## Title

# Later high school start time is associated with lower migraine frequency in adolescents. 

## Permalink

https://escholarship.org/uc/item/3mc7t5mb

## Journal

Headache, 61(2)
ISSN
0017-8748

## Authors

Gelfand, Amy A
Pavitt, Sara
Ross, Alexandra C et al.

## Publication Date

2021-02-01
DOI
10.1111/head. 14016

Peer reviewed

# Later High School Start Time is Associated with Lower Migraine Frequency in Adolescents 

Amy A. Gelfand ${ }^{1}$, Sara Pavitt ${ }^{1}$, Alexandra C. Ross ${ }^{1}$, Christina L. Szperka ${ }^{2}$, Samantha L. Irwin ${ }^{1}$, Suzanne Bertisch ${ }^{3}$, Katie L. Stone ${ }^{4,5}$, Remi Frazier ${ }^{6}$, Barbara Grimes ${ }^{4}$, I. Elaine Allen ${ }^{4}$<br>${ }^{1}$ Child \& Adolescent Headache Program, University of California, San Francisco, San Francisco, USA<br>${ }^{2}$ Division of Neurology, Children's Hospital of Philadelphia \& Departments of Neurology \& Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA<br>${ }^{3}$ Division of Sleep and Circadian Disorders, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA<br>${ }^{4}$ Department of Epidemiology \& Biostatistics, University of California, San Francisco, San Francisco, USA<br>${ }^{5}$ Research Institute, California Pacific Medical Center, San Francisco, CA<br>${ }^{6}$ Academic Research Systems, University of California, San Francisco, CA, USA


#### Abstract

Objective: To determine whether high school start time is associated with headache frequency in adolescents with migraine.

Background: Adolescence is marked by a physiologic delayed circadian phase, characterized by later bedtimes and wake times. The American Academy of Pediatrics (AAP) recommends that high schools start no earlier than 8:30 AM, but most high schools in the United States (U.S.) start earlier. The study hypothesis was that adolescents with migraine whose high schools start at 8:30


[^0]AM or later (late group) would have lower headache frequency than those whose schools start earlier than 8:30 AM (early group).

Methods: This was a cross-sectional internet survey study of U.S. high schoolers with migraine recruited online through social media. Comparisons were made between the late group and the early group. The primary outcome measure was self-reported headache days/month.

Results: 1,012 respondents constituted the analytic set: $n=503$ in the late group vs. $n=509$ in the early group. Mean (SD) self-reported headache days/month were 4.8 (4.6) vs. 7.7 (6.1) in the late and early groups, respectively ( $p<0.001$ ); mean difference -2.9 ( $95 \% \mathrm{CI}-2.2$ to -3.6 ). Mean (SD) self-reported hours of sleep on a school-night were: 7.9 (0.9) vs. 6.9 (1.3), $p<0.001$. Adjusting for total hours of sleep, sex, taking a migraine preventive, days of acute medication use, hours of homework, grade level and missing breakfast, mean (SD) self-reported headache days/month remained lower in the late group than the early group: 5.8 ( $95 \%$ CI 5.3 to 6.2) vs. 7.1 ( $95 \%$ CI 6.7 to 7.4 ), ( $p<0.001$ ); mean difference -1.3 ( $95 \% \mathrm{CI}-1.9$ to -0.7 ).

Conclusion: Adolescents with migraine who attend high schools that follow AAP recommendations for start times have lower self-reported headache frequency than those whose high schools start before 8:30 AM. If prospective studies confirm this finding, shifting to a later high school start time may be an effective strategy for migraine prevention in adolescents.

## Keywords

migraine; adolescent; sleep

## Introduction:

Migraine affects 8-12\% of adolescents and can cause missed school and substantial disability(1-3). When migraine frequency is high, adolescents often take preventive medication to try to decrease headache frequency and related disability. However, trials of pharmacologic strategies for migraine prevention in this age group have not generated consistent evidence of efficacy(4).

In 2019 the American Academy of Neurology (AAN) and the American Headache Society (AHS) issued new guidelines on migraine prevention in children and adolescents(4). These guidelines emphasize lifestyle management, advising clinicians to, "counsel patients and families that lifestyle and behavioral factors may influence headache frequency" and "educate patients and families to identify and modify migraine contributors that are potentially modifiable"(4). However, research into identifying which lifestyle and behavioral factors actually influence headache frequency in adolescents has been relatively modest, as has research into how to modify them.

Evidence from across the age spectrum suggests there is a relationship between sleep and migraine (5-9). Getting adequate sleep and maintaining a regular sleep schedule (i.e. minimizing variability of bedtime and wake-time on weekdays and weekends) is advice commonly given to adolescents with migraine(6,10). The American Academy of Sleep Medicine recommends that teenagers get 8-10 hours of sleep per night for optimum health(11). However, as adolescents develop, their circadian phase delays (12), and they
often cannot fall asleep until 11:00 PM or later(13). To accommodate adolescents' natural sleep physiology, the American Academy of Pediatrics (AAP) recommends that middle schools and high schools begin no earlier than 8:30 AM(13). According to the Centers for Disease Control and Prevention (CDC), however, only $18 \%$ of schools adhere to this recommendation(14). As a result of the misalignment between high school start times and adolescents' internal (circadian) clock, many adolescents do not achieve adequate sleep duration during the school week. A pilot study suggested that later high school start time may be associated with lower headache frequency in adolescents with migraine(15).

