Chemotherapy induced nausea and vomiting

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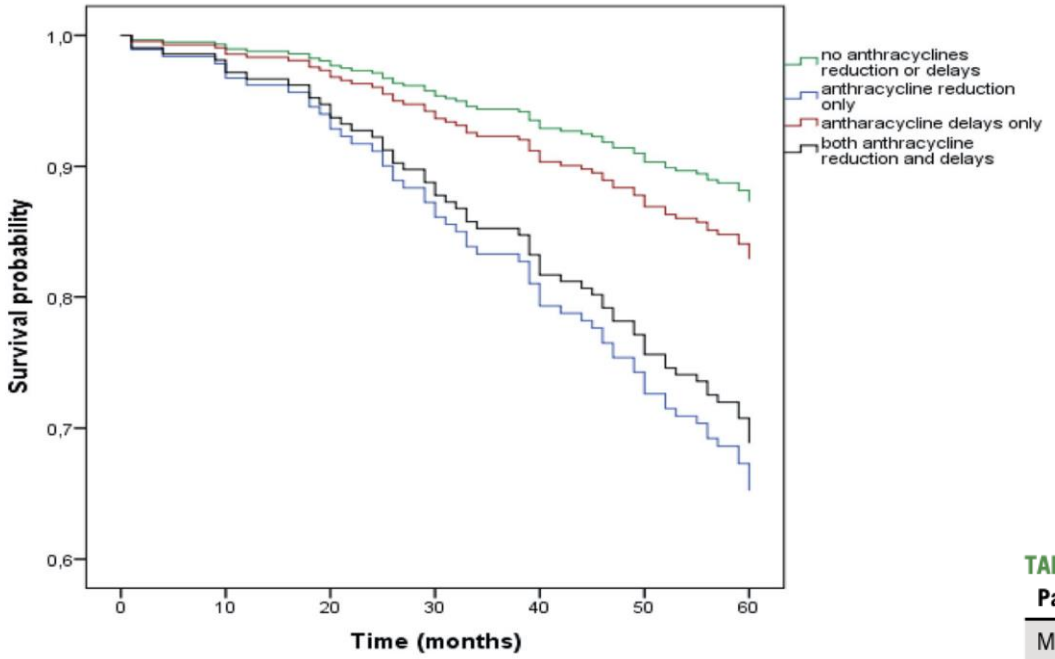
CINV – why does it matter to the patient?

- major concern by patients going into chemotherapy
- nausea and vomiting is a distressing symptom

Why does it matter to the caregiver?



Liutkauskiene *et al. BMC Cancer* (2018) 18:453

dose reduction of anthracycline of 15% in adjuvant therapy: 5 year survival 57.2% vs. 86.4%

TABLE 2. Patterns and Characteristics of ED Visits Made by Adults With Newly Diagnosed Cancer at a Safety-Net Health System (N = 11,282)

Pattern or Characteristic	Measure
Mean monthly ED* visits per 1,000 patient-months† (95% CI)	226.7 (226.5 to 226.9)
Primary presenting complaint	
Nausea/vomiting/diarrhea/dehydration	8.0
Fever/chills	5.6
Pain (excluding chest pain), headache	28.3
Extremity swelling/edema	4.1
Medication refill	2.2
Rash	0.8
Shortness of breath/cough	8.5
Chest pain	2.9

Hong et al, J Oncol. Pract 2019

Cancer induced nausea and vomiting then and now:

THE NEW YORK TIMES, THURSDAY, OCTOBER 15, 1981

Drug Stops Chemotherapy Ills

BOSTON, Oct. 14 (UPI) — An experimental drug called metoclopromide can eliminate the nausea and vomiting that accompany one of the most widely used and powerful treatments for cancer, according to a team of researchers.

The drug holds hope for other cancer patients suffering drug-induced nausea and vomiting. These symptoms are "the most frequent and debilitating acute side effects of chemotherapy for advanced cancer," the researchers wrote in the latest issue of The New England Journal of Medicine.

76 percent of the patients. The sedation was mild in all but one patient.

