Predictors of Allodynia in Persons with Migraine: Results from the 2017 Migraine in America Symptoms and Treatment (MAST) Study

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This study was funded and sponsored by Promius Pharma, a subsidiary of Dr. Reddy's Laboratories, Princeton, NJ, USA.

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Disclosures

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David W. Dodick, MD – Within the last 12 months, Dr. Dodick reports personal fees from Amgen, Alder, Allergan, Autonomic Technologies, Biohaven, Eli Lilly, eNeura, Foresight Capital, Neurolief, Zosano, WL Gore, Vedanta Associates, Promius Pharma, Nocira, Novartis, Electrocore, Teva, Ipsen, Impel, Satsuma, Charleston Laboratories, Theranica. Compensation for activities related to data safety monitoring committee from Axsome. Compensation related to CME content development: Healthlogix, Medicom Worldwide, Medlogix Communications, MedNet, Miller Medical Communications, PeerView Operation Services America, Web MD/Medscape, American Academy of Neurology, American Headache Society, PeerView Institute for Medical Education, Chameleon Communications, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket Medical Education, Global Scientific Communications, UpToDate, Meeting LogiX. Royalties from editorial or book publishing: Oxford University Press, Cambridge University Press, Wiley Blackwell, Sage, Wolters Kluwer Health. Consulting use agreement through employer: NeuroAssessment Systems, Myndshft. Hold equity in: Aural Analytics, Healint, Theranica, Second Opinion/Mobile Health, Epien. Board of Directors position: King-Devick Technologies, Ontologics.

Michael L. Reed, PhD – Employee of Vedanta Research, which has received support funded by Allergan, Inc., Colucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation.

Kristina Fanning, PhD – Employee of Vedanta Research, which has received support funded by Allergan, Inc., Colucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation.

Sagar Munjal, MD, MS – Employee of Dr. Reddy's Laboratories and owns stock in the company.

Aftab Alam, MBBS, MS, MBA – Employee of Dr. Reddy's Laboratories and owns stock in the company.

Dawn C. Buse, PhD – Received grant support and honoraria from Allergan, Avanir, Amgen/ Novartis, Biohaven, Eli Lilly, Promius Pharma and Teva. She is on the editorial boards of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine.

Todd J. Schwedt, MD – Consultant, Scientific Advisory Board, or Speaker: Allergan, Amgen, ATI, Avanir, Dr. Reddy's Laboratories, Nocira, Novartis, and Teva. Editor: Headache, Pain Medicine, and Cephalalgia journals.

Richard B. Lipton, MD – Dr. Richard B. Lipton is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (Program Director), 5U10 NS077308 (PI), 1RO1 AG042595 (Investigator), RO1 NS082432 (Investigator), K23 NS09610 (Mentor), K23AG049466 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation. He serves on the editorial board of Neurology and as senior advisor to Headache. He has reviewed for the NIA and NINDS, holds stock options in eNeura Therapeutics and Biohaven Holdings; serves as consultant, advisory board member, or has received honoraria from: American Academy of Neurology, Alder, Allergan, American Headache Society, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Colucid, Dr. Reddy's Laboratories, Electrocore, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta. He receives royalties from Wolff's Headache, 8th Edition, Oxford Press University, 2009, Wiley and Informa.

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Allodynia in Migraine – Background and Objectives

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Background

- Cutaneous allodynia is a common feature of acute migraine attacks[1-5]
- Allodynia predicts poor response to acute migraine treatment with triptans[5,6], and is a risk factor for headache recurrence and progression from episodic to chronic migraine[7]

Objectives

- Determine the influence of headache-day frequency and other covariates on the presence of allodynia
- Estimate the prevalence of allodynia in adults with migraine with and without acute medication overuse (AMO)
- To determine gender stratified risk of cutaneous allodynia and the differential influence of other covariates on the presence of allodynia in men and women

1. Selby G, et al. *JNNP* 1960;23:23-32 2. Burstein R, et al. *Ann Neurol* 2000;47:614-624 3. Bigal ME, et al. *Neurology* 2008;70:1525-1533 4. Lipton RB, et al. *Ann Neurol* 2008;63:148-158
5. Burstein R, et al. *Ann Neurol* 2005;55:19-26 6. Lipton RB, et al. *Headache* 2017;57:1026-1040 7. Lipton RB, et al. *Headache* 2016;56:1635-1648

MAST – Methods, Participants, and Data Collection

MAST 2017 Study

- US nationwide online research panel of Adults (18+) constructed to represent US population by age, gender, and income
- Web surveys collected from October 2016-January 2017 assessed migraine features and other factors
- Persons eligible for this sub-study:
  - Meet ICHD-3β[1] criteria for migraine
  - Had ≥3 headache days in past 3 months and ≥1 headache day in past 30 days
  - Used acute migraine prescription medication

1. Headache Classification Committee of the International Headache Society. *Cephalalgia* 2013;33:629–808.

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MAST – Methods, Participants, and Data Collection

