



**European antiemetic regulations
(restricting metoclopramide use)
increases admission rates due to
hyperemesis gravidarum.**

Lone Holst

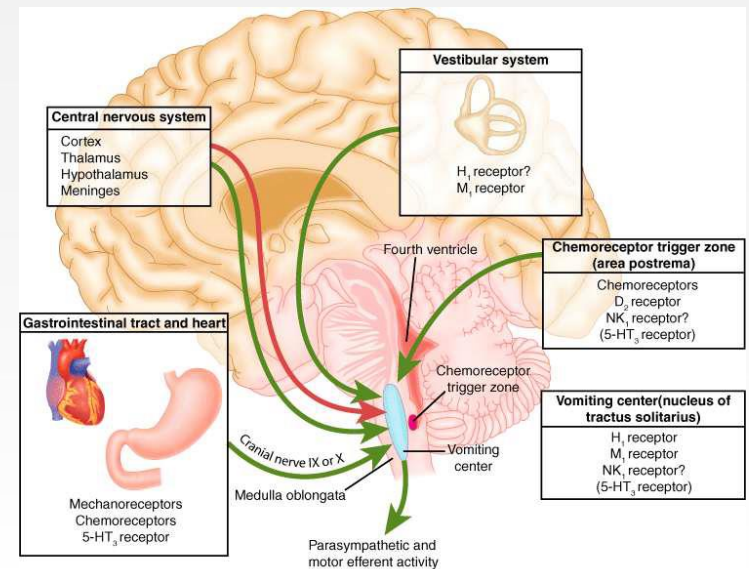
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Metoclopramide

- Included in guidelines on treatment of HG
- ATC-code A03F A01: Propulsive
- More important: Dopamin antagonist





Side effects

- Extrapyramidal disorders
- Tardive dyskinesias
- Increased risk with long-term or high-dose treatment
- BUT: most side effects occur within the first 5 days*

• *Svendsen K, Wood M et al. Reported time to onset of neurological adverse drug reactions among different age and gender groups using metoclopramide: an analysis of the global database Vigibase®. Eur J Clin Pharm 2018; 74:627-636





Safety documentation

- No associations with
 - Malformations^{1,2}
 - Spontaneous abortion¹
 - Stillbirth/perinatal death^{1,2}
 - Low birth weight²
 - Preterm delivery²

- 1) Pasternak B, Svanstrom H et al. JAMA 2013; 310: 1601-11.
- 2) Matok I, Gorodischer R, Koren G, Sheiner E, Wiznitzer A, Levy A. T. N Engl J Med. 2009 Jun 11;360(24):2528-35.





EMA recommendation

- European Medicines Agency's (EMA) Committee on Medicinal Products for Human Use (CHMP)
- First: July 2013
- Final legally binding decision, valid throughout the European Union (EU), on 20 December 2013.





Recommendation:

- Only short-term use up to 5 days
- Pregnancy is not mentioned in the recommendations

- <https://www.ema.europa.eu/en/medicines/human/referrals/metoclopramide-containing-medicines>
- https://www.ema.europa.eu/en/documents/referral/assessment-report-metoclopramide-containing-medicines_en.pdf





The hospital cohort

- Haukeland University Hospital, Bergen, Norway
- 2002 – 2016
- All women admitted with the diagnosis *Hyperemesis gravidarum*
- 893 women





Methods

- Review of patient records
 - Medication before admission
 - Medication during hospitalisation
 - Clinical patient characteristics
- Rate of admission is calculated based on number of births in the same period





Reported side effects

Drug	Pre-hospital*	In hospital
Meclizin	6	1
Metoclopramide	24	1
Prochlorperazine	9	3
Ondansetron	2	1
Promethazine	1	
Chlorpromazine	1	

