# ILLAMÅENDE OCH KRÄKNING VAD ÄR NYTT DE SISTA FEM ÅREN?

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### **PONV**

Postoperative Nausea and Vomiting Illamående och kräkning efter operation.



#### **PDNV**

PostDischarge Nausea and Vomiting Illamående och kräkning efter utskrivning.



2013 - 2018

Vad är nytt?

Historia – vad visste vi 2013?

Vad är publicerat? Vad är viktigt?





#### *Expertgruppsutlåtande*

## Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

Tong J. Gan, MD, MHS, FRCA,\* Pierre Diemunsch, MD, PhD,† Ashraf S. Habib, MB, FRCA,\* Anthony Kovac, MD,‡ Peter Kranke, MD, PhD, MBA,§ Tricia A. Meyer, PharmD, MS, FASHP, Mehernoor Watcha, MD,¶ Frances Chung, MBBS,# Shane Angus, AA-C, MS,\*\* Christian C. Apfel, MD, PhD,†† Sergio D. Bergese, MD,‡† Keith A. Candiotti, MD,§§ Matthew TV Chan, MB, BS, FANZCA, || Peter J. Davis, MD,¶¶ Vallire D. Hooper, PhD, RN, CPAN, FAAN,## Sandhya Lagoo-Deenadayalan, MD, PhD,\*\*\* Paul Myles, MD,††† Greg Nezat, CRNA, CDR, USN, PhD,§§§ Beverly K. Philip, MD,|||| and Martin R. Tramèr, MD, DPhil¶¶¶



# **Generell risk för PONV** 30%

Högriskgrupper 60-80%

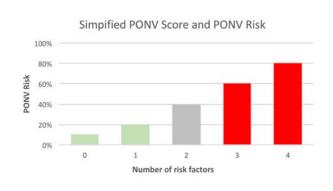


# Simplified PONV-score **Apfel Score**

Kvinna
Icke-rökare
Tidigare PONV o/e åksjuka
Postoperativa opioider













#### Table 1. Risk Factors for PONV in Adults

Table T. KISK	ractors for PONV III Addits
Evidence	Risk factors
Positive overall	Female sex (B1)
	History of PONV or motion sickness (B1)
	Nonsmoking (B1)
	Younger age (B1)
	General versus regional anesthesia (A1)
	Use of volatile anesthetics and nitrous oxide (A1)
	Postoperative opioids (A1)
	Duration of anesthesia (B1)
	Type of surgery (cholecystectomy, laparoscopic, gynecological) (B1)
Conflicting	ASA physical status (B1)
	Menstrual cycle (B1)
	Level of anesthetist's experience (B1)
	Muscle relaxant antagonists (A2)
Disproven or of	BMI (B1)
limited clinical	Anxiety (B1)
relevance	Nasogastric tube (A1)
	Supplemental oxygen (A1)
	Perioperative fasting (A2)
	Migraine (B1)

Consensus Guidelines for the Management of **Postoperative Nausea and Vomiting** 

Tong J. Gan, MD, Mrds, FRCA. \* Plante Demundou, MJ, FRQ. † Abrida S. 16666, MB. 1950.\* 100 March 1950. MB (M. 1950. MB (

PONV = postoperative nausea and vomiting; BMI = body mass index; MS = motion sickness.

#### **PROFYLAXPORTFÖLJEN**



# 5-HT3 antagonister (Ondansetron) Dopamin-2 antagonister (Droperidol, Haloperidol)

Steroider (Betamethasone)

Antihistaminer

Propofol (TIVA)

25%

Kombinerar vi ger det en **ADDITIV** effekt.



