

The AZ-PLM Nausea Study

A novel patient-centric collaboration

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patientslikeme®

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AstraZeneca 
Health Connects Us All

Your Presenters



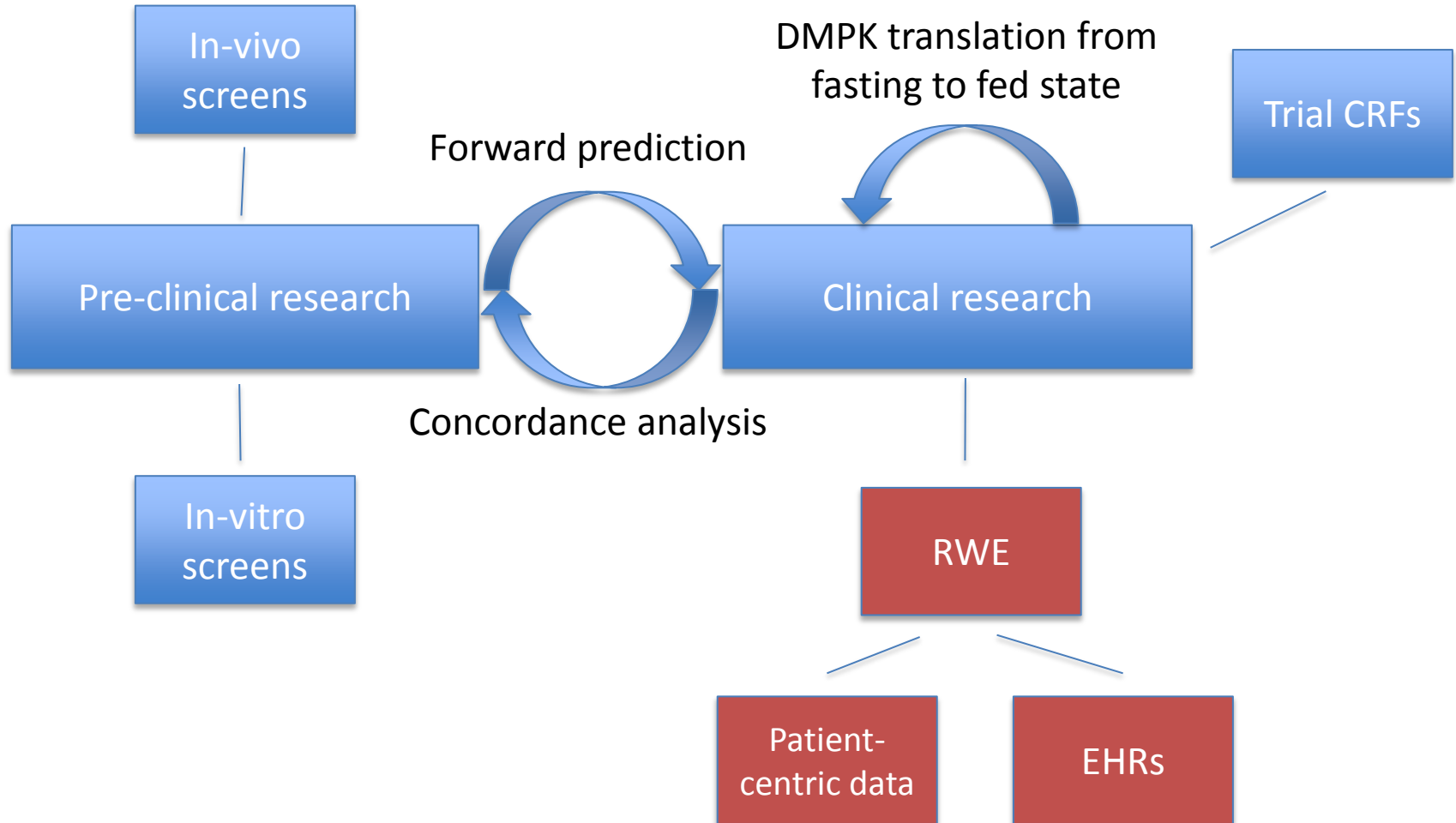
Jim Weatherall
Head, Advanced Analytics
Centre, Global Medicines
Development



Paul Wicks
Research Director,
PatientsLikeMe



How can we understand drug side effects?



Why PatientsLikeMe?

1. Differentiated from other patient online sites: more structured data collection, more scientific
2. PLM has over 30 peer-reviewed publications
3. Not so much a patient social media site...more an online patient-centric health research engine
4. Patients' perspectives are often overlooked *
5. *A complementary* form of Real World Evidence (RWE)

* e.g. Ethan Basch, "The Missing Voice of Patients in Drug-Safety Reporting", *The New England Journal of Medicine*, 2010

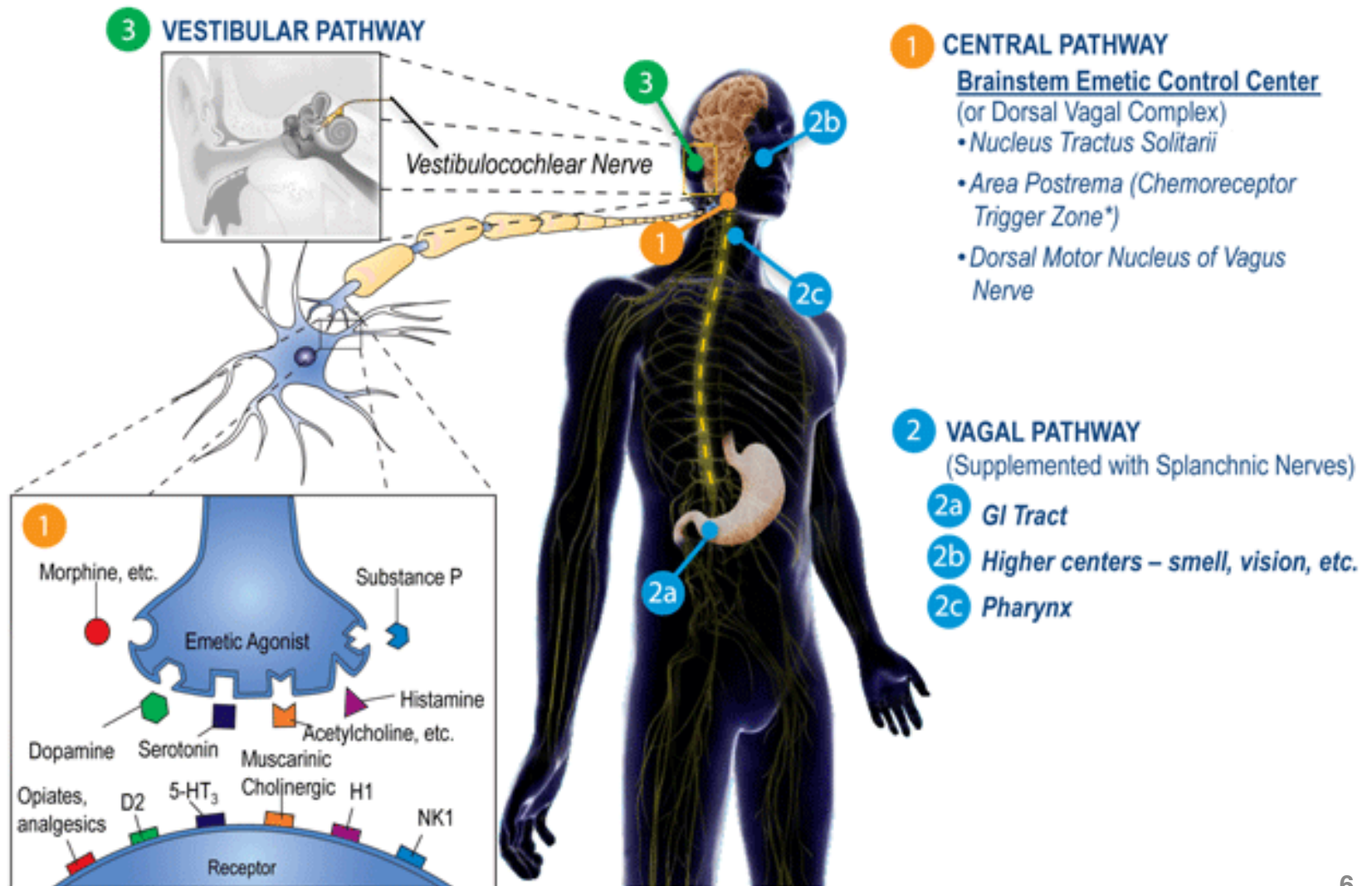
Why Nausea?