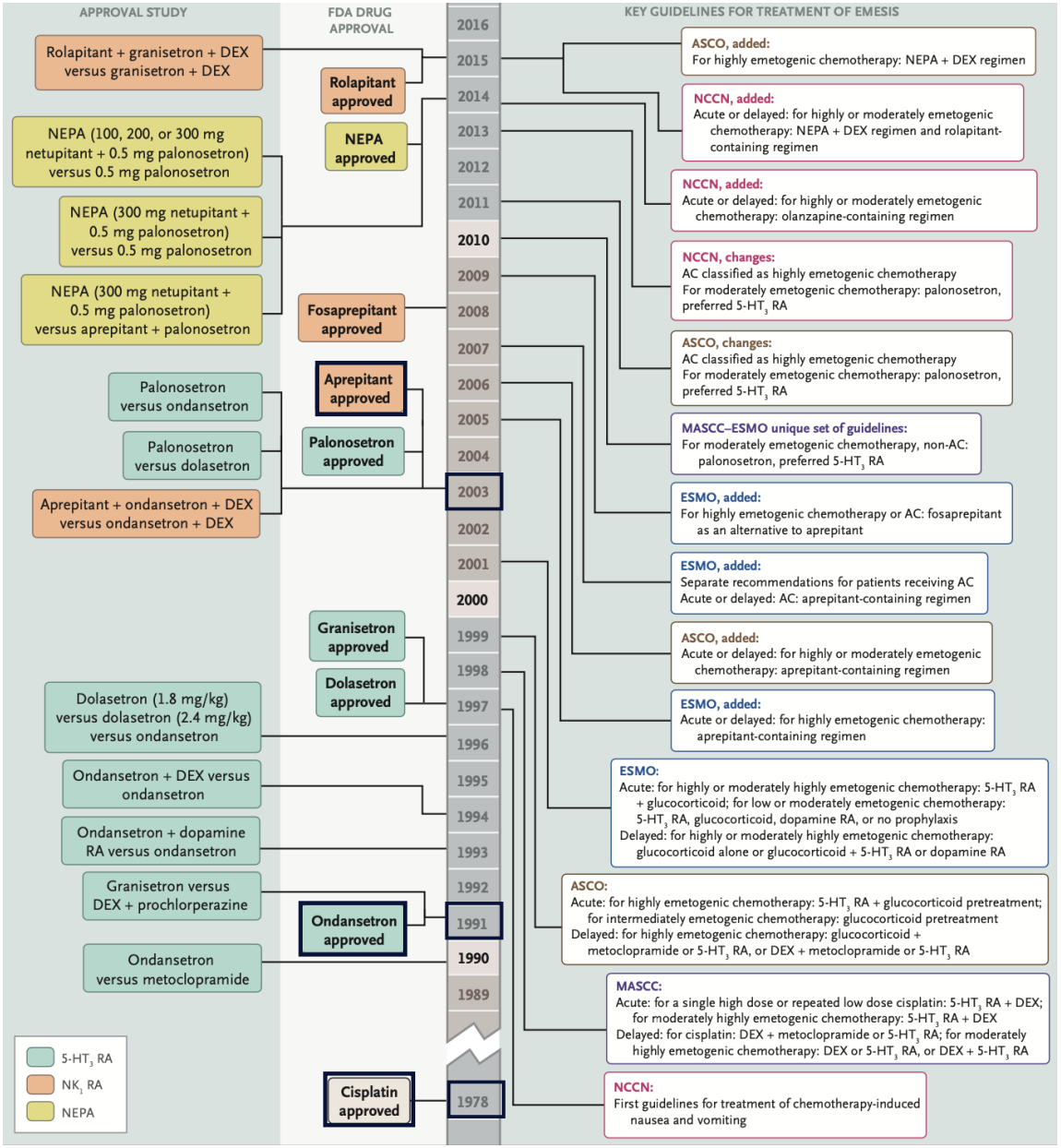
Other side effects were diarrhea, occasional headaches, chills or other minor problems, the study said, but none of these effects necessitated stopping the treatment.

The major drawback was that metoclopromide treatment took too long to be used on outpatients, the study said.

N.A.A.C.P. in South Carolina

Introduction of the most emetogenic cancer drug: 1978

Introduction of the most effective antiemetic: 2003!



Cancer induced nausea and vomiting then and now:

- Before introduction of Antiemetics:
  - 83% of patients nause and vomiting
- now: 13-35% depending on substances

Table 5 Ten most distressing side-effects of chemotherapy

Rank	1983	1995
1	Being sick (vomiting)	Feeling sick (nausea)
2	Feeling sick (nausea)	Loss of hair
3	Loss of hair	Being sick (vomiting)
4	Thought of coming for treatment	Constantly tired
5	Length of time treatment takes at the clinic (24)	Having to have an injection
6	Having to have an injection	Constipation (–)
7	Shortness of breath (15)	Thought of coming for treatment
8	Constantly tired	Affects family or partner
9	Difficulty sleeping (21)	Feeling low, miserable (depression) (14)
10	Affects family or partner	Feeling anxious or tense (13)

Numbers in parentheses indicate the ranking number in the opposite column.