Riskfaktorer	Perioperativa överväganden	Riskvärdering Ge minst:	Profylax
Apfel Score	Generell /Regional Inhalation / TIVA	Låg risk <b>Ingen profylax</b>	
1	Opioider		Betamethason
2	Ingreppstyp	Måttlig risk 1-2 profylax	Ondansetron
3	Analgesi		Droperidol
4	Patientens önskemål	Hög risk	•
<b>T</b>	Kostnadseffektivitet	2 eller mer profylax	TIVA



#### **VAD ÄR NYTT**

Risk

Riskfaktorer

Val av anestesimetod

Profylaktiska läkemedel

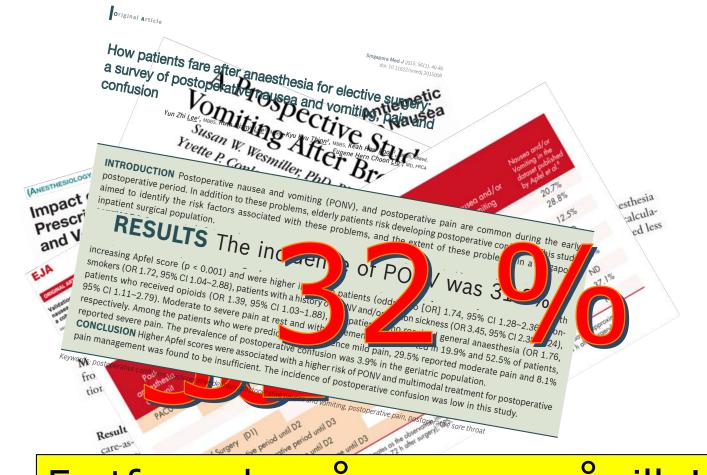
**PDNV** 

Genetik

Implementering av kunskapen



# <mark>NYTT!</mark> RISK FÖR PONV



Fortfarande många som mår illa!



#### **NYTT!** RISKFAKTORER PONV



Ålder < 50

Laparoskopi

Generell (vs Regional)

GAS (vs TIVA)

Anestesi/Operationstid

Inte så mycket ny kunskap om riskfaktorer.



#### **NYTT!** VAL AV ANESTESIMETOD

#### TIVA vs. GAS

#### **Metaanalys 2016**

#### [TIVA] vs [Gas + 1 profylax]

- 14 studier, 2000 patienter
- Ingen skillnad tidig PONV (0 2h)
- Ökad risk för sen PONV i TIVA-grupp.

#### **EJA**

Eur J Anaesthesiol 2016; 33:750-760

#### **ORIGINAL ARTICLE**

#### Total intravenous anaesthesia versus single-drug pharmacological antiemetic prophylaxis in adults

A systematic review and meta-analysis

Maximilian S. Schaefer\*, Peter Kranke\*, Stephanie Weibel, Robert Kreysing and Peter Kienbaum

BACKGROUND Postoperative nausea and vomiting anaesthesia and single-drug antiemetic prophylaxis, there (PONV) are among the most unfavourable anaesthetic outcomes attributed to the administration of inhaled anaesthetics. Accordingly, inhaled anaesthetics are frequently needs to be established based on robust data.

pharmacological prophylaxis with total intravenous anaesthesia (TIVA) for prevention of PONV.

were retrieved from MEDLINE, CENTRAL and EMBASE.

ELIGIBILITY CRITERIA Randomised controlled trials on adult patients undergoing general anaesthesia with at least one group receiving propofol-based intravenous anaesthesia without further antiemetic prophylaxis, and one group receiving inhalational anaesthesia with single-drug antiemetic STUDY REGISTRATION This systematic review with meta-

RESULTS Fourteen studies involving 2051 patients were included. Compared with TIVA, after inhalational

was no difference in the overall risk of PONV [relative risk (RR) 1.06, 95% confidence interval (CI) 0.85; 1.32, GRADE rating moderate], nor was there any difference substituted by propofol when patients are at risk of PONV. in the risk of postoperative vomiting (RR 1.17, 95% As, on some occasions, inhalational anaesthesia may be Cl 0.78; 1.76), need for rescue medication (RR 1.16, favourable, the relative impact of propofol anaesthesia 95% CI 0.68; 1.99) or early PONV (RR 1.06, 95% CI 0.88; 1.27). However, TIVA was associated with an increased risk of late PONV (RR 1.41, 95% CI 1.10; OBJECTIVE To compare the effectiveness of a single-drug

1.79, P=0.006). Six studies investigated other sideeffects associated with anaesthesia and found no differences between the two groups. Finally, there was DESIGN Systematic review of randomised controlled trials evidence of a publication bias that included smaller studies favouring TIVA.

