

# The Global Burden of Headache

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## Abstract

### Keywords

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- ▶ migraine
- ▶ tension-type headache
- ▶ medication-overuse headache
- ▶ burden of disease
- ▶ intervention
- ▶ structured headache services
- ▶ global campaign against headache

At the turn of the century, most of the world's population lived in regions where the prevalence of headache was unknown and its impact poorly understood. Lifting The Burden (LTB), a nonprofit organization in official relations with the World Health Organization, established the Global Campaign against Headache, with the ultimate purpose of reducing the burden of headache worldwide. First, the scope and scale of this burden had to be known. LTB embarked upon a program of population-based studies in countries in all world regions in order to achieve its aim. Its studies have demonstrated a high prevalence of headache disorders, including migraine, tension-type headache, and medication-overuse headache, and their associations with impaired quality of life, substantial lost productivity, and high economic costs in every country surveyed. Informed by these, the Global Burden of Disease study ranks headache disorders as the second leading cause of years lived with disability worldwide; migraine alone is third among people aged 15 to 49 years. With interventions urgently needed to reduce these burdens throughout the world, we review the epidemiological studies conducted by LTB, examine proposed interventions to improve provision of headache care including a three-tier system of structured headache services, and consider the challenges still remaining in providing effective, efficient, and equitable headache care especially in low-income countries.

The most common headache disorders worldwide are migraine, tension-type headache (TTH), and medication-overuse headache (MOH).<sup>1</sup> In recent years, the scale of the personal, societal, and economic burdens attributable to these disorders have increasingly been recognized, along with the extent of their contributions to global ill health. Behind this growing awareness has been the steady accrual, over 15 years, of more and better evidence.

In this regard, the Global Burden of Disease (GBD) studies have been highly informative (**Box 1**). GBD 2010 established TTH as the second most prevalent condition in the world (22%) and migraine third (15%), trailing only dental caries in the numbers of people affected.<sup>2</sup> GBD 2015 found that more

disability-adjusted life years (DALYs) were attributable worldwide to headache disorders than to all other neurologic disorders combined despite the fact that headache disorders have no impact on mortality.<sup>3</sup> Headache disorders ranked sixth among the leading causes of years lived with disability (YLDs) worldwide.<sup>3,4</sup> Migraine alone was seventh, and third in both men and women aged 15 to 49 years.<sup>4</sup> GBD 2000, the first iteration of GBD to include any headache disorder, ranked migraine 19th among causes of YLDs while ignoring TTH.<sup>3</sup>

Epidemiological data are essential to burden estimates. Where data are lacking, regionally or nationally, GBD does the best it can by extrapolating from areas adjacent or

### Box 1. The Global Burden of Disease studies

Performed reiteratively since 1990, Global Burden of Disease (GBD) is a worldwide collaboration recently described as “the most comprehensive worldwide observational epidemiological study to date”.<sup>71</sup> Now led by the Institute of Health Metrics and Evaluation, University of Seattle,<sup>72</sup> GBD estimates burden attributable to more than 300 diseases and injuries. It uses a number of metrics; among these, disability is measured in years lived with disability (YLDs) and early mortality in years of life lost (YLLs); disability-adjusted life years are the summation of YLDs and YLLs.

similar. It is imperfect methodology, generating inexact estimates. In 2000, more than half of the world’s population lived in regions where headache prevalence was unknown: the Western Pacific region (including China), Southeast Asia (including India), Eastern Mediterranean, (including the Middle East) and North Africa, most of sub-Saharan Africa and much of Eastern Europe.<sup>1</sup> With regard to headache, GBD 2000 was very poorly informed and its estimates unreliable.<sup>5</sup>

In 2003, the Global Campaign against Headache was launched in partnership with the World Health Organization (WHO).<sup>6,7</sup> Now led by *Lifting The Burden* (LTB), a United Kingdom registered nonprofit organization in Official Relations with the WHO,<sup>8</sup> the Campaign’s ultimate goal was and is to reduce the burden of headache worldwide. It is a goal not easily achieved, calling for implementation everywhere of headache services appropriate to local needs in a world of competing demands for limited resources. The Campaign’s first requirement was reliable knowledge of local needs, a requirement ill-served by GBD 2000 and the data then available. LTB’s first priority was therefore to fill the knowledge gaps.

