Anesthesia and Gender – what's the difference?

Hirslanden Anaesthesia Symposium 2024
personalised perioperative management in anaesthesia

Martin Schläpfer, Prof. Dr. med. et M.Sc.
Institut für Anästhesiologie, UniveristätsSpital Zürich

Universität Zürich[UZH] USZ Universitäts Spital Zürich

Conflicts of interests

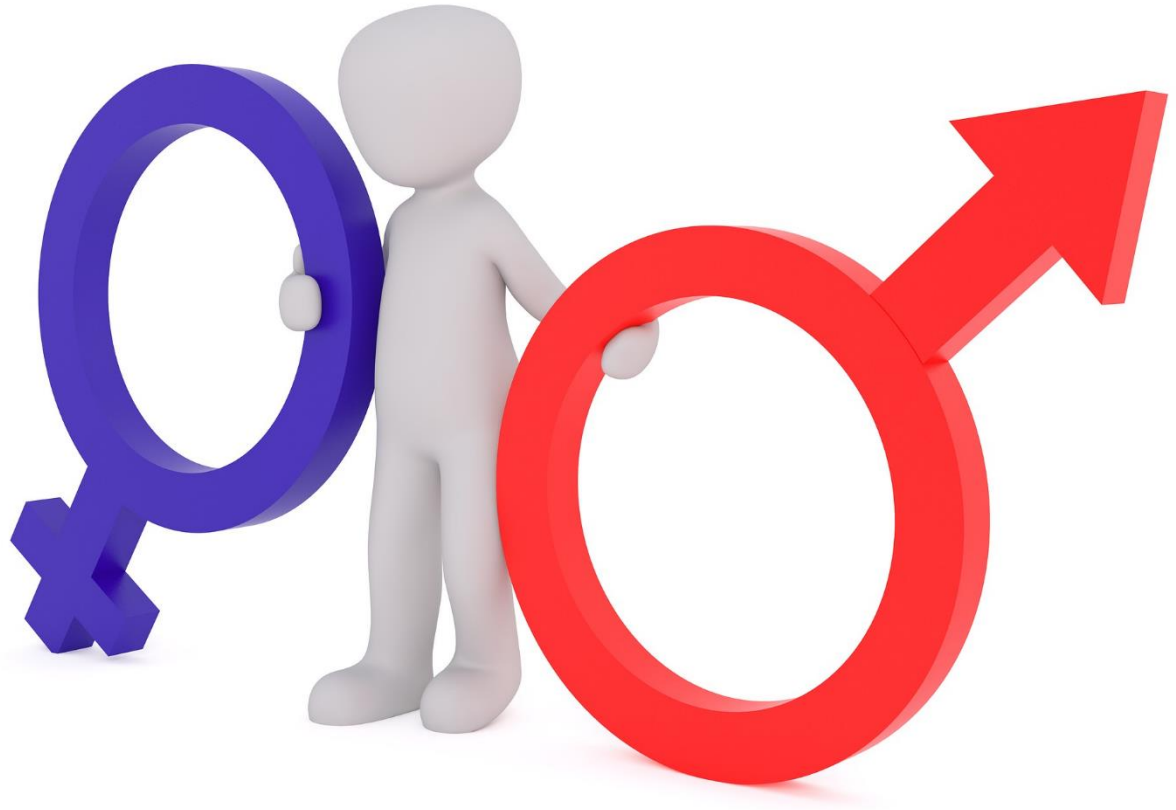
Research Grants

- Roche Diagnostics International
- Sedana Medical

Submitted patents

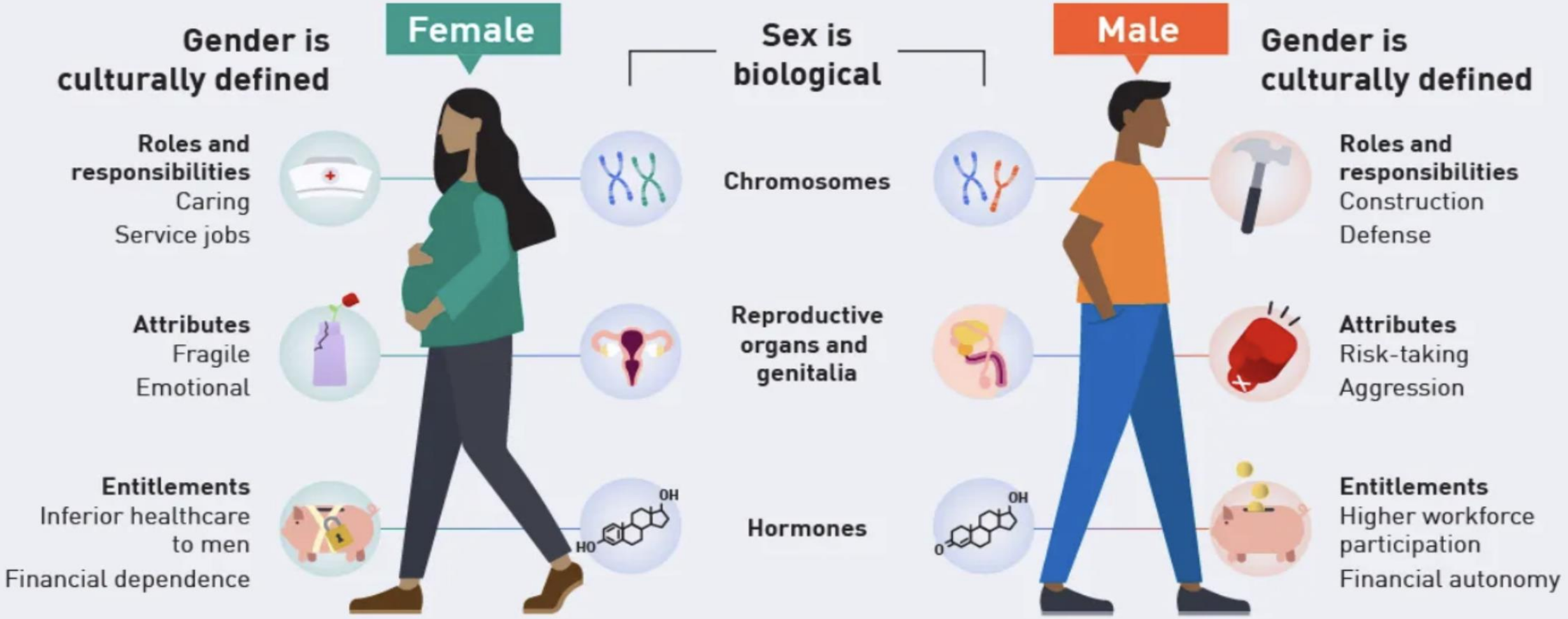
- for mitigating the negative effects of surgery and anesthesia with O_2/ CO_2 mixtures
- for an injectable formula to attenuate the harmful effects of sepsis

Are there sex/ gender differences in anesthesia? Are they relevant?



Source: www.pixabay.com

Sex versus Gender



THE LANCET

Source: Lancet Series on Gender Equality, Norms and Health. Paper 1, 2019

The most common complication after general anesthesia: postoperative nausea and vomiting (PONV)

The **most important risk factor** for the occurence **PONV** is «**female gender**».

Gan TJ et al. Anesthesia & Analgesia 2020

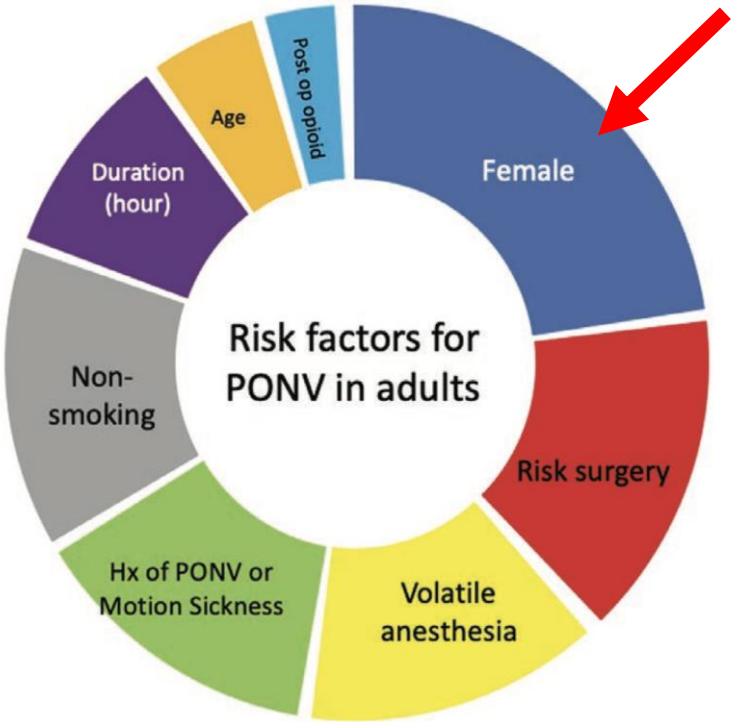


Figure 1. PONV risk factor summary. Intraoperative and postoperative risk factors of PONV in adults; the size of each segment is proportional to the odds ratios of PONV associated with each risk factors.[35] PONV indicates postoperative nausea and vomiting. Figure reused with permission from the American Society for Enhanced Recovery. For permission requests, contact info@aserhq.org.