We hypothesized that high school students with migraine who attend high schools that start at 8:30 AM or later will have lower headache frequency compared to those whose schools start earlier.

## Methods:

The UCSF Institutional Review Board approved this study (\#19-29816). Adolescents provided their assent to participate; the requirement for written parental consent was waived given the low-risk nature of the study. This manuscript represents the primary analysis of these data.

## Study design and recruitment:

This was a large, cross-sectional open internet survey study of high-school students in the U.S. who have migraine and attend school outside of the home (i.e. are not home-schooled or attending school online). Participants were recruited with social media advertisements (Facebook and Instagram) and directed to a screening website. The recruitment materials did not state the hypothesis of the study. Given that only $18 \%$ of high schools start at 8:30 AM or later(14), we hired a clinical research recruitment company to conduct primary research to identify regions and school districts with a higher concentration of late start times and focused our advertising in these regions. Once we had fully recruited the earlier start-time group, we closed enrollment of that arm and continued to recruit those from later start-time schools. Those who passed the screening questions could access the survey in REDCap (Research Electronic Data Capture), a secure, HIPPA compliant web-based database(16). Key questions were programmed with a completeness check, i.e. a prompt to query the participant if they left it blank, though participants still could leave questions blank if they desired.

To minimize the variance introduced by changes in sleep schedule over the course of the school year, we aimed to recruit the study sample over as short of a period as possible. Participants were told the survey would take approximately 10 minutes to complete and were given a $\$ 10$ gift card to thank them for their time.

## Inclusion and exclusion criteria:

To be eligible, participants needed to reside in the United States, read English, and be in $9^{\text {th }}$ to $12^{\text {th }}$ grade at a high school outside the home. Their school needed to have a consistent start time throughout the week. To determine migraine status we utilized the questions below to approximate International Classification of Headache Disorders (ICHD-3) diagnostic
criteria for migraine in adolescents(17). These same questions were used in our earlier


#### Abstract

study(15), but have not been validated against clinician interview. To be eligible the


 adolescent had to answer "Yes" to all four questions.1. Have you had at least 5 headaches in your life that were at least moderate or severe in intensity and that lasted for at least 2 hours?
2. With your headaches, is the pain ever throbbing and/or is it ever worse with movement (i.e. do you ever lay down with a bad headache or avoid moving?)
3. With your headaches, do lights and sounds ever bother you (even just a little bit) and/or do you ever have nausea (upset stomach)?
4. Have you been having headaches for at least 3 months?

## Primary outcome measure:

The primary outcome measure was headache days per month (self-reported). As in our previous study(15), this was asked as "How many headache days did you have in the last month?" The primary exposure variable was high school start time (in local time) dichotomized as before 8:30 AM (hereafter referred to as the "early" group) vs. 8:30 AM or later (i.e. the "late" group). School start time was based on respondent self-report.

## Demographic, clinical and lifestyle variables:

We collected sociodemographic, clinical and lifestyle variables thought to be associated with migraine frequency in adolescents. These included age, sex, frequency of acute medication use, how often they miss breakfast, how many hours of sleep they get on an average school night, and how variable their sleep schedule is (i.e. the amount of time that bedtimes and wake-times differ between weekends and weekdays, sometimes called "social jet lag")(3, 15, 18-20).

Sleep variables were asked in the survey as follows:

1. "How many HOURS of sleep do you usually get on a school night?"
2. "What time do you usually go to bed on a school night?"
3. "What time do you usually wake up on a school day?"
4. "What time do you usually go to bed on a weekend night?"
5. "What time do you usually wake up on a weekend day?"

One way to measure "social jetlag" is to calculate "sleep midpoint variability"(20), which for this study was defined as the difference between the midpoint of sleep (midpoint between sleep time and wake time) on a school night vs. on a weekend night.

Participants were asked for their zip code and their state of residence. States were grouped into 5 geographic regions(21). Zip code data were used to estimate the mean annual income in the respondent's zip code based upon Internal Revenue Service tax return data from 2017(22), as a marker for socioeconomic status.

All data were derived from participants' self-reported responses in the survey. Data were cleaned and values that fell outside of a realistic range for a given variable (e.g. school start time before 6:00 AM) were excluded.

Power calculation: In pharmacologic migraine preventive trials in both adults and pediatrics, mean headache days/month often differs by 1-2 days between the active arm(s) and the control arm(23-26). Hence, if later high school start time is associated with even 1 fewer headache day/month, this would be clinically important.

