Migraine Epidemiology: Results and Clinical Applications
Richard B. Lipton, M.D., F.A.H.S.
Albert Einstein College Of Medicine
<table>
<thead>
<tr>
<th>Disclosures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richard B. Lipton, MD, FAHS</td>
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<tr>
<th>Consulting fees/Honoraria</th>
<th>Alder, Allergan, Amgen, Avanir, Colucid, Dr. Reddy’s, Eli Lilly, Labrys, Merck, Novartis</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH, Alder, Allergan, Avanir, Colucid, Dr. Reddy’s, Eli Lilly, and Labrys</td>
<td>Research grants</td>
</tr>
<tr>
<td>Editorial Boards</td>
<td>Current Pain and Headache Reports, Journal of Headache and Pain, Pain Medicine, and Pain Pathways</td>
</tr>
</tbody>
</table>
Clinical lessons from migraine epidemiology

1. Migraine is common and disabling.
2. Headache days per month vary within person over time. Chronic migraine evolves from episodic migraine.
3. Evolution of CM is associated with well-characterized remediable risk factors.
4. Cardiovascular disease is common in migraine.
5. Cost and barriers to care

American Migraine Prevalence and Prevention Study

- ≈163,000 respondents age ≥12 years
- ≈29,000 reported “severe headache” within the preceding year
- ≈19,000 met ICHD-2 criteria for migraine

## Prevalence of Migraine and TTH

<table>
<thead>
<tr>
<th>Disorder</th>
<th>One-Year Period Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
</tr>
<tr>
<td>Migraine&lt;sup&gt;1&lt;/sup&gt;</td>
<td>18.6</td>
</tr>
<tr>
<td>Chronic migraine&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1.3</td>
</tr>
<tr>
<td>Episodic tension-type headache&lt;sup&gt;3&lt;/sup&gt;</td>
<td>42.0</td>
</tr>
<tr>
<td>Chronic tension-type headache&lt;sup&gt;3&lt;/sup&gt;</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Chronic Migraine: Greater Disability and Impact than Episodic Migraine

<table>
<thead>
<tr>
<th>Because of headache, on how many days* . . .</th>
<th>EM Mean (SD)</th>
<th>CM Mean (SD)</th>
<th>Rate Ratio EM vs CM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed work or school</td>
<td>0.54 (2.6)</td>
<td>2.4 (10.2)</td>
<td>4.1†</td>
</tr>
<tr>
<td>Productivity at work or school reduced 50%</td>
<td>1.7 (3.7)</td>
<td>10.4 (18.1)</td>
<td>5.8†</td>
</tr>
<tr>
<td>Missed household work</td>
<td>3.5 (5.4)</td>
<td>21.4 (23.3)</td>
<td>5.5†</td>
</tr>
<tr>
<td>Productivity in household work reduced 50%</td>
<td>2.6 (4.4)</td>
<td>18.7 (19.8)</td>
<td>6.2†</td>
</tr>
<tr>
<td>Missed family, social or leisure activities</td>
<td>1.7 (3.6)</td>
<td>10.5 (17.4)</td>
<td>5.5†</td>
</tr>
</tbody>
</table>

* MIDAS recall period = 3 months
† $P \leq 0.001$ after controlling for age, gender, and income

Clinical lessons from migraine epidemiology

1. Migraine is common and disabling.
2. Headache days per month vary within person over time. Chronic migraine evolves from episodic migraine.
3. Evolution of CM is associated with well-characterized remediable risk factors.
4. Cardiovascular disease is common in migraine.
5. Barriers to care
Episodic migraine can progress to chronic migraine due to treatment-related conditions, exogenous factors, headache features, and in patients with certain co-morbidities. The annual rate of progression from episodic to chronic migraine is about:

a. 2.5%
b. 7.5%
c. 12.5%
d. 20%
Persistent EM/CM Group Mean Headache Days/Month: AMPP 2005-2009

Persistent CM

Persistent EM

Lipton et al., In review

15 headache days/mo

Lipton et al. (In review)
15 headache days per month

Lipton et al. In review
EM at Baseline and CM in at Least one Follow-up Wave: CaMEO-3 month Follow-up Intervals

Lipton et al. In review
Clinical lessons from migraine epidemiology

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## Risk Factors for CM/CDH Onset

### Comorbidities
- Depression
- Anxiety
- Other pain disorders
- Obesity
- Asthma
- Snoring

### Exogenous Factors
- Stressful life events
- Head/Neck injury
- Caffeine

### Headache Features
- Attack frequency (headache days)
- Persistent, frequent nausea
- Allodynia

### Treatment-related
- Poor treatment efficacy
- Medication overuse

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Chronic migraine is comorbid with several medical and psychiatric conditions. What percentage of persons with chronic migraine also have depression?

