DOI:10.1017/cjn.2024.337
This is a manuscript accepted for publication in *Canadian Journal of Neurological Sciences*. This version may be subject to change during the production process.

Productivity Loss Associated with Disability from Migraine: A Canada-wide Cross-sectional Study

Hiten Naik[1,2]; Alexander Tam[3]; Logan Trenaman[4]; Larry Lynd[2,3]; Wei Zhang[2,3]

Affiliations:

1. Department of Medicine, The University of British Columbia, Vancouver, British Columbia, Canada
2. Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, British Columbia, Canada
3. Centre for Advancing Health Outcomes, Providence Research, Vancouver, British Columbia, Canada
4. Department of Health Systems and Population Health, School of Public Health, University of Washington, Seattle, Washington, USA

Correspondence: Wei Zhang, PhD, Faculty of Pharmaceutical Sciences, The University of British Columbia, 2405 Wesbrook Mall, Vancouver, British Columbia, V6T 1Z3, Email: wei.zhang@ubc.ca

Running title: Migraine and Productivity Loss

Keywords: migraine disorders; headache; health economics; patient-reported outcomes; work capacity evaluation; employment; disability leave; sick days; cross-sectional study

Word count (abstract): 248

Word count (main text): 3,142

Ethics Approval and Consent to Participate

The University of British Columbia Research Ethics Board (REB# H22-03211) approved this study. All participants provided electronic consent.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors have no competing interests to declare.

Funding

This study was supported by a grant-in-aid from Pfizer Canada.

Role of Funders

The funders had no role in the design and conduct of the study, data collection, management, analysis, and interpretation of the data, preparation, review, or approval of the manuscript, and decision to submit the manuscript for publication.

Authors' Contributions

LT, LL, and WZ conceived the study. HN, AT, and WZ were involved in data acquisition. AT conducted the statistical analysis. All authors were involved in data interpretation. HN wrote the first draft of the manuscript. All authors were involved in critically reviewing the manuscript for important intellectual content. All authors approved of the final manuscript.

Acknowledgments

The authors would like to thank Ms. Amanda Brar for her insights as a patient partner during the development of this study. Dr. Naik would like to acknowledge the support of The University of British Columbia Clinician Investigator Program and CAN-TAP-TALENT & Michael Smith Health Research BC Postdoctoral Fellowship. Dr. Trenaman would like to acknowledge the support of the Leo Greenawalt Endowed Professorship in Health Policy. Dr. Zhang would like to acknowledge the support of the Michael Smith Health Research BC Scholar Award.

Highlights

- Few studies in Canada have examined the relationship between migraine-related disability and productivity loss.
- In this cross-sectional study, employed adults living with migraine across Canada completed the Valuation of Lost Productivity (VOLP) questionnaire.
- After adjusting for relevant covariates, greater migraine-related disability was associated with more total, paid, and unpaid productivity loss.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Abstract

Background: Migraine can affect adults during their most productive years, yet few studies in Canada have examined the relationship between migraine-related disability and productivity loss. In particular, the impact of migraine on unpaid productivity loss has not been quantified.

Methods: In this cross-sectional study, employed adults living with migraine were recruited from across Canada to complete a web-based questionnaire. Migraine-related disability was assessed using the Migraine Disability Assessment (MIDAS) questionnaire, and productivity loss was evaluated using the Valuation of Lost Productivity (VOLP) questionnaire. Multiple regression models were used to quantify the association between migraine-related disability level and productivity loss after adjusting for relevant clinical, occupational, and sociodemographic covariates.

Results: There were 441 participants, of which 60.1% were female, and the mean (SD) age was 37.7 (10.9). Compared to participants with little to no migraine-related disability, hours of total productivity loss were higher among those with moderate disability (54.1 [95%CI: 10.2- 98.1] adjusted hours per 3 months) and severe disability (110.5 [95%CI: 65.5- 155.6] adjusted hours per 3 months); paid productivity loss was higher among participants with moderate disability (32.4 [95%CI: 3.1-61.8] adjusted hours per 3 months) and severe disability (61.6 [95%CI: 31.5-91.7] adjusted hours per 3 months); and unpaid productivity loss was greater in those with severe disability (43.5 [95%CI: 12.7-74.3] adjusted hours per 3 months).

Conclusions: Greater migraine-related disability was associated with more total, paid, and unpaid productivity loss among employed adults. These data will be valuable when evaluating the cost-effectiveness of emerging migraine therapies.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Introduction

Migraine poses a significant socioeconomic burden on society. It is estimated that over 1 billion people are affected by migraine worldwide [1], and of all medical conditions, migraine is responsible for the second-greatest number of years lived with disability [2]. Migraine impairs quality of life and has been linked to several chronic conditions, including insomnia, depression, anxiety, and gastric ulcers [3]. The direct healthcare costs related to health resource utilization and treatment of migraine are significant [4–6].

In economic evaluations, the indirect costs related to work productivity loss are also an important consideration, given that migraine disproportionately impacts working-age adults [7–9]. Multiple studies have shown that the productivity loss associated with migraine is substantial. [9–17]. However, additional research is needed for several reasons. First, there is a paucity of observational studies in North America that have captured data examining the impact of migraine on presenteeism (reduced productivity while at work), which may be a greater contributor to migraine-related productivity loss than absenteeism [15, 16, 18, 19]. Second, studies have not estimated productivity loss related to unpaid work (such as childcare and housework), which is an important consideration given that migraine is more common in women [7, 8, 20, 21]. Third, the productivity loss associated with different categories of migraine-related disability or severity is rarely evaluated [15, 17–19]. Fourth, most studies assessing productivity loss from migraine have used the Work Productivity and Activity Impairment (WPAI), which quantifies productivity losses as a percent impairment [6, 15, 19, 22–27]. Estimating productivity loss in hours would provide a more direct quantification of the cost burden [28].