A review in 2007 of the published epidemiological studies of headache noted frequent methodological shortcomings in study design, case definitions and ascertainment, sampling, data interpretation, and reporting.<sup>9</sup> LTB engaged an expert panel to develop consensus guidelines on the design and conduct of cross-sectional population-based studies of headache.<sup>10</sup> Questionnaires were produced to assess not only the prevalence of headache disorders but also many components of the burden attributable to them in adults<sup>11</sup> and children.<sup>12</sup> These were employed and validated in multiple countries,<sup>13</sup> along with an instrument to help health care providers evaluate and adjust headache treatment.<sup>14–16</sup> Population-based studies using these standardized methods in Georgia,<sup>17</sup> Moldova,<sup>18</sup> Lithuania,<sup>19</sup> Russia,<sup>20</sup> China,<sup>21</sup> India,<sup>22</sup> Nepal,<sup>23</sup> Pakistan,<sup>24</sup> Zambia,<sup>25</sup> Ethiopia,<sup>26</sup> Saudi Arabia (unpublished), Morocco (unpublished), and nine European Union countries<sup>27</sup> have provided data to successive iterations of GBD, each, as a consequence, better informed to make more dependable YLD estimates.<sup>28</sup> The result is a better,

albeit still incomplete, understanding of the impact of headache disorders worldwide.

Here, we review the recent population-based studies of headache prevalence and personal and societal burdens, interventions that might fill the yawning gaps in headache treatment,<sup>29</sup> and challenges remaining in the continuing quest for better diagnosis and efficient, cost-effective, and equitable treatment of headache disorders worldwide.

## Global Headache Epidemiology

Studies conducted by LTB with standardized methodology, on which we focus, are summarized in ►Tables 1 and 2.

### European Region

Studies in Georgia,<sup>17,30</sup> Lithuania,<sup>19</sup> Moldova,<sup>18</sup> and Russia<sup>20,31</sup> using standardized methodology found broadly similar results (►Table 1): 1-year prevalence of all headache disorders in the range of 53 to 75% and of migraine in the much narrower range of 16 to 20%. Except in Moldova (18%), the prevalence of TTH was consistently higher than that of migraine (31–42%). Having in mind its likely impact, headache occurring on  $\geq 15$  days per month was extraordinarily common (5–10%). The Eurolight Project, a cross-sectional study of more than 8,000 residents of Austria, France, Germany, Italy, Lithuania, Luxembourg, Netherlands, Spain, and the United Kingdom,<sup>27</sup> used methods somewhat at variance from LTB’s standardized methodology.<sup>32</sup> It found a lifetime headache prevalence of >90% and a 1-year prevalence of 79%, with almost equal proportions of migraine (35%) and TTH (38%) (►Table 1).

As might be expected, headache disorders were generally associated with impaired quality of life (QoL) across all countries. The effect was similar with all headache types in Georgia,<sup>30</sup> was greatest with headache on  $\geq 15$  days per month and, among episodic headaches, more with migraine than TTH, in Russia,<sup>31</sup> and was observed only with migraine and headache on  $\geq 15$  days per month, not TTH, in Lithuania.<sup>19</sup> Nearly a quarter (17.7% of males, 28% of females) of participants with migraine in Eurolight lost >10% of their productive time and nearly half (44.7% of males, 53% of females) of those with probable MOH (pMOH) lost >20%.<sup>27</sup> Societal impact was consequently high: the burden of indirect costs, attributable mostly to lost productivity, was equated to 1.5% lost gross domestic product (GDP) in Lithuania and to 1.8% lost GDP in Russia (►Table 2).<sup>19,31</sup>

Eurolight assessed impact in a range of additional domains, both ictal and interictal and both on people with headache and on others (their partners and children): in all of these domains, impact was high.<sup>27</sup> For example, one-quarter of people with migraine reported interictal symptoms, including anxiety in 11% and avoidance of activities with consequential lifestyle compromise in 15%; both of these were positively associated with frequency and severity of migraine attacks. One-third were reluctant to speak of their condition, many believing that family and friends (10%) or employers and colleagues (12%) failed to understand their headaches. Most importantly, since these were indicators of

**Table 1** Global 1-year prevalences of headache disorders: country estimates from Lifting The Burden cross-sectional studies using standardized methodology

Country	All headaches (%)	Migraine (%)	Tension-type headache (%)	All headaches on $\geq 15$ d/m (%)	Probable MOH (%) <sup>a</sup>
European Region					
European Union	79	35	38	7	3
Georgia	61	16	37	8	1
Lithuania	75	19	42	9	3
Moldova	53	18	18	5	–
Russia	62	20	31	10	7
Western Pacific Region					
China	24	9	11	1	0.6
South East Asia Region					
India	64	25	35	3	1
Nepal	85	35	41	8	2
Eastern Mediterranean Region					
Pakistan	77	22	45	7	1
Africa Region					
Ethiopia	45	18	21	3	1
Zambia	62	23	23	12	7

Abbreviation: MOH, medication-overuse headache.