- Frequent complaint of PatientsLikeMe members in various conditions as a side effect
- Poorly characterized from patients' perspective but seems highly variable
- Pre-clinical animal studies are poorly predictive of occurrence in humans *

* e.g. Percie du Sert et al, "Predicting the emetic liability of novel chemical entities: a comparative study", *British Journal of Pharmacology*, 2011

* e.g. Olson et al, "Concordance of the Toxicity of Pharmaceuticals in Humans and in Animals", *Regulatory Toxicology and Pharmacology*, 2000

Pathways to Nausea



Study segments

Retrospective
Data
Extraction &
Analysis

Prospective
Data
Collection

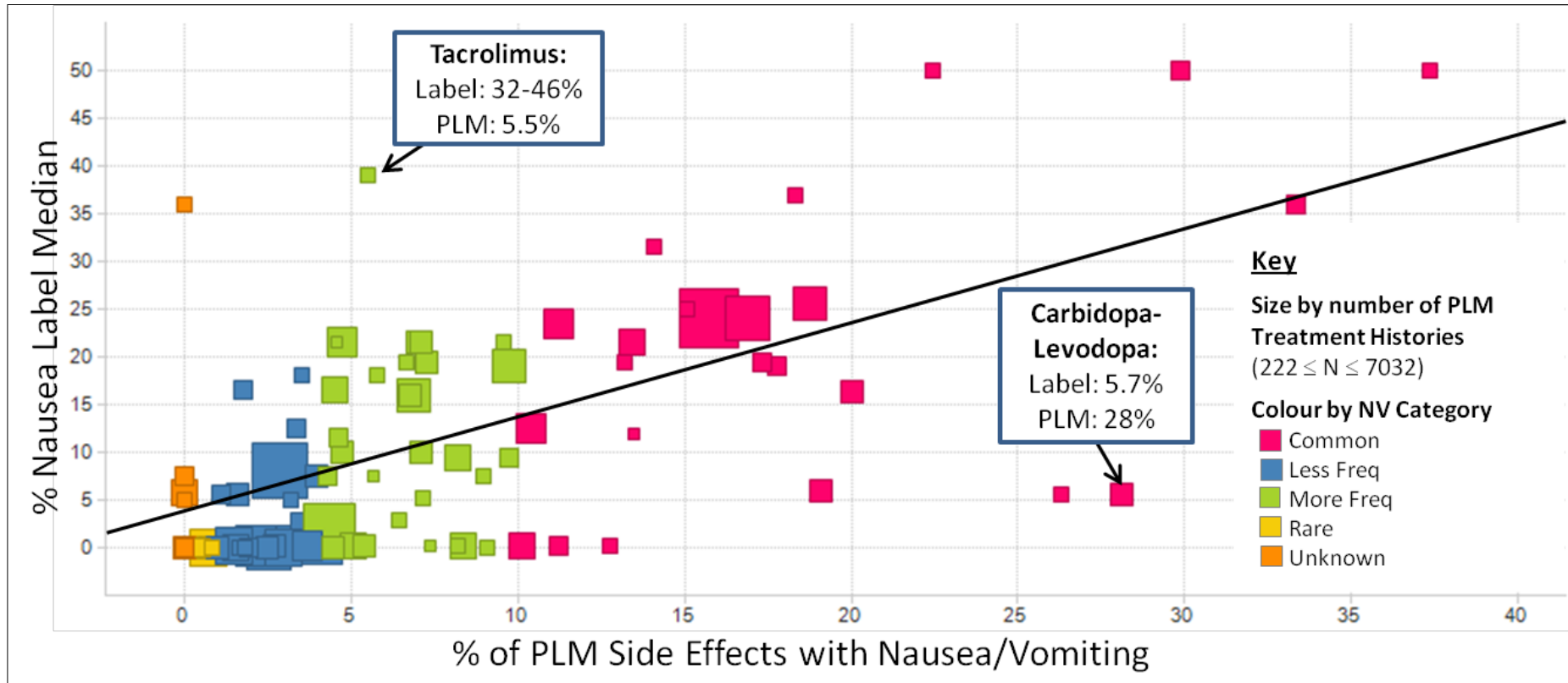
Final Data
Analysis &
Reporting

Condition by N	Patients with this condition	Patients reporting nausea	Patients reporting nausea nausea	% error in fraction
Major Depressive Disorder	1,310	1,048	1,048	18.4%
Bipolar I Disorder	11,804	796	812	0.1%
Generalized Anxiety Disorder	875	428	453%	1.7%
MDD (Multiple Sessions)	12,743	411	2.1%	0.1%
Bipolar II Disorder	725	378	51.3%	1.3%
Bipolar I Disorder	638	240	54.2%	2.0%
Bipolar II Disorder	888	290	27.2%	1.1%
PTSD (Post Traumatic Stress Disorder)	321	187	58.3%	2.8%
Migraine	271	109	58.7%	3.0%
Dysphagia	295	143	48.5%	2.8%
Schizophrenia	1,011	138	4.6%	0.4%
Schizophrenia (Lupus Encephalopathy)	1,176	97	8.2%	0.8%
AD (Attention Deficit)	1,254	80	6.7%	0.7%
ADHD (Attention Deficit/Hyperactivity Disorder)	249	78	31.3%	2.3%
Bipolar Disorder	260	75	28.8%	2.8%
Chronic Fatigue Syndrome	540	60	11.1%	1.4%
Social Anxiety Disorder	152	60	43.4%	4.0%
Neurotic Disorder	1,148	40	1.5%	0.1%
Panic Disorder	128	53	39.8%	4.1%
ICD (Obsessive Compulsive Disorder)	142	10	35.9%	4.0%
Substance Type 2	888	41	5.0%	0.7%
Borderline Personality Disorder	96	30	40.6%	5.0%
AD (Alcohol Use Disorder/Alcohol Use)	1,481	20	2.0%	0.4%
Alcohol Use Disorder	44	20	39.1%	6.1%
AD (Alcohol Use Disorder/Alcohol Use)	1,118	40	0.8%	0.1%