Further comprehensive and patient-centered valuations of productivity loss from migraine would be valuable for assessing the economic impact of this condition, particularly when considering the perspective of the employer and society. These data could also be used in cost-effectiveness analyses as new migraine therapies reach the market. Accordingly, we conducted a cross-sectional study that examined productivity loss among individuals with migraine across Canada. The study's primary objective was to examine the association between different levels of migraine-related disability and productivity loss.

Methods

Study Design and Participants

This was a cross-sectional study in which participants completed an online questionnaire. Participants were recruited from throughout Canada from an *Ipsos* market research panel. Potentially eligible members from the *Ipsos iSay* rewards community were invited to participate via the *Ipsos iSay* website, the mobile app, and/or text message (depending on the member's preferences). To be eligible, participants were required to be 19 or older, employed, a resident of Canada, have a history of migraine, and be able to comprehend English or French. The questionnaire was administered electronically by Qualtrics (Provo, Utah). Participants completed

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

eligibility screening questions through *Ipsos iSay* platform before electronically accessing the main study questionnaire. Through the eligibility screening, participants were considered to have a history of migraine if they reported being previously diagnosed by a clinician. We targeted 450 total participants for this study and set Qualtrics quotas to ensure an approximately equal distribution of respondents for different levels of migraine-related disability. Some participants were prevented from completing the questionnaire if their responses deemed them ineligible (e.g., unemployed) or the pre-determined quota had already been met.

This study was designed and executed in collaboration with a patient partner living with migraine and two additional patient partners with chronic disease (1 living with atopic dermatitis and 1 with alopecia areata). A draft of the questionnaire was piloted in 3 people with a history of migraine, 3 people with atopic dermatitis, and 1 person with alopecia areata. Questions related to productivity loss and demographics were the same for the 3 diseases. The questions related to disease history, severity, and treatment were disease-specific. After they completed the draft questionnaire, participants were interviewed for feedback, and appropriate revisions were made. The final questionnaire was available to study participants in English and French. Based on feedback from our patient partner, it was presented in dark mode to reduce possible migraine exacerbation from photophobia [29–31].

This study was approved by The University of British Columbia Research Ethics Board (REB# H22-03211). Recruitment for this study occurred between December 4, 2023, and February 12, 2024. Participants provided electronic consent before starting the questionnaire. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies [32].

Migraine-related Disability

Migraine-related disability was assessed using the Migraine Disability Assessment (MIDAS) questionnaire [33]. The first 5 items of the MIDAS ask about the number of days in the past 3 months that were affected by migraine: the number of missed work or school days; missed household chores days; missed non-work activity days; days at work or school where productivity was reduced by half or more; and days in which household work was reduced by half or more [33]. The total MIDAS score was derived by summing the total number of days affected by migraine [33]. Using previously established cut-offs, we categorized participants as having little to no disability (MIDAS score 0-5), mild disability (MIDAS score 6-10), moderate disability (MIDAS score 11-20), or severe disability (MIDAS score ≥21) [33].

The MIDAS questionnaire has 2 additional items. The sixth item asks about the number of days the participant has experienced headaches over the past 3 months, and the seventh item asks about the average severity of the headaches (on a scale of 0 to 10). These two items were used in sensitivity analyses.

Outcomes

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Productivity loss was measured using the Valuation of Lost Productivity (VOLP) questionnaire [34]. The VOLP consists of questions about health-related paid and unpaid productivity loss. The questions about productivity loss refer to health in general and are not migraine-specific. Paid productivity loss comprises absenteeism (number of absent workdays due to health) and presenteeism (hours actually taken to complete all work relative to the hours taken to complete the same work if not experiencing any health problems). Unpaid work loss represents the hours of paid and unpaid help received for unpaid work activities (such as childcare and housework) due to health [34]. It has been validated and used in other chronic conditions to estimate health-related productivity loss in hours over the preceding 3 months [34–38]. In this study, the primary outcome was total hours of productivity loss, calculated as the sum of paid productivity loss (from absenteeism and presenteeism) and unpaid productivity loss. The hours of total paid productivity loss, hours lost due to absenteeism, hours lost due to presenteeism, and hours of unpaid productivity loss were evaluated as secondary outcomes. Details regarding calculating the productivity loss outcomes using the VOLP are described in the **supplemental methods**.

An additional secondary outcome was the percent overall work impairment and percent activity impairment due to health as measured by the Work Productivity and Activity Impairment (WPAI)- General Health questionnaire. The WPAI is a validated measure that assesses the impact of health on work productivity and impairment of regular activities in the prior week [22, 39, 40]. Calculations for work and activity impairment using the WPAI are outlined in the **supplemental methods**.

Statistical Analysis

Mean values for each outcome were calculated for different levels of migraine-related disability based on MIDAS responses [33]. We then used ordinary least squares (OLS) regressions to measure the association between migraine-related disability level and the outcomes while adjusting for potential confounding variables. These additional covariates were pre-specified based on a review of the literature and were captured from questionnaire responses [8, 11, 35, 37, 41]. These included age, gender, ethnicity, marital status, education level, work income, household income, employment status (part of VOLP), work habits, and number of comorbidities. We chose to use OLS models for productivity loss outcomes based on previously published practical recommendations for regression model selection in productivity loss analyses [42].

We conducted sensitivity analyses based on responses to the two additional MIDAS items to determine if outcomes were associated with 1) the number of days with migraine over the past 3 months and 2) the average severity of migraine.

Statistical tests were two-sided, and the threshold for significance was $p<0.05$. Analyses were performed using R statistical software version 4.3.3 and Stata version 15.1 (StataCorp LLC, College Station, TX).

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Results

In total, 441 participants were included in the analyses. Due to incomplete or invalid responses, 10 participants were excluded from the VOLP analyses, and 17 were excluded from the WPAI analyses.