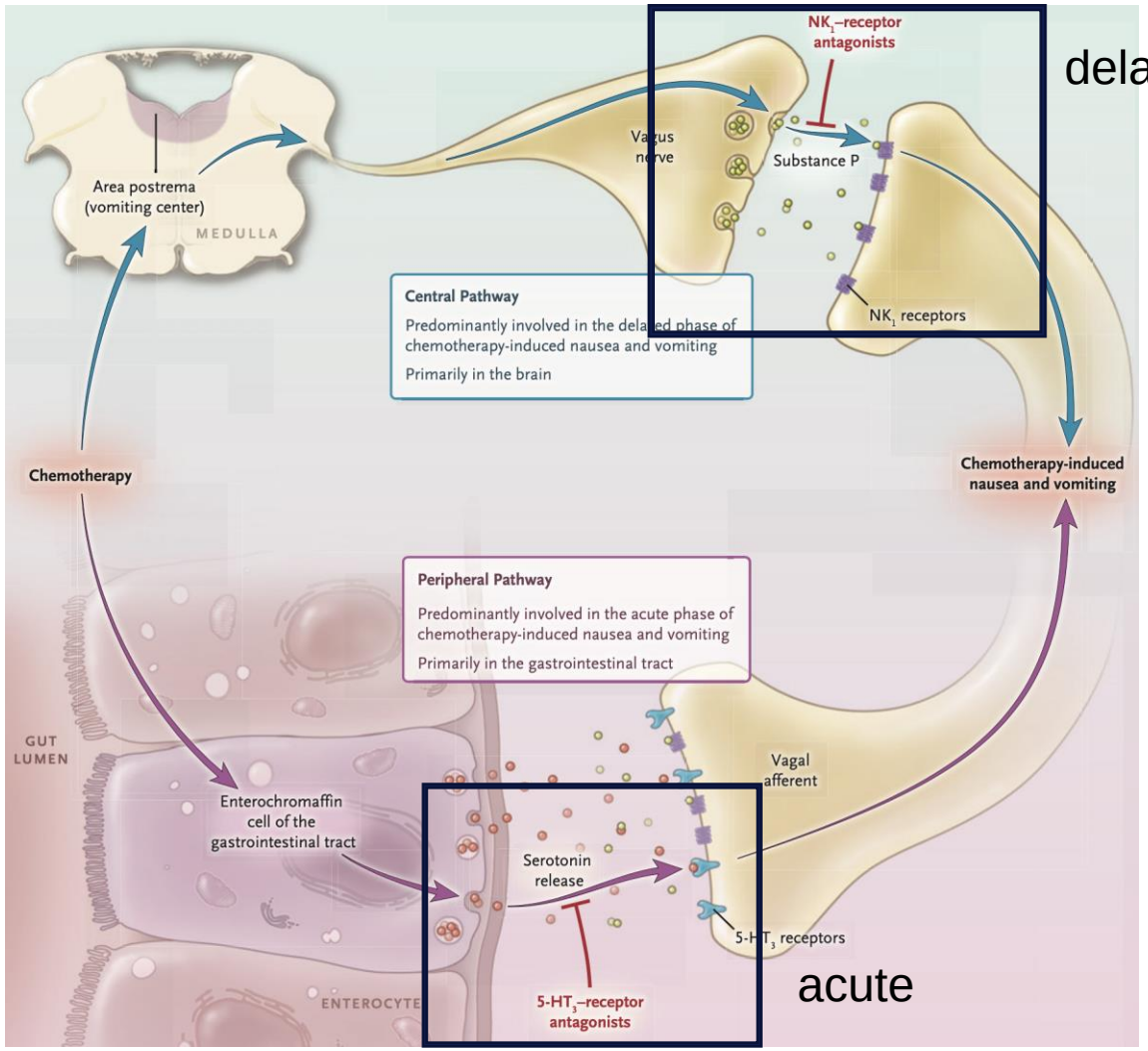
de Boer-Dennert et al, Br.. J. Cancer 1997

TABLE 4
Relative Severity of Side Effects for the Entire Group

Symptom	Rank
Affects my family or partner	1
Loss of hair	2
Constantly tired	3
Affects my work, home duties	4
Affects my social activities	5
Loss of sexual feeling	6
Giddiness on standing up	7
Diarrhea	8
Weight gain	9
Shortness of breath	10
Emesis	11
Feeling low (depression)	12
Irritability, bad temper	13
Numbness in fingers or toes	14
Loss of appetite	15

Carelle et al, Cancer 2002

Why does it happen?



Longo, NEJM 2016

Classification	Definition
Acute	Occuring with the first 24 hours after initiation, peaking after 5-6 hours
Delayed	Occurring from 24 hours to 2-5 days after chemotherapy

Who is affected?

Emetogenic potential	IV chemotherapy		Oral chemotherapy
High (>90%)	Anthracycline/cyclophosphamide combination Dacarbazine	Cisplatin Cyclophosphamide ≥1500 mg/m2	Procarbazine
Moderate (>30 to 90%)	Alemtuzumab Azacitidine Bendamustine Carboplatin Cyclophosphamide <1500 mg/m2 Cytarabine >1000 mg/m2	Daunorubicin, Doxorubicin, Epirubicin, Idarubicin Ifosfamide Irinotecan Oxaliplatin Trabectedin	Crizotinib Cyclophosphamide Imatinib Temozolomide Vinorelbine
Low (10-30%)	Aflibercept Bortezomib Brentuximab Cabazitaxel Cetuximab Cytarabine ≤1000 mg/m2 Docetaxel Eribulin Etoposide	5-Fluorouracil Gemcitabine Ipilimumab Methotrexate Nab-paclitaxel Paclitaxel Pegylated liposomal doxorubicin Pertuzumab Trastuzumab-emtansine	Afatinib Axatinib Capecitabine Everolimus Lapatinib Olaparib Sunitinib Thalidomide
Minimal (0 to <10%)	Bevacizumab Nivolumab Pembrolizumab	Trastuzumab Vinblastine, Vincristine, Vinorelbine	Melphalan Methotrexate Pomalidomide

adapted from ESMO + MASCC Guidelines

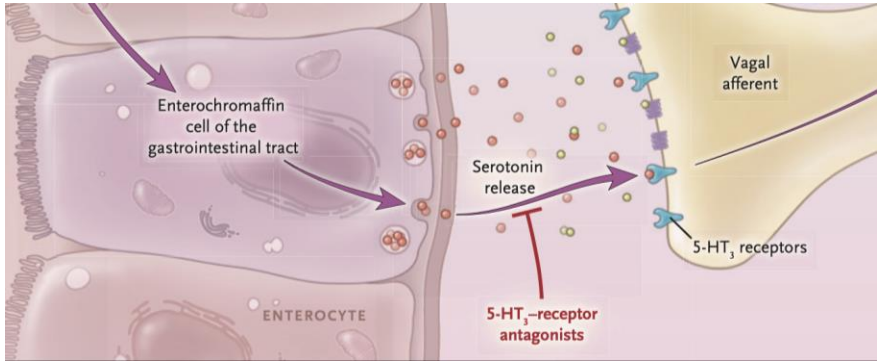
Annals of Oncology 27 (Supplement 5): v119–v133, 2016
doi:10.1093/annonc/mdw270

