

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The social burden of people with the migraine diagnosis in Japan: evidence from a population-based cross-sectional survey
AUTHORS	Igarashi, Hisaka; Ueda, Kaname; Jung, Sungeun; Cai, Zhihong; Chen, Yirong; Nakamura, Tomomi

VERSION 1 – REVIEW

REVIEWER	Paolo Martelletti Department of Clinical and Molecular Medicine, Sapienza University, Rome, Italy
REVIEW RETURNED	02-Jul-2020

GENERAL COMMENTS	<p>The Authors present an interesting manuscript on the burden of migraine in Japan in a wide sample of the population (n=25209). Self-reported migraine has been reported in 44.792 with an important lack of referral to a physician specialized in headache, highlighting the fact that migraine is underdiagnosed and undertreated also in Japan.</p> <p>The manuscript also reports interesting data on loss of productivity and work.</p> <p>I suggest to insert and discuss the following papers in order to make the manuscript more representative in respect to scientific evidences:</p> <p>PMID: 31699022; PMCID: PMC6836347. PMID: 30203163; PMCID: PMC6131678. PMID: 30482181; PMCID: PMC6755592. PMID: 31805851; PMCID: PMC6896325. PMID: 31888448; PMCID: PMC6937810.</p>
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REVIEWER	Akihiro Shindo Mie University Graduate School of Medicine, Japan
REVIEW RETURNED	13-Aug-2020

GENERAL COMMENTS	<p>Dr. Igarashi and colleagues present an important work on migraine in Japan. This is an interesting paper that may be a valuable work for the patients with not only migraine, but also other types of headaches. The results are clearly presented and there are a few points that need to be addressed.</p> <p>1. First, confirmation of the diagnosis with migraine is an important problem of this study. Several doctors tend to diagnose the patients with migraine easily, just when the patients complain headache. I think most of neurologists will make diagnosis of migraine with diagnostic criteria, but some of primary care doctors not so. How the authors confirm the diagnosis of this study?</p>
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	<p>2. Second, this study revealed over half of patients had no prescription for migraine from GPs and neurologists. Did the patients truly attend the doctor for headache? I think if the patients' chief complaint is headache, most of doctors will prescript some kind of medicine. Did the patients want the prescription for migraine? Even though when the patients need the medication, didn't the doctors prescript the medicine? If the patients got the pain-killer by themselves, please add the sentences.</p>
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VERSION 1 – AUTHOR RESPONSE

REVIEWER #1, Paolo Martelletti

Comment 1. The Authors present an interesting manuscript on the burden of migraine in Japan in a wide sample of the population (n=25209). Self-reported migraine has been reported in 44.792 with an important lack of referral to a physician specialized in headache, highlighting the fact that migraine is underdiagnosed and undertreated also in Japan.

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PMID: 31699022; PMCID: PMC6836347.

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PMID: 31805851; PMCID: PMC6896325.

PMID: 31888448; PMCID: PMC6937810.

Response and Action: We thank the reviewer for the comment. The suggested literature covers scientific evidences ranging from prevalence estimates of migraine to the burden of migraine and is a great addition to our current **Introduction** section. We have included the publication on the burden of headache disorders in China to provide evidence from Asia:

“Migraine is a common disabling headache disorder, known to impose a burden on both patients and societies worldwide[1–3].”

We have included information on the prevalence of East Asian migraineurs to provide more information on migraine prevalence in a broader region, which reads:

“The 1-year prevalence of migraine among adults in East Asia ranged from 6.0% to 14.3%[6]. In Japan, the prevalence has been estimated to be between 6.0 - 8.9%, with the 1-year prevalence among non-elderly adults reported at 6.0%[6–9].”

We also expanded our introduction on the burden of migraine to outside Japan to provide more context globally. The revised **Introduction** section now reads:

“A recent study of European migraine patients showed that suffering from at least 4 monthly headache days (MHDs) was associated with poorer health related quality of life (HRQoL), high healthcare resource utilizations (HCRU) and loss of work productivity compared to non-migraine controls[1]. In another study among migraine patients with at least 4 MHDs and had failed at least one preventive migraine treatment, impact of migraine on professional, private, and social domains were reported by 70%, 64% and 78% of the respondents, respectively[10]. Migraine was also reported to be associated with a high economic burden, with annual direct cost of chronic migraine substantially higher than that of episodic migraine[11].”