Preoperative assessment

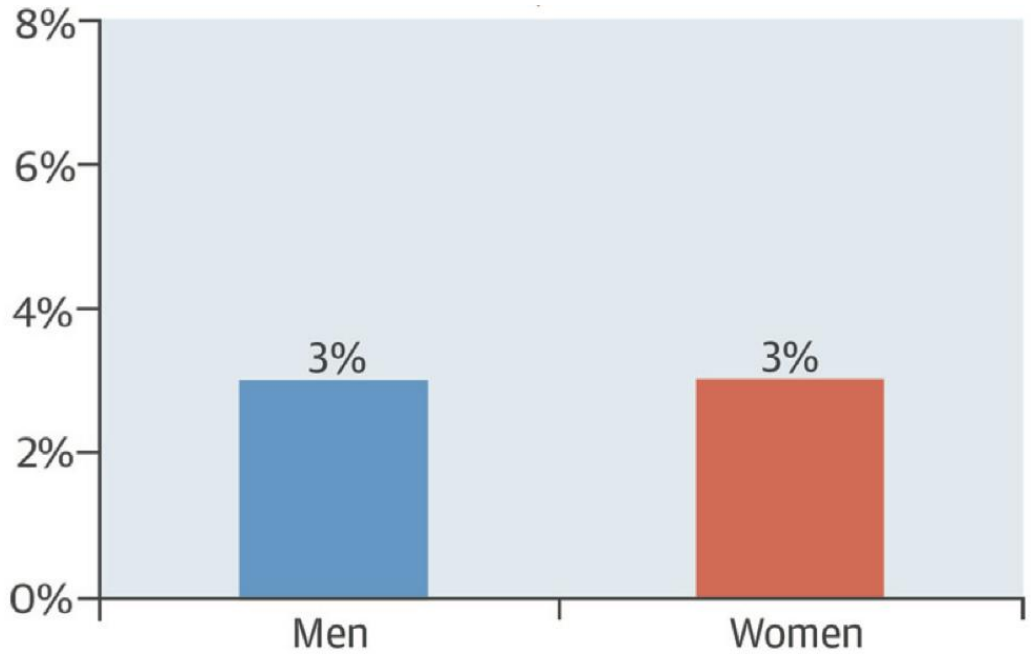
Cardiac disease and sex

- risk of arrhythmia: f>m
- risk of CVD: m>f

Preoperative assessment

CVD and sex

- recurrent ACS: f=m

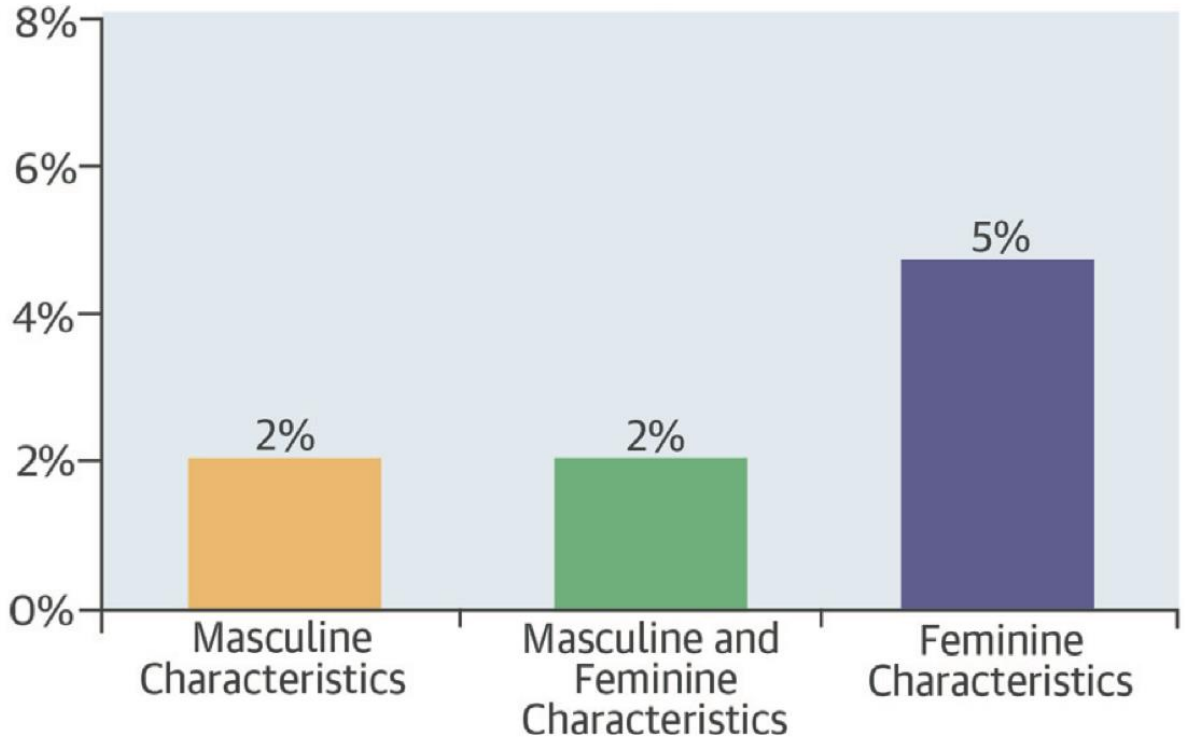


Pelletier, R. et al. J Am Coll Cardiol. 2016; 67(2):127-35.

Preoperative assessment

CVD and gender

- recurrent ACS: f>m
- ACS mortality: f>m



Preoperative assessment

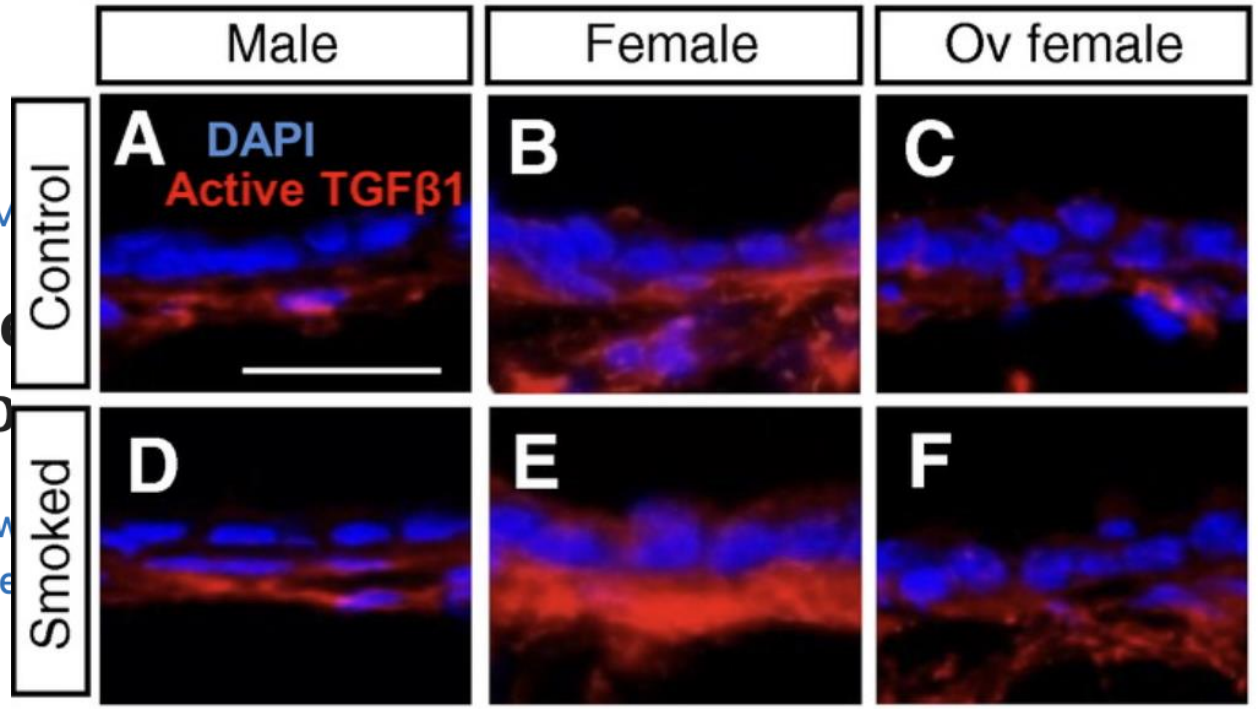
COPD and sex

- female lung more prone to COPD
- role of estrogen?