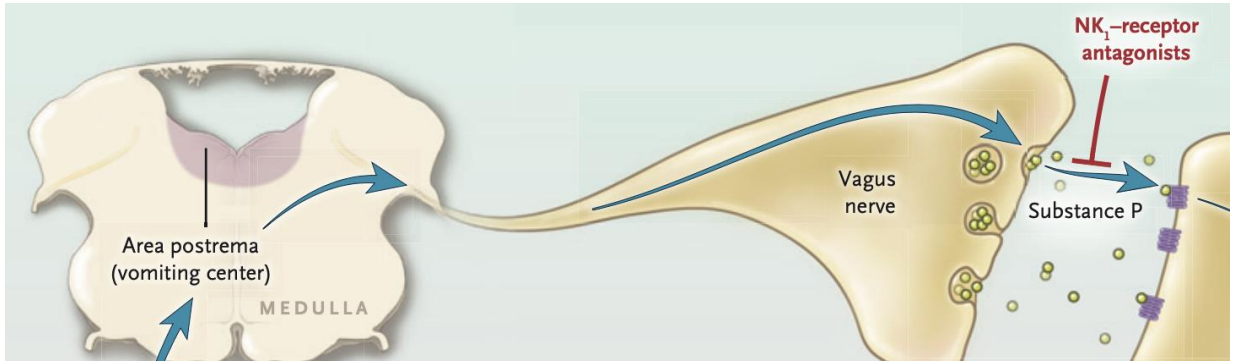
2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients

F. Roila[1], A. Molassiotis[2], J. Herrstedt[3], M. Aapro[4], R. J. Gralla[5], E. Bruera[6], R. A. Clark-Snow[7], L. L. Dupuis[8], L. H. Einhorn[9], P. Feyer[10], P. J. Hesketh[11], K. Jordan[12], I. Olver[13], B. L. Rapoport[14], J. Roscoe[15], C. H. Ruhlmann[3], D. Walsh[16], D. Warr[17] & M. van der Wetering[18] on behalf of the participants of the MASCC/ESMO Consensus Conference Copenhagen 2015*

[1]Medical Oncology, Santa Maria Hospital, Terni, Italy; [2]School of Nursing, The Hong Kong Polytechnic University, Hong Kong, China SAR; [3]Department of Oncology, Odense University Hospital, Odense, Denmark; [4]Clinique de Genolier, Multidisciplinary Oncology Institute, Genolier, Switzerland; [5]Albert Einstein College of Medicine, Jacobi Medical Center, New York; [6]Department of Palliative, Rehabilitation and Integrative Medicine, UT MD Anderson Cancer Center, Houston; [7]The University of Kansas Cancer Center, Westwood, Kansas, USA; [8]Department of Pharmacy and Research Institute, The Hospital for Sick Children, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada; [9]Division of Hematology–Oncology, Simon Cancer Center, Indiana University, Indianapolis, USA; [10]Department of Radiation Oncology, Vivantes Clinics, Neukoelln, Berlin, Germany; [11]Lahey Health Cancer Institute, Burlington, USA; [12]Department of Hematology/Oncology, Martin-Luther-University Halle-Wittemberg, Halle, Germany; [13]Sansom Institute for Health Research, University of South Australia, Adelaide, Australia; [14]Medical Oncology Centre of Rosebank, Johannesburg, South Africa; [15]Department of Surgery, University of Rochester Medical Center, Rochester, USA; [16]Academic Department of Palliative Medicine, Our Lady's Hospice and Care Services, Dublin, Ireland; [17]Cancer Clinical Research Unit, Princess Margaret Cancer Centre, Toronto, Canada; [18]Department of Paediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, The Netherlands

	Serotonin-Blockers	Substance P-Blockers	Cortisone
Substances	**Ondansetron**, Granisetron, Tropisetron, Dolasetron, Palonosetron	**Aprepitant**, Fosaprepitant, Rolapitant, Netupitant	**Dexamethasone**
Type of CINV	**Acute** + Delayed	Acute + **Delayed**	Acute + Delayed
Side effects	**constipation**	constipation, fatigue, hick-up	hyperglycemia, **sleeplessness**, psychiatiric side effects
Use	all types	Highly emetogenic chemotherapy	All types, enhances efficacy of subtances P-Blockers





MASCC-ESMO guidelines

Emetogenic risk level	Acute phase	Example	Delayed phase	Example
High	NK1-RA + 5-HT3-RA + dexamethasone +	Day 1: Aprepitant 125 mg once + Ondansetrone 8 mg twice daily + 12 mg dexamethsone once	NK1-RA + dexamethasone	Day 2+ 3: Aprepitant 80 mg + dexamthasone 8 mg p.o.
Moderate	5-HT3-RA + dexamethasone	Ondansetrone 8 mg + 8 mg dexamethasone	dexamethasone	
Low	5-HT3-RA or dexamethasone or dopamine receptor antagonist	Ondansetrone 8 mg or 8 mg dexamethasone or 10 mg metoclopramide	-	
Minimal	No fixed medication			