Characteristics of the study population are described in **Table 1.** The mean (SD) age was 37.7 (10.9); 60.1% were women, 75.5% were White, 81.6% worked full time, and 50.1% were sedentary at work. Of note, the no to little migraine-related disability level group had the greatest proportion of participants at the highest work income level (43.1% with over $100,000), and the severe migraine-related disability level group had the greatest proportion (45.5%) of participants with 2 or more comorbidities.

The migraine preventative strategies, treatments, and workplace accommodations reported by participants are reported in **Table S1**. The most commonly used strategies by participants to prevent migraine were lifestyle changes (73.0%) and oral medications (68.7%); the most common migraine treatment was oral medications (87.3%). Concerning workplace accommodations for health conditions, 38.1% reported being granted paid leave, and 28.8% had been granted flexible work arrangements.

The mean [SD] hours of total productivity loss in the past 3 months were higher at greater levels of migraine-related disability (61.0 [120.4] hours per 3 months for little to no disability, 105.9 [128.7] for mild disability, 132.3 [148.8] for moderate, and 196.5 [214.5] for severe) (**Table 2**). Specifically, paid productivity loss (including absenteeism and presenteeism) increased with migraine-related disability level (47.6 [106.4], 64.8 [99.1], 85.0 [96.3], and 119.8 [109.4], hours per 3 months, respectively), and so did the mean [SD] hours of unpaid productivity loss (16.5 [61.0], 40.4 [89.5], 46.8 [97.6], and 76.0 [166.9] hours per 3 months, respectively). The mean (SD) hours of absenteeism increased greatly with migraine-related disability level (7.0 [13.4], 13.9 [16.2], 29.4 [48.2], and 50.9 [56.2] hours per 3 months, respectively). However, the increase in mean [SD] hours of presenteeism across disability levels was not as pronounced (40.4 [102.1], 50.8 [96.1], 55.5 [84.0], and 68.7 [88.5] hours per 3 months, respectively), and for all levels, presenteeism contributed more to paid productivity loss than absenteeism.

The mean [SD] WPAI percent overall work impairment in the prior 7 days reported by participants also increased with migraine-related disability level (23.1 [22.4]% for little to no disability, 37.9 [26.2]% for mild disability, 49.5 [26.5]% for moderate, and 65.4 [22.4]% for severe disability), as did percent activity impairment (23.2 [22.2]%, 35.9 [23.9]%, 46.7 [23.0]%, and 58.5 [22.1]%, respectively).

In our multiple regression models, having severe migraine-related disability was associated with greater total productivity loss (110.5 [65.5, 155.6] adjusted hours, $p<0.001$), paid productivity loss (61.6 [31.5, 91.7] adjusted hours, $p<0.001$), and unpaid productivity loss (43.5

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

[12.7, 74.3] adjusted hours, $p<0.01$) compared with little to no disability (**Table 3; Table S2**). Additionally, moderate migraine-related disability was also associated with greater total and paid productivity loss compared with little to no disability (54.1 [10.2, 98.1] adjusted hours, $p<0.05$; 32.4 [3.1, 61.8] adjusted hours, $p<0.05$, respectively). Similarly, in models evaluating overall work impairment derived from WPAI responses, greater levels of migraine-related disability were associated with greater percent impairment (13.1% [6.2, 20.0], $p<0.001$ for mild; 23.0% [16.3, 29.8], $p<0.001$ for moderate; and 37.3% [30.3, 44.2], $p<0.001$ for severe disability compared with little to no disability) (**Table S3**).

In sensitivity analyses, more headache days over the past 3 months and greater average migraine severity were associated with greater total productivity loss, paid productivity loss, unpaid productivity loss, overall work impairment, and activity impairment (**Table S4**).

Discussion

In this cross-sectional study involving participants from across Canada, we compared productivity loss between individuals with different levels of migraine-related disability. We found that components of paid and unpaid productivity loss (as measured by VOLP), as well as work and activity impairment (as measured by WPAI), were higher in individuals with more disability from migraine.

This is one of the first observational studies to examine productivity loss among people with migraine in a Canadian context. As part of their study on the overall economic burden of migraine, Amoozegar et al. estimated the percentage of patients who had productivity loss after administering the WPAI questionnaire to 287 patients with migraine [16]. Our study builds on this work by including a larger cohort, estimating productivity loss in hours, measuring unpaid losses, and stratifying by migraine-related disability.

Our findings also contribute to accumulating evidence that migraine-related disability has a significant impact on work productivity loss [15, 18, 43]. For example, a recent study by Wong et al. evaluated WPAI outcomes by MIDAS level in employees within the banking sector in Malaysia [15]. Compared to this study, we observed that the percent overall work impairment and activity impairment for little to no, mild, and moderate disability levels were lower, but we observed greater impairment for severe disability. This Malaysian study also reported significant levels of productivity loss associated with just minimal levels of migraine-related disability [15]. Based on VOLP responses, individuals in our study with little to no migraine-related disability had an average of 61 hours of productivity loss over the prior 3 months. This finding is an indication that even mild or treated migraine disorder may result in significant occupational impairment.

Like the Malaysian study, our results showed that presenteeism (productivity loss at work) is significant among persons with migraine. Regardless of migraine-related disability level, presenteeism contributed more to paid productivity loss than absenteeism. This is a

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

relevant finding from the employer's perspective, as individuals with migraine have experienced stigma, and there is potential for migraine exacerbation in the workplace [18, 44–48]. Indeed, employers have become increasingly aware of the importance of developing work environments and programs that support people with migraine [48–50]. Studies have suggested that reducing screen time, implementing migraine-specific disease management programs, safe/ dark rooms, and referrals to occupational health could be beneficial for people with migraine [18, 50]. However, further research is needed to evaluate whether these interventions can reduce productivity loss [48, 50].