DATA SOURCES All available studies until 29 April 2015 CONCLUSION This meta-analysis confirms the results from indirect comparisons in individual studies: instead of substituting inhalational anaesthesia with propofol-based TIVA, a similar antiemetic effect can be achieved by adding singledrug pharmacological prophylaxis to the inhalational anaes-

> analysis was registered at PROSPERO (www.crd.york.ac.uk/ PROSPERO), study number CRD42015019571.

Published online 2 August 2016

#### Om GAS använd adekvat mängd antiemetika



#### **NYTT!** VAL AV ANESTESIMETOD

#### **OFA**

#### **OPIOID-FRI ANESTESI**

British Journal of Anaesthesia 112 (5): 906–11 (2014) Advance Access publication 18 February 2014 · doi:10.1093/big/aet551

Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis

P. Ziemann-Gimmel\*, A. A. Goldfarb, J. Koppman and R. T. Marema

#### **Classic:**

Gas + Fentanyl

TIVA:

Dex + Propofol + Ketamine

**Table 4** Comparison of PONV severity. CI, confidence interval; n/a, not applicable. \*Wilcoxon rank-sum test; †Fisher's exact test

Classic group (n=59)	TIVA group (n=60)	P-value	RR (95% CI)
37 (62.7%)	48 (80.0%)		
13 (22.0%)	9 (15.0%)		
2 (3.4%)	3 (5.0%)		
7 (11.9%)	0 (0%)	0.02*	n/a
7 (11.9%)	0 (0%)	0.006†	1.13 (1.02, 1.25)
5 (8.5%)	0 (0%)	0.02 <sup>†</sup>	1.09 (1.00, 1.19)
	group (n=59) 37 (62.7%) 13 (22.0%) 2 (3.4%) 7 (11.9%) 7 (11.9%)	group (n=59) group (n=60)  37 (62.7%) 48 (80.0%)  13 (22.0%) 9 (15.0%)  2 (3.4%) 3 (5.0%)  7 (11.9%) 0 (0%)  7 (11.9%) 0 (0%)	group (n=59) (n=60)  37 (62.7%) 48 (80.0%)  13 (22.0%) 9 (15.0%)  2 (3.4%) 3 (5.0%)  7 (11.9%) 0 (0%) 0.002*  7 (11.9%) 0 (0%) 0.006†



#### MÅNGA STUDIER!

Jämförelser, kombinationer, patientgrupper.

Kombinationer av läkemedel från olika grupper effektivt för att reducera PONV.

Säkerhet? Nya läkemedel?



# NYTT! PROFYLAKTISKA LÄKEMEDEL SÄKERHET

#### ÄR DET FARLIGT ATT GE STEROIDER?

Sårläkning, Infektioner, Sockerkontroll





#### ÄR DET FARLIGT ATT GE STEROIDER?

British Journal of Anaesthesia 110 (2): 191–200 (2013) Advance Access publication 5 December 2012 - doi:10.1093/bja/aes431 BJA

Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis

N. H. Waldron, C. A. Jones, T. J. Gan, T. K. Allen and A. S. Habib\*
Department of Anesthesiology, Duke University Medical Center, Box 3094, Durham, NC 27710, USA
\* Corresponding author. E-mail: habib001@mc.duke.edu

Meta-analys > 5000 patienter

4-5 mg lika bra som 8-10 mg på PONV.

Ingen skillnad i infektioner/sårläkning

Högre blodsocker postop





#### ÄR DET FARLIGT ATT GE STEROIDER?

BJA 2017

Intraoperative dexamethasone does not increase the risk of postoperative wound infection: a propensity score-matched post hoc analysis of the ENIGMA-II trial (EnDEX)

T. Corcoran $^{1,2,3,4,*}$ , J. Kasza $^4$ , T. G. Short $^5$ , E. O'Loughlin $^{2,6}$ , M. T. V. Chan $^7$ , K. Leslie $^{4,8,9}$ , A. Forbes $^4$ , M. Paech $^{1,2}$  and P. Myles $^{4,10}$ , for the ENIGMA-II investigators $^\dagger$ 

Sub-analys i studie om 70% N2O

Högriskpatienter, även diabetiker.

