

**Title:** Patient perspectives and experiences of preventive treatments and self-injectable devices for migraine: a focus group study

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**Authors:** Jaein Seo<sup>1,\*</sup>, Charlie A. Smith<sup>2</sup>, Caitlin Thomas<sup>2</sup>, Tommi Tervonen<sup>2,3</sup>, Asha Harandeen<sup>2</sup>, Janet H. Ford<sup>4</sup>, Virginia L. Stauffer<sup>4</sup>, Robert A Nicholson<sup>4</sup>, Kevin Harrison Duffy<sup>4</sup>, Antje Tockhorn-Heidenreich<sup>4</sup>

**\*Corresponding author:** Jaein Seo, Evidera. E-mail: [Jaein.Seo@evidera.com](mailto:Jaein.Seo@evidera.com).

<sup>1</sup> Patient-Centered Research, Evidera, Bethesda, MD, USA

<sup>2</sup> Patient-Centered Research, Evidera, London, UK

<sup>3</sup> Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

<sup>4</sup> Eli Lilly, Indianapolis, IN, USA

### **Online Resource 1: Literature review**

#### *Search strategy*

Literature was searched through the Ovid database, which includes key medical literature databases (e.g., EMBASE, MEDLINE). The objectives of the targeted literature review included identifying patient-relevant treatment aspects, referred to as 'value dimensions' that could be included in the focus group discussion, and could inform the attribute list in the quantitative phase of the study. Additional materials provided by Eli Lilly were also reviewed, including relevant clinical trials and device comparisons.

Separate search strategies were developed for qualitative studies (**Table 1-1**) and for quantitative preference studies (**Table 1-2**).

**Table 1-1 Search Terms for Qualitative Studies**

Description	#	Search Terms
Population	1	exp *Migraine Disorders/ or migraine.ti.
Outcome	2	*Patient Satisfaction/ or *Quality of Life/ or ('burden of illness' or 'patient perception' or 'treatment perception' or 'patient reported outcome' or 'patient-reported outcome' or 'patient satisfaction' or 'treatment satisfaction' or 'treatment importance' or 'quality of life' or QOL or HRQOL or 'patient reported' or 'self report' or 'self reported' or 'patient rated' or 'self assessment' or 'patient preference*' or 'treatment priorit\$' or 'impact of disease' or 'disease impact' or 'treatment theme').ti.
Study design	3	Qualitative Research/ or *"Surveys and Questionnaires"/ or *Interviews as Topic/ or (qualitative or interview\$ or questionnaire\$ or survey\$ or 'focus group' or 'live experience' or 'narrative analysis' or 'conceptual framework' or debriefing or 'content analysis' or 'discussion group' or ethnograph).ti.
Combined searches	4	1 and 2 and 3
Non-human studies <b>(to be filtered out)</b>	5	(animal\$ or mouse or mice or rat\$ or 'in vitro').ti. or limit 4 to (cats or cattle or chick embryo or dogs or goats or guinea pigs or hamsters or horses or mice or rabbits or rats or sheep or swine or animals)
Non-adult studies <b>(to be filtered out)</b>	6	(child or children or pediatric\$ or adolescent\$ or infant\$ or youth\$).ti. or limit 4 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)")
Publication types NOT of interest <b>(to be filtered out)</b>	7	limit 4 to (address or autobiography or bibliography or biography or comment or controlled clinical trial or editorial or letter or randomized controlled trial or "review" or "systematic review")
Combined searches	8	5 or 6 or 7
Combined searches	9	4 not 8
Remove duplicates	10	Remove duplicates from 9