Our study also observed that unpaid work significantly contributes to productivity loss in people with migraine. Unpaid work, such as caregiving can affect mental health, impair health-related quality of life (HRQOL), and has significant societal value [51, 52]. However, unpaid losses are not routinely considered in economic analyses and have not been accounted for in migraine productivity loss assessments until our study. Women are estimated to spend 2-10 times more time on unpaid work activities than men [53]. In the context of migraine – which are at least twice as prevalent in women - it is imperative to consider unpaid losses when examining the economic benefits of an intervention [7, 8, 54].

The results of this study highlight the economic value of developing effective migraine treatments. For example, recent randomized trials showed that 3 months of treatment with the calcitonin-gene-related peptide (CGRP) antagonist galcanezumab resulted in MIDAS score improvements of over 20 points [55, 56]. This level of improvement is enough to reduce migraine-related disability from severe to little or no symptoms; based on our data, this would represent an adjusted total productivity loss improvement of 110.5 hours in 3 months and an adjusted paid productivity loss improvement of 61.6 hours (i.e., nearly 2 full work weeks).

The productivity loss valuations reported in this study could be applied to future cost-effectiveness analyses. Over 2 decades ago, productivity loss valuations played a role in demonstrating the efficacy of triptans [57–59]; similar assessments will be required for CGRP receptor antagonists and other new migraine therapies [60]. Whereas recent cost-effectiveness analyses of CGRP receptor antagonists have used WPAI outcome data [50, 52], the VOLP should be considered as it was designed for use in economic evaluations or cost of illness studies and provides a more comprehensive assessment from a societal perspective [28]. Unlike WPAI, the VOLP estimates paid and unpaid work productivity loss in terms of time, which can then be valued in monetary terms [28].

However, it is prudent to consider the limitations of our study. As it was a cross-sectional analysis, causal relationships between migraine-related disability level and the outcomes cannot be established. Since we relied on online convenience sampling of participants and set quotas to ensure a similar number of participants for each disability level group, the study population should not be taken to represent all employed Canadian residents with migraine. In addition, VOLP and WPAI captured productivity loss due to health (any physical, mental, or emotional

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

problems or symptoms) as opposed to migraine-specific productivity loss. The VOLP was developed as a generic health instead of a disease-specific questionnaire because patients may have difficulty attributing their sick leaves or reduced work productivity to a specific disease, especially when they have multiple chronic health conditions, and because they are less likely to attribute the related treatment side effects or co-morbidities to a specific disease [28, 61]. The severe disability group was more likely to have at least 2 comorbidities and thus tended to have higher health-related productivity loss. Thus, the findings on the adjusted *differences* between different disability levels have more practical implications than the outcomes for a given disability level. Furthermore, we relied solely on self-report (as opposed to clinical records) to ascertain migraine diagnosis, which may have led to the inclusion of individuals who did not truly have a migraine disorder. Similarly, comorbidity information was captured from questionnaire responses and was not comprehensive; this may have resulted in unmeasured confounding.

Our study has several strengths. We captured data in two languages from regions across Canada and included participants from various socioeconomic backgrounds and workplaces. In contrast to previous productivity loss assessments of migraine in Canada, our study included larger sample size, and recruitment was not limited to specific clinics or patients with particular treatment profiles [16]. The diversity of our study population increases the generalizability of our findings- an important consideration given that productivity loss from migraine has been shown to differ by occupation and region [12]. Furthermore, all our study outcomes were patient-reported, and we applied a patient-oriented approach by engaging patient partners, which helped ensure that the procedures and results were centered on the values of individuals with migraine and other chronic diseases. Lastly, a major strength of our study was the selection of the outcome measures. Although the VOLP has not been previously applied to individuals with migraine, it has been used for several other diseases and permitted a comprehensive valuation of productivity loss, including paid and unpaid losses [34, 37, 38]. This was complemented by including the WPAI outcomes, allowing comparisons with other studies [6, 15, 19, 22, 24, 26, 27, 62, 63].

Conclusion

In conclusion, greater migraine-related disability was associated with greater total, paid, and unpaid productivity loss among employed adults. These findings demonstrate the economic impact of migraine and highlight the potential societal value of effective interventions.

List of Abbreviations

CGRP	Calcitonin-gene-related peptide
CI	Confidence interval
HRQOL	Health-related quality of life
MIDAS	Migraine Disability Assessment
SD	Standard deviation
VOLP	Valuation of Lost Productivity
WPAI	Work Productivity and Activity Impairment

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

References

[1] Safiri S, Pourfathi H, Eagan A, et al. Global, regional, and national burden of migraine in 204 countries and territories, 1990 to 2019. *Pain* 2022; 163: E293–E309.

[2] GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390: 1211–59.

[3] Buse DC, Reed ML, Fanning KM, et al. Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: Results of the migraine in America symptoms and treatment (MAST) study. *Journal of Headache and Pain*; 21. Epub ahead of print 2 March 2020. DOI: 10.1186/s10194-020-1084-y.

[4] Gilligan AM, Foster SA, Sainski-Nguyen A, et al. Direct and indirect costs among United States commercially insured employees with migraine. *J Occup Environ Med* 2018; 60: 1120–1127.

[5] Ford JH, Ye W, Nichols RM, et al. Treatment patterns and predictors of costs among patients with migraine: evidence from the United States medical expenditure panel survey. *J Med Econ* 2019; 22: 849–858.

[6] García-Azorín D, Moya-Alarcón C, Armada B, et al. Societal and economic burden of migraine in Spain: results from the 2020 National Health and Wellness Survey. *J Headache Pain* 2024; 25: 38.

[7] Schramm SH, Obermann M, Katsarava Z, et al. Epidemiological profiles of patients with chronic migraine and chronic tension-type headache. *J Headache Pain* 2013; 14: 1–8.

[8] Amiri P, Kazeminasab S, Nejadghaderi SA, et al. Migraine: A Review on Its History, Global Epidemiology, Risk Factors, and Comorbidities. *Frontiers in Neurology*; 12. Epub ahead of print 23 February 2022. DOI: 10.3389/fneur.2021.800605.