2000 hade fått steroider av 5000

Ingen skillnad i sår infektioner eller allvarliga händelser

Förefaller säkert för diabetiker





#### ÄR DET FARLIGT ATT GE STEROIDER?

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Dexamethasone versus standard treatment for postoperative nausea and vomiting in gastrointestinal surgery: randomised controlled trial (DREAMS Trial)

DREAMS Trial Collaborators and West Midlands Research Collaborative

#### Steroider:

Ingen högre risk för infektioner / sårläkning Försiktighet vid diabetes.

THICKUOHCI 1070 1070

Anastomosläckage 1.6% 3.1%

(Ej diabetiker)





#### Palonosetron (Aloxi<sup>(R)</sup>)

Långverkande (48h) 5-HT3 receptor blockare

Börjar komma mer studier

#### **Profylax under operation**

Kan vara bättre än våra vanliga profylax för PONV 0-48 h.

Tidseffekt?

(Gugale et al 2016, Chun et al 2014, Kim et al 2013)

Långverkande antiemetika börjar komma...





#### **Aprepitant** (Emend<sup>(R)</sup>)

Långverkande (48h) NK-1 receptor blockare

Annan angreppspunkt - annan receptor.

Mer på kräkning.

Vi vet att det fungerar och kostar (200kr). Kapsel/Oralt

Hur bra är det?





#### **Aprepitant**

#### Aprepitant as a fourth antiemetic prophylactic strategy in high-risk patients: a double-blind, randomized trial

L. C. de Morais<sup>1</sup> (6), A. M. Sousa<sup>1</sup>, G. F. Flora<sup>1</sup>, T. R. Grigio<sup>1</sup>, G. M. N. Guimarães<sup>1</sup> and H. A. Ashmawi<sup>2</sup>

Acta Anaesthesiologica Scandinavica 62 (2018) 483–492

Apfel 3-4. Laparotomier. Centrala opioider (spinal/epidural) TIVA, Ondansetron, Steroid.

	Per-protocol					
	Control group $n = 32$	Treatment group $n = 34$	<i>P</i> -value			
PONV 24 h	13 (40%)	5 (15%)	0.03			
0–2 h	1 (3%)	0	0.45			
2–24 h	12 (37%)	5 (14%)	0.04			



Pitanter lovande! Behövs fler studier!

<sup>&</sup>lt;sup>1</sup>Pain Service, Cancer Institute of the State of Sao Paulo from the University of Sao Paulo Medical School, Sao Paulo, Brazil

<sup>&</sup>lt;sup>2</sup>Pain Service, Hospital das Clínicas of the University of Sao Paulo Medical School, São Paulo, Brazil



#### **Amisulpride**

D2/D3 antagonist

Istället för droperidol, kan ges i låg dos. Mycket mindre biverkningar.





D2/D3 antagonist

Högrisk (Apfel>=2).

Amisulpride 5 mg 40% PONV

Placebo

69% PONV

Högrisk (Apfel>=3). n=1149

Kranke et al 2018

Kranke et al 2013

Inhalation + Ondansetron eller steroid.

Amisulpride 5 mg 42% PONV

Placebo **53% PONV** 

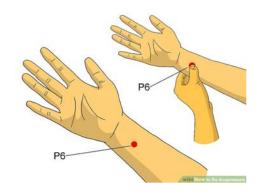
Kanske kommer en ny dopamin antagonist. Behöver jämföras mot droperidol och haloperidol.