Section One - Current Nausea

- Are you currently experiencing nausea or vomiting as a side effect of one of the medications you are taking?
 - Yes (continue to Q2 in this section)
 - No (skip to section two)
- How many days has it been since you last experienced nausea or vomiting from this medication? (If you experienced these today please enter 0)
 - Number of days (0-90)
- Which medication do you think is responsible for your nausea? (Please enter either the brand name or generic name, don't worry about spelling)
 - Open text box (one line)
- What dosage of this medication are you currently taking? (If possible please answer in units (e.g. milligrams) rather than the number of pills you take)
 - Open text box (one line)
- How often do you take the medication that is responsible for your nausea?
 - Multiple times a day
 - Once a day
 - Once every few days
 - Once a week
 - Once every few weeks
 - Once a month
 - Less than once a month
 - As needed

Correlation between PLM N/V Frequency vs Drug Label Frequency



A moderate correlation is seen between PLM and Drug Label side effect frequency data
 $R = 0.62$

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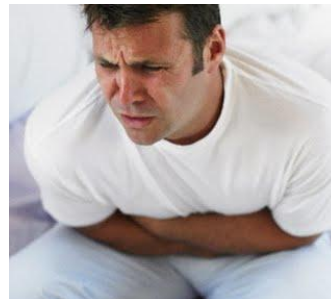
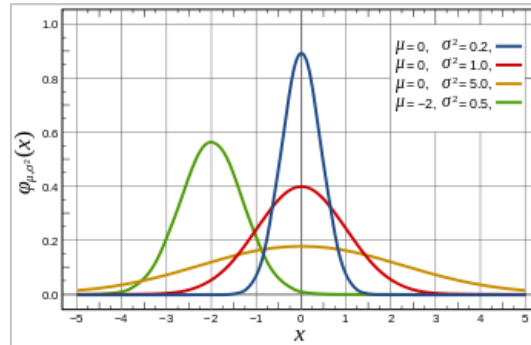
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Major Depressive Disorder	1,310	1,048	1,048	0.0%
Bipolar I Disorder	11,808	976	8.2%	0.1%
Generalized Anxiety Disorder	875	428	48.3%	1.7%
MDD (Multiple Sessions)	12,743	411	2.2%	0.1%
Bipolar II Disorder	725	378	52.1%	1.3%
Bipolar I Disorder	638	240	37.6%	2.0%
Alcohol Use Disorder	888	230	25.7%	1.1%
PTSD (Post Traumatic Stress Disorder)	321	187	58.3%	2.8%
Migraine	271	109	39.9%	3.0%
Dysphagia	295	143	48.5%	2.8%
Schizophrenia	1,011	138	13.7%	0.4%
Systemic Lupus Erythematosus	1,170	97	8.3%	0.8%
AD (Attention Deficit)	1,254	80	6.3%	0.7%
ADHD (Attention Deficit/Hyperactivity Disorder)	249	78	31.3%	2.3%
Bipolar Disorder	260	75	28.8%	2.8%
Chronic Fatigue Syndrome	540	60	11.1%	1.4%
Social Anxiety Disorder	152	60	39.5%	4.0%
Wernicke's Disease	1,148	40	3.5%	0.3%
Panic Disorder	128	53	41.4%	4.1%
CD (Obsessive Compulsive Disorder)	142	10	7.0%	0.9%
Substance Type 2	888	41	4.6%	0.7%
Borderline Personality Disorder	86	30	34.9%	5.0%
HIV (Human Immunodeficiency Virus)	1,481	20	1.3%	0.4%
Polysubstance Abuse	44	20	45.5%	6.1%
N/A (Neurological/Lateral Sclerosis)	1,118	40	3.6%	0.3%

Section One - Current Nausea

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Objectives - Shape of Nausea

Nausea can be characterised by:
Onset, duration, frequency,
severity, amelioration



Survey Instruments and Domains

Core Instruments

Demographics + SF1

Treatment Satisfaction (TSQM-II)

Quality of Life / Health State (EQ5D)

Adherence (Morisky Scale)

Illness Perception Questionnaire

PRO-CTCAE 7 Day Nausea / Vomiting + 24hr Screen

Work & Productivity (WPAI:NV)

(IF) Current Nausea

Cause of Nausea (Meds, condition, unknown)

Severity

Duration

Onset

Other Symptoms

Amelioration

Nausea Impact (Osoba NVQ5)

(IF) Current Vomiting

Cause of Vomiting (Meds, condition, unknown)

Severity

Duration

Onset

Other Symptoms

Amelioration

Vomiting Impact (Osoba NVQ5)

Are you experiencing nausea or vomiting? Please help us learn more! **PREVIEW (Edit Survey)**

0% complete

Dear Paul,

Are you experiencing nausea or vomiting? Whether you feel it's part of your health condition(s), a side effect of your medication, or it's just a temporary illness affecting you at the moment, we want to know more. We've partnered with the research team at drug manufacturer AstraZeneca® to learn more about how these unpleasant issues can affect you.

The survey should only take about 10-15 minutes to complete and as soon as we have analyzed the data we will share the overall results back with you and the rest of the community. We hope we can give patients and researchers better tools to describe their symptoms and perhaps even help people to live better with them on a daily basis.

To get started, click "Yes I'd like to participate" below, or if you have any questions please email research@patientslikeme.com

Best wishes

Paul Wicks, PhD.

R&D Director, PatientsLikeMe

Please answer the following questions as accurately as possible. The information that you provide will be managed according to our [Privacy Policy](#).

Basic Info



These questions will help researchers analyze trends and patterns. Your answers will also update your profile so you can better connect with patients like you.