[9] Seddik AH, Branner JC, Ostwald DA, et al. The socioeconomic burden of migraine: An evaluation of productivity losses due to migraine headaches based on a population study in Germany. *Cephalalgia* 2020; 40: 1551–1560.

[10] Allen D, Hines EW, Pazdernik V, et al. Four-year review of presenteeism data among employees of a large United States health care system: A retrospective prevalence study. *Hum Resour Health*; 16. Epub ahead of print 9 November 2018. DOI: 10.1186/s12960-018-0321-9.

[11] Landy SH, Runken MC, Bell CF, et al. Assessing the impact of migraine onset on work productivity. *J Occup Environ Med* 2011; 53: 74–81.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

[12] Rondinella S, Silipo DB. The effects of chronic migraine on labour productivity: Evidence from Italy. *Labour* 2023; 37: 1–32.

[13] Alkahtani RF, Alrumaih SS, Algezlan SS, et al. The Impact of Migraine Disease on Work Productivity and Quality of Life Among the Adults in Riyadh, Saudi Arabia. *Cureus*. Epub ahead of print 6 August 2022. DOI: 10.7759/cureus.27733.

[14] Husøy A, Katsarava Z, Steiner TJ. The relationship between headache-attributed disability and lost productivity: 3 Attack frequency is the dominating variable. *Journal of Headache and Pain*; 24. Epub ahead of print 1 December 2023. DOI: 10.1186/s10194-023-01546-9.

[15] Wong LP, Alias H, Bhoo-Pathy N, et al. Impact of migraine on workplace productivity and monetary loss: A study of employees in banking sector in Malaysia. *Journal of Headache and Pain*; 21. Epub ahead of print 8 June 2020. DOI: 10.1186/s10194-020-01144-z.

[16] Amoozegar F, Khan Z, Oviedo-Ovando M, et al. The Burden of Illness of Migraine in Canada: New Insights on Humanistic and Economic Cost. *Canadian Journal of Neurological Sciences* 2022; 49: 249–262.

[17] Kim Y, Han S, Suh HS. The impact of migraine and probable migraine on productivity loss in Korea: A cross-sectional online survey. *PLoS One*; 17. Epub ahead of print 1 November 2022. DOI: 10.1371/journal.pone.0277905.

[18] Haw NJ, Cabaluna IT, Kaw GE, et al. A cross-sectional study on the burden and impact of migraine on work productivity and quality of life in selected workplaces in the Philippines. *Journal of Headache and Pain*; 21. Epub ahead of print 1 December 2020. DOI: 10.1186/s10194-020-01191-6.

[19] Ishii R, Schwedt TJ, Dumkrieger G, et al. Chronic versus episodic migraine: The 15-day threshold does not adequately reflect substantial differences in disability across the full spectrum of headache frequency. *Headache* 2021; 61: 992–1003.

[20] Graves EB, Gerber BR, Berrigan PS, et al. Epidemiology and treatment utilization for Canadian patients with migraine: a literature review. *Journal of International Medical Research*; 50. Epub ahead of print 1 September 2022. DOI: 10.1177/03000605221126380.

[21] Delaruelle Z, Ivanova TA, Khan S, et al. Male and female sex hormones in primary headaches. *Journal of Headache and Pain*; 19. Epub ahead of print 29 November 2018. DOI: 10.1186/s10194-018-0922-7.

[22] Ford JH, Ye W, Ayer DW, et al. Validation and meaningful within-patient change in work productivity and activity impairment questionnaire (WPAI) for episodic or chronic migraine. *J Patient Rep Outcomes*; 7. Epub ahead of print 1 December 2023. DOI: 10.1186/s41687-023-00552-4.

[23] Stafford MR, Hareendran A, Ng-Mak DS, et al. *EQ-5D^{TM}-derived utility values for different levels of migraine severity from a UK sample of migraineurs*, http://www.hqlo.com/content/10/1/65 (2012).

[24] Spierings ELH, Ning X, Ramirez Campos V, et al. Improvements in quality of life and work productivity with up to 6 months of fremanezumab treatment in patients with episodic and chronic migraine and documented inadequate response to 2 to 4 classes of migraine-preventive medications in the phase 3b FOCUS study. *Headache* 2021; 61: 1376–1386.

[25] Barbanti P, Goadsby PJ, Lambru G, et al. Effects of eptinezumab on self-reported work productivity in adults with migraine and prior preventive treatment failure in the randomized, double-blind, placebo-controlled DELIVER study. *Journal of Headache and Pain*; 23. Epub ahead of print 1 December 2022. DOI: 10.1186/s10194-022-01521-w.

[26] Caronna E, Gallardo VJ, Alpuente A, et al. Epidemiology, work and economic impact of migraine in a large hospital cohort: time to raise awareness and promote sustainability. *J Neurol* 2022; 269: 1456–1462.

[27] Sumelahti ML, Sumanen M, Sumanen MS, et al. My Migraine Voice survey: Disease impact on healthcare resource utilization, personal and working life in Finland. *Journal of Headache and Pain*; 21. Epub ahead of print 29 September 2020. DOI: 10.1186/s10194-020-01185-4.

[28] Zhang W, Bansback N, Boonen A, et al. Development of a composite questionnaire, the valuation of lost productivity, to value productivity losses: Application in rheumatoid arthritis. *Value in Health* 2012; 15: 46–54.

[29] Tian P, Xu G, Han C, et al. Effects of Paradigm Color and Screen Brightness on Visual Fatigue in Light Environment of Night Based on Eye Tracker and EEG Acquisition Equipment. *Sensors*; 22. Epub ahead of print 1 June 2022. DOI: 10.3390/s22114082.

[30] Noseda R, Bernstein CA, Nir RR, et al. Migraine photophobia originating in cone-driven retinal pathways. *Brain* 2016; 139: 1971–1986.

