PKU test. From the top: the CCS Minilancet used in the SL group, the Microlance used in the LL group, and the Microlance needle (0.9 × 40 mm) used in the VP group.

The 3 P's of Helping your Baby during Vaccinations
A Parent's Guide: Babies up to 1 year old

Vaccine injections can be painful and stressful for babies and parents, but you can really make a difference.

Plan Ahead

For your baby's next vaccine injection, plan with your health care provider to:

1) Apply topical anaesthetics to numb the skin – these are medicines you can buy at a pharmacy without a prescription.
2) Give your baby sugar water for comfort – make sugar water at home or at the clinic by mixing 1 teaspoon of sugar with 2 teaspoons of water.
3) Distract your baby – choose an age-appropriate item to bring.

Read the 3 P's of vaccination pain management below and combine these strategies to improve pain relief.
For more information and a video, visit the **SickKids** (The Hospital for Sick Children, Toronto, Canada) website:
www.aboutkidshealth.ca/pain-free-injections

Before Injection

STEP 1: PHARMACOLOGICAL (PAIN MEDICINE)

TOPICAL ANAESTHETICS

- Available products: lidocaine (Maxilene™), tetracaine (Ametop™), lidocaine-prilocaine (EMLA™).
- Apply to either the upper outer part of the leg (infants less than 1 year), or upper arm (infants 1 year old), 30 to 60 minutes before injection – check product instructions.
- If 2 or more injections are planned, apply to both legs or arms.
- May cause temporary reddening or whitening of skin – this is normal. If there is a rash, talk to your doctor – it could be an allergic reaction.
- Avoid acetaminophen (Tylenol™), ibuprofen (Advil™), ice and cold sprays before injection– they have not been proven to reduce injection pain. After injection, acetaminophen or ibuprofen may be used to relieve fever or discomfort.

SUGAR WATER

- Give your baby sugar water to drink right before the injection.

During Vaccine Injection

STEP 2: PHYSICAL (BODY POSITION AND ACTIVITY)

HOLD

- Hold your baby close during injection – in a hug or on your lap. This feels good and helps your baby stay still.
- Avoid holding your baby too tightly – this can increase pain and distress.

BREASTFEED

- Start breastfeeding your baby before injection and continue during and after injection.
- If 1 injection is planned, position your baby to expose 1 leg; expose both legs for 2 or more injections.
- If the baby cannot be breastfed, offer a bottle or pacifier starting before injection and continue during and after injection.

STEP 3: PSYCHOLOGICAL (THOUGHTS AND BEHAVIOURS)

BREATHE DEEPLY

- Stay calm and use your normal speaking voice. This helps your baby stay calm – babies look to their parents for how to act and feel.
- If you are nervous, take a few slow, deep breaths to calm yourself before and during injection – breathe so your stomach expands, not your chest. You can do this while holding your baby.

DISTRACT

- Help keep your baby's attention away from the injection.
- Distractions you can use: rocking, cuddling, singing, talking, sucking (breast-feeding or pacifier). Distract with objects or toys (bubbles, pop-up books, rattles) when your baby is calm enough to do so; otherwise, distress can be increased.

These are scientifically proven ways of reducing pain in babies during vaccine injections.
Think about what worked and plan ahead to make the next vaccination less painful.

HELP inKidS SickKids aboutkidshealth

"Clinical Practice Guideline: Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline" – Adapted from, *CMAJ December 14, 2010 182:E843-E855* by permission of the publisher.
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SUGGESTIE 3

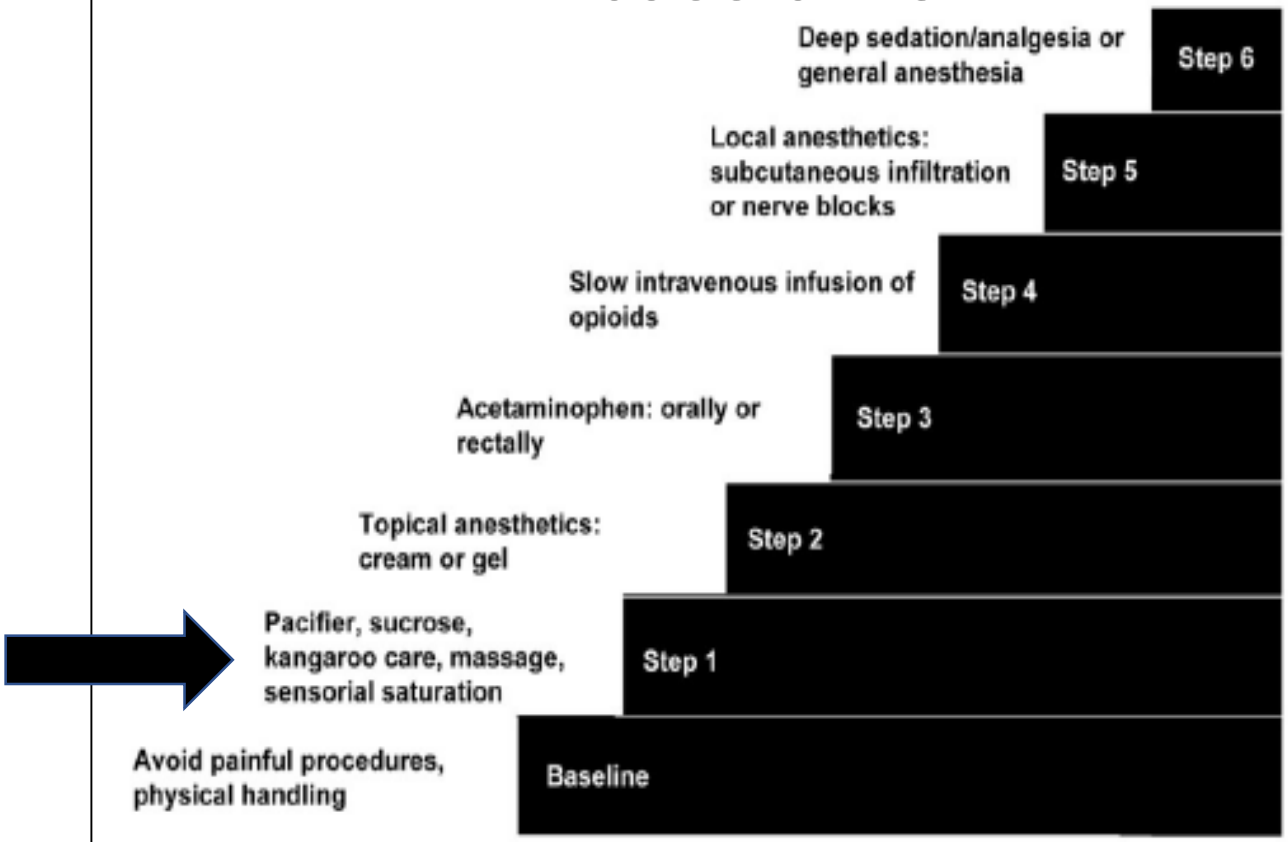
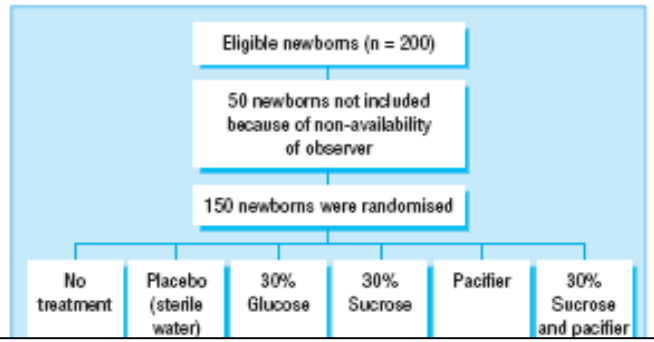


Figure 1. Stepwise approach to neonatal analgesia.



Acta Pædiatr 86: 787–8. 1997

INVITED COMMENTARY

Calming minds or killing pain in newborn infants?

S Lindahl

Department of Anaesthesiology and Intensive Care, Karolinska Hospital and Institute, Stockholm, Sweden

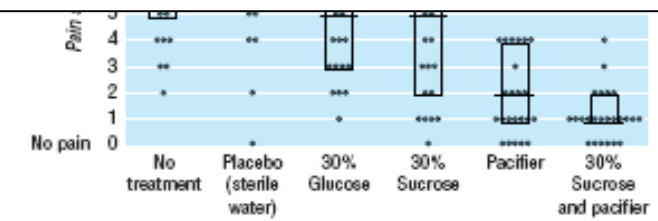


Fig 2 Pain evaluation with DAN scale (0 to 10) during venepuncture in 150 newborns randomised to six equal sized groups, with values for individual infants, median values, and interquartile ranges (for 30% sucrose and pacifier lower quartile coincides with median value)

Oral sucrose as an analgesic drug for procedural pain in newborn infants: a randomised controlled trial

Rebeccah Slater, Laura Cornelissen*, Lorenzo Fabrizi*, Debbie Patten, Jan Yoxen, Alan Worley, Stewart Boyd, Judith Meek†, Maria Fitzgerald†