a. 10%
b. 20%
c. 30%
d. 50%
CM Has Greater Psychiatric and Medical Comorbidities than EM at Cross-section

<table>
<thead>
<tr>
<th>Comorbid Condition</th>
<th>EM (n=10,609)</th>
<th>CM (n=655)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression\textsuperscript{a}</td>
<td>17.2%</td>
<td>30.2%</td>
<td>2.1 (17.4–2.5)</td>
</tr>
<tr>
<td>Anxiety Disorders\textsuperscript{b}</td>
<td>18.8%</td>
<td>30.2%</td>
<td>1.9 (1.6–2.2)</td>
</tr>
<tr>
<td>Other Chronic Pain Disorders\textsuperscript{b}</td>
<td>15.1%</td>
<td>31.5%</td>
<td>2.6 (2.2–3.1)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Defined as PHQ-9 sum score \geq 15  
\textsuperscript{b} Based on subject report of physician diagnosis

CI= 95% confidence interval

Severity of Depression Predicts New Onset CM

Data from AMPP Study, 2005–2007

- Severe: 2.53*; 95%CI (1.52–4.21)
- Moderately–Severe: 2.35*; 95%CI (1.53–3.62)
- Moderate: 1.77*; 95%CI (1.25–2.52)
- None/Mild

*P<0.05

Persistent frequent nausea occurs in 43.7% of episodic migraine.

Risk of progression to chronic migraine increases 2-fold when frequent nausea persists over time.

Conclusions:

- Persistent frequent nausea could be a marker for the risk of progression to chronic migraine.
- Persistent frequent nausea could contribute to the cause of progression to chronic migraine.
- Effective management of nausea could improve headache treatment, outcomes in episodic migraine.

Data from AMPP Study; Reed et al. *Headache*. 2015;55:76–87.
Rates of New-Onset Chronic Migraine by Acute Treatment Efficacy Status

**Progressing from EM to CM (%)**

- **Very Poor**
  - N=308
  - 6.8%

- **Poor**
  - N=1,919
  - 4.4%

- **Moderate**
  - N=1,132
  - 2.7%

- **Maximal**
  - N=1,266
  - 1.9%

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**OR**

- OR, 3.08; 95% CI (1.79-5.29), P<0.001*

- OR, 1.64; 95% CI (1.08-2.49), P<0.019*

- OR, 1.15; 95% CI (0.70-1.88), P<0.587

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*Adjusted for age, sex, and annual household income

Use of Barbiturates and Opioids Predicts New Onset Chronic Migraine

Comorbid pain predicts the onset of CM and persistence of CM: Results from the CaMEO Study

- Pain was assessed using the Total Pain Index
- Number of pain locations occurring most or all of the time were examined
  - Excluding head pain, 8 pain locations were possible
- Examined the cross-sectional relationship of number of pain locations and migraine type for EM, CM (not daily) and daily CM.
- Examined the predictive validity of the number of pain locations on the onset of CM in persons with EM and on the persistence of CM using binary logistic regression analysis
Number of pain locations by migraine group: Cross-sectional analysis

- Mean (SD) number of pain locations with pain most or all of the time and headache frequency

![Bar chart showing number of pain locations by headache frequency and migraine group]

- CM-Non-Daily
  - Twice as many pain locations as EM
  - RR: 2.04 (95% CI, 1.9–2.2)

- CM-Daily
  - 46% more pain locations than CM Non-Daily
  - RR: 1.46 (95% CI, 1.13–1.89)

Scher et al., Submitted
Number of pain locations and the onset of CM in persons with EM over 3 months: Longitudinal analysis

<table>
<thead>
<tr>
<th>Baseline HA Status</th>
<th>Increased Odds of CM with Each Additional Pain Location</th>
<th>Adjusted for Demographics</th>
<th>Adjusted for Demographics and Baseline Headache Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted for Demographics</td>
<td></td>
</tr>
<tr>
<td>Baseline EM (transition to CM)</td>
<td>43% (OR 1.43 [95% CI, 1.33–1.53])</td>
<td>42% (OR 1.42 [95% CI, 1.33–1.52])</td>
<td>30% (OR 1.30 [95% CI, 1.21–1.40])</td>
</tr>
</tbody>
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Note: For two pain locations the OR is 1.96 and for 3 it is 2.7

Data for baseline and 3-month follow-up. **Bolded values** are statistically significant.
### Number of pain locations and the onset or maintenance CM at 3 months: Longitudinal analysis