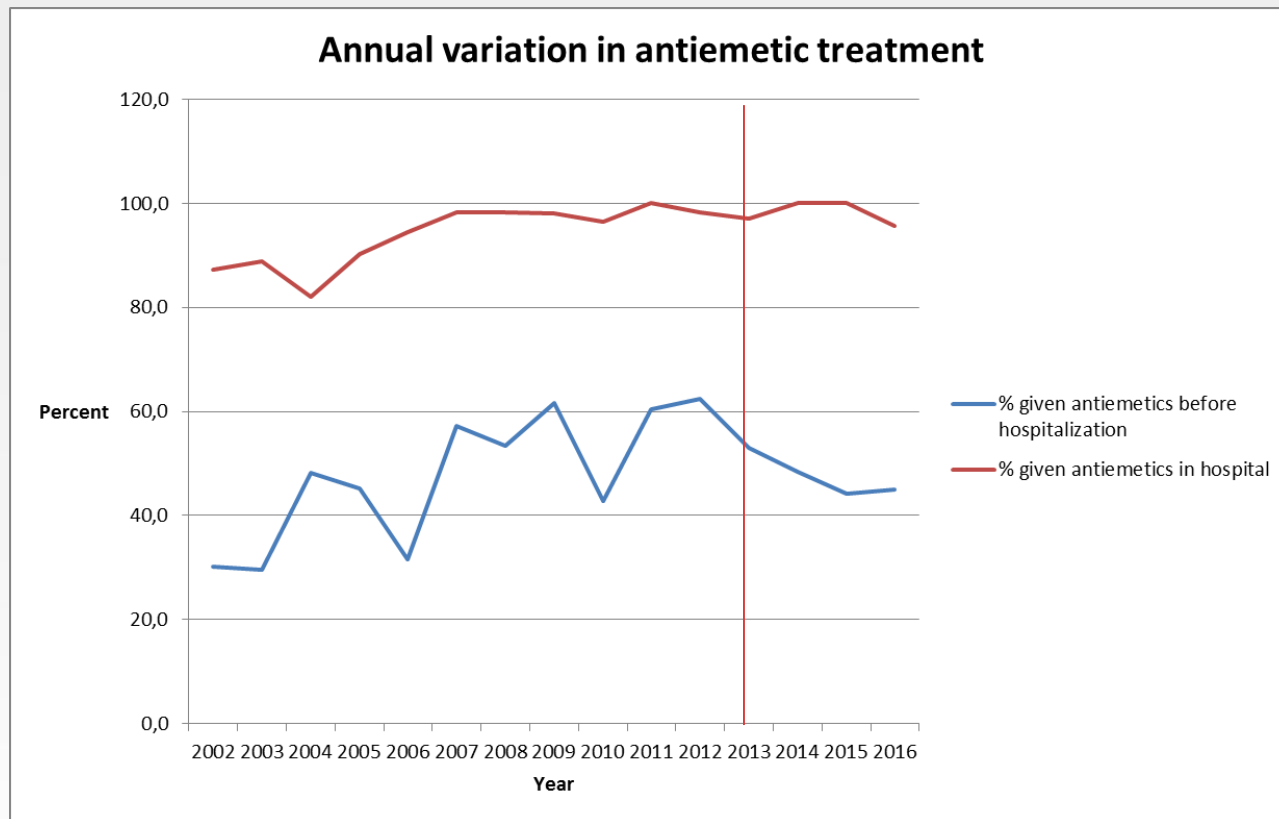
*This or earlier pregnancies

Only 6 women (0.8%) experienced side effects in hospital



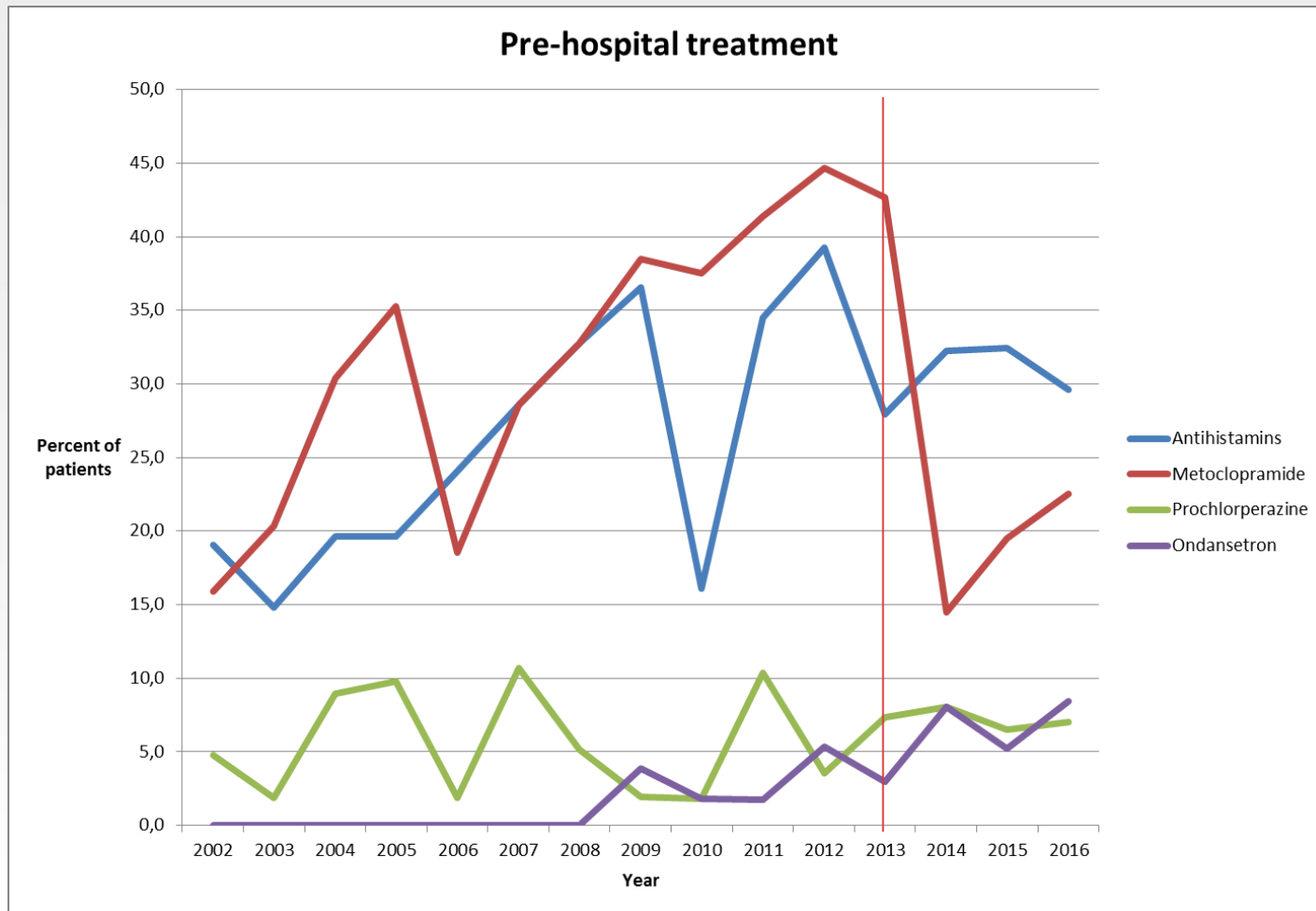


All antiemetics before and during hospitalisation