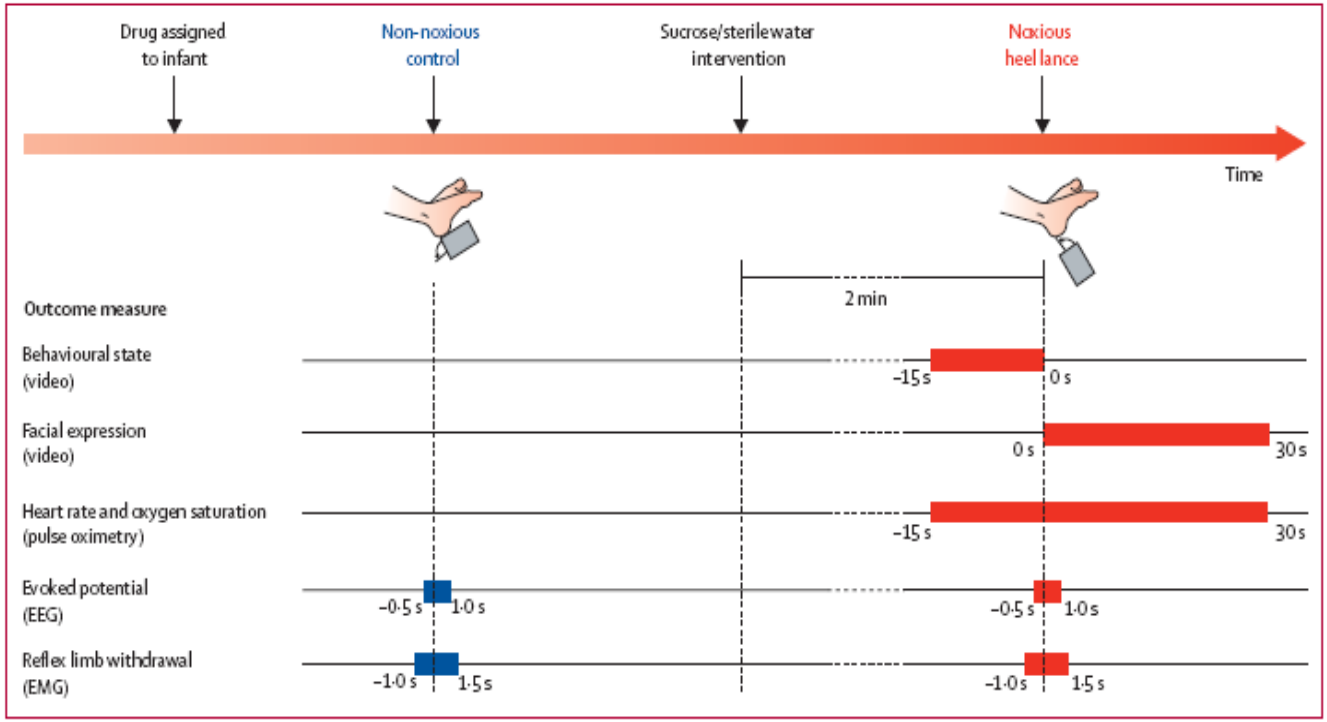


Figure 1: Experimental time line
EEG=electroencephalography. EMG=electromyography.

Oral sucrose as an analgesic drug for procedural pain in newborn infants: a randomised controlled trial

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	Sucrose (N=20)	Sterile water (N=24)	p value
Primary outcome			
Nociceptive-specific brain activity (mean weight)	0·10 (0·04–0·16)	0·08 (0·04–0·12)	0·46
Secondary outcomes			
Mean baseline heart rate (bpm)	132·6 (124·3–140·9)	131·8 (122·2–141·5)	0·90
Mean baseline oxygen saturation (%)	99·4% (98·8–100·1)	97·4% (95·0–99·8)	0·13
Baseline behavioural score (from PIPP)	1·3 (0·8–1·7)	1·3 (0·8–1·8)	0·91
PIPP score	5·8 (3·7–7·8)	8·5 (7·3–9·8)	0·02
Latency to change in facial expression (s)	3·8 (1·3–6·4)	3·5 (1·0–6·1)	0·86
Facial non-responders	7/20 (35%)	0/24 (0%)	<0·0001
Mean nociceptive reflex withdrawal activity (μV)	36·11 (24·20–48·02)	30·82 (18·51–43·13)	0·49
Mean latency to nociceptive reflex withdrawal activity (ms)	363·3 (256·4–470·1)	413·5 (262·0–564·9)	0·56

Data are mean (95% CI) or n/N (%). bpm=beats per min. PIPP=premature infant pain profile.

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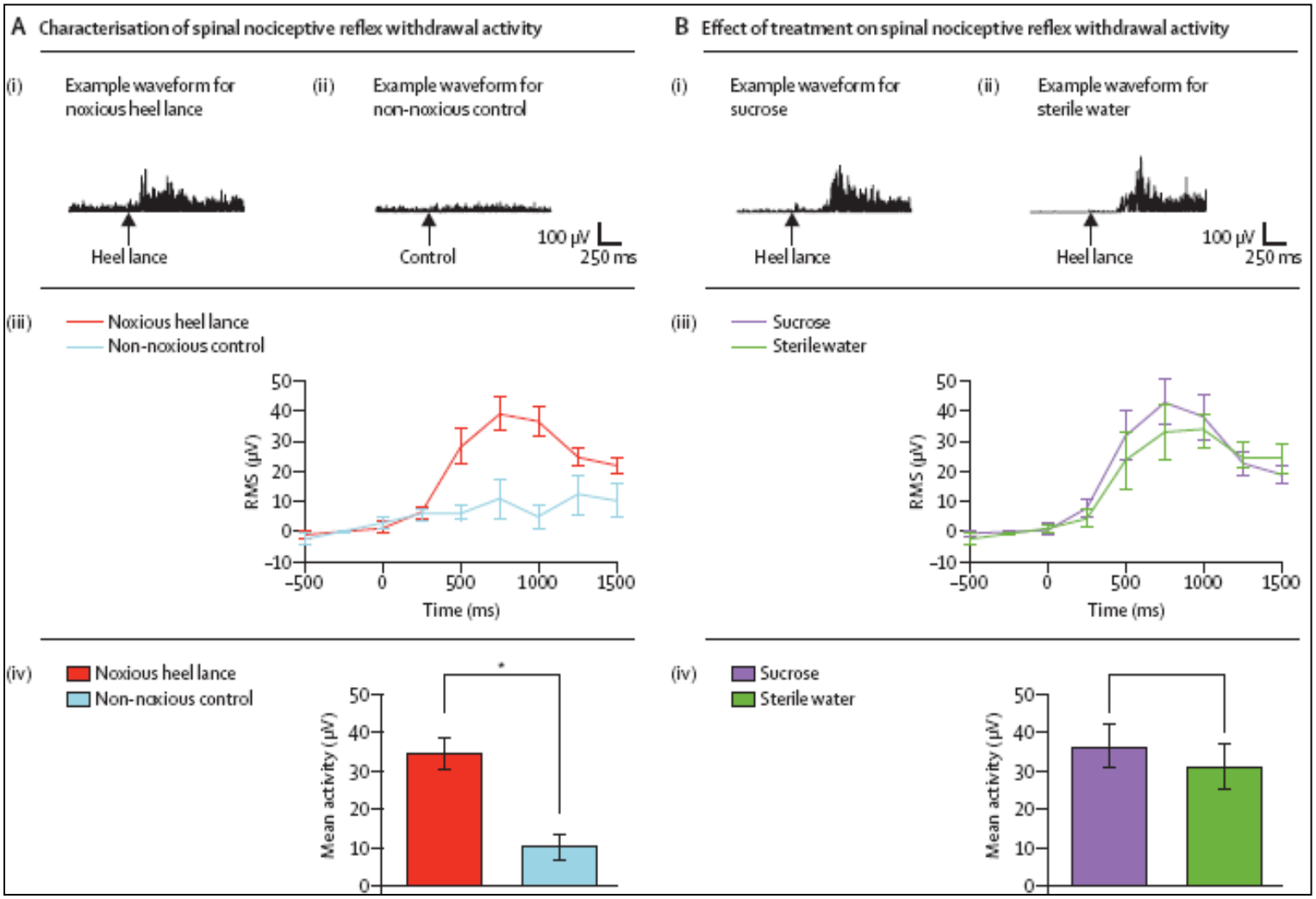


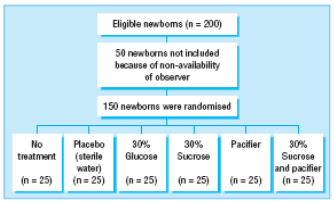
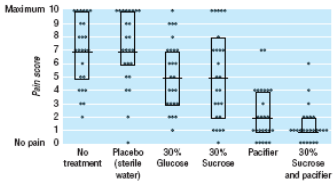


Fig 1 Trial profile and participant flow; all randomised newborns completed trial