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- Additional variables assessed
  - Sociodemographic (age, gender, race, income, employment, education, BMI, health insurance, smoking status, marital status)
  - Acute Medication Overuse (ICHD-3β)
  - Headache Frequency and Intensity
  - Migraine Symptom Severity Score (MSSS)*
  - Anxiety/Depression Score (PHQ-4)
  - Allodynia Symptom Score (ASC-12)

*A composite index that incorporates information about 7 headache features (unilateral pain, pulsatile pain, moderate or severe pain intensity, routine activities worsen pain, nausea, photophobia, phonophobia)

MAST Study Sample Results

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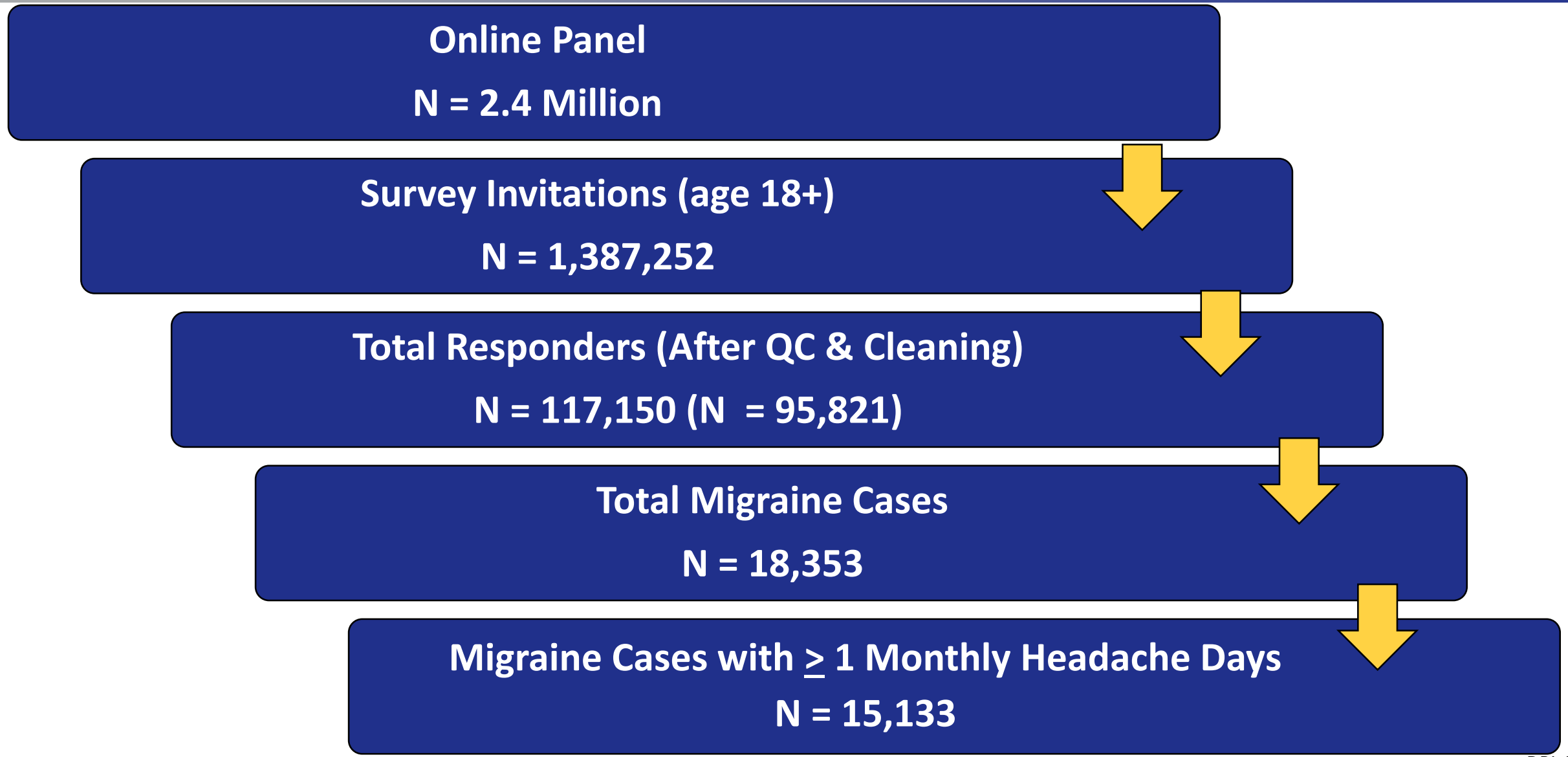

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Baseline Features Associated with Allodynia

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Sociodemographic	No Allodynia N = 9,095 (60.1%)	Allodynia N = 6,038 (39.9%)	Total N = 15,133 (%)	*P* Value
Females	6216 (68.3%)	4833 (80%)	11049 (73%)	<.001
Mean Age	44	41	43	<.001
Unmarried	4026 (44.4%)	2899 (48.2%)	6925 (45.9%)	<.001
Less than 4-year Degree	3638 (40%)	2656 (44%)	6294 (41.6%)	<.001
Current Smoker	851 (9.4%)	870 (14.4%)	1721 (11.4%)	<.001
Employed Full/Part Time	2529 (27.8%)	1890 (31.3%)	4419 (29.2%)	<.001