**Table 1-2 Search Terms for Quantitative Preference Studies**

Description	#	Search Terms
Population	1	exp *Migraine Disorders/ or migraine.ti.
Outcomes	2	*Patient Preference/ or ('patient preference\$' or preference\$ or 'acceptable risk' or 'acceptable benefit' or 'marginal rate of substitute' or 'attribute importance' or 'person trade off' or PTO or 'willingness to pay' or WTP or 'willingness to wait' or WTW).ti.
Study design	3	*Choice Behavior/ or ('discrete choice' or 'discrete-choice' or 'conjoint analysis' or 'multi criteria decision analysis' or 'multicriteria decision analysis' or 'best worst scaling' or 'best-worst scaling' or 'benefit risk' or 'thresholding' or 'stated preference\$' or 'choice experiment').ti,ab.
Combined searches	4	1 and (2 or 3)
Non-human studies (to be filtered out)	5	(animal\$ or mouse or mice or rat\$ or 'in vitro').ti. or limit 4 to (cats or cattle or chick embryo or dogs or goats or guinea pigs or hamsters or horses or mice or rabbits or rats or sheep or swine or animals)
Non-adult studies (to be filtered out)	6	(child or children or pediatric\$ or adolescent\$ or infant\$ or youth\$).ti. or limit 4 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)")
Publication types NOT of interest (to be filtered out)	7	limit 4 to (address or autobiography or bibliography or biography or comment or controlled clinical trial or editorial or letter or randomized controlled trial or "review" or "systematic review")
Combined searches	8	5 or 6 or 7
Combined searches	9	4 not 8
Remove duplicates	10	Remove duplicates from 9

Screening was carried out independently by two reviewers and conflicts were resolved by discussion. Study eligibility criteria are listed in **Table 1-3**.

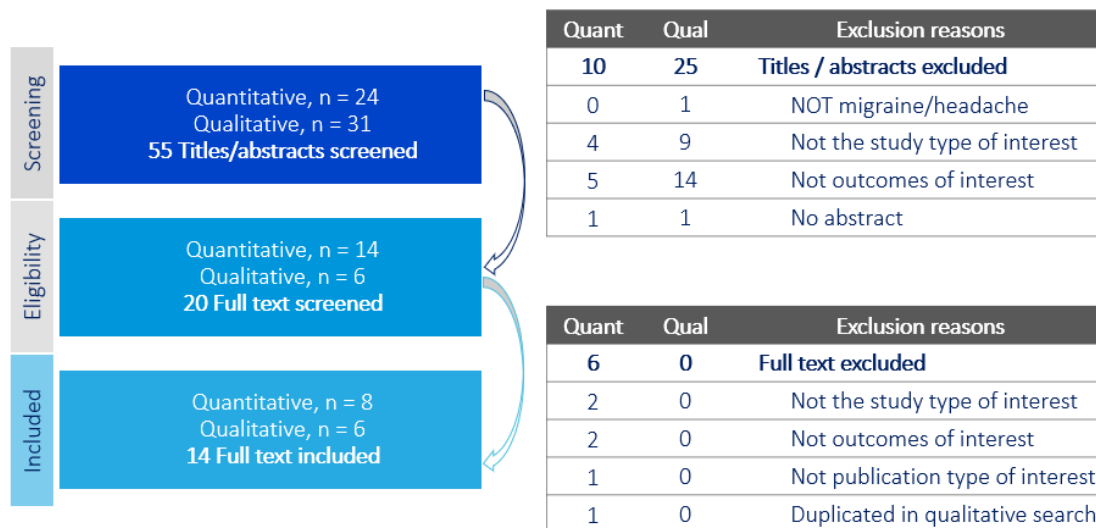
**Table 1-3 Study Eligibility Criteria**

Category	Inclusion Criteria	Exclusion Criteria
<b>Population</b>	Adult patients with migraine	Non-adult patients
	Quantitative studies	Publications of studies with the following designs:
	Patient preference studies (e.g., DCE, BWS, SW, MCDA, thresholding, BRA)	Animal studies
	Qualitative studies	In-vitro/ex-vivo studies
<b>Study design</b>	PROs	Gene expression/protein expression studies
	Interviews	Case studies/case series
	Focus groups	Publications that are not of studies (e.g., reviews, editorials, conference abstracts) will also be excluded
<b>Language</b>	English-language articles	N/A

Abbreviations: DCE = discrete choice experiment; BWS = best-worst scaling; MCDA = multiple criteria decision analysis; BRA = benefit-risk analysis; PRO = patient reported outcomes; N/A = not applicable