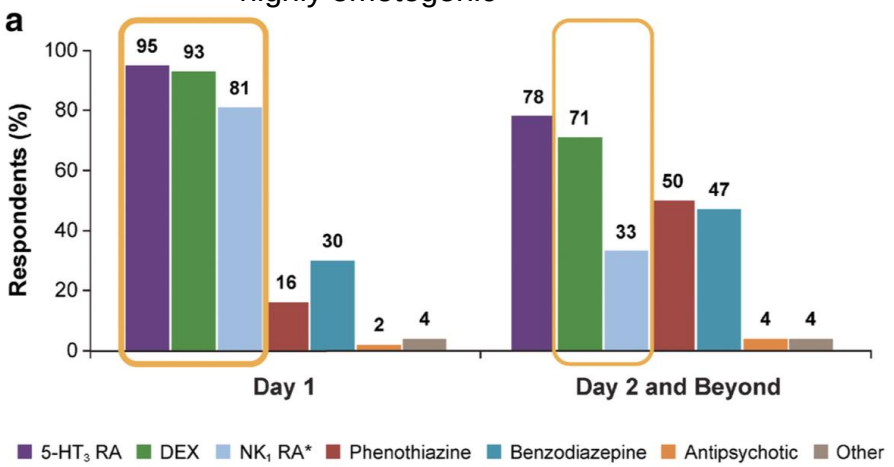
Support Care Cancer (2018) 26:557–564
DOI 10.1007/s00520-017-3866-6

ORIGINAL ARTICLE

Chemotherapy-induced nausea and vomiting (CINV) and adherence to antiemetic guidelines: results of a survey of oncology nurses

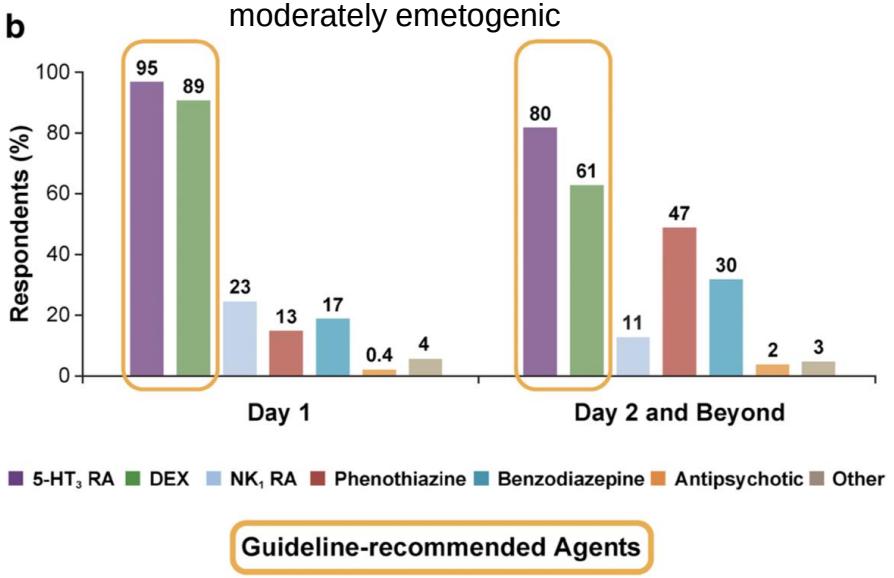
Rebecca Clark-Snow[1] · Mary Lou Affronti[2] · Cynthia N. Rittenberg[3]

highly emetogenic



*During Day 2 and beyond, an oral NK_1 RA (aprepitant) would be considered guideline-recommended if it had been administered on Day 1