[31] Choi JY, Oh K, Kim BJ, et al. Usefulness of a photophobia questionnaire in patients with migraine. *Cephalalgia* 2009; 29: 953–959.

[32] von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008; 61: 344–349.

[33] Stewart WF, Lipton RB, Dowson AJ, et al. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology* 2001; 56: S20–S28.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

[34] Zhang W, Bansback N, Kopec J, et al. Measuring time input loss among patients with rheumatoid arthritis: Validity and reliability of the valuation of lost productivity questionnaire. *J Occup Environ Med* 2011; 53: 530–536.

[35] Zhang W, Li KH, Gobis B, et al. Work Productivity Losses and Associated Risk Factors Among University Employees in the CAMMPUS Wellness Program. *J Occup Environ Med* 2020; 62: 25–29.

[36] Zhang W, Sun H, Gelfand A, et al. Working From Home During the COVID-19 Pandemic: The Association With Work Productivity Loss Among Patients and Caregivers. *J Occup Environ Med* 2022; 64: E677–E684.

[37] Rodriguez Llorian E, Zhang W, Khakban A, et al. Productivity loss among people with early multiple sclerosis: A Canadian study. *Multiple Sclerosis Journal* 2022; 28: 1414–1423.

[38] Gelfand A, Sou J, Sawatzky R, et al. Valuation of Lost Productivity in Caregivers: A Validation Study. *Front Psychol*; 12. Epub ahead of print 27 August 2021. DOI: 10.3389/fpsyg.2021.727871.

[39] Zhang W, Bansback N, Boonen A, et al. Validity of the work productivity and activity impairment questionnaire-general health version in patients with rheumatoid arthritis. *Arthritis Res Ther*; 12, http://arthritis-research.com/content/12/5/R177 (2010, accessed 19 March 2024).

[40] Reilly MC, Zbrozek AS, Dukes EM. The Validity and Reproducibility of a Work Productivity and Activity Impairment Instrument. *Pharmacoeconomics* 1993; 4: 353–365.

[41] Buse DC, Manack A, Serrano D, et al. Sociodemographic and comorbidity profiles of chronic migraine and episodic migraine sufferers. *J Neurol Neurosurg Psychiatry* 2010; 81: 428–432.

[42] Zhang W, Sun H. How to analyze work productivity loss due to health problems in randomized controlled trials? A simulation study. *BMC Med Res Methodol*; 21. Epub ahead of print 1 December 2021. DOI: 10.1186/s12874-021-01330-w.

[43] Domingues RB, Picon IS, VESCOVi J, et al. Assessment of work productivity and activity impairment (WPAI) questionnaire for migraine with the help of a smartphone app. *Arq Neuropsiquiatr* 2020; 78: 468–472.

[44] Parikh SK, Kempner J, Young WB. Stigma and Migraine: Developing Effective Interventions. *Current Pain and Headache Reports*; 25. Epub ahead of print 1 November 2021. DOI: 10.1007/s11916-021-00982-z.

[45] Parikh SK, Young WB. Migraine: Stigma in Society. *Current Pain and Headache Reports*; 23. Epub ahead of print 1 January 2019. DOI: 10.1007/s11916-019-0743-7.

[46] Begasse de Dhaem O, Sakai F. Migraine in the workplace. *eNeurologicalSci*; 27. Epub ahead of print 1 June 2022. DOI: 10.1016/j.ensci.2022.100408.

[47] Shimizu T, Sakai F, Miyake H, et al. Disability, quality of life, productivity impairment and employer costs of migraine in the workplace. *Journal of Headache and Pain*; 22. Epub ahead of print 1 December 2021. DOI: 10.1186/s10194-021-01243-5.

[48] Vicente-Herrero T, Burke TA, Laínez MJA. The impact of a worksite migraine intervention program on work productivity, productivity costs, and non-workplace impairment among Spanish postal service employees from an employer perspective. *Current Medical Research and Opinion* 2004; 20: 1805–1814.

[49] Begasse de Dhaem O. Migraines Are a Serious Problem. Employers Can Help. *Harvard Business Review*, 2021.

[50] Begasse de Dhaem O, Gharedaghi MH, Bain P, et al. Identification of work accommodations and interventions associated with work productivity in adults with migraine: A scoping review. *Cephalalgia* 2021; 41: 760–773.

[51] Pinquart M, Sörensen S. Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychol Aging* 2003; 18: 250–267.

[52] Seedat S, Rondon M. Women's wellbeing and the burden of unpaid work. *The BMJ*; 374. Epub ahead of print 31 August 2021. DOI: 10.1136/bmj.n1972.

[53] Ferrant G, Pesando M, Nowacka K. *Unpaid Care Work: The missing link in the analysis of gender gaps in labour outcomes*. 2014.

[54] Nicolas PV, Aikaterini P, Tomas B, et al. Burden of Migraine in Europe Using Self-Reported Digital Diary Data from the Migraine Buddy Application. *Neurol Ther* 2018; 7: 321–332.

[55] Tepper SJ, Ailani J, Ford JH, et al. Effects of Galcanezumab on Health-Related Quality of Life and Disability in Patients with Previous Failure of 2–4 Migraine Preventive Medication Categories: Results from a Phase IIIb Randomized, Placebo-Controlled, Multicenter Clinical Trial (CONQUER). *Clin Drug Investig* 2022; 42: 263–275.

[56] Ford J, Tassorelli C, Leroux E, et al. Changes in patient functioning and disability: results from a phase 3, double-blind, randomized, placebo-controlled clinical trial evaluating galcanezumab for chronic migraine prevention (REGAIN). *Quality of Life Research* 2021; 30: 105–115.