> Am J Respir Crit Care M

Sex Difference
Model of Chro

Anthony Tam [1] [2], Andrew
Harvey O Coxson [1] [2], Ste



Preoperative assessment

Further differences

- coagulation disturbances
- frailty
- risk tolerance

Physiological differences in females

Cardiac		Respiratory	
Cardiac mass	↓*	Lung volumes	↓
Diastolic function	↓	Maximal expiratory flow rates	↓
Left ventricular ejection fraction	→	Lung diffusion surface	↓
Stroke volume	↓	Exercise-induced hypoxemia	↑
Cardiac output	→	Ventilatory response to hypercapnia	↓
Resting heart rate	↑ **	Ventilatory response to hypoxia	↓
Cardiac cycle length	↓***	Apneic threshold	↓
Blood pressure	↓$	Airway diameter	↓
Coronary arteries diameter	↓		
Collateral coronary circulation	↓		
Q-T interval	↑		
Baroreflex sensitivity	↑		

Ref: Filipescu D, et al. Best Pract Res Clin Anaesthesiol. 2021

Physiological differences in females

Neurocognitive		Metabolic		Renal	
Neuronal density	↓	Basal metabolic rate	↓$$	Creatinine clearance	↓
Neuronal processing	↑	Sedentary energy expenditure	↓	Glomerular filtration rate	↓→#
Stress glucocorticoid response	↑	Core body temperature	→↑++	Renal blood flow	→
Pain threshold	↑			Renal vascular resistance	→
Sleep	Disturbed			Filtration fraction	→
				Plasma renin	↓&

Ref: Filipescu D, et al. Best Pract Res Clin Anaesthesiol. 2021

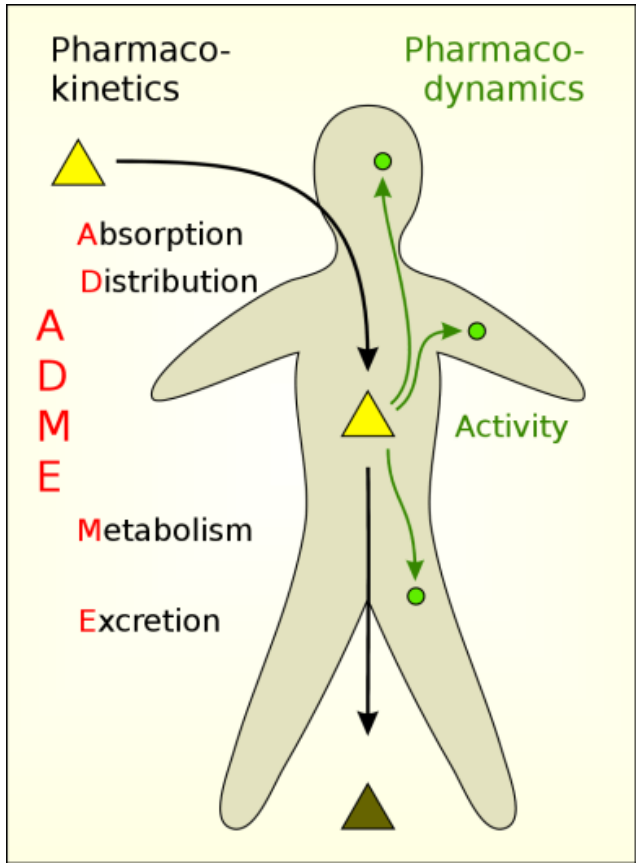
Physiological differences in females

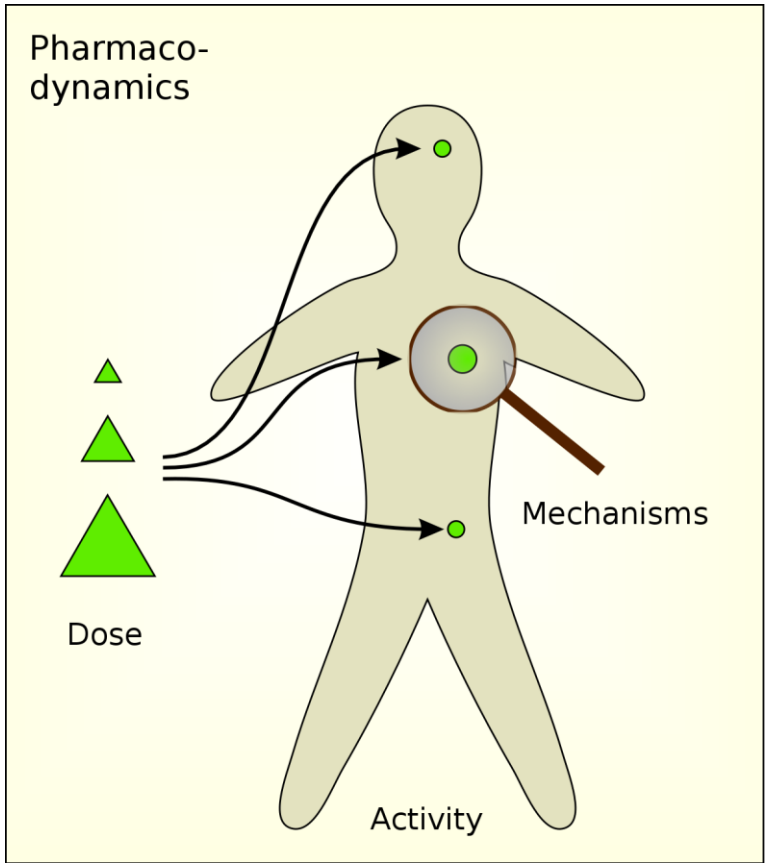
Physiological and pharmacological variables in women as compared to men

Body fat	↑ (5–10%)
Muscle mass	↓ (10%)
Total body water	↓ (15–20%)
Bone mass	↓

Ref: Filipescu D, et al. Best Pract Res Clin Anaesthesiol. 2021

Propofol – Short repetition on pharmacokinetics and pharmacodynamics





Source: www.wikipedia.com

Propofol

Clinical Science | May 1999

Women Emerge from General Anesthesia with Propofol/Alfentanil/Nitrous Oxide Faster than Men FREE

Tong J. Gan, MB, FRCA, FFARCSI; Peter S. Glass, MB, FFA(SA); Jeff Sigl, PhD; Peter Sebel, MB, BS, PhD, FFARSCI; Fredrick Payne, MD; Carl Rosow, MD, PhD; Patricia Embree, CRNA

+ Author and Article Information

Anesthesiology May 1999, Vol. 90, 1283–1287.

Table 2. Bispectral Index (BIS) Data and Recovery Parameters

	Male (n = 96)	Female (n = 178)	*P* Value
Intraoperative average BIS*	47 ± 9	47 ± 8	0.84
Prerecovery average BIS†	51 ± 10	53 ± 12	0.22
Time interval: propofol off to open eyes (min)	11.2 ± 8.6	7.0 ± 5.2	0.0001
	9.0 (20.8)‡	6.4 (13.1)‡	0.0001§
Time interval: propofol off to responds to verbal command (min)	11.7 ± 8.6	8.1 ± 6.2	0.001
	9.4 (22.0)‡	7.0 (14.6)‡	0.001§

Data are mean ± SD.

* Intraoperative average BIS = average value from start of procedure to 15 min before discontinuation of propofol.

† Prerecovery average BIS = average BIS value over 15 min before discontinuation of propofol.