1 Vo P, Fang J, Bilitou A, *et al.* Patients’ perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom. *J Headache Pain* 2018;**19**:82. doi:10.1186/s10194-018-0907-6
[PMID: 30203163; PMCID: PMC6131678]

2 Yao C, Wang Y, Wang L, *et al.* Burden of headache disorders in China, 1990-2017: findings from the Global Burden of Disease Study 2017. *J Headache Pain* 2019;**20**:102. doi:10.1186/s10194-019-1048-2
[PMID: 31699022; PMCID: PMC6836347]

6 Takeshima T, Wan Q, Zhang Y, *et al.* Prevalence, burden, and clinical management of migraine in China, Japan, and South Korea: a comprehensive review of the literature. *J Headache Pain* 2019;**20**:111. doi:10.1186/s10194-019-1062-4
[PMID: 31805851; PMCID: PMC6896325]

10 Martelletti P, Schwedt TJ, Lanteri-Minet M, *et al.* My Migraine Voice survey: a global study of disease burden among individuals with migraine for whom preventive treatments have failed. *J Headache Pain* 2018;**19**:115. doi:10.1186/s10194-018-0946-z
[PMID: 30482181; PMCID: PMC6755592]

11 Negro A, Sciattella P, Rossi D, *et al.* Cost of chronic and episodic migraine patients in continuous treatment for two years in a tertiary level headache Centre. *J Headache Pain* 2019;**20**:120. doi:10.1186/s10194-019-1068-y
[PMID: 31888448; PMCID: PMC6937810]

REVIEWER #2, Akihiro Shindo

Dr. Igarashi and colleagues present an important work on migraine in Japan. This is an interesting paper that may be a valuable work for the patients with not only migraine, but also other types of headaches. The results are clearly presented and there are a few points that need to be addressed.

Comment 1. First, confirmation of the diagnosis with migraine is an important problem of this study. Several doctors tend to diagnose the patients with migraine easily, just when the patients complain headache. I think most of neurologists will make diagnosis of migraine with

diagnostic criteria, but some of primary care doctors not so. How the authors confirm the diagnosis of this study?

Response and Action: We thank the reviewer for this great point. We agree that diagnosis of migraine is an important aspect in migraine research, however, data used in this study came from an online self-administered survey. All information was self-reported by the respondents and we could not verify or confirm migraine diagnosis in this study. This has been mentioned in the **Discussion** section as a limitation of the study, and we have added more clarity on the confirmation of migraine diagnosis. It now reads:

“As all data are self-reported, no verification of migraine diagnosis or patient reported outcomes was conducted, and data is subject to recall bias.”

Comment 2. Second, this study revealed over half of patients had no prescription for migraine from GPs and neurologists. Did the patients truly attend the doctor for headache? I think if the patients' chief complaint is headache, most of doctors will prescribe some kind of medicine. Did the patients want the prescription for migraine? Even though when the patients need the medication, didn't the doctors prescribe the medicine? If the patients got the pain-killer by themselves, please add the sentences.

Response and Action: We thank the reviewer for this comment. Due to the self-reported nature of this study, we were not able to verify if patients had truly visited the doctor for headache. Among all diagnosed migraine patients, more than half (53.6%) were not *currently* taking prescription medication (Rx). As the question in the survey focused only on current use of Rx, we could not infer why the patient had previously taken Rx and decided to discontinue or why the patient was never given any Rx to treat migraine during their consultation with the doctors. Among patients not currently taking Rx, 14.6% had used OTC or herbal product to treat migraine (Table 1). We have added this additional information in the text in the **Results** section, **Treatment use in migraine patients**, which reads:

“Of the migraine patients not currently taking Rx, 99 (14.6%) had used OTC or herbal product to treat migraine.”

Although treatment use for migraine and discontinuation would be of interest, due to the design of the survey, comprehensive information on treatment use and reasons for not taking Rx or for discontinuation of Rx were not available. This was included as a limitation in the current **Discussion** section, which reads:

“Due to the design of the survey, the reasons for not taking Rx or for discontinuation of Rx (e.g. less migraine episodes or lack of efficacy) were not reported and could not be concluded.”

VERSION 2 – REVIEW

REVIEWER	Akihiro Shindo Department of Neurology, Department of Dementia Prevention and Therapeutics, Graduate School of Medicine, Mie University
REVIEW RETURNED	23-Sep-2020
GENERAL COMMENTS	The second version of this manuscript has been revised well. I think this manuscript will is now acceptable.