[Intervention Review]

Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting

Cochrane review 2015



Måttlig kvalitet på studier

Effekt motsvarande antiemetika

Behövs studier som sätter in P6 i en multimodal strategi.



doi: 10.1093/bja/aew375

#### Chewing gum for the treatment of postoperative nausea and vomiting: a pilot randomized controlled trial

J. N. Darvall<sup>1,2,3,\*</sup>, M. Handscombe<sup>1</sup> and K. Leslie<sup>1,3,4,5</sup>

<sup>3</sup>Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, Melbourne, Victoria, Australia, <sup>2</sup>Royal Melbourne Hospital Clinical School, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Victoria, Australia, <sup>3</sup>Anaesthesia, Perioperative and Pain Medicine Unit, University of Melbourne, Melbourne, Victoria, Australia, <sup>4</sup>Department of Pharmacology and Therapeutics, University of Melbourne, Melbourne, Victoria, Australia and <sup>5</sup>Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

\*Corresponding author. E-mail: jai.darvall@mh.org.au

#### Ondansetron vs.

**PONV 28%** 

Funkade 39%

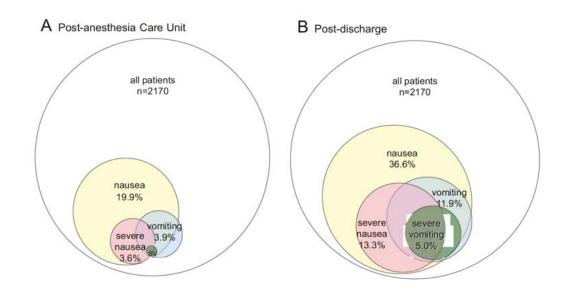


PONV 31% Funkade 75%





## PostDischarge Nausea and Vomiting Illamående och kräkning efter utskrivning vid dagkirurgi.



Många mår illa först hemma!

75-86





## PostDischarge Nausea and Vomiting Illamående och kräkning efter utskrivning vid dagkirurgi.

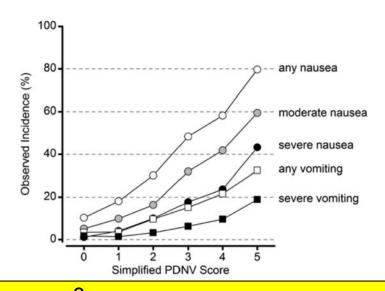
Kvinna

**Tidigare PONV** 

Yngre än 50 år

Opioider på UVA

Illamående på UVA



Vi kan värdera risk för illamående hemma innan de skrivs ut från dagvården!



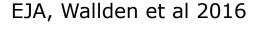


## PostDischarge Nausea and Vomiting Illamående och kräkning efter utskrivning vid dagkirurgi.

Table 2 Risk of nausea and/or vomiting in each time interval

Post- anaesthesia care unit	Immediately postsurgery, after discharge, until Day 1 (noon)	Postop. Day 1 (noon)– Day 2 (noon)	Postop. Day 2 (noon) – Day 3 (noon)	Nausea	Vomiting	Nausea and/or vomiting	Nausea and/or Vomiting in the dataset published by Apfel et al. <sup>6</sup>
PACU				16.9%	6.0%	18.8%	20.7%
	DPS			20.9%	6.3%	22.7%	28.8%
		D1-D2		9.3%	1.6%	9.7%	12.5%
			D2-D3	7.2%	0.5%	7.4%	ND
Day of Su	rgery (D1)			29.5%	10.2%	32.3%	38.5%
Posto	operative period until	D2		32.7%	11.4%	36.0%	44.8%
	Postoperative p	eriod until D3		33.6%	11.6%	34.0%	ND
Postdischarge until D2			24.6%	7.7%	26.9%	37.1%	
	Pos	stdischarge until D3		24.6%	6.7%	28.1%	ND

The comparisons with the cohort published by Apfel et al.<sup>6</sup> are estimates as the observation intervals are not exactly the same. D1-D2, postoperative day 1 (approximately 24–48 h after surgery); D2-D3, postoperative day 2 (approximately 48–72 h after surgery); DPS, immediate postsurgical day (approximately 0–24 h after surgery); PACU, post-anaesthesia care unit; ND, no data.