Baseline Features Associated with Allodynia

MAST 2017 Study

Respondent and Headache Features	No Allodynia N = 9,095 (60.1%)	Allodynia N = 6,038 (39.9%)	Total N = 15,133 (%)	*P* Value
Psychological Distress (PHQ-4)	1556 (17.1%)	2013 (33.3%)	3569 (23.6%)	<.001
Monthly Headache Days [mean ± SD]	4.90 ± 5.49	6.56 ± 6.65	5.56 ± 6.03	<.001
Pain Intensity Rating [mean ± SD]	6.41 ± 1.67	7.07 ± 1.56	6.67 ± 1.66	<.001
MSSS [mean ± SD]	15.93 ± 3.00	17.64 ± 2.66	16.61 ± 2.99	<.001
Medication Overuse	976 (11.9%)	1131 (20.7%)	2107 (15.4%)	<.001

MSSS = Migraine Symptom Severity Score

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Risk of Cutaneous Allodynia

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Sociodemographics	Model 1 Sociodemographic OR (95% CI)	Model 2 Add MHDs OR (95% CI)	Model 3 Add Responder/HA Characteristics OR (95% CI)
Age	0.99 (0.98, 0.99)	0.99 (0.98, 0.99)	0.99 (0.98, 0.99)
Women	1.78 (1.65, 1.93)	1.76 (1.62, 1.91)	1.70 (1.56, 1.86)
Household Income	0.97 (0.96, 0.99)	0.98 (0.96, 1.00)	1.00 (0.98, 1.03)
White	1.15 (1.05, 1.25)	1.11 (1.02, 1.22)	1.13 (1.03, 1.25)
Current Smoker	1.69 (1.53, 1.88)	1.62 (1.46, 1.8)	1.37 (1.22, 1.55)
Not Employed Full Time	1.27 (1.17, 1.38)	1.23 (1.13, 1.33)	1.19 (1.08, 1.3)
MHD (5-9 Days)		1.49 (1.36, 1.62)	1.23 (1.12, 1.36)
MHD (10-14 Days)		1.64 (1.44, 1.86)	1.22 (1.05, 1.41)
MHD (≥ 15 Days)		2.09 (1.86, 2.35)	1.36 (1.18, 1.57)
Medication Overuse			1.23 (1.09, 1.38)
MSSS			1.17 (1.15, 1.19)
Pain Intensity			1.11 (1.08, 1.14)
Depression and Anxiety Symptomology (PHQ-4)			1.83 (1.67, 2.00)

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Gender Stratified Risk of Cutaneous Allodynia

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Fully Adjusted Model	Males OR (95% CI)	Females OR (95% CI)
Age	0.97 (0.97, 0.98)	0.99 (0.99, 1.00)
Household Income	1.08 (1.01, 1.15)	0.97 (0.94, 1.01)
White	1.31 (1.03, 1.67)	1.08 (0.97, 1.21)
Current Smoker	1.63 (1.32, 2.01)	1.17 (1.01, 1.35)
Not Employed Full Time	1.18 (0.95, 1.47)	1.20 (1.09, 1.33)
MHD (5-9 Days)	1.17 (0.95, 1.43)	1.25 (1.12, 1.39)
MHD (10-14 Days)	1.02 (0.75, 1.39)	1.27 (1.07, 1.49)
MHD (≥ 15 Days)	1.16 (0.86, 1.57)	1.46 (1.24, 1.72)
Medication Overuse	1.57 (1.25, 1.98)	1.10 (0.96, 1.26)
MSSS	1.17 (1.13, 1.21)	1.17 (1.15, 1.19)
Pain Intensity	1.14 (1.07, 1.20)	1.09 (1.05, 1.12)
Depression and Anxiety Symptomology (PHQ-4)	2.17 (1.82, 2.60)	1.69 (1.53, 1.88)

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Conclusions

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- Allodynia is common (40%) in persons with migraine
- Symptoms of depression and anxiety, acute medication overuse, and each 1-point increase in MSSS were associated with an 83%, 23%, and 17% increased likelihood of having allodynia
- Increasing income category, being white, and acute medication overuse increased the odds of having allodynia in men
- Being unemployed and having frequent migraine headache days was associated with greater likelihood of allodynia in women

Conclusions

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- Other factors associated with the presence of allodynia included increasing MSSS, headache frequency, headache intensity, being female, being white, and smoking
- Allodynia reported in 50.3% of those with AMO compared 37.5% without AMO ($P < .001$)
- Cutaneous allodynia and MO are strongly associated even after adjusting for covariates, which supports the clinical approach of minimizing the overuse of acute medications
- A prospective, longitudinal study would help clarify the directionality of these associations

Thank You!

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