Our previous study(15) was powered around an anticipated mean difference of 1.5 headache days/month (SD 3) between groups based upon the results of a placebo-controlled trial of topiramate for migraine prevention in adolescents(24). The observed difference was smaller than anticipated ( -0.8 day ( $95 \%$ CI -2.3 to 0.7 ), while the observed variance was higher- 5 days in the late start group and 7 days in the early start group). A revised power calculation suggested that $n=445$ respondents per group would be needed to have $80 \%$ power to detect a difference of 1 headache day per month, assuming a standard deviation of 6 and a two-sided test with alpha=0.05. Assuming $10 \%$ would not complete the survey, we aimed to enroll 500 per group, or $n=1,000$ total.

Statistical methods: Descriptive statistics and summaries were calculated by the two school start time groups using means and standard deviations (or medians and interquartile ranges) for continuous (interval and ratio) variables and frequencies and percentages for categorical (nominal and ordinal) variables.

The outcome variable, headache days/month, was examined for linearity and found to be skewed, hence the median (interquartile range) is also reported. Comparisons between groups were made using Mann-Whitney tests, indepenent groups Student $t$-tests (comparing groups assuming equal variance in each group), and Chi-squared tests as appropriate. Analyses were two-tailed with an a priori level of significance of $p<0.05$.

Univariate analyses examining the relationship between individual predictors and headache days/month were performed using linear regression modeling. Multivariable linear regression modeling was performed to adjust for potential confounders of the association between headache days/month and the primary predictor of interest, school start time. Variables that were associated with headache frequency in univariate regression models were adjusted for in the initial multivariable model (model \#1). Given that a minimum of 8 hours of sleep is recommend for adolescents(11), we wanted to examine for both a threshold effect at 8 hours of sleep, as well as to examine whether total sleep time (as a continuous variable) made a difference. Therefore, in model \#2 we substituted getting at least 8 hours of sleep for total sleep time in the model. While acute medication use frequency in this study was generally not so high as to raise concern for medication overuse headache as a driver of headache frequency, we included it in our most conservative models (models \#1 and \#2), but then removed it in subsequent models (\#3-5) as a sensitivity analysis. In order to examine whether sleep schedule variability, and/or total sleep time were major drivers of the observed association between high school start time and headache frequency, we removed sleep schedule variability in model \#4 and then both of these variables in model \#5.

As headache days per month is not a truly continuous variable (i.e. responses are limited to $0-30$ ), we validated our results by also using Poisson regression models.

Analyses were performed using SAS 9.4 (Cary, NC) and Stata 16.0 (College Station, TX).

## Results:

We enrolled 1,012 adolescents between February 28 and March 13, 2020. Fortunately, this time frame did not overlap with significant shelter-in-place efforts related to the COVID-19 pandemic.

A total of 1,362 potential participants screened in REDCap for eligibility; there were $n=204$ screen failures ( $15.0 \%$ ). Reasons for screen failure were: not meeting criteria for migraine ( $n=140$ ), not being in $9^{\text {th }}-12^{\text {th }}$ grade ( $n=22$ ), not attending high school outside the home ( $n=70$ ), not living in the United States ( $n=1$ ) and/or not assenting to complete the survey $(n=2)$; respondents could screen fail for more than one reason. Of the 1,158 who screen passed, $1,012(87.4 \%)$ provided survey data, $n=509$ in the early group and $n=503$ in the late group. There were respondents from all 50 states.

Table 1 shows demographic, clinical, school and sleep schedule-related variables by group. Age did not differ between groups, although grade distribution was somewhat different. There was a higher proportion of girls in the early group ( $61.9 \%$ vs. $56.1 \%$ ), though this difference was not statistically significant. Respondents' geographic distribution differed between cohorts, with more in the early-start group coming from the West. However, geographic region was not a significant predictor of monthly headache days in models examining school start times. Estimated mean income did not differ between groups.

Adolescents with migraine in the early group had a higher self-reported headache frequency than those in the late group, mean (SD): 7.7 (6.1) vs. $4.8(4.6),(p<0.001)$, for a difference of 2.9 headache days/month ( $95 \%$ CI for the difference 2.2 to 3.6 ). They were also more likely to have $\geq 15$ headache days per month, had a higher mean PedMIDAS score, and used acute headache medication more often (Table 1). Interestingly, those in the late group were more likely to be on a migraine preventive: $39.2 \%$ (197/503) vs. $27.9 \%$ (142/509), ( $p<0.001$ ). Adjusting for the difference in migraine preventive use in linear regression modelling, the mean difference in headache days between groups was 3.2 days ( $95 \%$ CI 2.5 to 3.9).