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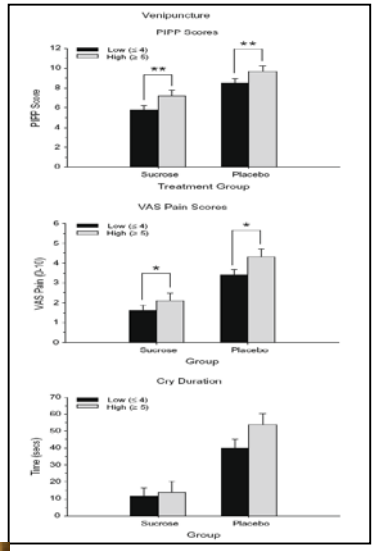
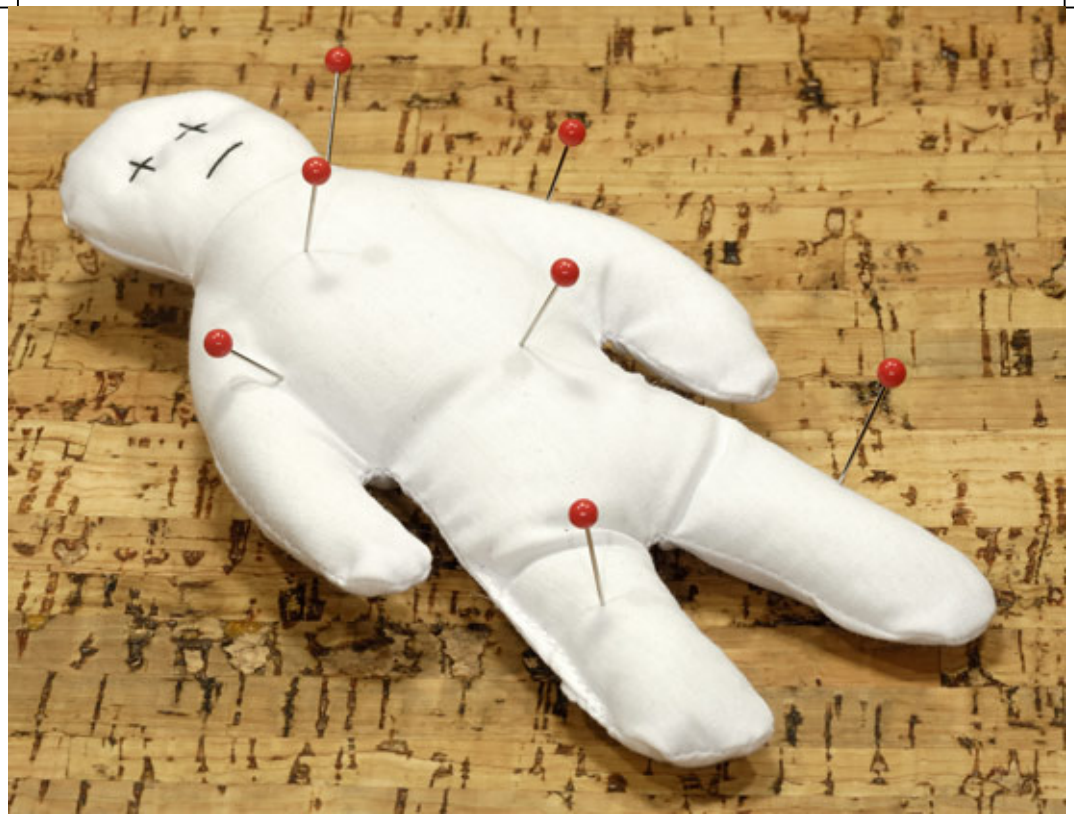
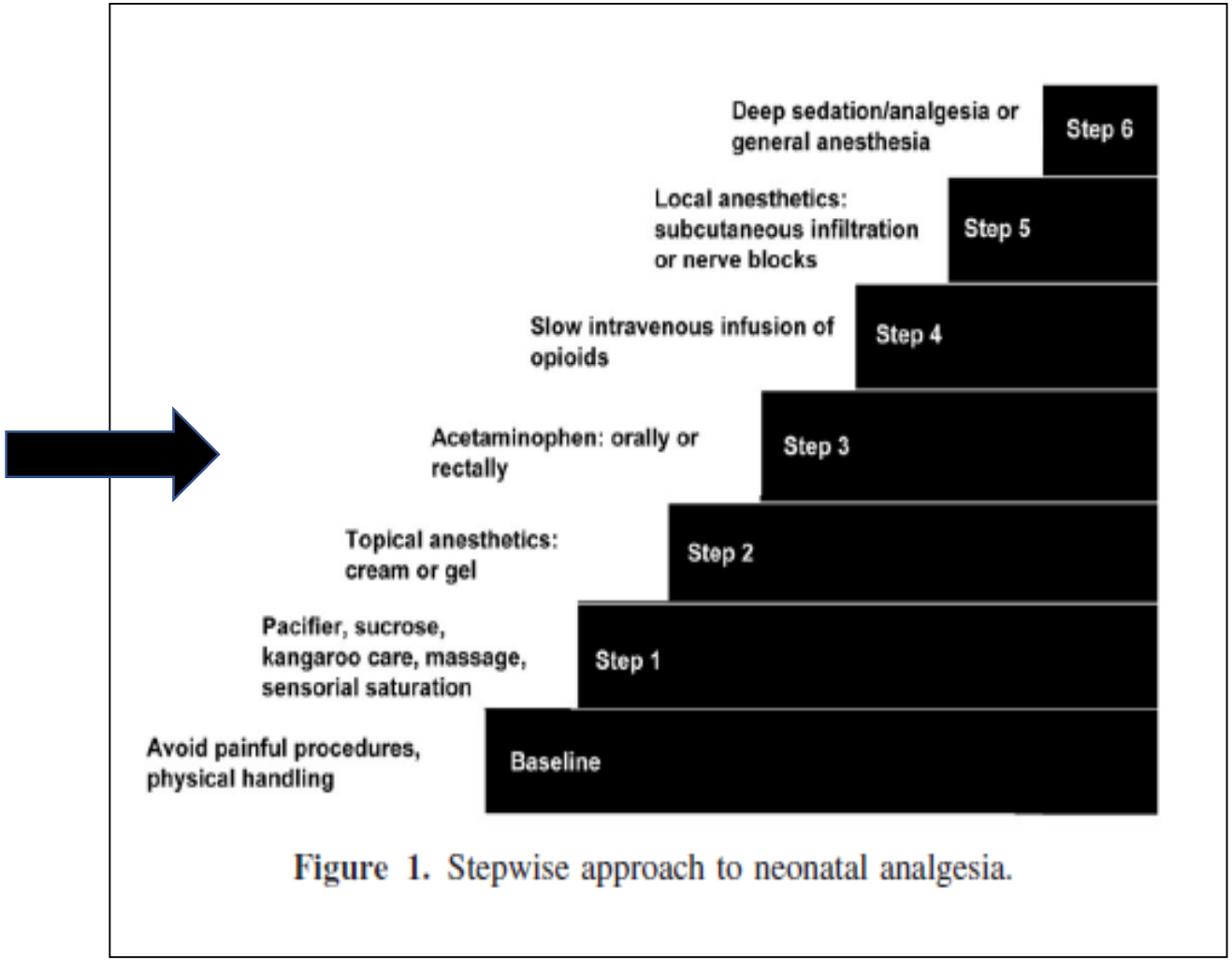




suggestie 4: beperkt effect – if any – in neonates, proven in infants

Table 15.3 Reported papers on the analgesic effects of tetracaine/amethocaine in neonates (type of procedure highlighted)

Reference	Study design and results
Shah et al. [88]	Randomized, double-blind, placebo-controlled trial, *intramuscular injection* (vitamin K) in 110 term neonates, topical amethocaine gel 4 %. There were no differences in crying duration, in pain score and only the latency to cry was somewhat longer in the treated group. Topical amethocaine gel 4 % was ineffective in reducing pain intramuscular injection of vitamin K in full-term neonates
Jain A et al. [89]	Randomized, double-blind, placebo-controlled trial in 40 (pre)term neonates during *venipuncture*. Topical amethocaine provided effective pain relief (crying, neonatal facial coding system) during venipuncture in the newborn when used as single technique for analgesia
Lemyre et al. [90]	Randomized, double-blind, placebo-controlled trial in 142 preterm (from 24 weeks onward) infants during *venipuncture*. Tetracaine did not significantly decrease procedural pain in infants undergoing a venipuncture, when used in combination with routine sucrose administration
Lemyre et al. [91]	Randomized, double-blind, placebo-controlled trial in 54 preterm neonates on the add-on effect of tetracaine gel in addition to sucrose to treat procedural pain related to *peripherally inserted central catheter (PICC) placement*. Tetracaine 4 % when applied for 30 min was not beneficial in decreasing procedural pain associated with a PICC in very small infants
Jain et al. [92]	Randomized, double-blind, placebo-controlled trial in 60 (pre)term neonates during *heel prick blood sampling*. Topical amethocaine gel does not have a clinically important effect on the pain of heel prick blood sampling. Its use for this purpose cannot therefore be recommended



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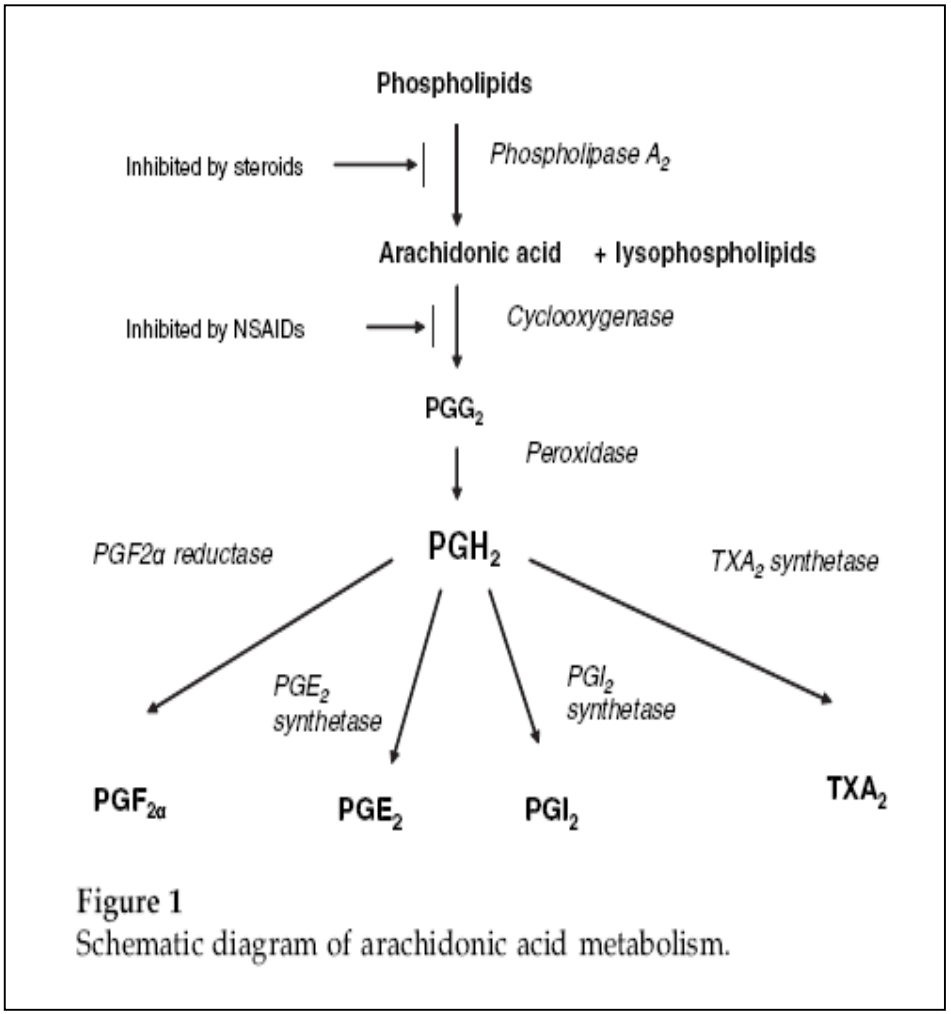


Figure 1
Schematic diagram of arachidonic acid metabolism.

L-arginine-nitric oxide (NO) pathway

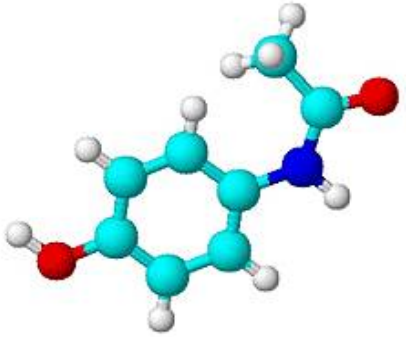
Substance P mediated

NMDA (N-methyl D-aspartate)

Serotonergic pain pathways

cannabinoid pathways, through paracetamol metabolite (p-amino phenol + arachnidonic acid, Subsequent cannabinoid receptor activation (through vanillin receptor – act as ligand)

how does paracetamol 'work' (pharmacodynamics)



mg/l, plasma

— **10**

— **20**

antipyretic ? lower

— **> 25**

analgesic ceiling or not ?
any type of pain syndrome ?
median conc 10 mg/l

Dutch formulary[13]		
Oral	Loading dose	Not sufficiently supported by clinical evidence
	Maintenance	60 mg/kg/d, > 32 wk PMA 30 mg/kg/d, 28–32 wk PMA
Rectal	Loading dose	30 mg/kg, < 32 wk PMA
	Maintenance	20 mg/kg, 28–32 wk PMA 20 mg/kg, q8h in term neonates 20 mg/kg, q12h in preterm neonates
Intravenous		Off label in preterm neonates
	Loading dose	20 mg/kg, irrespective of age
	Maintenance	10 mg/kg, max 40 mg/kg/d, in term cases 10 mg/kg, max 30 mg/kg/d, 31–36 wk PMA 10 mg/kg, max 20 mg/kg/d, < 31 wk PMA

PMA = postmenstrual age (in weeks).