Birth date

1981

August

24

Gender

Male

Female

Country of Residence

United Kingdom

Next »

Study segments

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Final Data
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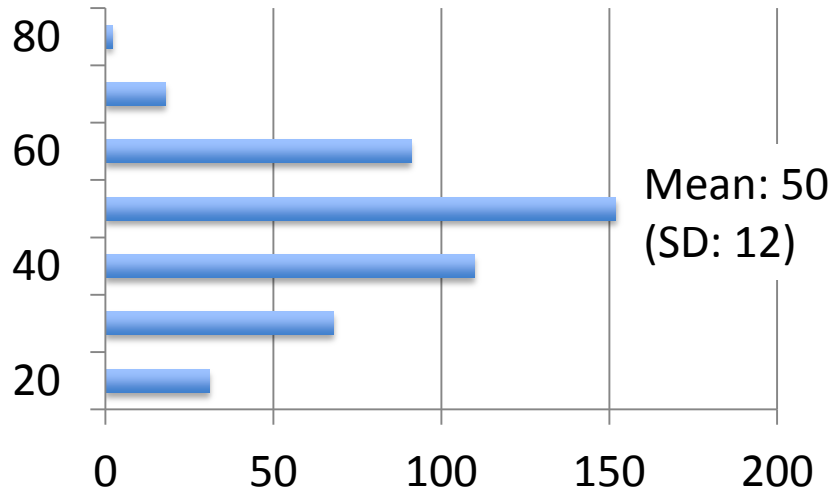
Condition by N	Patients with this condition	primary	Patients reporting nausea	Patients reporting nausea	N of error in fraction
Major Depressive Disorder	1,310	1,310	1,310	1,310	0.0%
Bipolar I Disorder	11,804	11,804	11,804	11,804	0.1%
Generalized Anxiety Disorder	875	875	875	875	1.7%
MDD (Multiple Sclerosis)	12,743	12,743	12,743	12,743	0.1%
Bipolar II Disorder	725	725	725	725	1.3%
Bipolar I Disorder	638	638	638	638	2.0%
Alcohol Use Disorder	888	888	888	888	1.1%
PTSD (Post Traumatic Stress Disorder)	321	321	321	321	2.8%
Migraine	271	271	271	271	3.0%
Dysphagia	295	295	295	295	2.8%
Schizophrenia	1,011	1,011	1,011	1,011	0.4%
Systemic Lupus Erythematosus	1,176	1,176	1,176	1,176	0.8%
AD (Attention Deficit)	1,254	1,254	1,254	1,254	0.7%
ADHD (Attention Deficit/Hyperactivity Disorder)	249	249	249	249	2.3%
Bipolar Disorder	260	260	260	260	2.8%
Chronic Fatigue Syndrome	540	540	540	540	1.4%
Social Anxiety Disorder	152	152	152	152	4.0%
Wetmore's Disease	1,148	1,148	1,148	1,148	0.1%
Panic Disorder	128	128	128	128	4.1%
ICD (Obsessive Compulsive Disorder)	142	142	142	142	4.0%
Substance Type 2	888	888	888	888	0.7%
Borderline Personality Disorder	36	36	36	36	5.0%
HIV (Human Immunodeficiency Virus)	1,481	1,481	1,481	1,481	0.8%
Poliovirus Infection	44	44	44	44	6.1%
N/A (Neurological/Lateral Sclerosis)	1,118	1,118	1,118	1,118	0.1%

Section One - Current Nausea

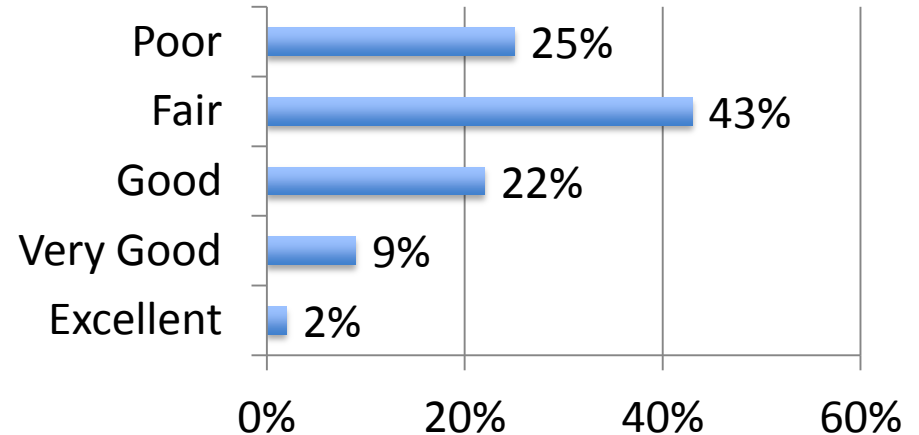
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 - Once every few weeks
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Participant Characteristics (N=472)

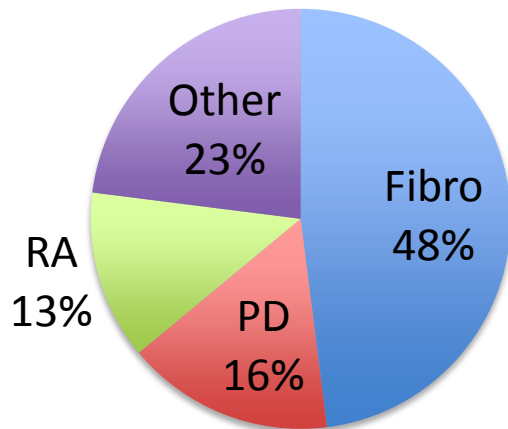
Age Distribution



In general, would you say your health is:

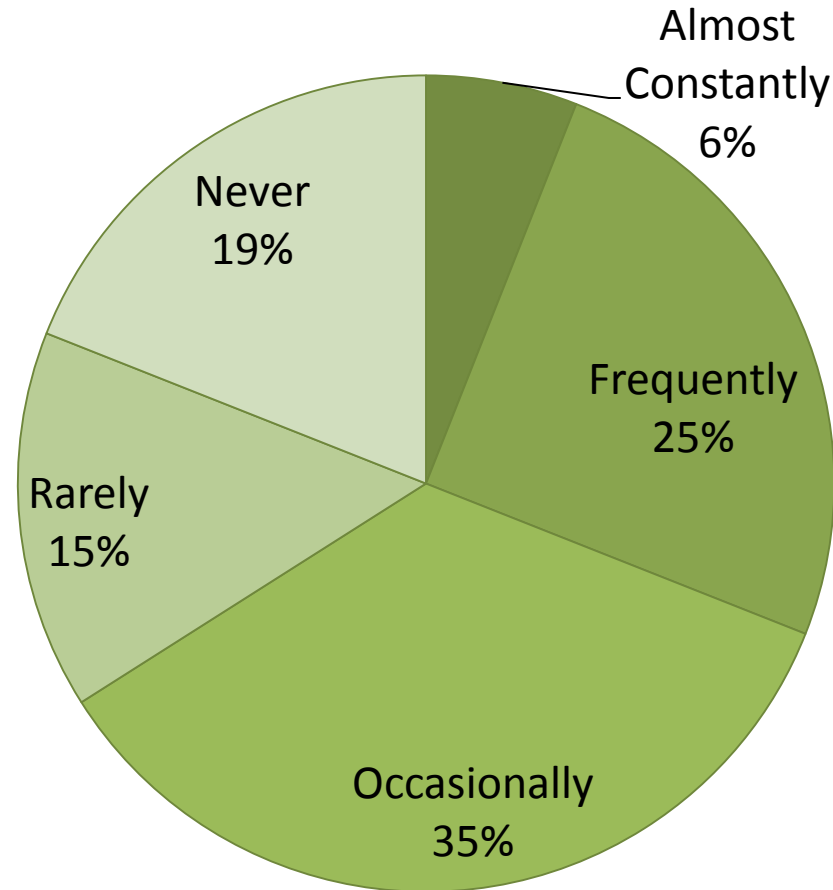


Primary Condition

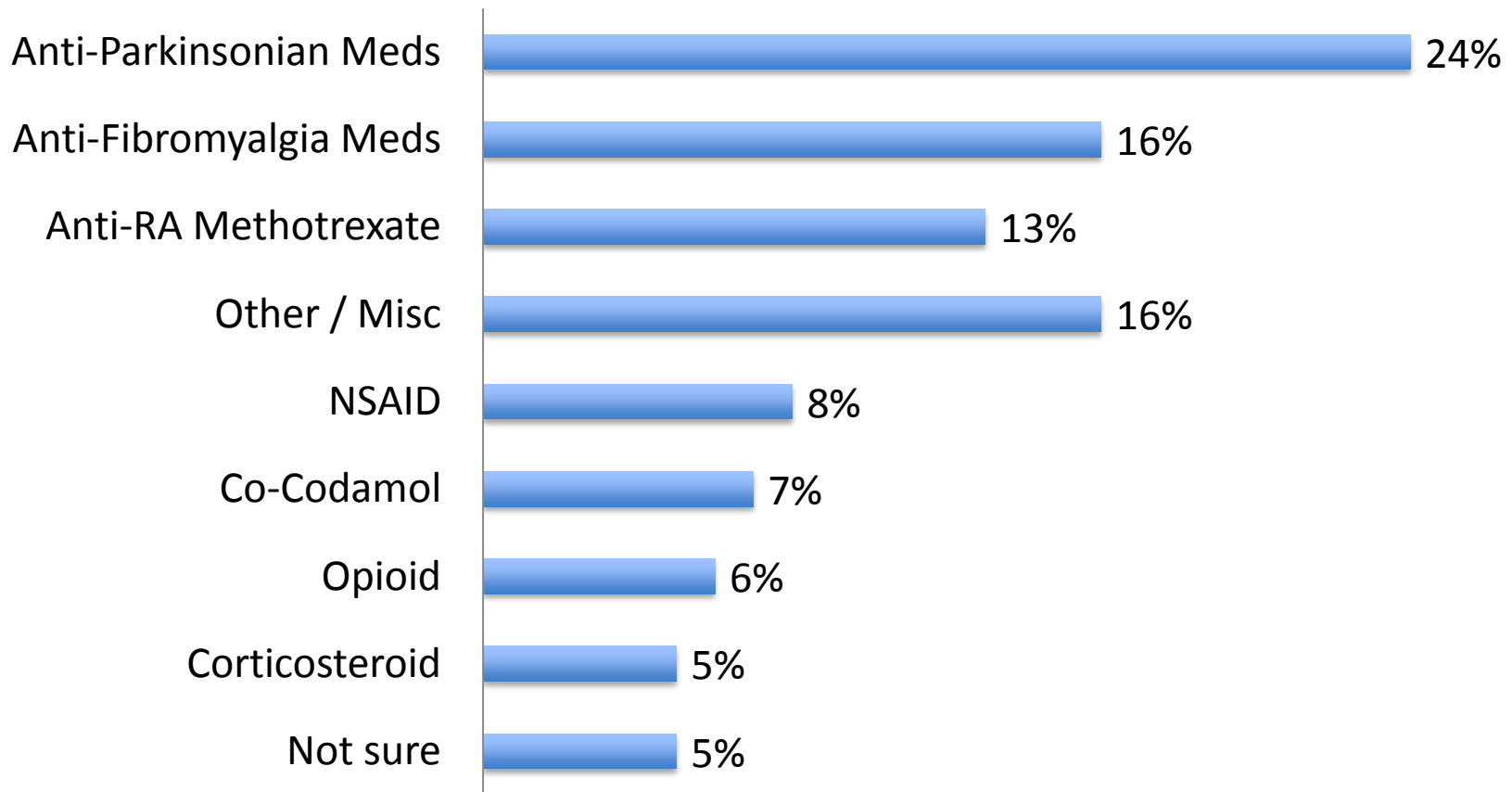


- Sex:
 - 85% Female
 - 15% Male
- Do you experience any medication side effects at all?
 - 79% Yes
 - 18% No
 - 3% N/A

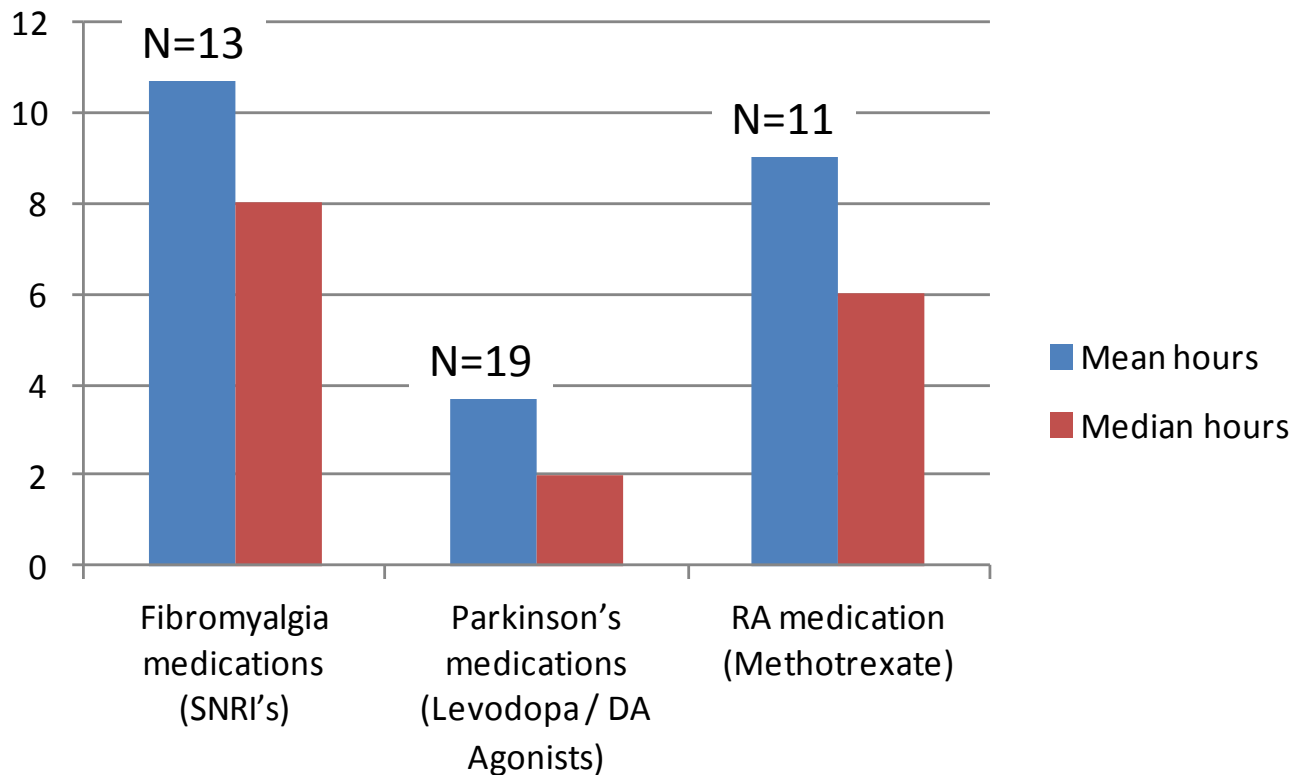
“In the last 7 days, how often did you have nausea?”