As compared to the early group, those in the late group were more likely to attend a public high school ( $80.9 \%(407 / 509)$ vs. $75.8 \%(386 / 509 ; p=0.050)$ and reported having fewer hours of homework per night (mean (SD): 1.7 (0.7) vs. 2.5 (1.4), $p<0.001$ ), getting more total hours of sleep on a school-night (mean (SD): 7.9 (0.9) vs. 6.9 (1.3) $p<0.001$ ), being more likely to get at least 8 hours of sleep on a school-night ( $55.7 \%$ (280/503) vs. $33.0 \%$ (168/509), $p<0.001$ ), and missing fewer weekday breakfasts (mean (SD): 1.6 (1.5) vs. 2.3 (2.0), $p<0.001$ ). However, when breakfast eating was examined as a binary outcome (i.e. proportion missing breakfast at least once per week vs. not) the late start group was more likely to miss breakfast at least once during a school week ( $72.6 \%$ (365/503) vs. $65.8 \%$ (335/509), $p=0.020$ ).

Interestingly, mean weeknight bedtime was earlier in the late group (10:19 PM vs. 10:58 PM, $p<0.001$ ), as was weekend bedtime (11:15 PM vs. 11:30 PM, $p=0.006$ ). Wake-up time on a typical school day was later in the late group (7:11 AM vs. 6:25 AM, $p<0.001$ ), as was weekend wake-up time (9:03 AM vs. 8:45 AM, $p<0.001$ ). Students in the late group left the house later, on average, on school mornings (8:02 AM vs. 7:15 AM, $p<0.001$ ). Duration of commute to school did not differ between groups.

Table 2 examines the associations between headache frequency and sociodemographic and clinical predictors. In table 3, multivariable linear regression models depict the relationship between school start time and headache frequency, adjusting for covariates of interest. In all models, headache frequency remained different between start time groups. Poisson regression modeling yielded similar differences between groups (data not shown).

## Discussion:

In this study, later high school start-time was associated with lower self-reported headache frequency in adolescents with migraine. Even after adjusting for possible confounders such as total sleep time and missing breakfast, headache frequency remained lower in those whose schools follow American Academy of Pediatrics guidelines and start no earlier than 8:30 AM (i.e. the late group). The mean difference between headache days/month between the late and early start time groups was -1.3 days ( $95 \%$ CI -1.9 to -0.7 ). While causal inference is limited in this observational study, this finding suggests that starting school at 8:30 AM or later may have the potential to improve migraine frequency in adolescents.

The magnitude of the observed effect size in this study, i.e. a mean difference of -1.3 days lower in the late group ( $95 \% \mathrm{CI}-1.9$ to -0.7 ), observed in the most conservative multivariable model (model \#1), is similar to that seen in pharmacologic migraine prevention trials in both adolescents and adults(24-26). For example, in a trial of topiramate vs. placebo in 12-17 year-olds with episodic migraine, those receiving topiramate 100 $\mathrm{mg} /$ day had a mean of 2.0 (SD 2.9) migraine days in the last 4 -weeks of the 12 -week double-blind maintenance phase, whereas those in the placebo arm had a mean of 3.5 (SD 3.5) migraine days in the same time period, for a mean difference of 1.5 days(24). In the PREEMPT trials of onabotulinum A toxin injections vs. placebo for chronic migraine prevention in adults, mean difference in headache days/28-days was -1.4 ( $95 \% \mathrm{CI}-0.4$ to $-2.4)$ in PREEMPT 1 and $-2.3(-1.3$ to -3.3$)$ in PREEMPT $2(25,26)$. If these findings are confirmed in future research utilizing prospective headache diaries, this would suggest that shifting to a later high school start-time is a modifiable, society-level behavioral intervention that could translate to thousands of fewer migraine days and fewer missed days of school for adolescents nationally.

Compared to adults, adolescents enjoy comparatively less control over their day-to-day schedules. Similarly, their families' schedules are often bound by the school schedules of their local school districts. While 2019 AHS/AAN guidelines on migraine prevention in children and adolescents note that "recurrent headache in adolescents is associated with....poor sleep habits", and recommend that clinicians counsel patients and families that behavioral factors "may influence headache frequency"(4), the results of our study suggests
that changes in sleep habits may be best advocated for at the societal level. Improving sleep can be a difficult task with the structure of the American school system. Adolescents experience a dramatic delay in the daily timing of the sleep-wake cycle(12), yet society often requires them to wake up early for school. The results of our study suggest that as pediatric providers, efforts to advocate for change in school policy have the potential to improve adolescents' circadian alignment and make a substantive difference in headache frequency on a population level. In 2019, California became the first state to legislate that high schools begin no earlier than 8:30 AM, a change that will be implemented in the 2022-2023 school year(27). Additionally, in 2020, the COVID-19 pandemic has led to wide scale change in how students attend school. As we rethink what a typical school day looks like, the time may be ripe for changing school start time as well. In the meantime, providers of adolescents with migraine can consider advocating for a 504 plan $^{1}$ that includes the recommendation that the student be excused from first period class if their school starts before 8:30 AM.

The influence of lifestyle and behavior on migraine frequency is complex. This can make it challenging to study, however, it is important that lifestyle advice for preventing migraine be studied with the same rigor as pharmacologic interventions in order to optimize care yet avoid unnecessarily restricting the lives of young people and their families.