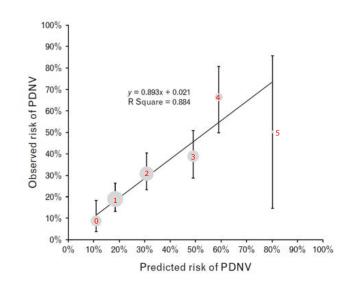






#### Validering på ett svenskt material

Kvinna
Tidigare PONV
Yngre än 50 år
Opioider på UVA
Illamående på UVA



EJA, Wallden et al 2016

PDNV-score funkar i Sverige också!



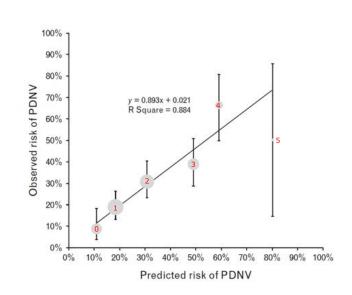


Kan vi förebygga PDNV?

Riskbedömning innan hemgång

Ge riktad profylax

**POSTPAL-studien** 







Blodprov preoperativt för att värdera risk....

#### Varianter av receptorer

Varianter av hur läkemedel metaboliseras.



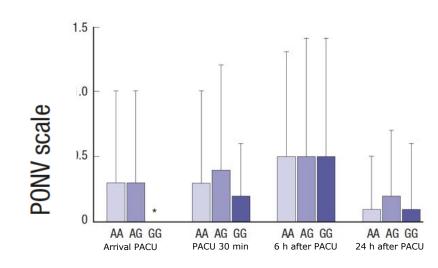


#### Varianter av receptorer

Fåtal studier. Utfall av illamående eller effekt av läkemedel.

5-HT3
Muscarin typ 3
NK-1
DA2 **µ-Opioid** 

A118G SNP



J Korean Med Sci 2015; 30: 651-657





Men...

Associationer är svaga med enskilda varianter
Förklarar inte den variabilitet vi ser mellan individer i PONV.

Troligen finns oupptäckta varianter.

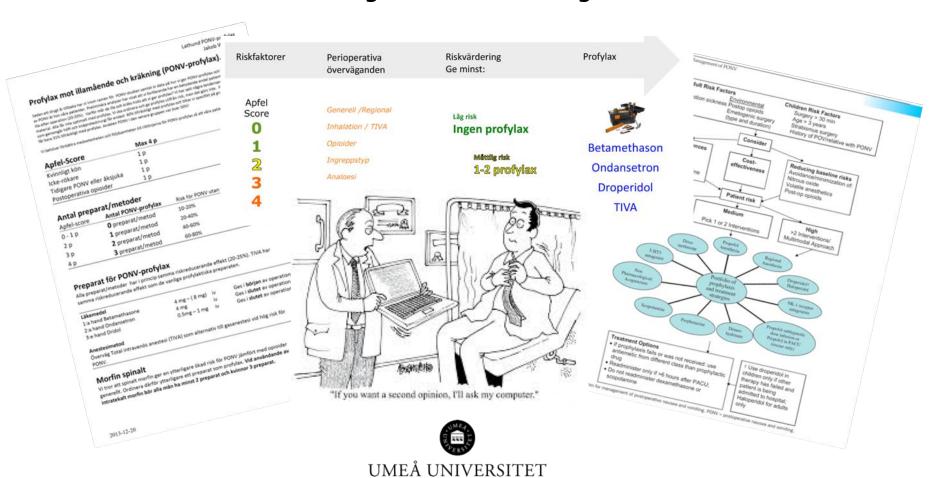
Genetik – Inget konklusivt idag. Kanske i framtiden...





#### **IMPLEMENTERING AV KUNSKAP**

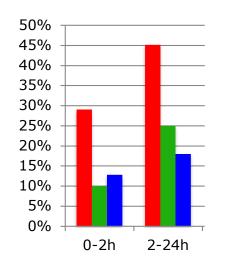
#### Hur fungerar det i verkligheten?