Pacifici, Curr Ther Research 2015

suggestie 4: paracetamol werkt, soms…

standard rectale dosis paracetamol is onvoldoende

lagere bio-availabiliteit

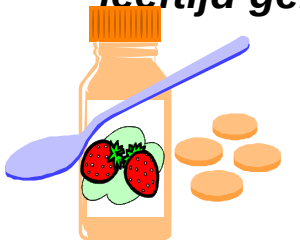
vertraagde absorptie

belangrijke variabiliteit

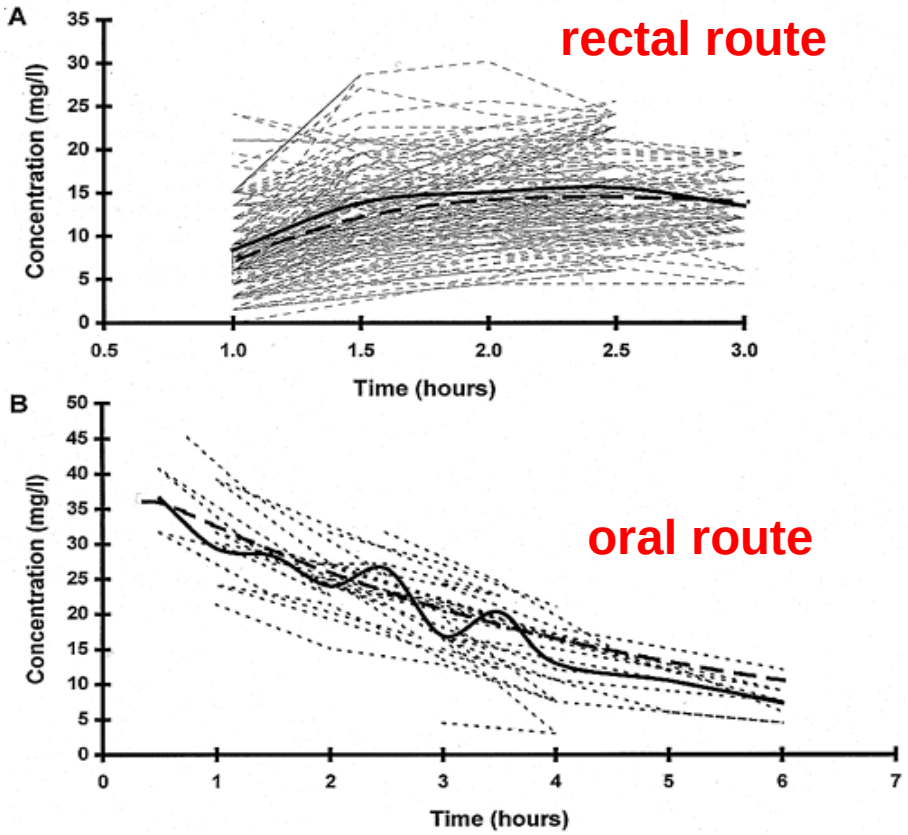
oral > iv > rectal

denk aan een oplaaddosis: distributie volume

leeftijd gerelateerde veranderingen in klaring zijn eerder beperkt



rectaal of oraal, 20 mg/kg single dose na NKO heelkunde



Anderson et al. Anesthesiology 1999

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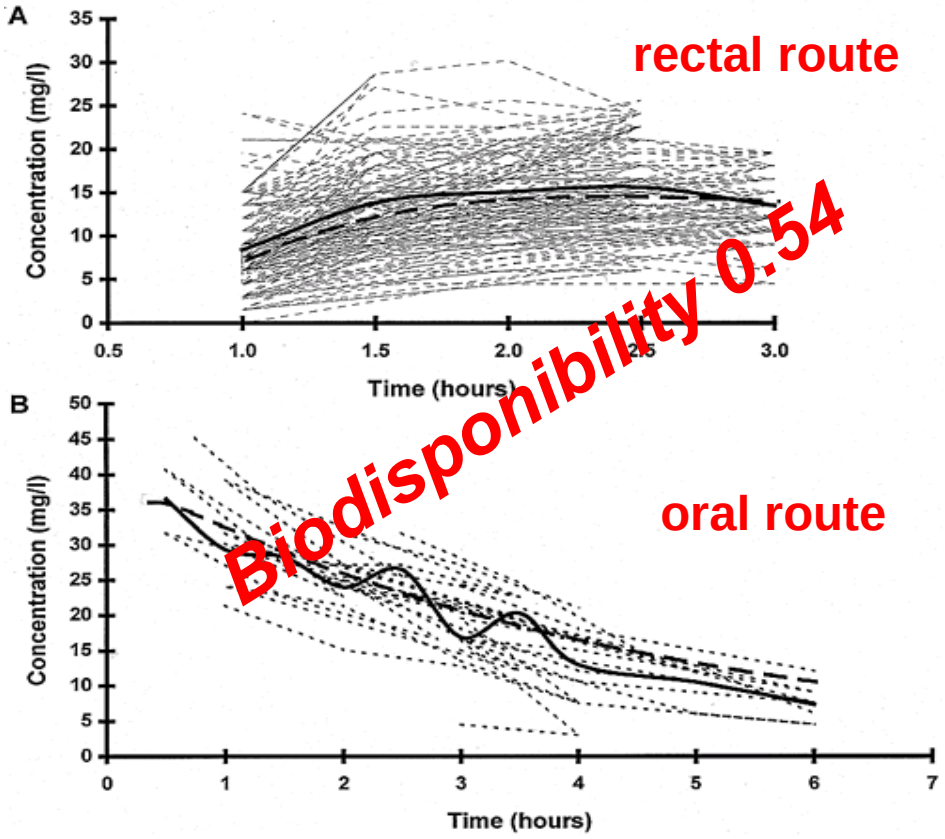
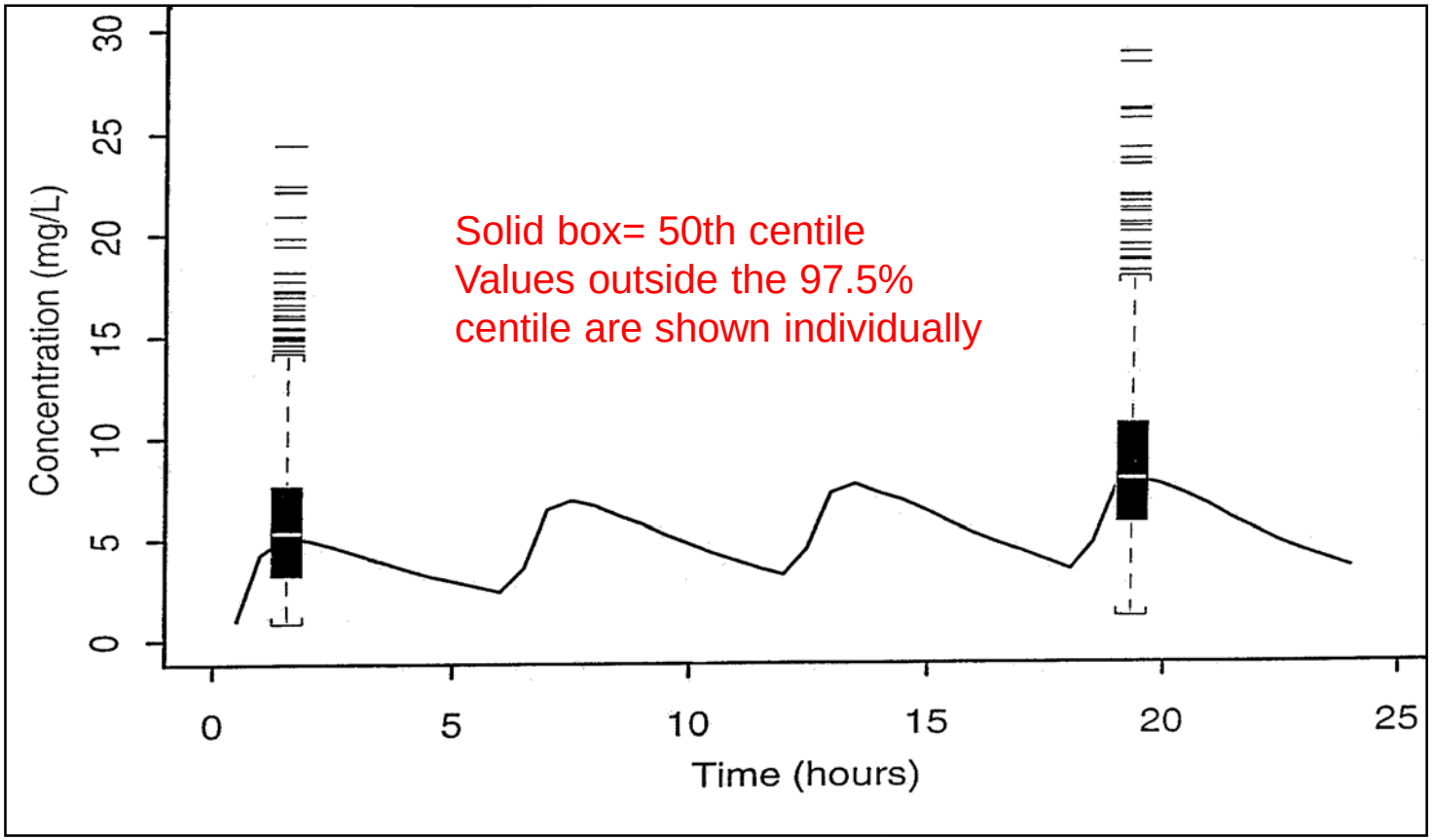