‡ Median (90th percentile).

§ Statistical results from the Mann Whitney test.

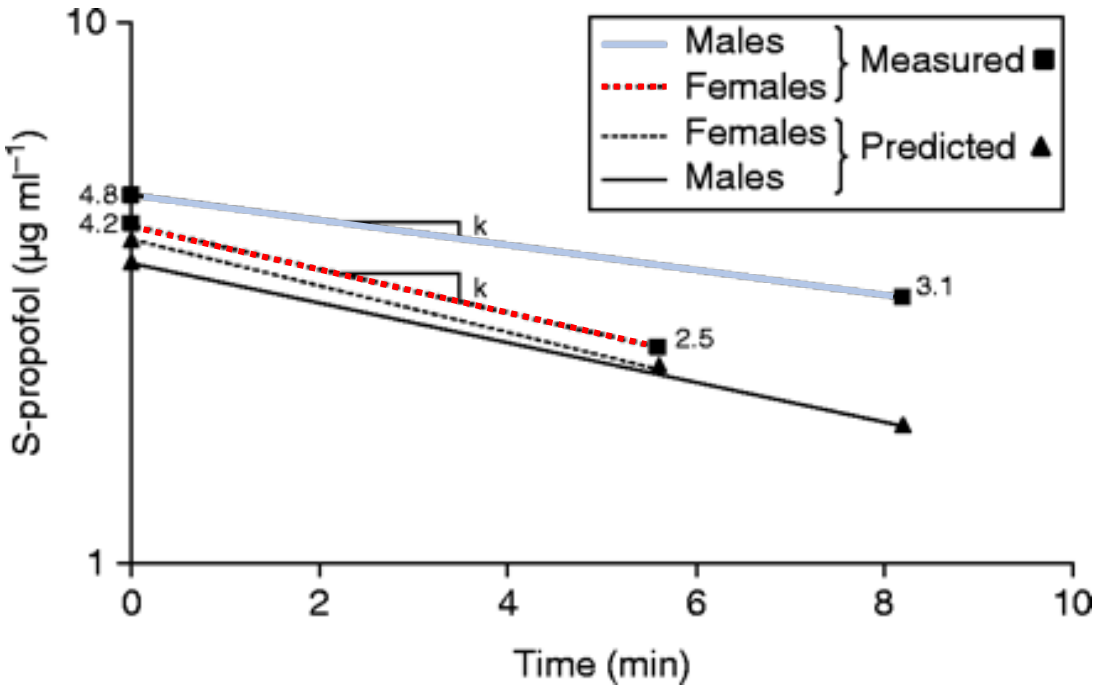
Propofol – pharmacokinetic differences

Why do women wake up faster than men from propofol anaesthesia? FREE

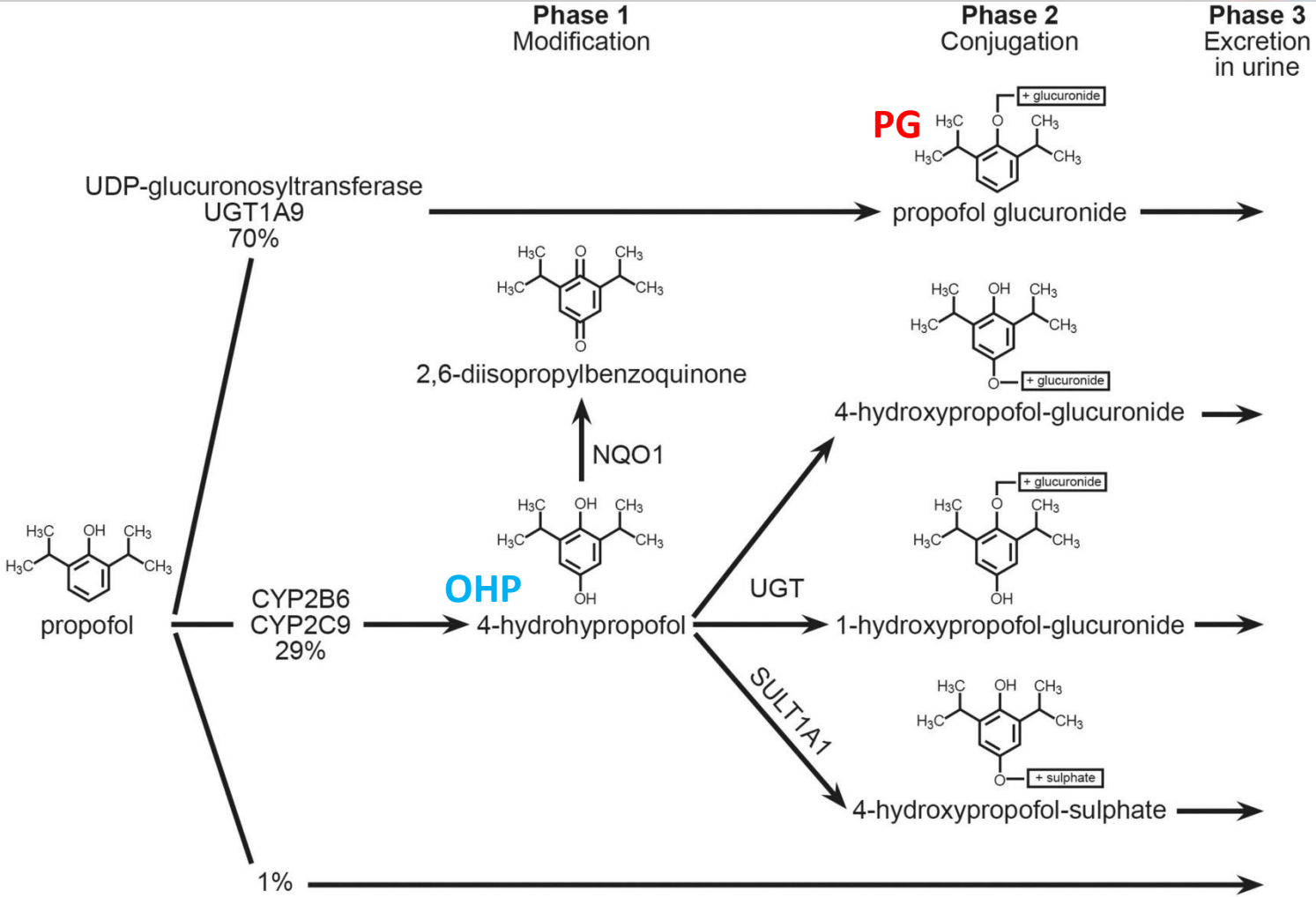
S. C. Hoymork ✉, J. Raeder

BJA: British Journal of Anaesthesia, Volume 95, Issue 5, November 2005, Pages 627–633,
https://doi.org/10.1093/bja/aei245