**“Which medication do you think is causing your nausea?” (N=84)



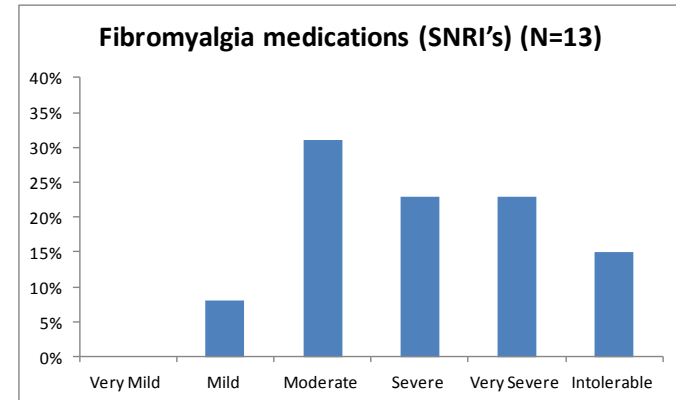
Does Duration of Nausea Vary by Medication Type? (Q: “For about how many hours a day did the nausea last?”) (Yes)



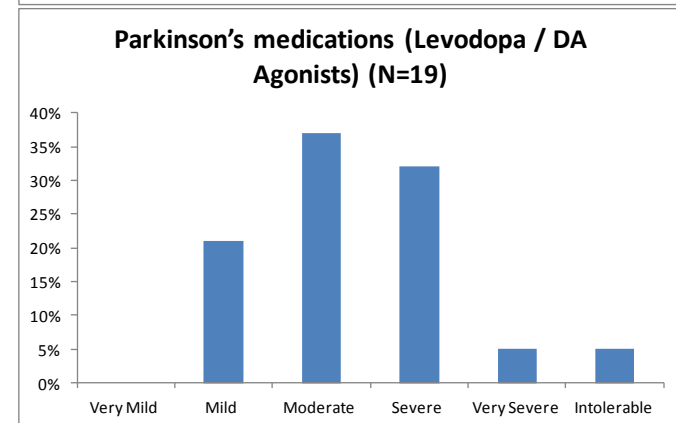
Kruskal Wallis Chi Square (2 df) = 8.448, p=0.015

Does Severity of Nausea Vary by Medication Type? (Q: “How would you describe the nausea at its worst”) (No)

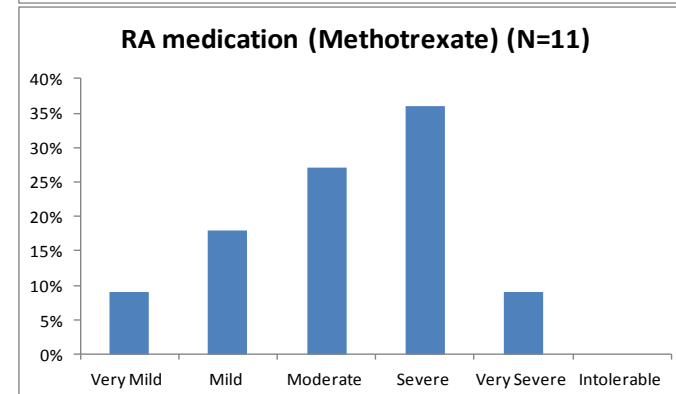
Fibromyalgia medications →



Parkinson's medications →



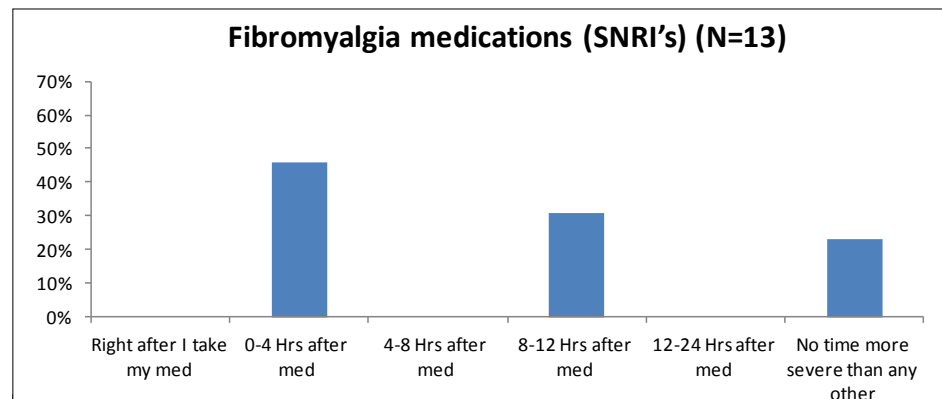
RA medication →



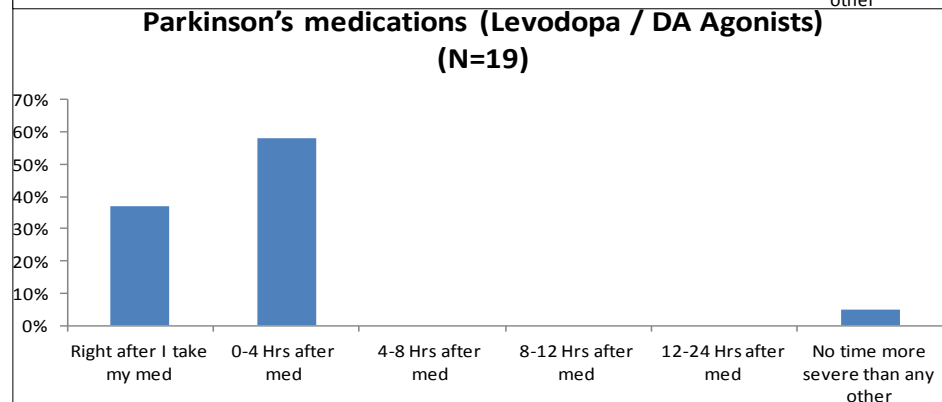
Chi-Square (df 10) = 8.724, p=0.558 (n.s.)