Strengths of this study include the national recruitment strategy, using social media and collection of all data during a 2 -week period, minimizing temporal effects from fluctuations due to school vacations, etc. There are also several limitations. All data were self-reported and recall based. Migraine status was not confirmed by a clinician and the questions used to ascertain migraine status have not been validated against the gold-standard of a clinician interview; however, this was necessary for practical purposes and ICHD-3 criteria were used to craft the survey questions. It is possible that individuals could have completed the survey more than once. Respondents in this study had a higher mean estimated income, and were more likely to be on a migraine preventive, compared to those in previous studies(2, 29). As with all observational studies, unmeasured or residual confounding factors could still account for some or all of the observed associations. For example, school districts that start later may also be more attuned to things that support adolescent health generally. However, as our sample represented all states and estimated mean income did not differ between groups, it does not seem to be an effect due to socioeconomic or geographic differences. To address the above shortcomings, future observational studies could utilize research grade actigraphs to collect sleep data, as well as prospective sleep and headache diaries, and ideally sample the same school districts pre- and post-implementation of a change in school start time.

If this study's findings are confirmed, shifting to later high school start times could be an evidence-based strategy for migraine prevention in adolescents. If broadly implemented, this

[^1]could lead to thousands of fewer headache days and missed school days in adolescents annually.

## Acknowledgments

Funding: UCSF Resource Allocation Program grant

| Abbreviations: |  |
| :--- | :--- | :--- |
| CHAMP | Childhood \& Adolescent Migraine Prevention |
| AAP | American Academy of Pediatrics |
| AHS | American Academy of Neurology |
| CDC | American Headache Society |
| SD | Centers for Disease Control and Prevention |
| SE | Standard deviation |
| IQR | Standard error |
| PedMIDAS | Pediatric Migraine Disability Score |
| U.S. | United States |
| ICHD | International Classification of Headache Disorders |
| CI | Confidence Interval |
| REDCap | Research Electronic Data Capture |

## References:

1. Arruda MA, Bigal ME. Migraine and migraine subtypes in preadolescent children: association with school performance. Neurology. 2012;79(18):1881-8. [PubMed: 23109652]
2. Lipton RB, Manack A, Ricci JA, Chee E, Turkel CC, Winner P. Prevalence and burden of chronic migraine in adolescents: results of the chronic daily headache in adolescents study (C-dAS). Headache. 2011;51(5):693-706. [PubMed: 21521206]
3. Victor TW, Hu X, Campbell JC, Buse DC, Lipton RB. Migraine prevalence by age and sex in the United States: a life-span study. Cephalalgia : an international journal of headache. 2010;30(9):1065-72. [PubMed: 20713557]
4. Oskoui M, Pringsheim T, Billinghurst L, Potrebic S, Gersz EM, Gloss D, et al. Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Headache. 2019;59(8):1144-57. [PubMed: 31529477]
5. Guidetti V, Dosi C, Bruni O. The relationship between sleep and headache in children: implications for treatment. Cephalalgia : an international journal of headache. 2014;34(10):767-76. [PubMed: 24973419]
6. Bruni O, Galli F, Guidetti V. Sleep hygiene and migraine in children and adolescents. Cephalalgia : an international journal of headache. 1999;19 Suppl 25:57-9. [PubMed: 10668125]