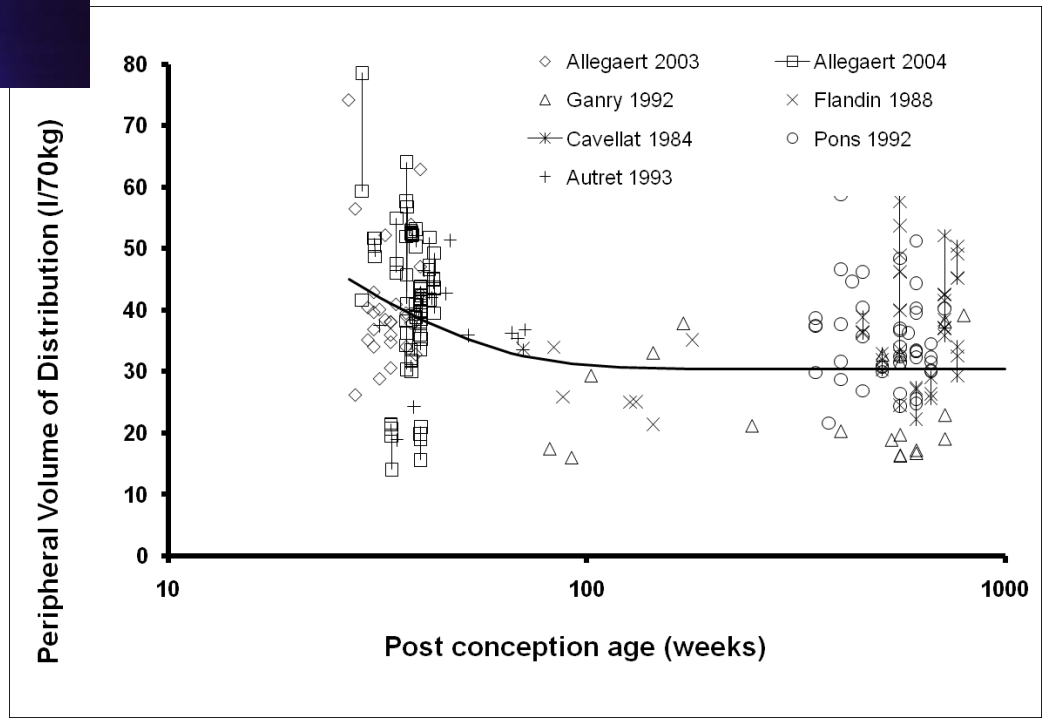
Anderson et al. Anesthesiology 1999

hogere doseringen rectaal ?



Anderson et al. Anesthesiology 1999

body water/paracetamol distribution



Anderson BJ *et al*, Paediatr Anaesth 2004

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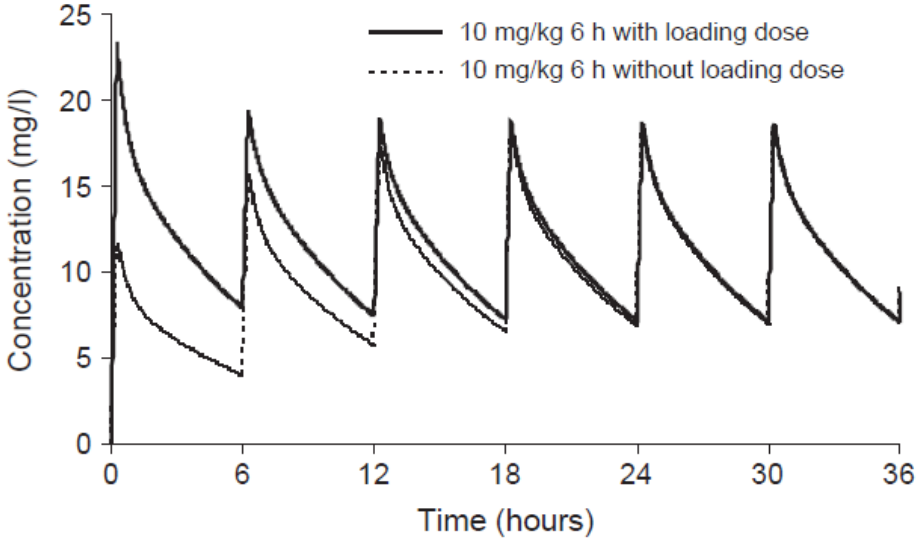
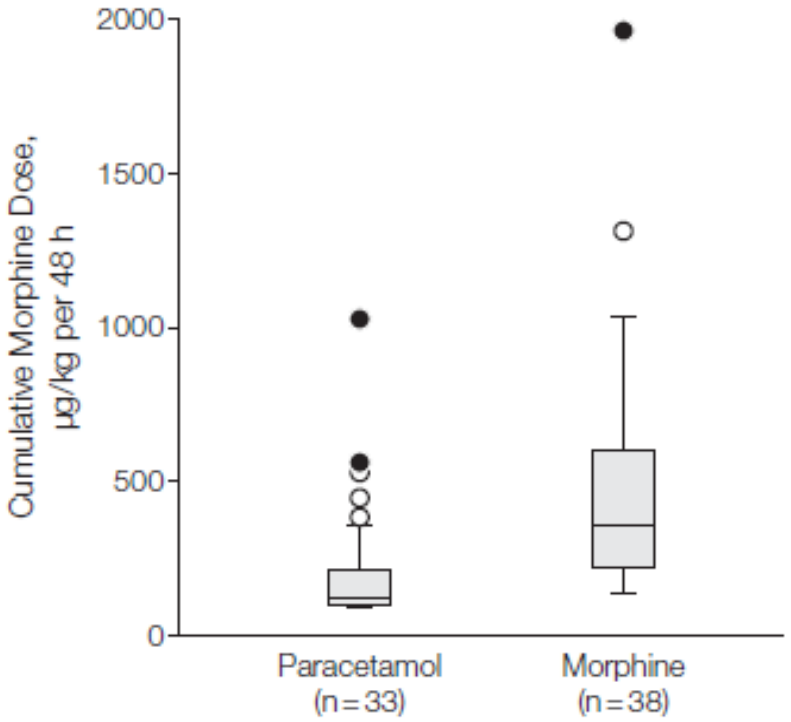


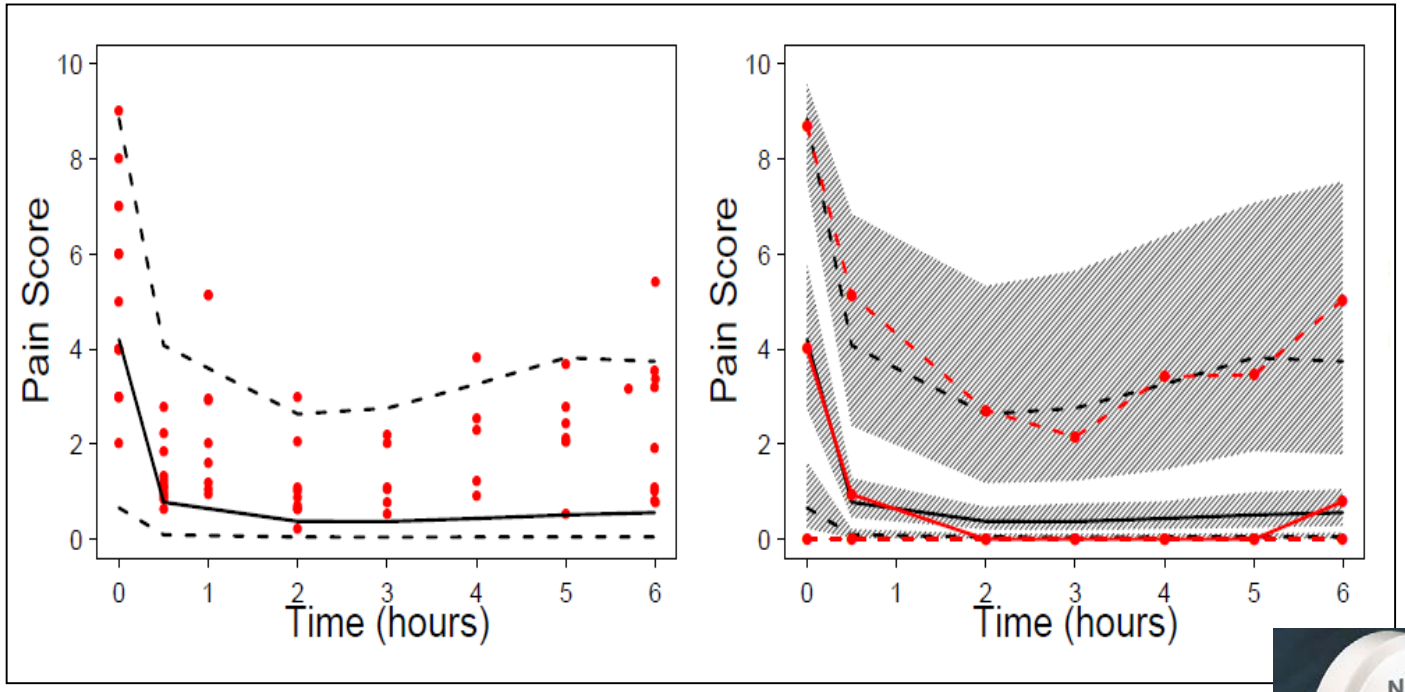
Figure 3 A typical concentration profile for neonates of 28–44 weeks' premenstrual age given a paracetamol loading dose of 20 mg/kg (black continuous line) or not given a loading dose (grey continuous line), followed by a maintenance dose of 10 mg/kg every 6 h. A mean concentration of 11 mg/l is achieved.

pooled iv paracetamol in neonates. Arch Dis Child 2011

Figure 2. Cumulative Morphine Dose for Morphine and Paracetamol Study Groups Over 48 Postoperative Hours



Ceelie et al. JAMA 2013



Pediatr Anesth, 2014

after procedural pain (heel prick), uniform negative

Reference	Study design and pain model	Paracetamol dosing	Results
Shah et al. Arch Dis Child Fetal Neonatal Ed 1998	Double blind placebo controlled trial 75 term neonates, heel prick. Facial action pain scores and cry score.	Single oral paracetamol 20 mg/kg or placebo, 60 to 90 min before prick.	No differences in facial action pain scores, nor in cry score.
Bonetto et al. Arch Argent Pediatr 2008	Prospective randomized trial 76 term neonates, heel prick pain scores (NIPS, neonatal infant pain score>4)	Placebo, dextrose (25%) EMLA or oral paracetamol (20 mg/kg, 60 min)	NIPS<4 similar between placebo, paracetamol or ELMA (47, 42 and 63 %). Oral dextrose most effective (84% NIPS<4, NNT 2.7)
Badiee et al. Saudi Med J 2009	Randomized placebo controlled trial in 72 preterm (mean 32 weeks) neonates, heel prick PIPP (premature infant pain profile) score	Single (high dose) oral paracetamol (40 mg/kg) 90 minutes before prick.	PIPP scores placebo (9,7, SD 4.2) were similar to paracetamol (11.1, SD 3.8)