#### Hur fungerar det i verkligheten?

Dagkirurgi, Sundsvalls Sjukhus Kirurgi och Ortopedi Prospektiv observationstudie upp till 72 timmar. n=110



■Mindre (n=31)

■Optimal (n=40)

■Mer (n=39)



# Impact of Risk Assessments on Prophylactic Antiemetic Prescription and the Incidence of Postoperative Nausea and Vomiting

(ANESTHESIOLOGY 2014; 120:343-54)

A Cluster-randomized Trial

Teus H. Kappen, M.D., Karel G.M. Moons, Ph.D., Leo van Wolfswinkel, M.D., Ph.D., Cornelis J. Kalkman, M.D., Ph.D., Yvonne Vergouwe, Ph.D., Wilton A. van Klei, M.D., Ph.D.

**Methods:** A single-center, cluster-randomized trial was performed in 12,032 elective surgical patients receiving anesthesia from 79 anesthesiologists. Anesthesiologists were randomized to either exposure or nonexposure to automated risk calculations for PONV (without patient-specific recommendations on prophylactic antiemetics). Anesthesiologists who treated less

#### Med beslutsstöd för PONV-risk gavs mer PONV-profylax

men ... PONV 43% vs 41%





British Journal of Anaesthesia 114 (2): 252–60 (2015) Advance Access publication 1 October 2014 · doi:10.1093/bja/aeu321 BJA

Impact of adding therapeutic recommendations to risk assessments from a prediction model for postoperative nausea and vomiting<sup>†</sup>

T. H. Kappen<sup>1\*</sup>, Y. Vergouwe<sup>2,3</sup>, L. van Wolfswinkel<sup>1</sup>, C. J. Kalkman<sup>1</sup>, K. G. M. Moons<sup>1,2</sup> and W. A. van Klei<sup>1</sup>

#### Beslutsstöd PONV-risk + rekommendation

Gav i snitt 0.5 mer PONV-profylax

Reducerade PONV (OR 0.6)

Riskbedömning med beslutsstöd kan reducera PONV.





# NÅGOT VÄLDIGT ENKELT...

British Journal of Anaesthesia, 120(1): 156-163 (2018)

Simplified algorithm for the prevention of postoperative nausea and vomiting: a before-and-after study

G. Dewinter<sup>1</sup>, W. Staelens<sup>1</sup>, E. Veef<sup>1</sup>, A. Teunkens<sup>1</sup>, M. Van de Velde<sup>1,2</sup> and S. Rex<sup>1,2,\*</sup>

<sup>1</sup>Department of Anaesthesiology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium and <sup>2</sup>Department of Cardiovascular Sciences, KU Leuven, Herestraat 49, 3000 Leuven, Belgium



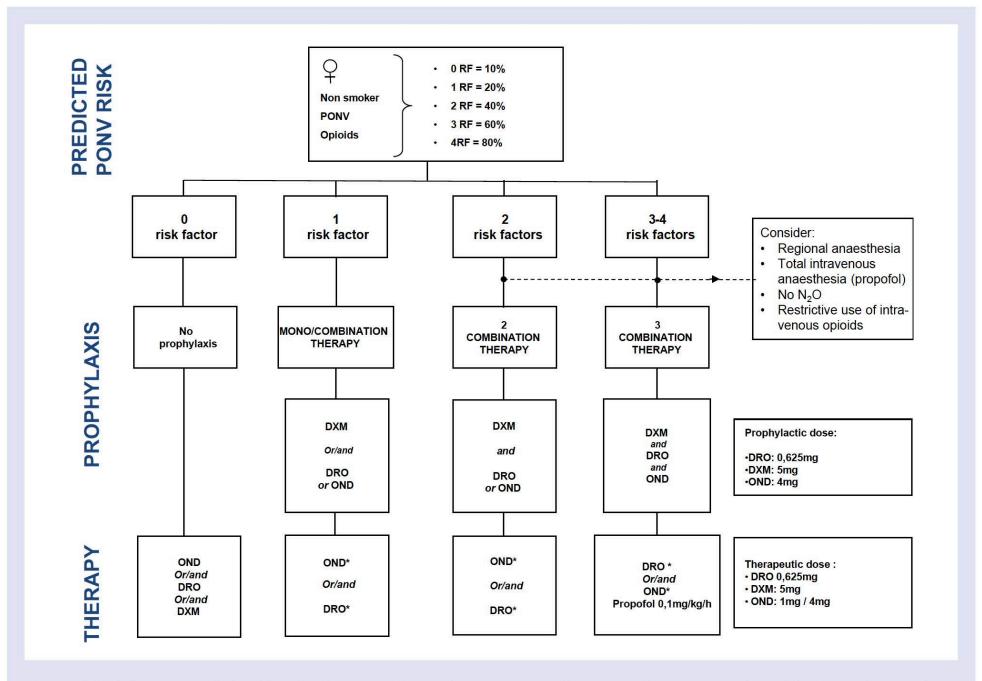
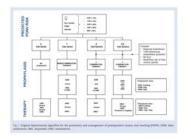