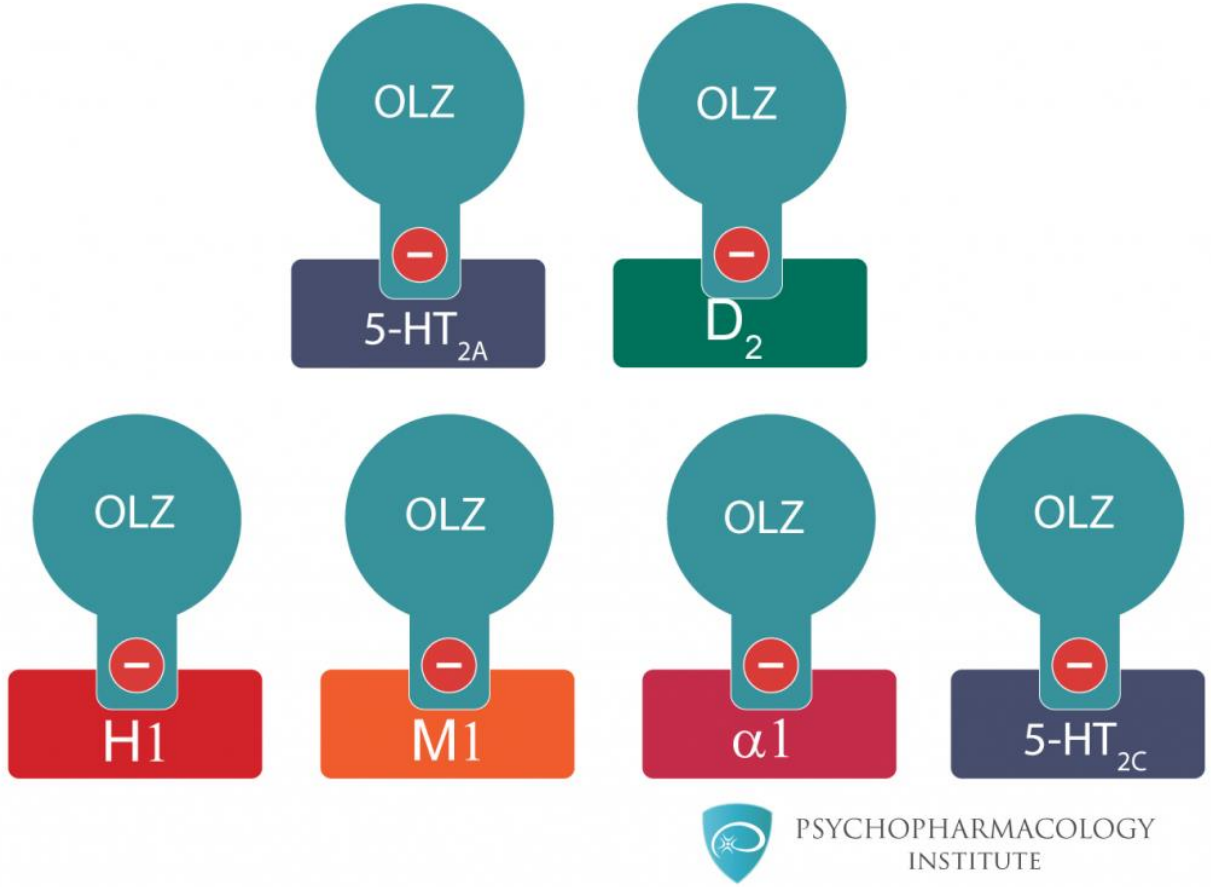
moderately emetogenic



underuse of correct medication for delayed nauses

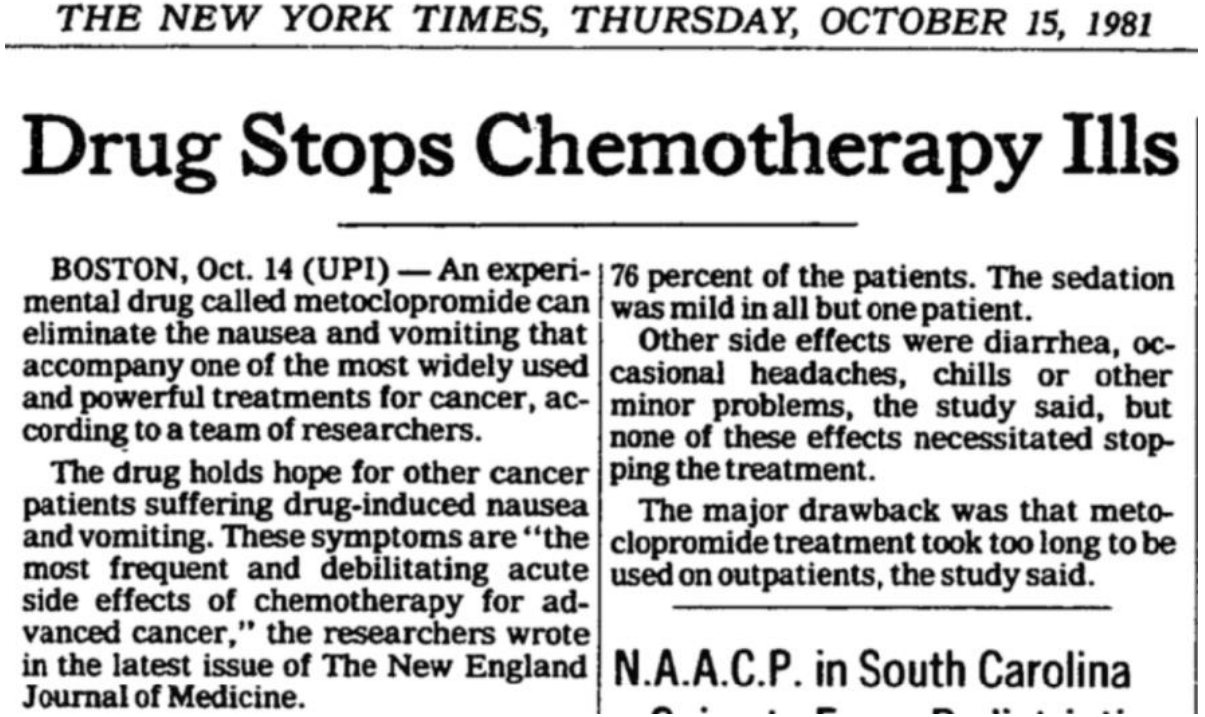
Olanzapine

- antipsychotic drug used in treatment for schizophrenia
- blocks various receptors (dopamine, serotonin, histamine)
- additional treatment in patients not controlled under standard regimens
- **delayed and breakthrough vomiting**
- **educate patients!**



Dopamine receptor antagonists

- **metoclopramide** one of the first antiemetic drugs used in cancer
- blocks dopamine receptors causing enhanced motility and accelerated gastric emptying
- in higher doses also blocks serotonin receptors in chemoreceptor trigger zone of the CNS - dose limitations due to neurological side effects: 3x10 mg i.v. or p.o.
- no major role in treatment of acute and delayed CINV
- role in breakthrough CINV



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76 percent of the patients. The sedation was mild in all but one patient.