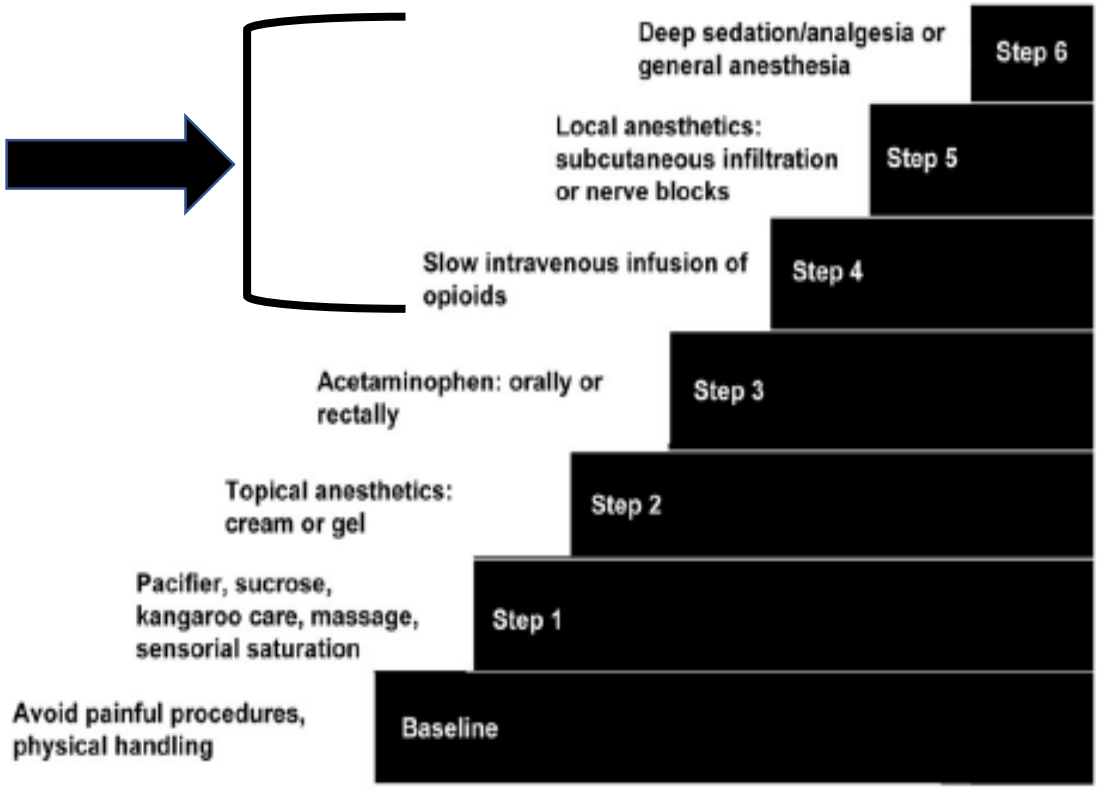
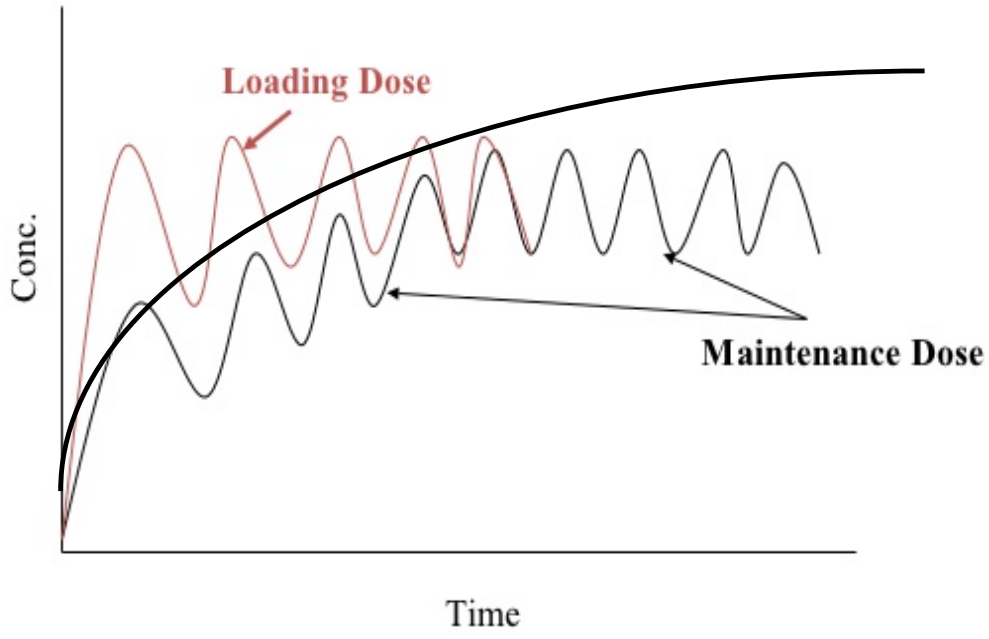


Figure 1. Stepwise approach to neonatal analgesia.

Table 2 Dose suggestions for systemic analgesics in the surgical term neonate are formulated based on the currently available evidence on pharmacokinetics or dynamics of these analgesics in neonates (iv= intravenous) [4, 5, 10, 12]

	Route	Loading dose	Maintenance dose
Morphine	iv	50–100 μg/kg	10–30 μg/kg/h
Fentanyl	iv	1–3 μg/kg	1–5 μg/kg/h
Tramadol	iv	2 mg/kg/30 min	6–8 mg/kg/day
Paracetamol	Oral	20 mg/kg	4×10 mg/kg/day
	Rectal	40 mg/kg	4×20 mg/kg/day
	iv	20 mg/kg	4×10 mg/kg/day

OPLADEN IS VAN BELANG, NOG MEER BIJ PASGEBORENEN



NIKS DOEN IS GEEN OPTIE

PREVENTIEVE MAATREGELEN BESTAAT EN WERKEN

PROCEDURALE PIJNSTILLING

PRO EN CO VAN SUCROSE EN DE VARIANTEN
PRO EN CO VAN TOPISCHE LOCALE ANALGETICA

PARACETAMOL WERKT, SOMS

MILDE PIJNBEELDEN
MORPHINE SPAREND
PROCEDURALE PIJNSTILLING

OPLADEN IS VAN BELANG, NOG MEER BIJ PASGEBORENEN

Belgian Association for Paediatric Anaesthesiology
Section of the Belgian Society for Anaesthesia and Reanimation

KINDER ZIEKENHUIS UZ LEUVEN

Pediatrisch Pijnsymposium 2018

De weg naar minder pediatrische pijn

Zaterdag 28 april 2018

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Air Liquide HEALTHCARE

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janssen

#dewegnaarminderpijn2018

Ontwenning na een opname op de PICU : Wat kunnen we doen?

Dr. S. Maebe, kinderarts-intensivist

UZ LEUVEN | INTENSIEVE GENEESKUNDE

Inhoud

- Achtergrond en definities
- Diagnose
  - Kliniek
  - Risicofactoren
  - Type medicatie
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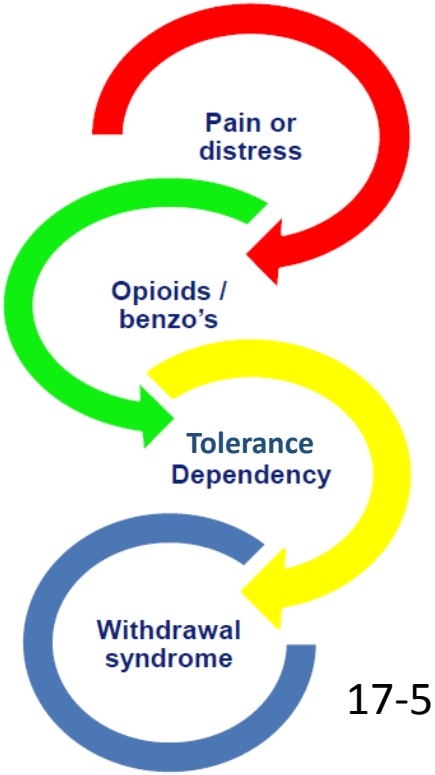
Achtergrond en definitie

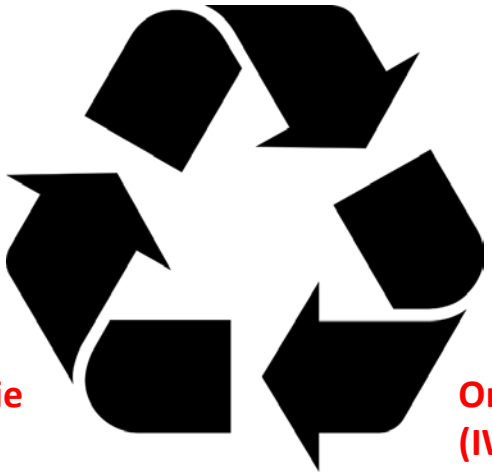


17-57 %

Achtergrond en definities

Fysische afhankelijkheid

Nood aan het verderzetten van de toediening van een product om de ontwikkeling van ontwenning te voorkomen



Tolerantie

Een bepaalde dosis van een product wordt ineffectief of een hogere dosis van het product is nodig om hetzelfde effect te bekomen

Ontwenning
(IWS: iatrogenic withdrawal syndrome)

Klinisch syndroom dat optreedt na stoppen of omschakelen van een product na verlengde blootstelling aan dat product

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Diagnose: Kliniek

- **Klinisch syndroom** dat optreedt na stoppen of omschakelen van een product na verlengde blootstelling aan dat product