## Results

Fifty-five studies were identified from the search, including 24 quantitative and 31 qualitative studies. There were reduced to 14 quantitative and 6 qualitative studies following the title and abstract screening. Further 6 quantitative studies were excluded after full-text screening. The most frequent reason for excluding studies was not outcomes of interest (n=21) followed by not the study type of interest (n=15). As a result, 14 papers were included in the literature review (n=6 qualitative and n=8 quantitative; **Fig. 1-1**). No study considered preventive treatment for migraine other than Mansfield et al. 2019 and Peres et al. 2007; other studies considered acute treatments or did not specify treatment of interest.



**Fig. 1-1 PRISMA flow chart**

The following data were extracted:

- **Study characterization:** Authors; Data source; Study title; Study objective; Study year(s); Included countries; Sample size; Migraine severity; Treatments assessed
- **Outcomes and results:**
  - *Quantitative studies:* Preference elicitation method; Attributes and levels; Key findings (i.e. parameter estimates; trade-off measures; relative attribute importance)
  - *Qualitative studies:* Identified themes and subthemes; Patient experiences and relevant attributes; patient reported outcomes that were considered or developed

A total of 28 potentially relevant characteristics of migraine treatments were identified from the targeted literature review, consisting of 13 benefit measures, 11 risk measures, and 4 other measures (**Fig. 1-2**).

- **Benefit measures:** symptom free and symptom relief (pertinent to acute treatment) were commonly reported (n = 9) followed by impact on work and social life/physical activities (n = 8), sustained benefit (n = 6), and onset of action (n = 5).
- **Risk measures:** discrete adverse events from oral medications were reported mostly including cognitive problems (n = 4), loss of function (n = 3), fatigue (n = 3), emotional impact of migraine (n = 3), drowsiness (n = 2), and weight gain (n = 2). Further adverse events were explored from trial studies with self-injectable preventive treatments such as injection site reaction and infection.
- **Other measures:** mode and frequency of administration (n = 3) and ease of use (n = 1) were also identified as non-clinical measures.

The most relevant and recently published study, Mansfield et al. (2019), focused on preventive treatments for migraine and included the following attributes: 'reduction in headache days per month,' 'frequency of limitations with physical activities,' 'cognition problems,' 'weight gain,' 'how the medicine is taken,' and 'monthly out-of-pocket cost.'

	Quantitative studies								Qualitative studies						
	Gonzalez, 2013	Lenert L, 2003	Levitán, 2011	Lipton, 2005	Mansfield, 2019	Pascual, 2001	Peres, 2007	Smelt, 2014	Bagley, 2012	Caro, 1998	Cottrell, 2002	Davis, 2002	Hareendran, 2017	Palacios, 2017	
Benefit measures	Migraine Severity	●													
	Migraine Duration	●													
	Impact on work and social life/physical activities	●	●			●			●	●		●	●	●	
	Symptom free phase (severity/duration/headache elimination)	●						●	●	●		●			
	Chance headache returns/sustained response	●	●	●	●					●		●			
	Onset of action		●	●				●	●				●		
	Pain relief (duration, severity)		●	●	●				●	●		●			
	Photophobia relief		●	●					●	●					
	Nausea/vomiting relief		●	●					●	●					
	Headache relief			●											
	Phonophobia relief			●											
	Reduction in headache days per month					●									
	Works no matter when you take it during a migraine attack									●					
	Risk measures	Chest related adverse events			●										
		Thinking and memory problems/concentration					●		●	●	●				
Weight gain						●		●							
Tolerability							●								
Fatigue								●	●	●					
Loss of function (e.g., speech, arms/legs)				●					●				●		
Emotional impact of migraine									●		●			●	
Impact on sleep										●					
Drug interactions										●					
Drowsiness										●		●			
Addiction														●	
Others		Mode and frequency of administration					●		●				●		
		Out of pocket cost/price					●	●	●						
	Type of treatment (prescription vs. vitamin)							●							
	Ease of use											●			

**Fig. 1-2 Literature Review Summary – Synthesis of Benefits, Risks and Other Measures**

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