Fig 1. Original departmental algorithm for the prevention and management of postoperative nausea and vomiting (PONV). DXM, dexamethasone; DRO, droperidol; OND, ondansetron.



	Före (n=211)	
PONV 1 h	14%	
PONV 24 h	33%	
Enligt algoritm?	18%	



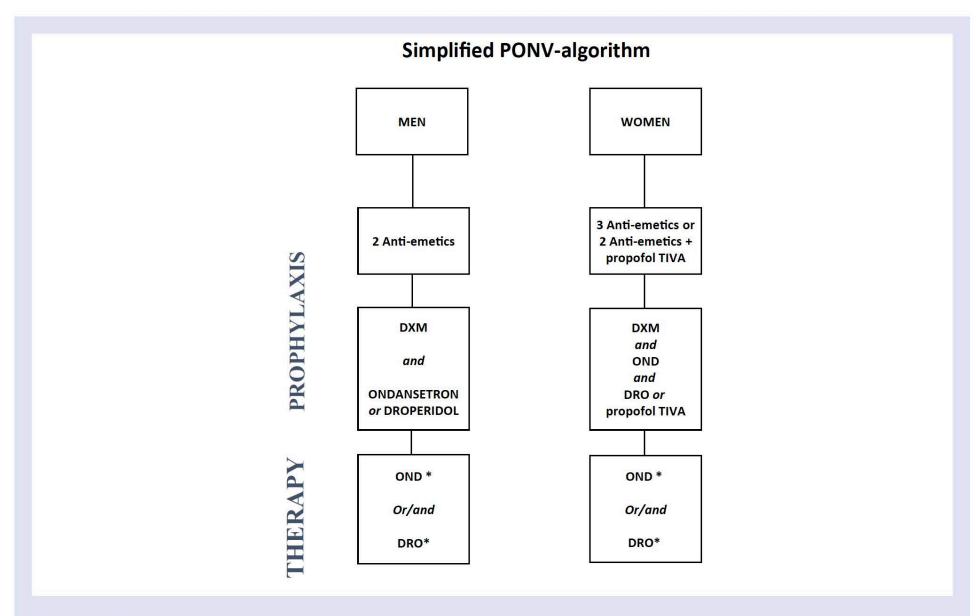
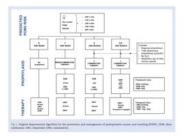
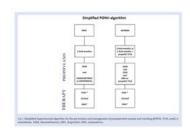


Fig 2. Simplified departmental algorithm for the prevention and management of postoperative nausea and vomiting (PONV). TIVA, total i.v. anaesthesia. DXM, dexamethasone; DRO, droperidol; OND, ondansetron.





	Före (n=211)	Efter (n=201)
PONV 1 h	14%	11%
PONV 24 h	33%	22%
Enligt algoritm?	18%	46%



**EJA** 

Eur J Anaesthesiol 2018; 35:407-465

#### **GUIDELINES**

Pre-operative evaluation of adults undergoing elective noncardiac surgery

Updated guideline from the European Society of Anaesthesiology

Implementera riktlinjer för PONV som är lokalt anpassade!

Använd preoperativ PONV-score!

Riskanpassad multimodoal strategi för att reducera PONV.

Mät PONV!



# TACK!