Does Onset of Nausea Vary by Medication Type? (Q: “When was the nausea worst?”) (Yes)

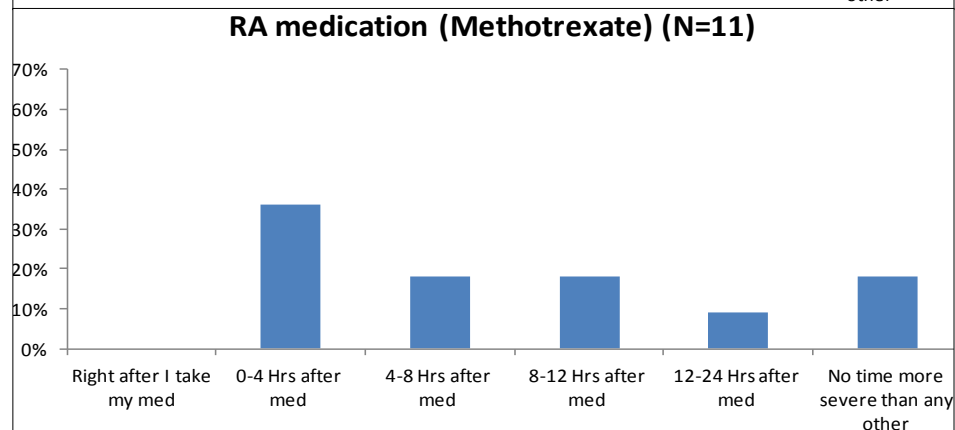
Fibromyalgia medications →



Parkinson's medications →



RA medication →

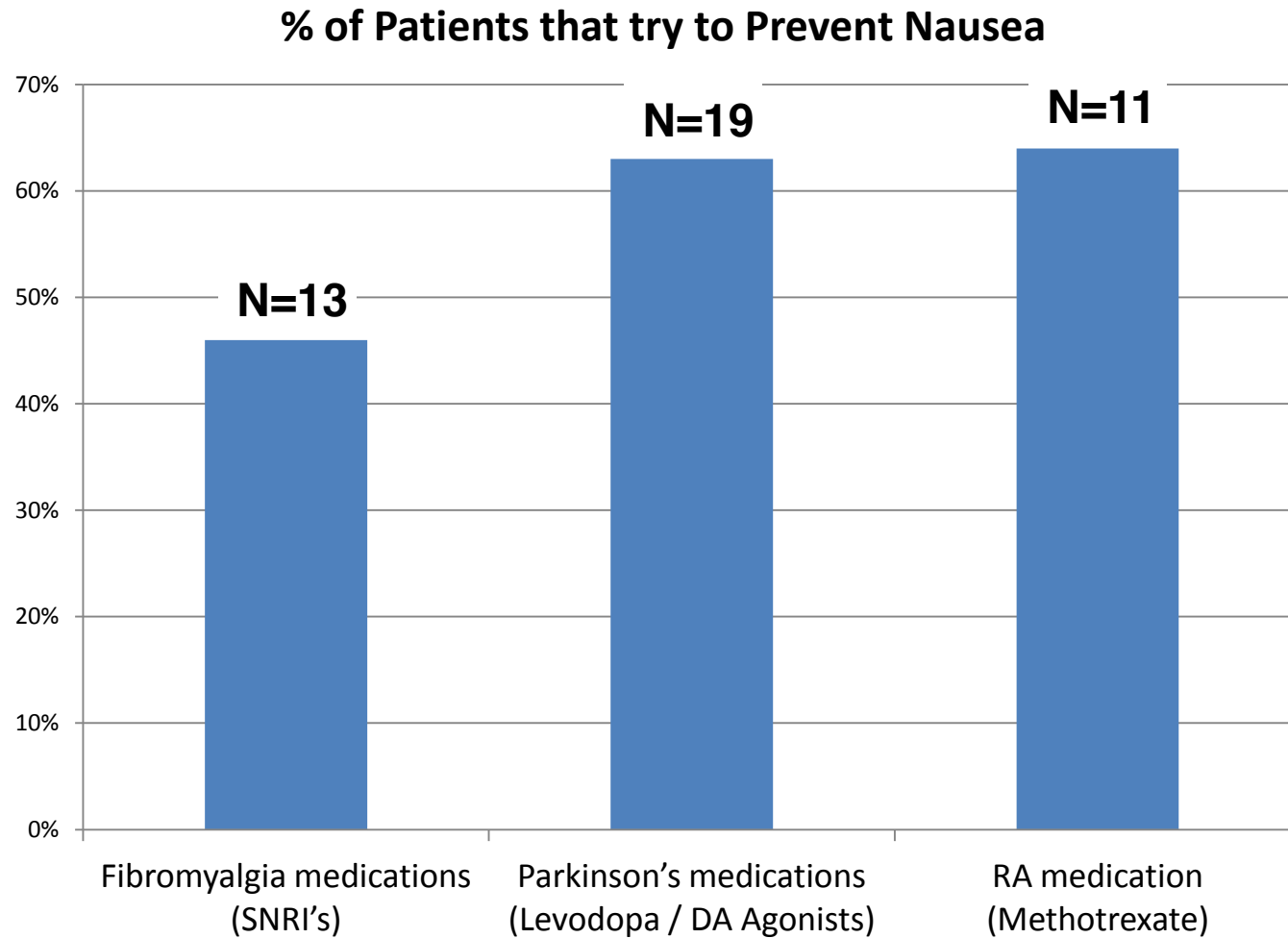


Chi-Square (df 10) = 25.630, p=0.004**

Do Co-occurring Symptoms Vary by Medication Type? (Q: “When you're experiencing nausea, what other symptoms do you normally experience at the same time? ”) (Maybe)

	Dizziness	Lightheaded	Feeling hot	Feeling cold	Stomach pain	Bloating	Diarrhea	Constipation	Heartburn	Burping	Palpitations	Headaches	Migraine	None of the above
FM Meds (N=13)	31%	54%	31%	39%	46%	31%	31%	23%	23%	31%	15%	31%	31%	15%
PD Meds (N=19)	20%	35%	10%	5%	30%	0%	5%	20%	5%	15%	10%	20%	0%	20%
RA Meds (N=11)	36%	55%	27%	27%	46%	36%	27%	9%	18%	9%	27%	64%	0%	0%

Can Nausea caused by Different Medication be Ameliorated to a Different Degree? (Q: “Do you do anything to try and prevent nausea?”) (No)



Chi Square (2 df) = 1.101, p=0.577

Can we tell “shape” by medication?