7. Bruni O, Fabrizi P, Ottaviano S, Cortesi F, Giannotti F, Guidetti V. Prevalence of sleep disorders in childhood and adolescence with headache: a case-control study. Cephalalgia : an international journal of headache. 1997;17(4):492-8. [PubMed: 9209768]
8. Woldeamanuel YW, Cowan RP. The impact of regular lifestyle behavior in migraine: a prevalence case-referent study. J Neurol. 2016.
9. Ong JC, Taylor HL, Park M, Burgess HJ, Fox RS, Snyder S, et al. Can Circadian Dysregulation Exacerbate Migraines? Headache. 2018;58(7):1040-51. [PubMed: 29727473]
10. Hershey AD, Powers SW, Coffey CS, Eklund DD, Chamberlin LA, Korbee LL, et al. Childhood and Adolescent Migraine Prevention (CHAMP) study: a double-blinded, placebo-controlled, comparative effectiveness study of amitriptyline, topiramate, and placebo in the prevention of childhood and adolescent migraine. Headache. 2013;53(5):799-816. [PubMed: 23594025]
11. Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, et al. Recommended Amount of Sleep for Pediatric Populations: A Consensus Statement of the American Academy of Sleep Medicine. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2016;12(6):785-6. [PubMed: 27250809]
12. Hummer DL, Lee TM. Daily timing of the adolescent sleep phase: Insights from a cross-species comparison. Neurosci Biobehav Rev. 2016;70:171-81. [PubMed: 27450579]
13. Adolescent Sleep Working G, Committee on A, Council on School H. School start times for adolescents. Pediatrics. 2014;134(3):642-9. [PubMed: 25156998]
14. Wheaton AG, Ferro GA, Croft JB. School Start Times for Middle School and High School Students - United States, 2011-12 School Year. MMWR Morb Mortal Wkly Rep. 2015;64(30):809-13. [PubMed: 26247433]
15. Gelfand AA, Pavitt S, Greene K, Szperka CL, Irwin S, Grimes B, et al. High School Start Time and Migraine Frequency in High School Students. Headache. 2019.
16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. Journal of biomedical informatics. 2009;42(2):377-81. [PubMed: 18929686]
17. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia : an international journal of headache. 2018;38(1):1-211.
18. Torres-Ferrus M, Vila-Sala C, Quintana M, Ajanovic S, Gallardo VJ, Gomez JB, et al. Headache, comorbidities and lifestyle in an adolescent population (The TEENs Study). Cephalalgia : an international journal of headache. 2019;39(1):91-9. [PubMed: 29771141]
19. Kedia S, Ginde AA, Grubenhoff JA, Kempe A, Hershey AD, Powers SW. Monthly variation of United States pediatric headache emergency department visits. Cephalalgia : an international journal of headache. 2014;34(6):473-8. [PubMed: 24335850]
20. Cespedes Feliciano EM, Rifas-Shiman SL, Quante M, Redline S, Oken E, Taveras EM. Chronotype, Social Jet Lag, and Cardiometabolic Risk Factors in Early Adolescence. JAMA Pediatr. 2019.
21. Geographic N. United States Regions [Available from: https://media.nationalgeographic.org/assets/ file/us-regions-map.pdf.
22. Service IR. SOI Tax Stats - Individual Income Tax Statistics - ZIP Code Data 2017 [Available from: https://www.irs.gov/statistics/soi-tax-stats-individual-income-tax-statistics-zip-code-datasoi.
23. Powers SW, Coffey CS, Chamberlin LA, Ecklund DJ, Klingner EA, Yankey JW, et al. Trial of Amitriptyline, Topiramate, and Placebo for Pediatric Migraine. N Engl J Med. 2017;376(2):11524. [PubMed: 27788026]
24. Lewis D, Winner P, Saper J, Ness S, Polverejan E, Wang S, et al. Randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of topiramate for migraine prevention in pediatric subjects 12 to 17 years of age. Pediatrics. 2009;123(3):924-34. [PubMed: 19255022]
25. Aurora SK, Dodick DW, Turkel CC, DeGryse RE, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind,
randomized, placebo-controlled phase of the PREEMPT 1 trial. Cephalalgia. 2010;30(7):793-803. [PubMed: 20647170]
26. Diener HC, Dodick DW, Aurora SK, Turkel CC, DeGryse RE, Lipton RB, et al.

OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. Cephalalgia. 2010;30(7):804-14. [PubMed: 20647171]
27. 328 CSBN. Senate Bill 328 https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml? bill_id=201920200SB328: California Legislative Information; 2019 [
28. Didier HA, Curone M, Tullo V, Didier AH, Cornalba R, Gianni AB, et al. Usefulness of an occlusal device in the treatment of medication overuse headache and persistent idiopathic facial pain: preliminary results. Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2017;38(Suppl 1):57-61.
29. Wang SJ, Fuh JL, Lu SR, Juang KD. Chronic daily headache in adolescents: prevalence, impact, and medication overuse. Neurology. 2006;66(2):193-7. [PubMed: 16434652]

Table 1:
Sociodemographic and clinical characteristics of survey respondents, U.S. high schoolers with migraine; $n=503$ whose high schools start at 8:30 AM or later vs. $n=509$ who start before 8:30 AM

|  | $\underset{(n=509)}{\substack{\text { Before 8:30 } \\(n M}}$ | 8:30 AM or Later ( $n=503$ ) | $p$-value |
| :---: | :---: | :---: | :---: |
| Sociodemographics: |  |  |  |
| Age, years, mean (SD); (range) | 16.5 (1.1); (13-19) | 16.4 (1.3); (13-19) | 0.374 |
| Grade; $n(\%)$ |  |  |  |
| 9th | 64 (12.6\%) | 63 (12.5\%) | $<0.001$ |
| 10th | 122 (24.0\%) | 113 (22.5\%) |  |
| 11th | 153 (30.1\%) | 252 (50.1\%) |  |
| 12th | 170 (33.4\%) | 75 (14.9\%) |  |
| Sex assigned at birth; $n(\%)$ |  |  |  |
| Male | 194 (38.1\%) | 221 (43.9\%) | 0.060 |
| Female | 315 (61.9\%) | 282 (56.1\%) |  |
|  |  |  |  |
| Gender identity; $n$ (\%) |  |  |  |
| Male | 196 (38.5\%) | 222 (44.1\%) | 0.069 |
| Female | 313 (61.5\%) | 281 (55.9\%) |  |
|  |  |  |  |
| Geographic distribution, $\boldsymbol{n}$ (\%) |  |  |  |
| Northeast | 94 (18.5\%) | 119 (23.7\%) | $<0.001$ |
| Southeast | 85 (16.7\%) | 147 (29.2\%) |  |
| Midwest | 61 (12.0\%) | 85 (16.9\%) |  |
| Southwest | 39 (7.7\%) | 62 (12.3\%) |  |
| West | 230 (45.2\%) | 90 (17.9\%) |  |
|  |  |  |  |
| Income* for zip code in which respondent resides; mean (SD) | $\begin{gathered} \$ 95,000(\$ 93,000) \\ (n=473) \end{gathered}$ | $\begin{gathered} \$ 89,000(\$ 88,000) \\ (n=447) \end{gathered}$ | 0.280 |
| Migraine: |  |  |  |
| Headache days in the last month; mean (SD), median (IQR) | $\begin{gathered} 7.7(6.1), \\ 6.0(3.0-10.0) \end{gathered}$ | $\begin{gathered} 4.8(4.6), \\ 3.0(2.0-6.0) \end{gathered}$ | <0.001 |
| Had a headache on day of survey completion; $n(\%)$ | $\begin{gathered} 273(53.6 \%) \\ (n=502) \end{gathered}$ | $\begin{gathered} 240(47.7 \%) \\ (n=497) \end{gathered}$ | 0.054 |
| Had $\geq 15$ headache days in the last month; $n(\%)$ | 70 (13.8\%) | 30 (6.0\%) | $<0.001$ |
| Days of acute headache medication use in the last month; mean (SD) | 4.7 (4.9) | 3.2 (3.4) | <0.001 |
| Currently on a migraine preventive; $n(\%)$ | 142 (27.9\%) | 197 (39.2\%) | <0.001 |
| PedMIDAS score; mean (SD) | 43.3 (41.2) | 36.7 (33.2) | 0.005 |


|  | $\underset{(n=509)}{\substack{\text { Before } 8: 30 ~ A M ~}}$ | $\text { 8:30 } \underset{(n=503)}{\text { AM or Later }}$ | $p$-value |
| :---: | :---: | :---: | :---: |
| School: |  |  |  |
| Mean school start time | 7:56 AM | 8:43 AM | NA |
| Attend a public high school; $n$ (\%) | 386 (75.8\%) | 407 (80.9\%) | 0.050 |
| Hours of homework on a typical school night; mean (SD) | $\begin{aligned} & 2.5(1.4) \\ & (n=508) \end{aligned}$ | $\begin{aligned} & 1.7(0.7) \\ & (n=503) \end{aligned}$ | <0.001 |
| Sleep: |  |  |  |
| Typical bedtime on a school night (mean) | 10:58 PM | 10:19 PM | <0.001 |
| Typical bedtime on a weekend night (mean) | 11:30 PM | 11:15 PM | 0.006 |
| Typical wake-up time on a school day (mean) | 6:25 AM | 7:11 AM | <0.001 |
| Typical wake-up time on a weekend day (mean) | 8:45 AM | 9:03 AM | $<0.001$ |
| Sleep midpoint variability (minutes); median (range) | 80 (0-360) | 75 (0-360) | 0.956 |
| Total hours of sleep on a typical school night; mean (SD) | 6.9 (1.3) | 7.9 (0.9) | $<0.001$ |
| Total hours of sleep on a typical weekend night; mean (SD) | 9.3 (1.6) | 9.8 (1.3) | <0.001 |
| Students who get at least 8 hours of sleep on an average school night; $n(\%)$ | 168 (33.0\%) | 280 (55.7\%) | <0.001 |
|  |  |  |  |
| Morning routine: |  |  |  |
| Time of leaving home needed to reach school on time; mean | 7:15 AM | 8:02 AM | $<0.001$ |
| Duration of commute to school (minutes); mean (SD) | 24.4 (15.4) | 24.2 (9.9) | 0.842 |
| Miss breakfast at least once during a 5-day school week; $n(\%)$ | 335 (65.8\%) | 365 (72.6\%) | 0.020 |
| Average number of missed breakfasts in a 5-day school week; mean (SD) | 2.3 (2.0) | 1.6 (1.5) | $<0.001$ |

SD=Standard deviation; IQR=Interquartile range; PedMIDAS=Pediatric Migraine Disability Score; NA=Not applicable.
Mean (SD) income is rounded to the nearest $\$ 1,000$.