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<tr>
<th>Baseline HA Status</th>
<th>Increased Odds of CM with Each Additional Pain Location</th>
<th>Adjusted for Demographics</th>
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<td><strong>30%</strong> (OR 1.30 [95% CI, 1.21–1.40])</td>
</tr>
<tr>
<td>Baseline CM (remaining CM)</td>
<td><strong>16%</strong> (OR 1.16 [95% CI, 1.08–1.25])</td>
<td><strong>15%</strong> (OR 1.15 [95% CI, 1.07–1.25])</td>
<td><strong>6%</strong> (OR 1.06 [95% CI, 0.97–1.16])</td>
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Data for baseline and 3-month follow-up. **Bolded values** are statistically significant.
Prevent Onset of Chronic Migraine in Your Patients with Episodic Migraine

<table>
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<tr>
<th>Risk Factor</th>
<th>Treatment/ Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment patterns</td>
<td>Monitor and modify medication use, consider preventive other non-oral treatments, and behavioral interventions*</td>
</tr>
<tr>
<td>Attack frequency</td>
<td>Reduction/Prevention with pharmacologic and behavioral interventions</td>
</tr>
<tr>
<td>Nausea</td>
<td>Antiemetics in acute treatment, early or non-oral attack treatment, preventive medications, avoidance of aggravating medications</td>
</tr>
<tr>
<td>Obesity</td>
<td>Weight loss, Exercise, Behavioral Interventions</td>
</tr>
<tr>
<td>Stress</td>
<td>Behavioral interventions, Exercise, Lifestyle modification</td>
</tr>
<tr>
<td>Snoring</td>
<td>Diagnose and treat sleep apnea, Weight loss</td>
</tr>
<tr>
<td>Allodynia</td>
<td>Manage migraine attack frequency and treat migraine early</td>
</tr>
<tr>
<td>Depression</td>
<td>Assess, Treat/Refer with pharmacologic and behavioral therapies</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Assess, Treat/Refer with pharmacologic and behavioral therapies</td>
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*Biofeedback, cognitive behavioral therapy, relaxation training, stress management
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CVD increases with age and in men

Percentage of Women and Men With Episodic Migraine Who Self-Reported Medically Diagnosed Cardiovascular Events, Conditions or Procedure

Events: MI, CVA, TIA; Conditions: Angina, claudication; Procedures: coronary angioplasty, CABG, endarterectomy, peripheral bypass surgery

Buse et al, Headache; 2016
Yet, there are more women than men with migraine who have CVD

Projected Number of Women and Men in the US Population With One or More CV Events, Conditions or Procedures

<table>
<thead>
<tr>
<th>Age</th>
<th>22–39</th>
<th>40–59</th>
<th>≥60</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>130,000</td>
<td>357,000</td>
<td>178,000</td>
<td>665,000</td>
</tr>
<tr>
<td>Women</td>
<td>449,000</td>
<td>1,012,000</td>
<td>518,000</td>
<td>1,979,000</td>
</tr>
<tr>
<td>TOTAL</td>
<td>579,000</td>
<td>1,369,000</td>
<td>696,000</td>
<td>2,644,000</td>
</tr>
</tbody>
</table>

2.6 million Americans with migraine and CV contraindications to triptans

Source: Buse et al. Headache, 2016
Chronic Migraine: Lower Employment Status than Episodic Migraine (%)
Chronic Migraine: Greater Healthcare Resource Use than Episodic Migraine

Visits in 12 months (mean)

Episodic Migraine
Chronic Migraine

Emergency HA
PCP HA
Emergency non-HA
PCP non-HA

0.22
0.79
0.44
2.79
0.48
2.48
0.6
4.47

HA, Headache; PCP, Primary Care Physician

*P<0.05

Assessing Barriers to Care in Episodic Migraine: AMPP

EM and HA-related disability*
N=775

Consulting

Consulters
n=353, 45.5%

Consulters
n=306, 86.7%

Entire cohort (%)
45.5

Diagnosed

Diagnosed Consulters
n=306, 86.7%

Nonconsulters
n=422, 54.5%

Undiagnosed Consulters
n=47, 13.3%

Treated, Diagnosed Consulters
n=204, 66.7%

Appropriate Acute Treatment

Inadequately treated, Undiagnosed Consulters
n=102, 33.3%

*MIDAS Grade >5 (Mild or greater)

Assessing Barriers to Care in CM: CaMEO

CM and HA-related disability*  
N=1254

Entire cohort (%)  
40.8

Consulting  
Consulters  
n=512, 40.8%

Diagnosed  
Diagnosed Consulters  
n=126, 24.6%

Appropriate Acute Treatment  
Treated, Diagnosed Consulters  
n=56, 44.4%

Nonconsulters  
n=742, 59.2%

Diagnosed Consulters  
Undiagnosed Consulters  
n=386, 75.4%

Untreated, Undiagnosed Consulters  
n=70, 55.6%

*MIDAS Grade ≥2

Dodick DW, et al. AHS Annual Scientific Meeting 2014
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5. Cost and barriers to care