Published: 16 September 2005 **Article history** ▾

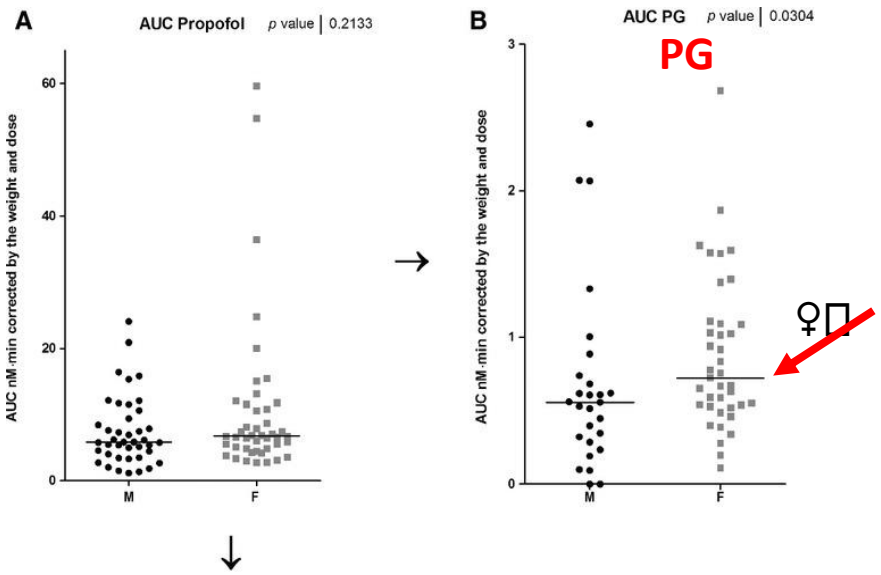


Propofol metabolism



Budic I et al.: Front Med (Lausanne). 2022 Feb 28:9:809393

Propofol – pharmacokinetic differences



Choong E. et al. Basic Clin Pharma Tox,
Volume: 113, Issue: 2, Pages: 126-131

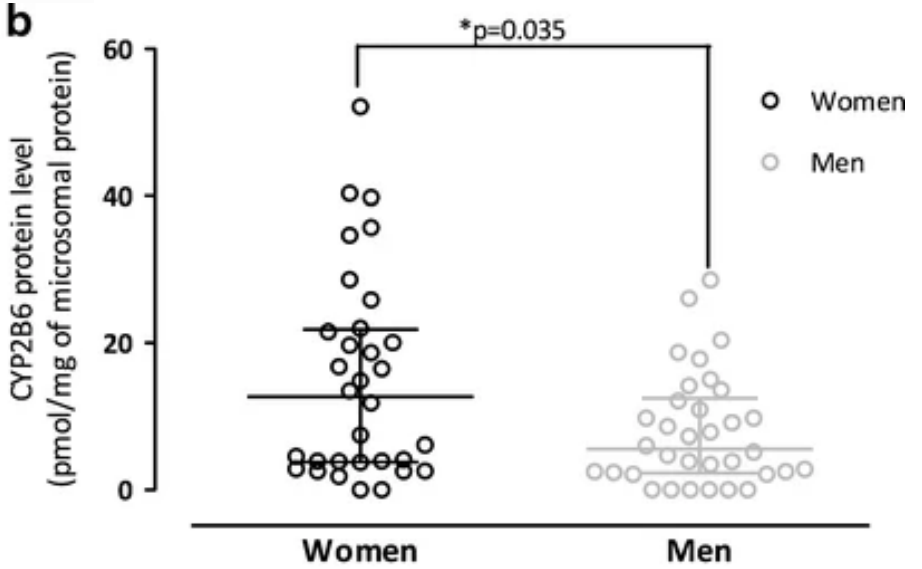
Propofol – pharmacokinetic differences

Pharmacokinetics and Disposition | Published: 18 October 2011

Influence of sex on propofol metabolism, a pilot study: implications for propofol anesthesia

Irena Loryan, Marja Lindqvist, Inger Johansson, Masahiro Hiratsuka, Ilse van der Heiden, Ron HN van Schaik, Jan Jakobsson & Magnus Ingelman-Sundberg

European Journal of Clinical Pharmacology **68**, 397–406 (2012) | Cite this article




not all
That's Folks!

Propofol – pharmacodynamic (?) differences

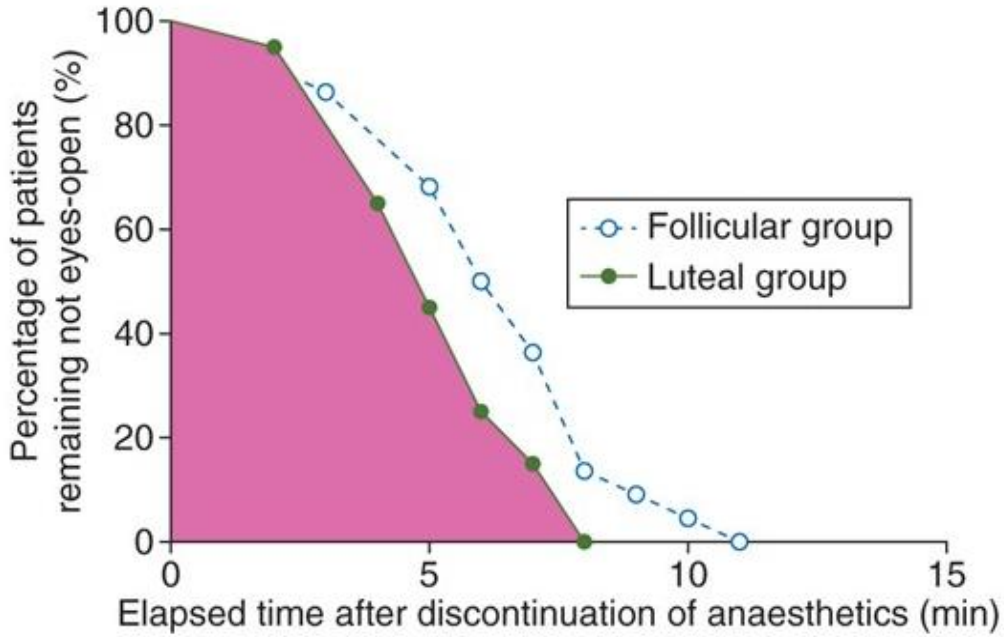
Propofol EC_{50} for inducing loss of consciousness is lower in the luteal phase of the menstrual cycle FREE

F. Fu, X. Chen ✉, Y. Feng, Y. Shen, Z. Feng, B. Bein

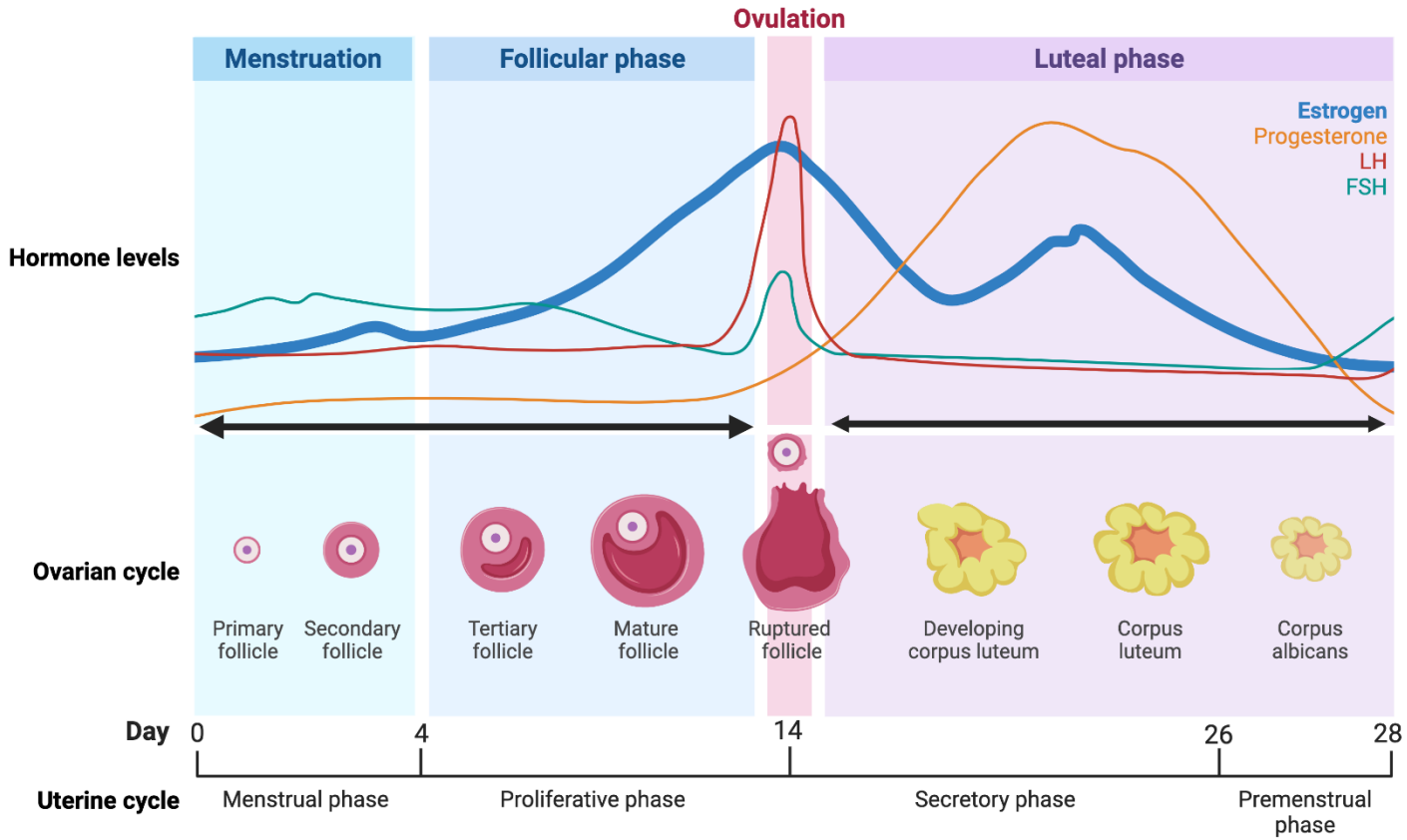
BJA: British Journal of Anaesthesia, Volume 112, Issue 3, March 2014, Pages 506–513,