[57] Schulman EA, Cady RK, Henry D, et al. *Effectiveness of Sumatriptan in Reducing Productivity Loss Due to Migraine: Results of a Randomized, Double-Blind, Placebo-Controlled Clinical Trial*. 2000.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

[58] Miller DW, Martin BC, Loo CM. Sumatriptan and Lost Productivity Time: A Time Series Analysis of Diary Data. *Clin Ther* 1996; 18: 1263–1275.

[59] Cady RC, Ryan R, Jhingran P, et al. *Sumatriptan Injection Reduces Productivity Loss During a Migraine Attack Results of a Double-blind, Placebo-Controlled Trial*. 1998.

[60] Zobdeh F, ben Kraiem A, Attwood MM, et al. Pharmacological treatment of migraine: Drug classes, mechanisms of action, clinical trials and new treatments. *British Journal of Pharmacology* 2021; 178: 4588–4607.

[61] Zhang W, Bansback N, Anis AH. Measuring and valuing productivity loss due to poor health: A critical review. *Soc Sci Med* 2011; 72: 185–192.

[62] Barbanti P, Goadsby PJ, Lambru G, et al. Effects of eptinezumab on self-reported work productivity in adults with migraine and prior preventive treatment failure in the randomized, double-blind, placebo-controlled DELIVER study. *Journal of Headache and Pain*; 23. Epub ahead of print 1 December 2022. DOI: 10.1186/s10194-022-01521-w.

[63] Doane MJ, Gupta S, Vo P, et al. Associations Between Headache-Free Days and Patient-Reported Outcomes Among Migraine Patients: A Cross-Sectional Analysis of Survey Data in Europe. *Pain Therapy* 2019; 203–216.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Tables

Table 1: Characteristics of the study population

Characteristic	Migraine-related disability level				All
	Little to no (MIDAS 0-5) N (%)	Mild (MIDAS 6-10) N (%)	Moderate (MIDAS 11-20) N (%)	Severe (MIDAS ≥21) N (%)	N (%)
Total, row %	109 (24.7)	111 (25.2)	111 (25.2)	110 (24.9)	441 (100)
Questionnaire language					
English	96 (88.1)	101 (91.0)	103 (92.8)	102 (92.7)	402 (91.2)
French	13 (11.9)	10 (9.0)	8 (7.2)	8 (7.3)	39 (8.8)
Gender[a]					
Man	65 (59.6)	42 (37.8)	38 (34.2)	31 (28.2)	176 (39.9)
Woman	44 (40.4)	69 (62.2)	73 (65.8)	79 (71.8)	265 (60.1)
Age, mean (SD)	36.6 (12.7)	38.8 (10.1)	38.2 (9.5)	37.3 (11.0)	37.7 (10.9)
Province or region					
Alberta	40 (36.7)	21 (18.9)	25 (22.5)	22 (20.0)	108 (24.5)
Atlantic Canada[b]	≤5 (≤4.6)	10 (9.0)	13 (11.7)	≤5 (≤4.5)	30 (6.8)
British Columbia	≤5 (≤4.6)	8 (7.2)	15 (13.5)	10 (9.1)	37 (8.4)
Manitoba	≤5 (≤4.6)	≤5 (≤4.5)	≤5 (≤4.5)	≤5 (≤4.5)	7 (1.6)
Ontario	30 (27.5)	43 (38.7)	36 (32.4)	53 (48.2)	162 (36.7)
Quebec	29 (26.6)	21 (18.9)	16 (14.4)	15 (13.6)	81 (18.4)
Saskatchewan	≤5 (≤4.6)	8 (7.2)	≤5 (≤4.5)	≤5 (≤4.5)	14 (3.2)
Territories[c]	≤5 (≤4.6)	≤5 (≤4.5)	≤5 (≤4.5)	≤5 (≤4.5)	≤5 (≤4.5)
Race/ ethnicity					
Other race/ ethnicity[d]	23 (23.1)	20 (18.0)	26 (23.4)	39 (35.5)	108 (24.5)
White	86 (78.9)	91 (82.0)	85 (76.6)	71 64.5)	333 (75.5)
Marital status					
Not married or common-law	66 (60.6)	35 (31.5)	38 (34.2)	49 (44.5)	188

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

					(42.6)
Married or common-law	43 (39.4)	76 (68.5)	73 (65.8)	61 (55.5)	253 (57.4)
Education					
No university or college education	63 (57.8)	55 (49.5)	66 (59.5)	64 (58.2)	248 (56.2)
University or college education	46 (42.2)	56 (50.5)	45 (40.5)	46 (41.8)	193 (43.8)
Work income					
<$50,000	31 (28.4)	28 (25.2)	28 (25.2)	33 (30.0)	120 (27.2)
$50,000- $99,999	31 (28.4)	52 (46.8)	39 (35.1)	49 (44.5)	171 (38.8)
≥$100,000	47 (43.1)	31 (27.9)	44 (39.6)	28 (25.5)	150 (34.0)
Household income					
<$50,000	16 (14.7)	16 (14.4)	20 (18.0)	24 (21.8)	76 (17.2)
$50,000- $99,999	17 (15.6)	27 (24.3)	23 (20.7)	37 (33.6)	104 (23.6)
$100,000- $149,999	36 (33.0)	40 (36.0)	35 (31.5)	28 (25.5)	139 (31.5)
≥$150,000	40 (36.7)	28 (25.2)	33 (29.7)	21 (19.1)	122 (27.7)
Number of comorbidities[e]					
0	57 (52.3)	36 (32.4)	33 (29.7)	31 (28.2)	157 (35.6)
1	35 (32.1)	47 (42.3)	45 (40.5)	29 (26.4)	156 (35.4)
≥2	17 (15.6)	28 (25.2)	33 (29.7)	50 (45.5)	128 (29.0)
Employment status					
Working full-time	93 (85.3)	93 (83.8)	94 (84.7)	80 (72.7)	360 (81.6)
Working part-time, self-employed, or other	16 (14.7)	18 (16.2)	17 (15.3)	30 (27.3)	81 (18.4)
Workdays per week, mean (SD)	4.8 (0.9)	4.8 (1.0)	4.9 (0.7)	4.8 (0.9)	4.8 (0.9)
Work hours per week, mean (SD)	33.0 (13.1)	34.9 (11.8)	33.7(12.6)	33.3 (14.2)	33.7 (12.9)
Work habits					