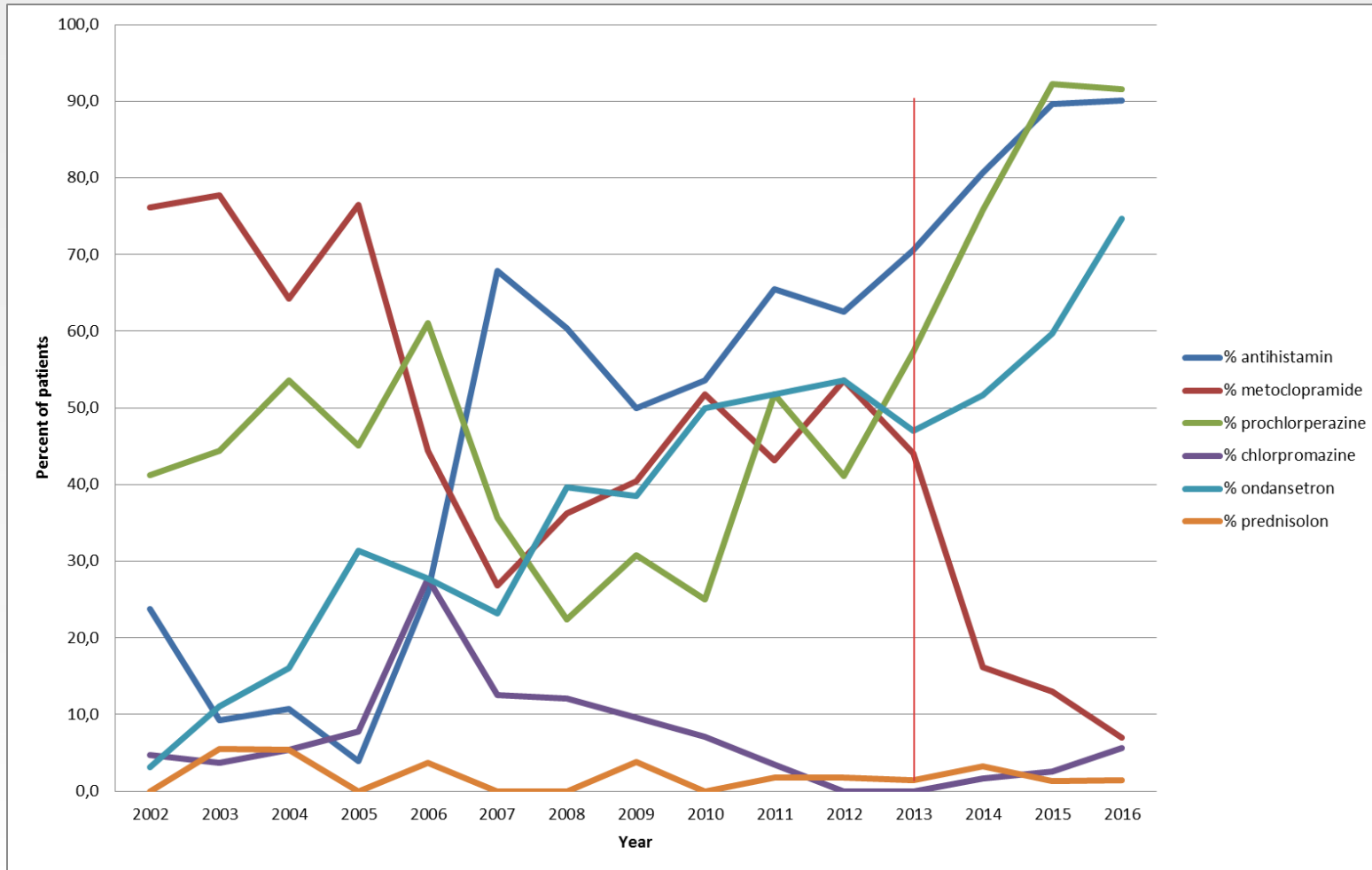


Pre-hospital treatment



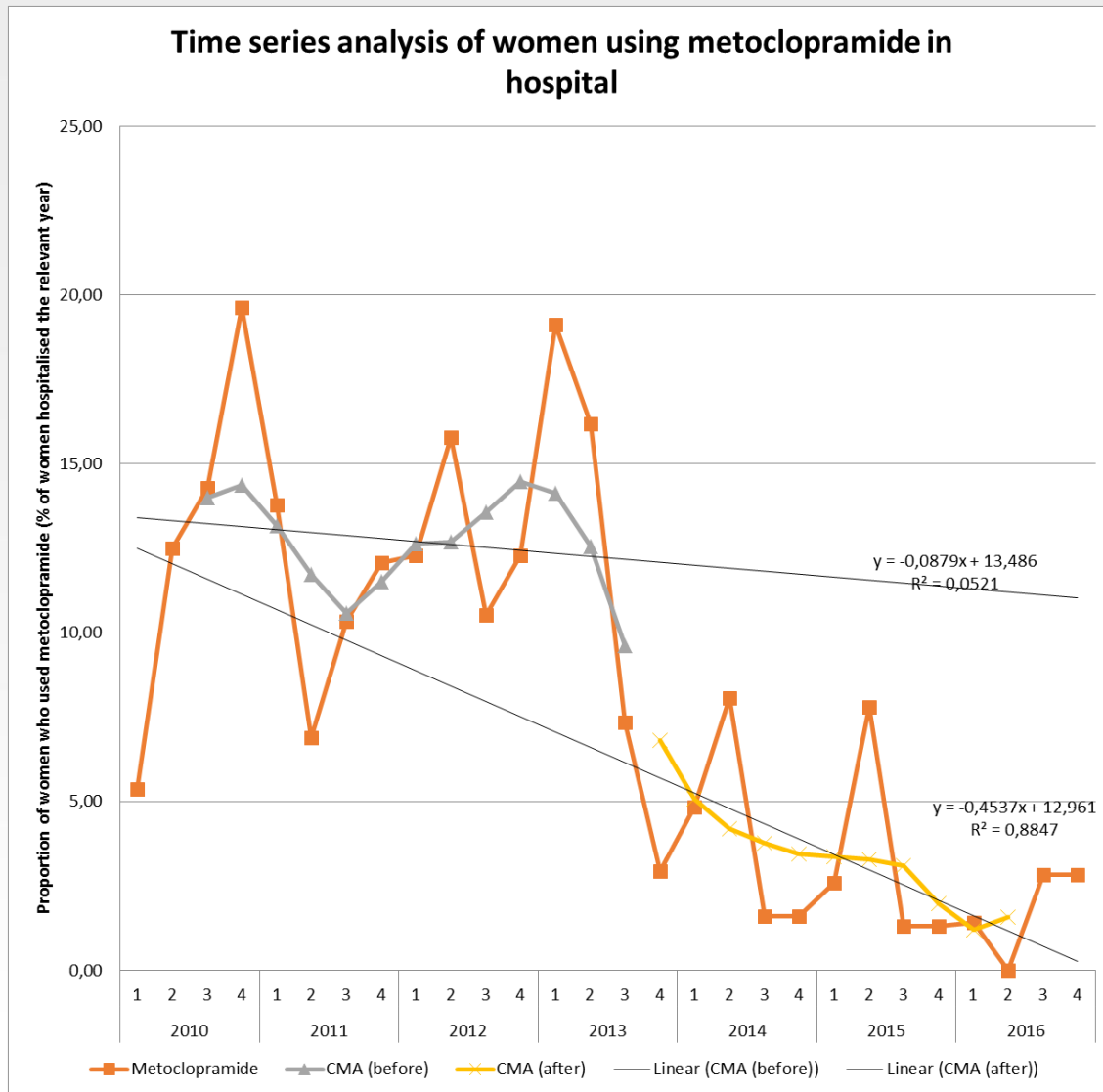


In-hospital antiemetic treatment





Did the use change?





Use of antiemetics - summary

	2002-4	2011-13	2014-16	p
Antiemetics before hospital	36%	58%		p<0,001
		58%	46%	p<0,001
Metoclopramide before hospital		41%	19%	p<0,001
HG admission rate	0.0106		0.0124	p=0.047





Conclusions

- Use of metoclopramide is significantly reduced
- A smaller proportion of women treated for HG before hospitalisation
- Admission rate due to HG increased from 2011-13 to 2014-16





**Thank you for your
attention.**



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