Emergence time from anaesthesia

Fig 3



Propofol – pharmacodynamic (?) differences



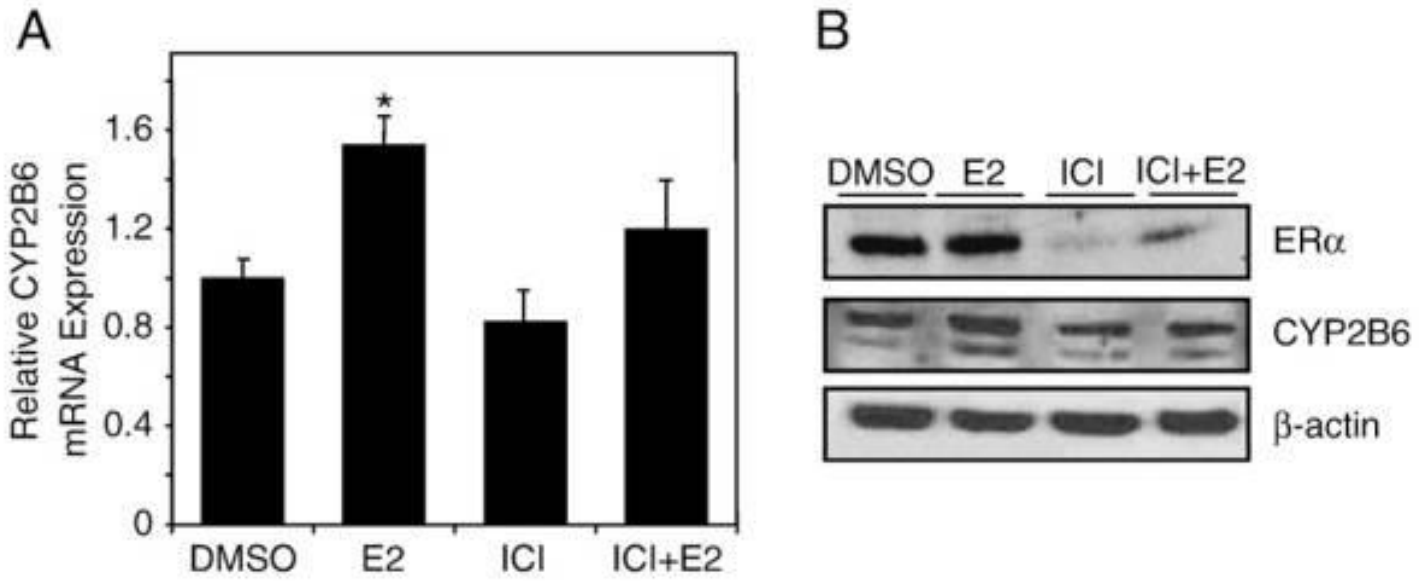
Created with Biorender.com

Potential reason for pharmacokinetic differences?

Biochim Biophys Acta. 2010 May-Jun; 1799(5-6): 469–479.
Published online 2010 Jan 14. doi: 10.1016/j.bbagrm.2010.01.005

Estrogen receptor-dependent regulation of *CYP2B6* in human breast cancer cells

Raymond Lo,[a] Lyle Burgoon,[b] Laura MacPherson,[a] Shaimaa Ahmed,[a] and Jason Matthews[a,*]



Propofol – ethnic differences

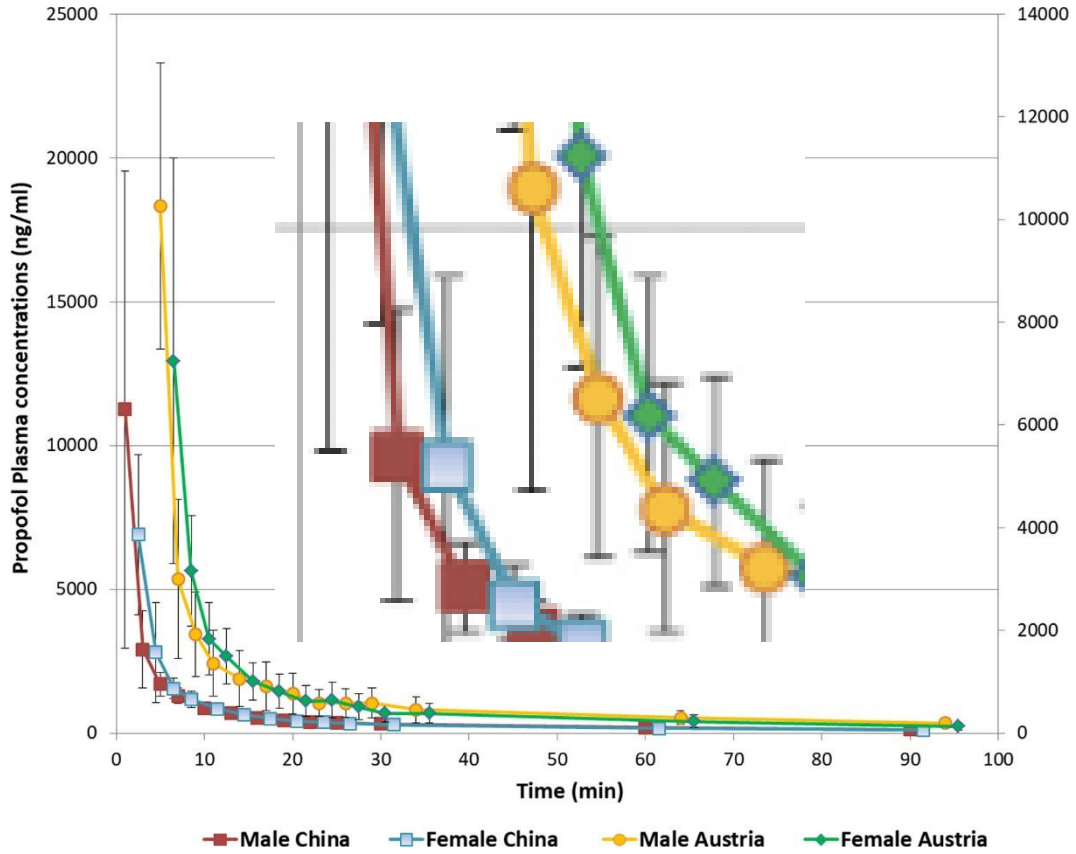
Fundamental & Clinical Pharmacology

ORIGINAL ARTICLE | Full Access

Location matters: Overlooked ethnic-geographic effect in China and Austria on propofol/cisatracurium sex differences among a population pharmacokinetic/pharmacodynamic (PopPK/PD) covariate analysis in men, women, and one transgender subject

Ashraf A. Dahaba, Zhaoyang Xiao, Xiaoling Zhu, Karl Oettl, Hailong Dong, Lize Xiong, Sieglinde Zelzer, Shuiyu Zhao, Gilbert Reibnegger