Other side effects were diarrhea, occasional headaches, chills or other minor problems, the study said, but none of these effects necessitated stopping the treatment.

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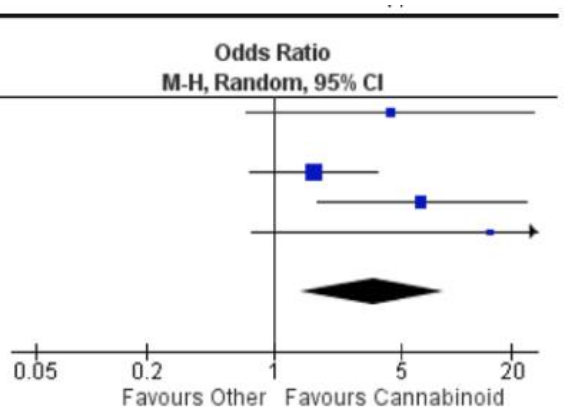
N.A.A.C.P. in South Carolina

Cannabinoids (dronabinole, nabilone)

- stimulate cannabinoid CB2 receptor in the brain stem
- side effects include sedation, euphoria, dysphoria and hallucinations
- no clear picture in available data (low patient numbers, poor quality of trials)
- no recommendation from ESMO or ASCO

	Cannabinoid		Other			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Chang et al 1979	6	15	2	15	18.5%	4.33 [0.71, 26.53]
Chang et al 1981	0	8	0	8		Not estimable
Frytak et al 1979	16	38	24	78	45.1%	1.64 [0.73, 3.66]
Meiri et al 2007	40	50	5	13	28.3%	6.40 [1.72, 23.83]
Sallan et al 1975	5	15	0	14	8.1%	15.19 [0.75, 305.73]
Total (95% CI)		**126**		**128**	**100.0%**	**3.45 [1.39, 8.58]**
Total events	67		31			

Heterogeneity: Tau² = 0.31; Chi² = 4.70, df = 3 (P = 0.20); I² = 36%
Test for overall effect: Z = 2.67 (P = 0.008)

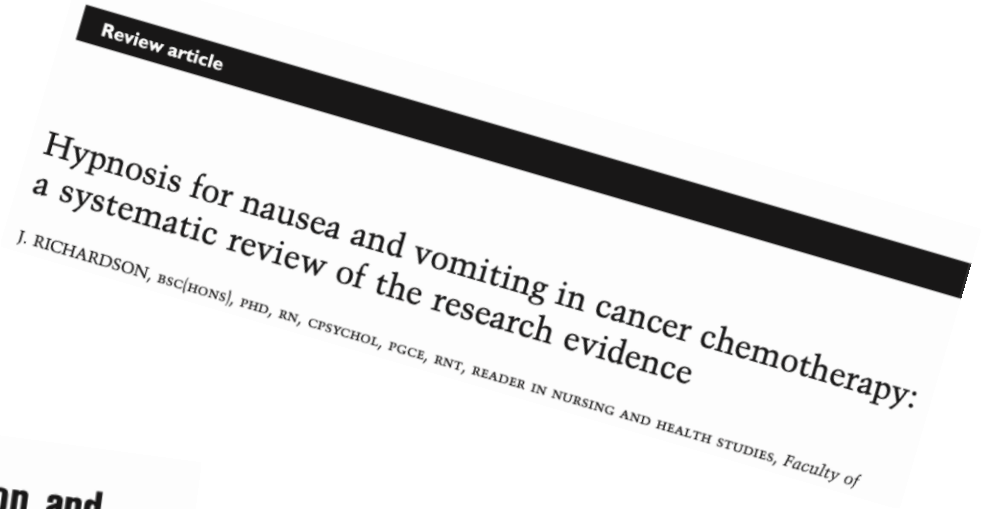


Chow et al, Supp. Cancer Care 2020

Alternative options?

Efficacy of Ginger (*Zingiber officinale*) in Ameliorating Chemotherapy-Induced Nausea and Vomiting and Chemotherapy-Related Outcomes: A Systematic Review Update and Meta-Analysis