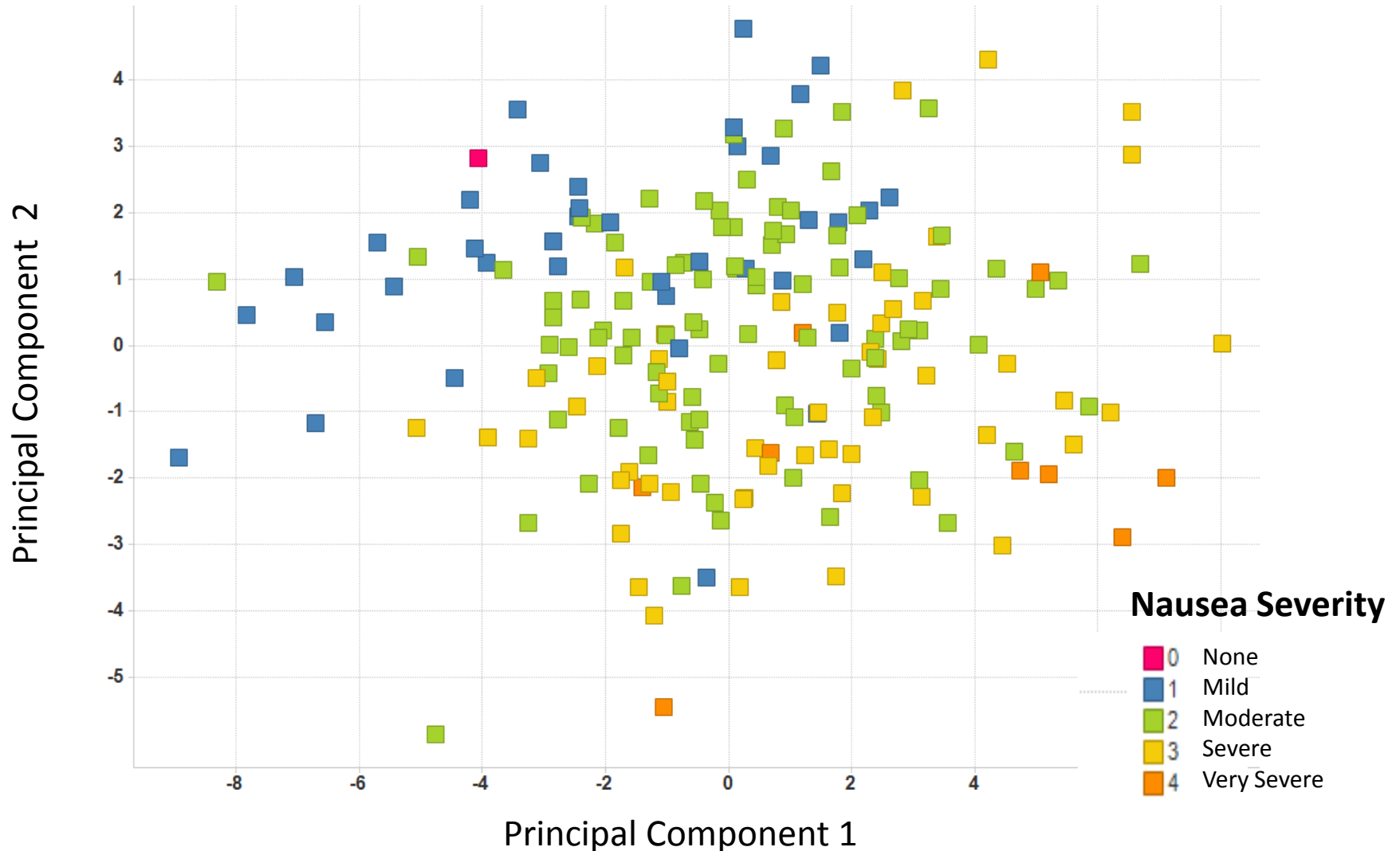
N&V Shape Variable	Different Pattern Across FM/PD/RA?
Duration	YES
Severity	NO
Onset	YES
Other symptoms	MAYBE
Amelioration	NO

Note: Due to the low numbers of patients in each disease category, we recommend that these preliminary findings be validated in a larger sample

Do these look like distinct “shapes” of nausea?

Indication of Treatment	Duration of Nausea	Onset of Nausea	Co-Occurring Symptoms
Fibromyalgia	8 hours a day	Hours after taking it	Lightheaded, Stomach Pain (15% none)
Parkinson's Disease	2 hours a day	Immediate after taking it	Lightheaded, Stomach Pain (20% none)
Rheumatoid Arthritis	6 hours a day	Heterogeneous	Headaches, Lightheaded (0% none)

Multivariate Analysis of PLM data - towards a better understanding of patient experience?



How PLM & AZ Worked Together

- Co-Location, F2F collaborative team building
- Multi-Disciplinary Team, with wide & flexible use of subject matter experts
- Shared Raw Data Set
- Sharing of confidential trial results
- Transparency with patients
- Mutual benefit and shared commitment to success

Summary versus objectives

PRIMARY: Investigate the feasibility of a future collaborative relationship between AZ & PLM

1. We showed that such a collaboration can work
2. Regular F2F sessions and flexible use of experts really helps
3. Learnings from contracting and planning process

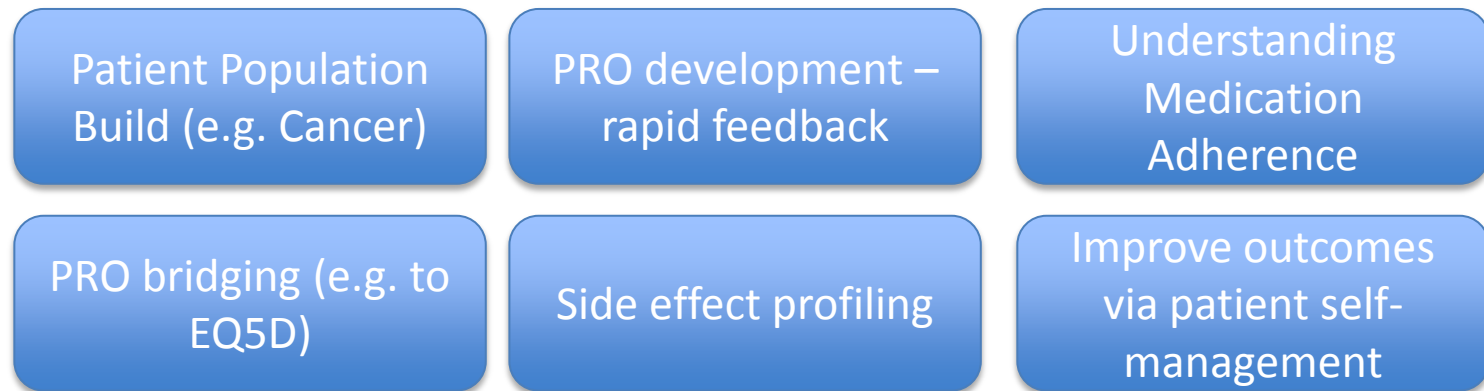
SECONDARY: Gain specific insights regarding patient experience of nausea & vomiting

1. The data was amenable to exploration and hypothesis generation
2. N decreases rapidly when filtering through the responder population
3. Scale-up would allow confirmation and more multivariate side-effect shape definition

Outlook

- AZ can collaborate with PLM to gain value in the areas of *patient-centric* understanding of disease, treatments and side-effects 
- The outputs are not fuel for submissions or reimbursement dossiers...yet 

Future Directions



Thank You!