- Combinatie van verschillende mogelijk symptomen

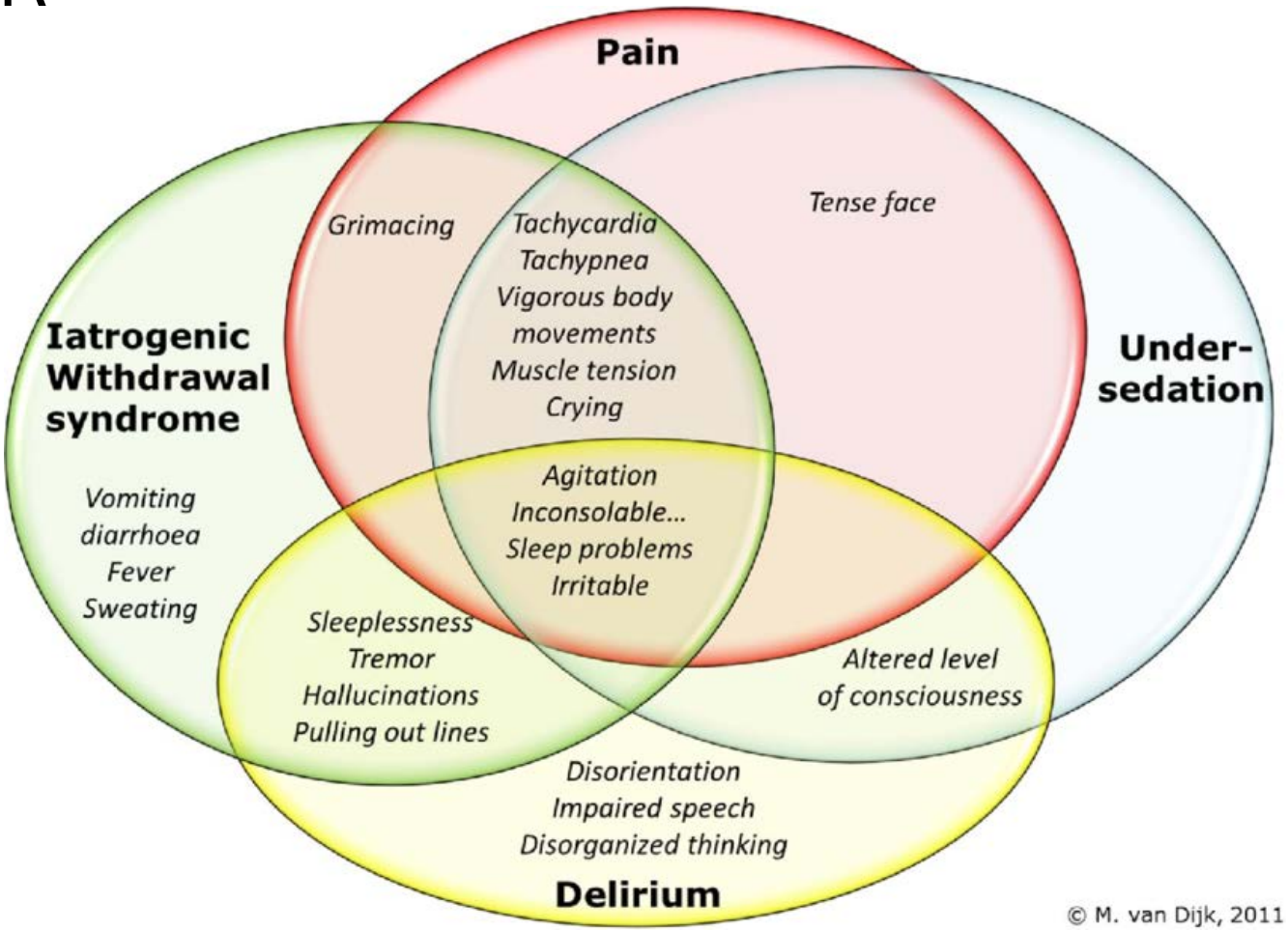
- Onder te verdelen in 3 hoofdgroepen
  - Centraal zenuwstelsel
  - GI stelsel
  - Sympathisch zenuwstelsel

Diagnose: kliniek

Centraal zenuwstelsel	Gastro-intestinaal stelsel	Sympathisch zenuwstelsel
Agitatie, rusteloosheid, irritabiliteit, **ontroostbaar huilen**, hoge schrei, **jitteriness**, hyperactiviteit, **angst**, **distress**, gedragsproblemen, zwakte, kippenvel**, niezen**, mydriase, **slaapstoornissen**, nachtmerries, **hallucinaties**, verwardheid, **tremor**, **twitching/jerking**, **abnormale bewegingen**, bewegingsstoornissen, stuipen, myoclonieën, hyperreflexie, hyperactieve Moro reflex, clonus, aphasie, bewusteloosheid, thrombocytose, **hypertonie**	**Braken**, regurgitatie, overdreven zuigreflex, nausea, moeizame voeding, **diarree**	**Grimassen**, **geeuwen**, **tachypnee**, **hypertensie**, **tachycardie**, nasale congestie, neusvleugelen, gebloemd zijn, **hoge aspiratienood**, vervellen, **koorts**, **zweten**

Opm: GI symtomen werden enkel beschreven ikv opioid withdrawal

MAAR·


Pain
Grimacing
Tachycardia
Tachypnea
Vigorous body movements
Muscle tension
Crying
Tense face
Iatrogenic Withdrawal syndrome
Vomiting
diarrhoea
Fever
Sweating
Under-sedation
Agitation
Inconsolable…
Sleep problems
Irritable
Sleeplessness
Tremor
Hallucinations
Pulling out lines
Altered level of consciousness
Disorientation
Impaired speech
Disorganized thinking
Delirium
© M. van Dijk, 2011

Diagnose: kliniek

- Overlap tussen symptomen van angst, pijn, delier en ontwenning!
- Hoe onderscheid maken:

1. Sluit andere oorzaken uit, ontwenning is een uitsluitingsdiagnose!

Bv shock, CNS infectie, CVA, sepsis, metabole ontregeling, delier

2. Gebruik gevalideerde monitoringtools
   - Withdrawal Assessment Tool (WAT-1)
   - Sophia Observation withdrawal Symptoms-scale (SOS)

3. Correlatie in de tijd met stoppen van medicatie: 1-72h

WITHDRAWAL ASSESSMENT TOOL VERSION 1 (WAT – 1)

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Patient Identifier														
	Date:													
	Time:													
Information from patient record, previous 12 hours														
Any loose /watery stools	No = 0 Yes = 1													
Any vomiting/wretching/gagging	No = 0 Yes = 1													
Temperature > 37.8°C	No = 0 Yes = 1													
2 minute pre-stimulus observation														
State	SBS[1] ≤ 0 or asleep/awake/calm = 0 SBS[1] ≥ +1 or awake/distressed = 1													
Tremor	None/mild = 0 Moderate/severe = 1													
Any sweating	No = 0 Yes = 1													
Uncoordinated/repetitive movement	None/mild = 0 Moderate/severe = 1													
Yawning or sneezing	None or 1 = 0 ≥2 = 1													
1 minute stimulus observation														
Startle to touch	None/mild = 0 Moderate/severe = 1													
Muscle tone	Normal = 0 Increased = 1													
Post-stimulus recovery														
Time to gain calm state (SBS[1] ≤ 0)	< 2min = 0 2 - 5min = 1 > 5 min = 2													
Total Score (0-12)														

SOS - Sophia Observation withdrawal Symptoms-scale
(Children 0 – 16 years)

Sticker with patient's name

Date _____

Time _____

Observer _____

Step 1		Explanation
Heart rate	/min.	*Enter highest rate in past 4 hours if present, otherwise read the monitor first or feel pulse.*
Breathing rate (tachypnoe)	/min.	*Enter highest rate in past 4 hours if present, otherwise read the monitor first or count breathing.*
Baseline value heart rate	/min.	*Please turn over for instruction on determining baseline value.*
Baseline value breathing rate	/min.	*Please turn over for instruction on determining baseline value.*

Step 2	Tick if yes	
Autonomic dysfunction		
1 Tachycardia	☐	*Yes if heart rate exceeds baseline value by ≥ 15%.*
2 Tachypnea	☐	*Yes if breathing rate exceeds baseline value by ≥ 15%.*
3 Fever	☐	*Yes if body temperature exceeded 38.4 °C in past 4 hours.*
4 Sweating	☐	*Not caused by room temperature, clothing, swaddling e.g.*
Central nervous system irritability		
5 Agitation	☐	*Yes if child shows at least one of these signs: irritable, restless, agitated, fidgety.*
6 Anxiety	☐	*Unrest or anxious face (eyes wide open, eyebrows tense and raised). Behavior can vary from panicky to draw back.*
7 Tremors: ***(pick one)***		*Slight, involuntary rhythmic movements of hand and/or feet.*
• Spontaneous	☐	*Note: please turn over for instructions.*
• In response to environmental stimuli	☐	
8 Motor disturbance: ***(pick one of four)***		
Slight muscle jerks:		*Involuntary, of forearms/lower legs, muscle twitching.*
• Spontaneous	☐	
• In response to environmental stimuli	☐	
Uncontrolled, robust movements:		*Choreoathetosis of arms, legs and/or head.*
• Spontaneous	☐	
• In response to environmental stimuli	☐	
9 Increased muscle tension	☐	*Clenched fists or tense clenched toes.*
10 Inconsolable crying	☐	*Yes if child cannot be consoled by parents or by offering distraction, e.g. pacifier, food; or game playing for older children. Score silent crying in intubated children.*

Best KM, Boullata JI, Curley MA. Risk factors associated with iatrogenic opioid and benzodiazepine withdrawal in critically ill pediatric patients: a systematic review and conceptual model. Pediatr Crit Care Med. 2015

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Diagnose: risicofactoren

Patient	Process	System
• **Duur > 5 dagen** • **Cumulatieve dosis** • **Leeftijd** • Cognitieve beperking • Ernst van ziekte • Farmacogenetica	• Gebruik protocols • Continue versus intermittente toediening • Soort medicatie • >3 medicaties	• Staffing • Toegelaten medicatie buiten PICU • Team approach

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Diagnose: types medicatie

1/ Veel evidentie voor ontwenning na verlengde toediening

- Opiaten
  - Bv fentanyl, morfine
- Benzodiazepines
  - Bv midazolam, lorazepam
- Barbituraten
  - Bv pentothal

2/ Evidentie uit case reports/series, kleine observationele studies

- Propofol
- Isoflurane (inhalatie-anestheticum)
- Chloralhydraat
- α2-agonisten (clonidine, dexmedetomidine)

3/ Medicatie waarbij ontwenning niet is beschreven

- Ketamine – wel tolerantie

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Behandeling: Algemene principes en preventie

Belangrijk:

Wat volgt is afgeleid uit :

- Beschikbare literatuur: schaars, geen RCT, veel variatie in gewoontes
- Selectie van PICU guidelines:
  - Nederland: Sophia kinderziekenhuis, Rotterdam
  - Canada: Sick Kids, Toronto
  - US: Children's hospital of Philadelphia
  - US: Natiowide Children's, Columbus, Ohio
  - Nieuw-Zeeland: Starship Children's Hospital, Auckland
  - UK: GOSH, London
  - UK: Nottingham Children's hospital
  - Australië: RCH, Melbourne

=> Veelal gebaseerd op expert opinion en lokale gewoontes !