First published: 29 May 2021 | https://doi.org/10.1111/fcp.12704

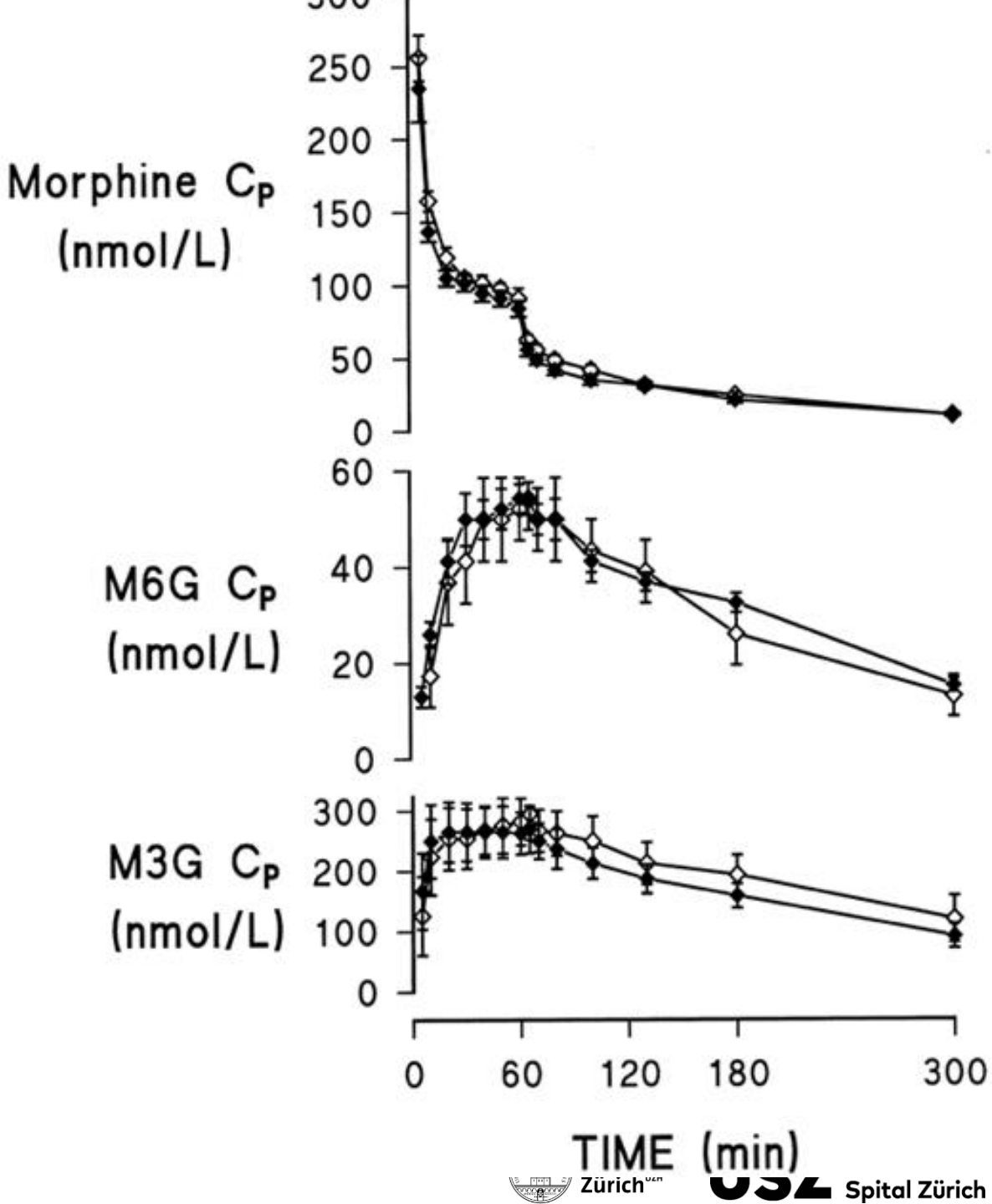


Morphine – no pharmakokinetic differences with regard to metabolite formation

Sex Differences in Morphine Analgesia: An Experimental Study in Healthy Volunteers

Elise Sarton, M.D., Ph.D.; Erik Olofsen, M.Sc.; Raymonda Romberg, B.Sc.; Jan den Hartigh, Ph.D.; Benjamin Kest, Ph.D.; Diederik Nieuwenhuijs, M.D.; Anton Burm, M.Sc., Ph.D.; Luc Teppema, Ph.D.; Albert Dahan, M.D., Ph.D.

Anesthesiology November 2000, Vol. 93, 1245–1254.



Morphine – clinical differences in humans

Do sex differences exist in opioid analgesia? A systematic review and meta-analysis of human experimental and clinical studies

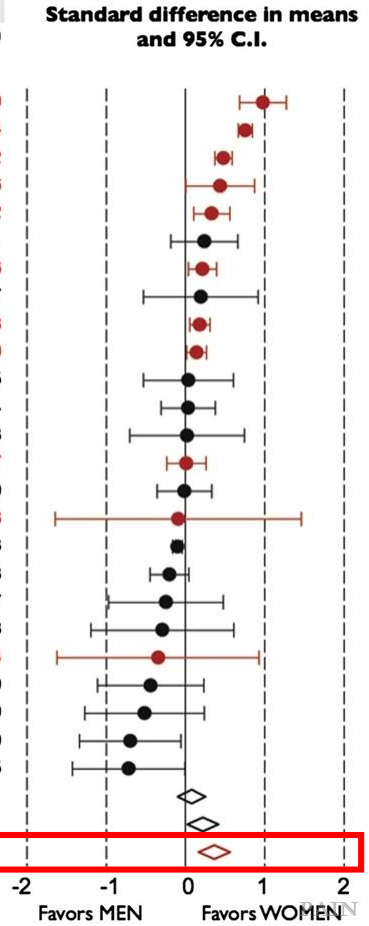
Niesters, Marieke[a]; Dahan, Albert[a,*]; Kest, Benjamin[b,c]; Zacny, James[d]; Stijnen, Theo[e]; Aarts, Leon[a]; Sarton, Elise[a]

Author Information

Pain: October 2010 - Volume 151 - Issue 1 - p 61-68
doi: 10.1016/j.pain.2010.06.012

Clinical studies on μ-opioids

Study	Std diff in means	SE	*P*-value	Relative weight (%)	MEN (n)	WOMEN (n)
[24] de Kock 1991	0.977	0.150	0.000	4.90	111	89
[17] Chia 2002	0.754	0.045	0.000	5.63	854	1444
[16] Chang 2006	0.478	0.056	0.000	5.58	646	662
[9] Burns 1989	0.438	0.222	0.048	4.20	38	46
[63] Sidebotham 1997	0.331	0.116	0.004	5.20	158	142
[14] Chang 2006	0.238	0.217	0.272	4.26	33	61
[43] Joels 2003	0.213	0.091	0.020	5.38	235	246
[5] Bijur 2008c	0.194	0.369	0.600	2.87	13	17
[49] Macintyre 1995	0.180	0.065	0.006	5.54	486	453
[65] Tsui 1996	0.141	0.063	0.025	5.55	494	510
[51] Miller 2004	0.036	0.286	0.899	3.58	24	25
[7] Birnbaum 2007	0.034	0.175	0.845	4.67	82	54
[5] Bijur 2008a	0.020	0.368	0.958	2.87	17	13
[38] Glasson 2002	0.010	0.126	0.938	5.12	115	137
[12] Cepeda 2003	-0.013	0.208	0.952	4.34	30	99
[4] Bennett 1982	-0.091	0.791	0.909	1.03	2	8
[1] Aubrun 2005	-0.102	0.031	0.001	5.67	2344	1933
[30] Fukuda 2009	-0.202	0.126	0.108	5.12	97	183
[40] Gourlay 1988	-0.246	0.370	0.507	2.86	13	17
[64] Tamsen 1982	-0.292	0.459	0.524	2.25	12	8
[22] Dahlstrom 1982	-0.344	0.650	0.597	1.40	6	4
[6] Bijur 2006	-0.439	0.343	0.201	3.07	16	19
[5] Bijur 2008b	-0.516	0.385	0.180	2.75	11	19
[46] Lehmann 1988	-0.696	0.326	0.033	3.22	21	19
[45] Larijani 2004	-0.716	0.361	0.047	2.93	12	25
ALL STUDIES	**0.094**	**0.089**	**0.286**			
ALL PCA STUDIES	**0.219**	**0.100**	**0.028**			
PCA MORPHINE STUDIES	**0.364**	**0.102**	**0.003**			



Morphine – clinical differences in humans

Do sex differences exist in opioid analgesia? A systematic review and meta-analysis of human experimental and clinical studies