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Sedentary at work	56 (51.4)	55 (49.5)	62 (55.9)	48 (43.6)	221 (50.1)
Mildly active at work	41 (37.6)	43 (38.7)	35 (31.5)	46 (41.8)	165 (37.4)
Moderate to strenuous activity at work	12 (11.0)	13 (11.7)	14 (12.6)	16 (14.5)	55 (12.5)
Work-from-home					
No work-from-home	44 (40.4)	36 (32.4)	39 (35.1)	44 (40.0)	163 (37.0)
Work from home at least part of the time	65 (59.6)	75 (67.6)	72 (64.9)	66 (60.0)	278 (63.0)

Legend: All percentages represent column proportions unless otherwise indicated. [a]"Non-binary person" was an option provided for gender, but no participants selected this. [b]Atlantic Canada includes the provinces Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.[c]Territiories include Yukon, Northwest Territories, and Nunavut.[d]Other race/ethnicity includes South Asian (e.g., East Indian, Pakistani, Sri Lankan, etc.), Chinese, First Nations, Southeast Asian (e.g., Vietnamese, Cambodian, Malaysian, Laotian, etc.), West Asian, Filipino, Latin American, Métis, Korean, Japanese, Arab, Inuit, Black, Indigenous/ Aboriginal (not included elsewhere), Other, and mixed (i.e., more than one) ethnicities. [e]Comorbidities include asthma, arthritis or osteoporosis, back problems, cancer, cardiovascular disease, chronic obstructive pulmonary disease (COPD), diabetes, mental health conditions, neurologic conditions, digestive diseases, fibromyalgia or chronic fatigue syndrome, kidney disease, liver disease or gallbladder problems, other. Abbreviations: MIDAS- migraine disability assessment; SD- standard deviation.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Table 2. Productivity loss and percentage impairment by migraine-related disability level

Outcomes	Migraine-related disability level				All
	Little to no (MIDAS 0-5) Mean (SD) N=109	**Mild (MIDAS 6-10)** Mean (SD) N=111	**Moderate (MIDAS 11-20)** Mean (SD) N=111	**Severe (MIDAS ≥20)** Mean (SD) N=110	**All** N=441
VOLP (last 3 months)					
Total work productivity loss hours†	61.0 (120.4)	105.9 (128.7)	132.3 (148.8)	196.5 (214.5)	124.8 (164.8)
Paid work productivity loss hours†	47.6 (106.4)	64.8 (99.1)	85.0 (96.3)	119.8 (109.4)	79.8 (106.0)
Absenteeism loss hours	7.0 (13.4)	13.9 (16.2)	29.4 (48.2)	50.9 (56.2)	25.3 (41.9)
Presenteeism loss hours†	40.4 (102.1)	50.8 (96.1)	55.5 (84.0)	68.7 (88.5)	54.1 (93.0)
Unpaid work productivity loss hours	16.5 (61.0)	40.4 (89.5)	46.8 (97.6)	76.0 (166.9)	45.0 (112.4)
WPAI (last 7 days)					
Percent overall work impairment*	23.1 (22.4)	37.9 (26.2)	49.5 (26.5)	65.4 (22.4)	44.1 (28.9)
Percent activity impairment	23.2 (22.2)	35.9 (23.9)	46.7 (23.0)	58.5 (22.1)	41.1 (26.2)

Legend: Abbreviations: MIDAS- migraine disability assessment; SD- standard deviation; VOLP- Valuation of Lost Productivity; WPAI- Work Productivity and Activity Impairment. †Sample size N=431 and 10 participants did not provide valid answers for questions related to presenteeism. *Sample size for the WPAI percent work impairment outcome N=424 and 17 participants had valid

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

question skip patterns (not currently employed (working for pay), or 0 hours missed because of health problems and 0 hours worked in the past 7 days). N for missing by migraine disability level is not provided due to small cell counts.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press

Table 3: Multiple regression models for productivity loss and percentage impairment by migraine-related disability level

Outcomes	Migraine-related disability level			
	Little to no (MIDAS 0-5)	**Mild (MIDAS 6-10)** Coefficient (95%CI)	**Moderate (MIDAS 11-20)** Coefficient (95%CI)	**Severe (MIDAS ≥21)** Coefficient (95%CI)
VOLP (last 3 months)				
Total productivity loss hours	[Reference]	37.4 (-6.5, 81.4)	54.1 (10.2, 98.1)*	110.5 (65.5, 155.6)***
Paid productivity loss hours	[Reference]	16.8 (-12.5, 46.1)	32.4 (3.1, 61.8)*	61.6 (31.5, 91.7)***
Unpaid productivity loss hours	[Reference]	15.6 (-14.2, 45.5)	17.3 (-12.7, 47.2)	43.5 (12.7, 74.3)**
WPAI (last 7 days)				
Percent overall work impairment	[Reference]	13.1 (6.2, 20.0)***	23.0 (16.3, 29.8)***	37.3 (30.3, 44.2)***
Percent activity impairment	[Reference]	11.7 (5.4, 17.9)***	20.9 (14.7, 27.2)***	31.2 (24.7, 37.7)***

Legend: Models are adjusted for gender, age, ethnicity, marital status, education, household income, employment status, work habits, and the number of comorbidities reported. Complete models are reported in **Table S2** and **Table S3**. Abbreviations: MIDAS- migraine disability assessment. WPAI- work productivity and impairment; VOLP- value of lost productivity. *p<0.05; **p<0.01; ***p<0.001.

https://doi.org/10.1017/cjn.2024.337 Published online by Cambridge University Press