Behandeling: Algemene principes en preventie

1) Correct gebruik van analgosedatie: dosis, duur, combinatie

2) Inventariseren van gebruikte producten, duur en cumulatieve dosis om risico in te schatten
3) Evalueer andere redenen om medicatie verder te zetten

   Bv nood aan opiaten voor pijncontrole, benzo ikv convulsies

4) Start monitoren van ontwenning bij start afbouw
   - Gebruiken van WAT-1 of SOS

Behandeling: Algemene principes en preventie

5) Langere toediening = tragere afbouw
   - < 5 dagen: stop zonder afbouw, WAT-1/SOS overwegen
   - 5-10(14) dagen: dosisreductie per 10-20% van **originele dosis** 1x/24u
   - > 10(14) dagen: Dosisreductie per 5-10% van originele dosis 1x/24u

6) Volgorde igv meerdere analgosedativa
   1. Opiaten - Benzodiazepines
   2. Chloral hydraat (afbouw nodig??)
   3. Clonidine verderzetten tot stop opiaten en benzodiazepines, dan afbouw tot stop

Behandeling: Algemene principes en preventie

6) Vroegtijdige switch naar langwerkende preparaten en enterale toediening zo mogelijk
   - Gebruik van aangepaste conversie tabellen
   - IV opiaten → morfine, methadone
   - IV benzodiazepines → diazepam, lorazepam
   - IV clonidine → PO clonidine
   - Continue infuus halveren bij 1^{e} PO dosis, stop bij 2^{e} dosis

7) Na afbouw tot lage dosis, verleng interval vooraleer te stoppen

8) Scoor tot 48-72h na stoppen van alle medicatie

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Behandeling: niet farmacologisch

1. Beperkt omgevingsstimuli
2. Zuigelingen: inbakeren, borstvoeding, wiegen, tutje
3. Oudere kinderen: massage, relaxatietherapie
4. Aangepaste voeding

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Behandeling: farmacologisch

1. Optreden van ontwenning tijdens afbouw opioiden/benzodiazepines
   - Geef een extra dosis van het opioid: bv. 50% van laatste intermittente dosis of 50% van laatste uurdosis van een continu infuus
   - Verhoog het onderhoud weer naar de vorige dosis/infuussnelheid
   - Bouw niet opnieuw af de volgende 24u
   - Overweeg om trager af te bouwen en/of slechts 1 product ipv 2

Behandeling: farmacologisch

2. Bij onvoldoende effect van voorgaande maatregelen
   - Als pt ook benzodiazepines krijgt: extra dosis (bv lorazepam 0,1 mg/kg)

   en overweeg verhogen onderhoudsdosis
   - Overweeg associëren clonidine *
     - PO 1 – max 5 mcg/kg/dosis
     - IV 0,5-3 mcg/kg/u

3. Chloral hydraat
   - Gebruikt als sedativum geassocieerd aan opiaten/benzodiazepines (enteraal)
   - Gebruik om ontwenning te behandelen??
   - Nood aan afbouw niet duidelijk, mogelijk niet nodig als reeds benzodiazepine
   - Dosis 10-20 mg/kg 4x/d tijdens afbouw, dan interval verlengen

   OF overweeg stop en rescue dosis 10-20 mg/kg indien ontwenning

Behandeling: farmacologisch

4. Clonidine
   - Bouw als laatste af
   - Te snelle afbouw geeft vnl sympathische symptomen (bv hypertensie)

   → bloedrukmonitoring is aangewezen

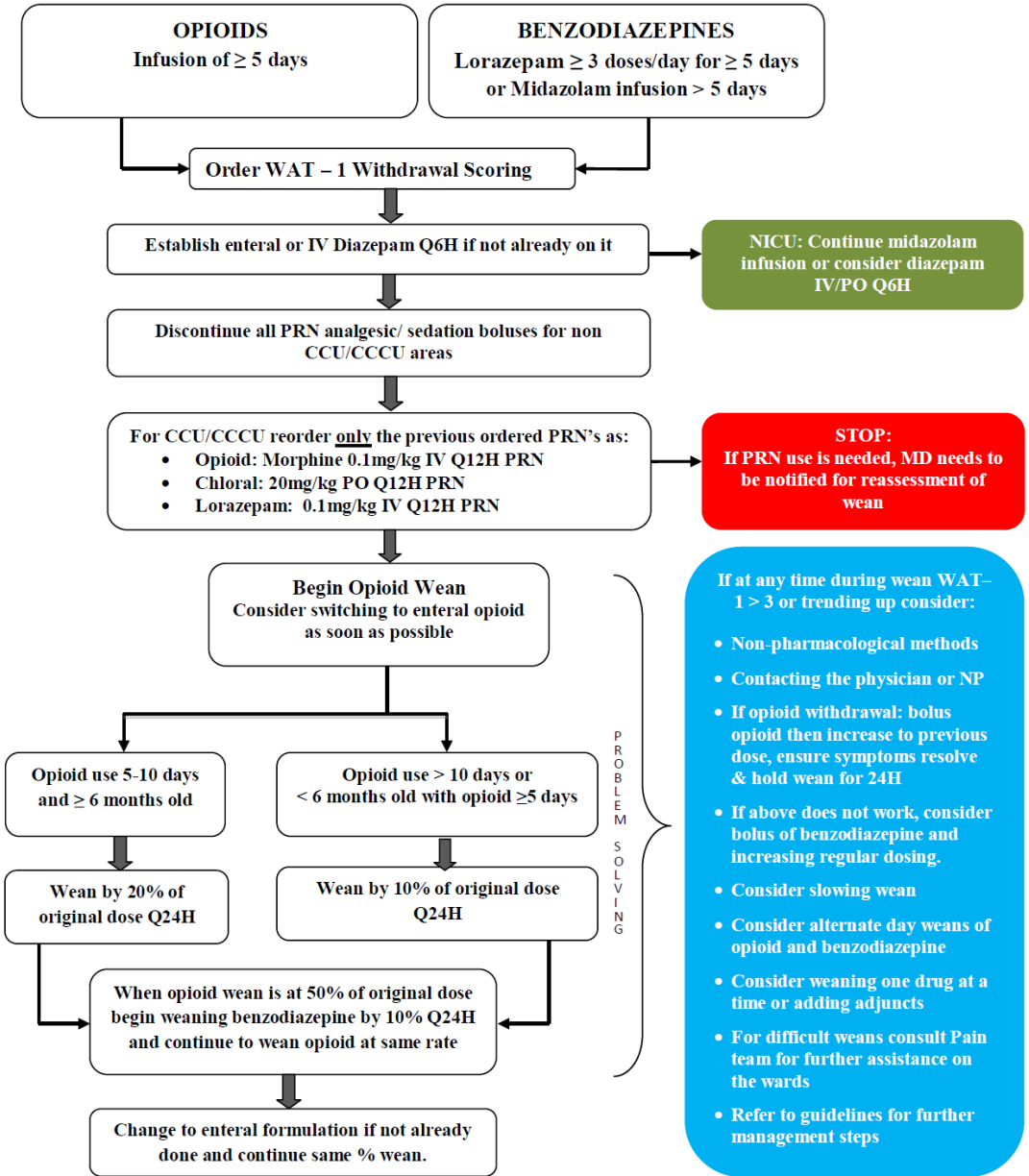
   → Afbouwen per 10-20 % 1x/24-48u

   → Vanaf dosis 0,5-1 mcg/kg: verleng interval

Behandeling: farmacologisch

- Wat met dexmedetomidine?
  - Hyperselectieve α2-agonist
  - Doel: ‘conscious sedation’
  - Bij ons enkel IV, op PICU (US ook PO beschikbaar)
  - Bijwerking: vnl. bradycardie, hypotensie
  - Gebruik: geassocieerd als sedativum of ikv ontwenning
  - Geleidelijk afbouwen, risico op ontwenning/rebound hypertensie
  - Off label bij kinderen
  - Geen evidence based informatie over gebruik bij kritiek zieke kinderen

Weaning Algorithm for Combination Use of Opioids and Benzodiazepines



Aandachtspunten

- Afbouw is steeds in percentage van de originele dosis !

  → afbouw per 20% = stop na 5 dagen
- Methadone kan QT verlenging veroorzaken
- Actieve metabolieten van morfine kunnen accumuleren bij patiënten met nierfalen
- Chloralhydraat kan verlengde werking hebben bij jonge kinderen, patiënten met lever/nier finsufficiëntie

Take home messages

- Ontwenning komt frequent voor in (ex) PICU-populatie
- Vooral geassocieerd aan leeftijd, duur en cumulatieve dosis
- Best beschreven bij opioiden en benzodiazepines,

  maar ook bij propofol, inhalalatie-anesthestica, chloralhydraat, α2 agonisten
- Preventieve maatregelen bij afbouw, ook niet farmacologisch
- Gebruik gevalideerde assessment tools WAT-1 of SOS
- Lokale protocols, heterogeen, weinig evidence based informatie

VRAGEN?

Belangrijkste referenties

- Best KM et al. Patient, process, and system predictors of iatrogenic withdrawal syndrome in critically ill children. Crit Care Med. 2017 Jan;45(1):e7-e15
- Vet NJ et al. Sedation in critically ill children with respiratory failure. Front Pediatr. 2016 Aug 24;4:89
- Harris J et al. Clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children: an ESPNIC position statement for healthcare professionals. Intensive Care Med (2016) 42:972-986
- Best KM, Boullata JI, Curley MA. Risk factors associated with iatrogenic opioid and benzodiazepine withdrawal in critically ill pediatric patients: a systematic review and conceptual model. Pediatr Crit Care Med. 2015 Feb;16(2):175-83
- Ista E, Tibboel D, van Dijk M Opioid and benzodiazepine withdrawal syndrome: can we predict and prevent it? Pediatr Crit Care Med. 2015 Feb;16(2):195-6
- Anand KJ et al. Tolerance and withdrawal from prolonged opioid use in critically ill children. Pediatrics. 2010 May;125(5):e1208-25
- Birchley G. Opioid and benzodiazepine withdrawal syndromes in the paediatric Intensive care unit: a review of recent literature. Nurs Crit Care. 2009 Jan-Feb;14(1):26-37
- Franck LS et al. The Withdrawal Assessment Tool-1 (WAT-1): an assessment instrument for monitoring opioid and benzodiazepine withdrawal symptoms in pediatric patients. Pediatr Crit Care Med. 2008 Nov;9(6):573-80
- Ista E. et al. Withdrawal symptoms in children after long-term administration of sedatives and/or analgesics: a literature review. "Assessment remains troublesome". Intensive Care Med. 2007 Aug;33(8):1396-406
- Tobias JD. Tolerance, withdrawal, and physical dependency after long-term sedation and analgesia of children in the pediatric intensive care unit. Crit Care Med. 2000 Jun;28(6):2122-32

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