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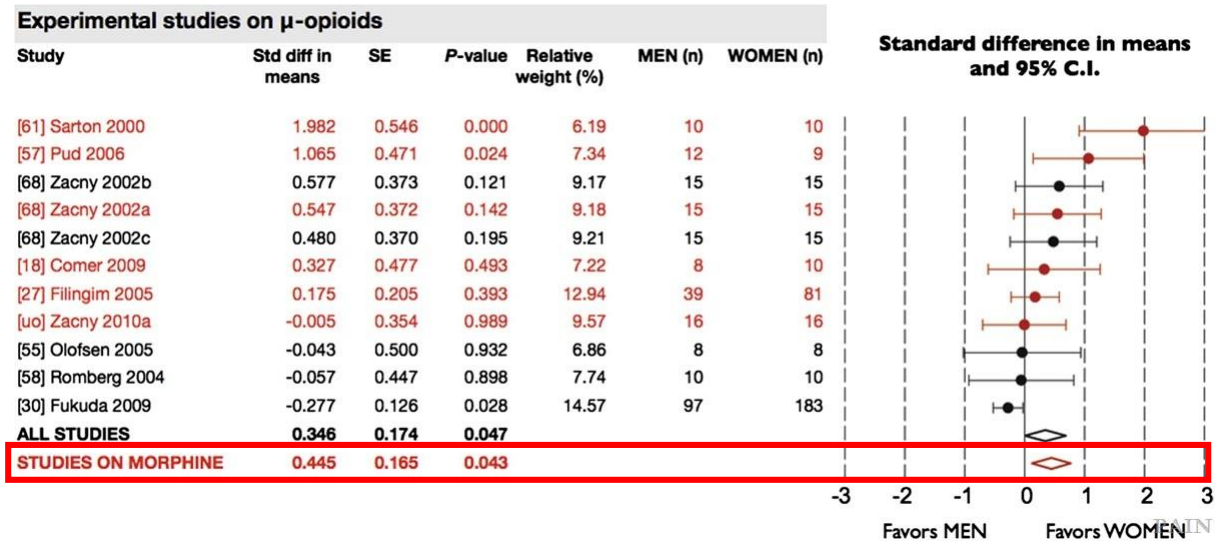
doi: 10.1016/j.pain.2010.06.012



Morphine – clinical differences in humans

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Pharmacological Research

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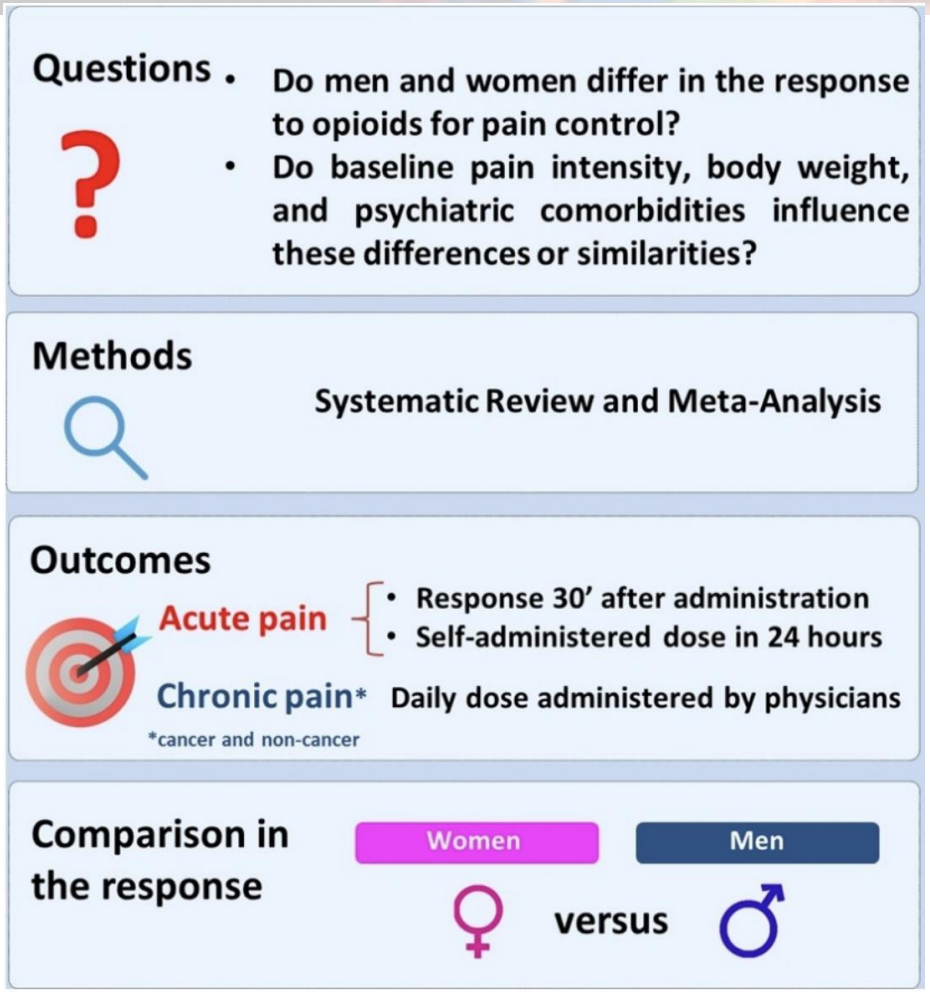
Invited Review

Sex differences in the response to opioids for pain relief: A systematic review and meta-analysis

Claudia Pisanu[a], Flavia Franconi[b], Gian Luigi Gessa[a], Sergio Mameli[c], Giovanni Maria Pisanu[c], Ilaria Campesi[d], Lorenzo Leggio[e,f,g,1], Roberta Agabio[a,*,1]

published 2019, graphical abstract



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Results

Acute pain: Response after 30'	♀ = ♂	**Participants**	563
		Comparisons	13
		Evidence quality	⊕⊕⊕ Moderate
Acute pain: Self-administered dose in 24 hrs	♀ < ♂	**Participants**	3,598
		Comparisons	11
		Evidence quality	⊕⊕⊕ Moderate
Chronic cancer pain: Daily dose	♀ = ♂	**Participants**	708
		Comparisons	6
		Evidence quality	⊕ Very low
Chronic non-cancer pain: Daily dose	♀ < ♂	**Participants**	1,952
		Comparisons	10
		Evidence quality	⊕⊕ Low

Morphine – clinical differences in humans

Prediction of Opioid-Induced Respiratory Depression on Inpatient Wards Using Continuous Capnography and Oximetry: An International Prospective, Observational Trial

Ashish K. Khanna, MD,*† Sergio D. Bergese, MD,‡§ Carla R. Jungquist, NP, PhD,‖ Hiroshi Morimatsu, MD, PhD,¶ Shoichi Uezono, MD,# Simon Lee, MD,** Lian Kah Ti, MBBS, MMed,†† Richard D. Urman, MD,‡‡ Robert McIntyre Jr, MD,§§ Carlos Tornero, MD, PhD,‖‖ Albert Dahan, MD, PhD,¶¶ Leif Saager, Dr Med,##*** Toby N. Weingarten, MD,††† Maria Wittmann, MD,‡‡‡ Dennis Auckley, MD,§§§ Luca Brazzi, MD, PhD,‖‖‖ Morgan Le Guen, MD, PhD,¶¶¶ Roy Soto, MD,### Frank Schramm, MD,**** Sabry Ayad, MD,†††† Roop Kaw, MD,†††† Paola Di Stefano, MSc,‡‡‡‡ Daniel I. Sessler, MD,§§§§ Alberto Uribe, MD,‡ Vanessa Moll, MD, PhD,** Susan J. Dempsey, MN,§§‖‖‖‖ Wolfgang Buhre, MD,¶¶¶¶ and Frank J. Overdyk, MD,#### on behalf of the PRediction of Opioid-induced respiratory Depression In patients monitored by capnoGraphY (PRODIGY) Group Collaborators

www.anesthesia-analgesia.org October 2020 • Volume 131 • Number 4

Table 3. Multivariable Model Prediction of Respiratory Depression, PRODIGY Scoring System, and Utilization

	Multivariable Model Predictors				
Clinical Characteristic	**Estimate**	**Standard Error**	**OR (95% CI)**	**Pr > |t|**	**Points if Clinical Characteristic = "Yes"**
Age (y)					
<60	Reference	…	…	…	0
≥60 to <70	0.8077	0.1458	2.243 (1.685–2.985)	<0.0001	8
≥70 to <80	1.2323	0.1805	3.429 (2.407–4.886)	<0.0001	12
≥80	1.5647	0.3657	4.781 (2.333–9.798)	<0.0001	16
Sex (M)	0.7550	0.1284	2.128 (1.654–2.737)	<0.0001	8
Opioid naive	0.2912	0.1652	1.338 (0.968–1.850)	0.0782	3
Sleep disorders	0.4755	0.1998	1.609 (1.087–2.381)	0.0175	5
Chronic heart failure	0.7494	0.4085	2.116 (0.949–4.715)	0.0668	7
					"Sum = PRODIGY Score"

Anesthesia and sex differences

... to be continued

Picture by Samuel Regan-Asante