Table 2:
Univariate linear regression models examining variables associated with headache frequency

|  | Difference between groups in headache <br> days/month (95\% confidence interval) |
| :--- | :--- |
| High School Start time before 8:30 AM | $2.9(2.2$ to 3.6$)$ |
| Being on a migraine preventive medication | $2.6(1.9$ to 3.3$)$ |
| Female sex (as determined at birth) | $1.4(0.7$ to 2.1$)$ |
| Getting at least 8 hours of sleep on weeknights | $-1.9(-2.6$ to -1.2$)$ |
| Hours of sleep on a school night (per hour) | $-1.2(-1.4$ to -0.9$)$ |
| Hours of sleep on a weekend night (per hour) | $-0.3(-0.5$ to -0.1$)$ |
| Age (per year) | $-0.2(-0.5$ to 0.1$)$ |
| Days of acute medication use (per day of use) | $0.9(0.8$ to 1.0$)$ |
| Hours of homework on a school night (per hour of homework) | $0.7(0.4$ to 1.0$)$ |
| Days of missed breakfast per 5-day school week (per day of missed breakfast) | $1.0(0.8$ to 1.1$)$ |
| Sleep midpoint variability (per 100 minutes) | $0.7(0.1$ to 1.3$)$ |
| Grade: <br> 9 th <br> $10^{\text {th }}$ <br> $11^{\text {th }}$ <br> $12^{\text {th }}$ | Reference |

## Table 3:

Multivariate regression models examining headache days/month, by cohort (late start vs. early start), adjusting for covariates.

| Variables in the model: | Mean (95\% CI) headache days/month in the late start vs. early start groups | Mean difference (95\% CI) between groups in headache days/month |
| :---: | :---: | :---: |
| Unadjusted headache frequency | 4.8 (4.3 to 5.3) vs. 7.7 (7.2 to 8.1) | -2.9 (-2.2 to -3.6) |
| Model \#1: Adjusted for 1) total hours of sleep on school nights 2) sleep midpoint variability, 3) frequency of acute medication use, 4) being on a migraine preventive, 5) sex, 6) homework hours, 7) missing breakfast and 8) grade level | 5.8 (5.3 to 6.2) vs. 7.1 (6.7 to 7.4) | -1.3 (-1.9 to -0.7) |
| Model \#2: Adjusted for 1) getting at least 8 hours of sleep on school nights, 2) sleep midpoint variability, 3) frequency of acute medication use, 4) being on a migraine preventive, 5) sex, 6) homework hours, 7) missing breakfast, and 8) grade level | 5.6 (5.2 to 6.0) vs. 7.1 (6.7 to 7.5) | -1.5 (-2.0 to -0.9) |
| Model \#3: Adjusted for 1) total hours sleep on school nights, 2) sleep midpoint variability, 3) being on a migraine preventive, 4) sex, 5) homework hours, 6) breakfast missing, and 7) grade level | 5.7 (5.2 to 6.2) vs. 7.7 (7.2 to 8.2) | $-2.0(-2.7$ to -1.3$)$ |
| Model \#4: 1) Total hours sleep on school nights, 2) being on a migraine preventive, 3) sex, 4) homework hours, 5) breakfast missing, and 6) grade level | 5.7 (5.2 to 6.2) vs. 7.7 (7.2 to 8.2) | $-2.0(-2.7$ to -1.3$)$ |
| Model \#5: Adjusted for 1) sleep midpoint variability, 2) being on a migraine preventive, 3) sex, 4) homework hours, 5) breakfast missing, and 6) grade level | 5.5 (5.0 to 6.0) vs. 7.8 (7.4 to 8.3) | $-2.4(-3.0$ to -1.7$)$ |


[^0]:    Corresponding Author: Amy A. Gelfand, MD, $55016^{\text {th }}$ St., $4^{\text {th }}$ Floor, San Francisco, CA 94158, amy.gelfand@ucsf.edu, Phone: 415-502-1914.
    Disclosures:
    AAG: Has received consulting fees from Advanced Clinical, Biohaven and Satsuma. She has received honoraria from UpToDate (for authorship) and JAMA Neurology (as an associate editor). Receives grant support from Amgen and the Duke Clinical Research Institute. Her spouse reports research support (to UCSF) from Genentech for a clinical trial, honoraria for editorial work from Dynamed Plus, and personal compensation for medical-legal consulting.
    SP: No conflicts of interest
    ACR: No conflicts of interest
    CLS: Dr. Szperka has consulted for Teva and Lundbeck. Dr. Szperka receives salary support from the NIH NINDS K23NS102521.
    SLI: Dr. Irwin receives honoraria for authoring a chapter for the Canadian Pharmacy Association (CPhA), compensation for consulting work with Impel NeuroPharma Inc. and research support from the Duke Clinical Research Institute.
    SB: Has received consulting fees from Merck, Dohme \& Sharpe and Eisai, Inc. Received grant support from ApniMed.
    KS: Has received grant support from Merck \& Co
    RF: No conflicts of interest
    BG: No conflicts of interest
    IEA: No conflicts of interest

[^1]:    ${ }^{1}$ A 504 plan is a formal plan developed under Section 504 of the Rehabilitation Act28. Didier HA, Curone M, Tullo V, Didier AH, Cornalba R, Gianni AB , et al. Usefulness of an occlusal device in the treatment of medication overuse headache and persistent idiopathic facial pain: preliminary results. Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2017;38(Suppl 1):57-61.to provide students with disabilities, including migraine, necessary accommodations to facilitate equality in learning