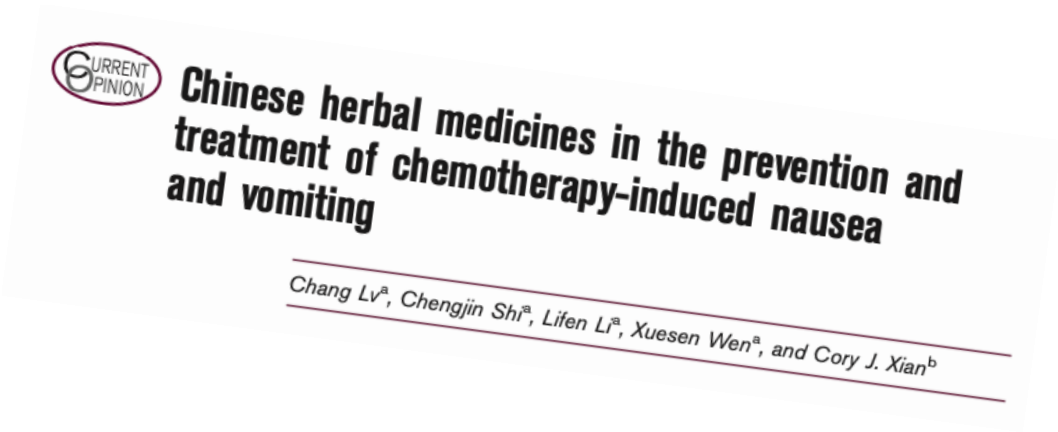
Megan Crichton, MNutr&Diet, APD*; Skye Marshall, PhD, APD*; Wolfgang Marx, PhD, APD*; Alexandra L. McCarthy, PhD, RN, MN; Elizabeth Isenring, PhD, AdvAPD‡



Review article

Hypnosis for nausea and vomiting in cancer chemotherapy: a systematic review of the research evidence

J. RICHARDSON, BSC(HONS), PHD, RN, CPSYCHOL, PGCE, RNT, READER IN NURSING AND HEALTH STUDIES, *Faculty of*



CURRENT OPINION

Chinese herbal medicines in the prevention and treatment of chemotherapy-induced nausea and vomiting

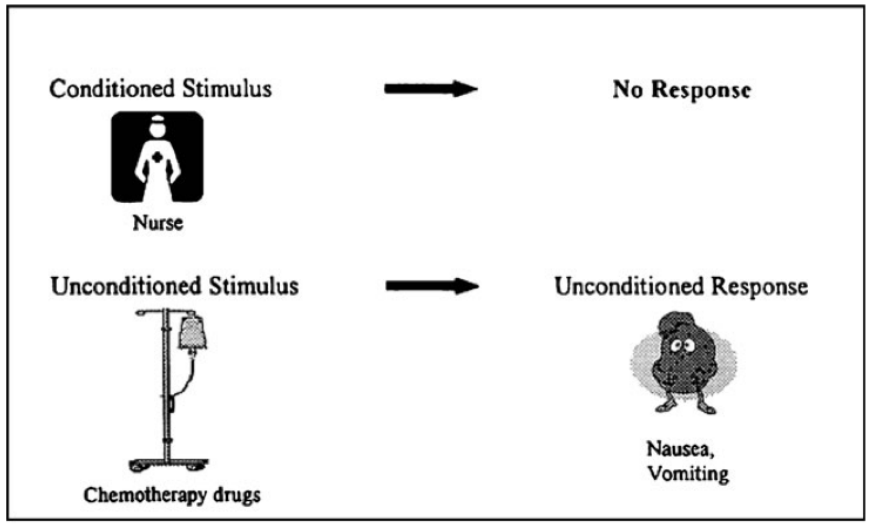
Chang Lv[a], *Chengjin Shi*[a], *Lifen Li*[a], *Xuesen Wen*[a], and *Cory J. Xian*[b]

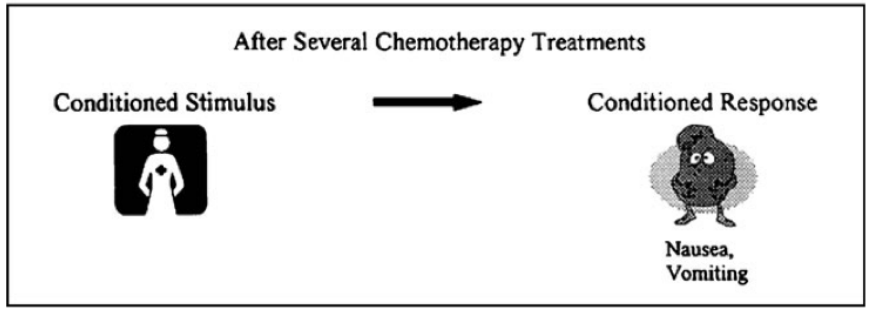
Anticipatory nausea and vomiting

- Nausea around 10%, vomiting around 3%

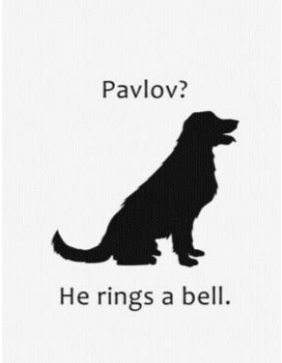
Table 1 Risk factors for ANV

Age less than 50
Nausea/vomiting after last chemotherapy session
Expectations of post-treatment nausea
Anxiety (both state and trait)
Susceptibility to motion sickness
Sweating or feeling warm all over after last chemotherapy session





Treatment	
Behavioural techniques	e.g. progressive relaxation training, hypnosis
Drug intervention: Benzodiazapines	**For example the day of the chemotherapy: Alprazolam 0.5-2 mg/d, Lorazepam 2 mg, diazepam**



Some final thoughts

- Educate your patients!
- Ask them how they did!
- Escalate antiemetic drugs!
- Consider anticipatory CINV!

The best prevention is the optimal treatment of CINV!

Thank you for your attention!