<sup>a</sup>MOH in *Lifting The Burden* studies is reported as “probable MOH” (headache on  $\geq 15$  days per month associated with medication overuse) because, in cross-sectional studies, causation cannot be ascertained.

**Table 2** Lost productive time from paid and household work as proportions of total available time, and lost GDP, due to headache: country estimates from Lifting The Burden cross-sectional studies using standardized methodology

Country	Per person lost productive time								Overall lost GDP
	From paid work				From household work				
	Migraine (%)	Tension-type headache (%)	All headaches on $\geq 15$ d/m (%)	Probable MOH (%) <sup>a</sup>	Migraine (%)	Tension-type headache (%)	All headaches on $\geq 15$ d/m (%)	Probable MOH (%) <sup>a</sup>	
European Region									
Lithuania	4	1	4	6	5	2	11	14	1.5
Russia	3	1	9	–	3	2	11	–	1.8
Western Pacific Region									
China	4	3	7	–	4	2	6	–	1.9
South East Asian Region									
India	2	1	8	6	2	1	5	11	1.7
Nepal	3	1	–	12	4	1	–	10	–
African Region									
Ethiopia	5	2	8	29	5	1	11	16	1.6
Zambia	6	2	–	7	5	1	–	5	1.9

Abbreviations: GDP, gross domestic product; MOH, medication-overuse headache.

<sup>a</sup>MOH in *Lifting The Burden* studies is reported as “probable MOH” (headache on  $\geq 15$  days per month associated with medication overuse) because, in cross-sectional studies, causation cannot be ascertained.

lifelong disadvantage, significant numbers reported negative impacts on educational attainment (12%), earning potential (6%), and/or careers (7%). Furthermore, both migraine and pMOH, but not TTH, were associated with significantly elevated risk of anxiety (19 and 39%, respectively), depression (7 and 17%), or both (5 and 14%) as comorbid disorders.<sup>33,34</sup>

### Asian Regions

Population-based studies have been completed in China,<sup>21,35</sup> India,<sup>22,36,37</sup> Nepal,<sup>23,38</sup> and Pakistan,<sup>24</sup> all with LTB's standardized methods and questionnaire. Similar results from India and Nepal (South East Asia) and from Pakistan (Eastern Mediterranean) contrast with those from China (Western Pacific), where headache appears to be generally much less prevalent than in other regions (►Table 1). One-year prevalence of all headache disorders ranged from 64% (India) to 85% (Nepal), except in China, where it was only 24%. Approximately one-quarter of participants reported migraine in India and Pakistan and one-third in Nepal, but only 9% in China. Similarly, prevalence of TTH ranged within 35 to 45%, except in China (11%). The disparity between China and the other countries is more likely, given its size, to have a genetic rather than cultural or environmental basis. In all these countries, as in Europe, women were more likely than men to report migraine and, similarly, headache on  $\geq 15$  days per month. Migraine in Nepal was strongly associated with living at altitudes above 1,000 m, a factor largely explaining its very high prevalence (in the lowland areas adjacent to India, prevalence was similar to that observed in India).<sup>23</sup> Despite the differences in prevalence, the socioeconomic impact of headaches disorders was similar in China<sup>21</sup> and India<sup>36</sup> (►Table 2).

LTB pioneered the collection of data on headache occurring on the day prior to interview ("headache yesterday" [HY]), enabling not only the estimation of 1-day (point) prevalence but also characterization of burden without reliance on recall over several months. In India, the 1-day headache prevalence was 5.9%; taking into account the reported duration of HY, this signaled that 1.7% of the population had headache at any moment.<sup>37</sup> More than 80% of those with HY reported at least some lost productivity, such that a 3% daily loss in overall productivity was estimated at the population level. In China, despite the much lower 1-year headache prevalence, 1-day prevalence was not so different at 4.8%, with 1.8% of China's population having headache at any moment.<sup>35</sup> Headache lasted all day in one-third of those reporting HY (6%), but the impact on productivity was lower than in India. Just more than one-quarter of those with HY could do nothing or less than half of what they would otherwise have expected, with lost productivity at population level estimated at a still substantial 1.3%.

In India, as in Europe,<sup>33</sup> the personal impact of headache was high in other respects, with 10 to 12% of participants reporting a lack of understanding among friends, family, employers, and colleagues, and 6 to 12% reporting negative impact on their educational attainment, earning potential, and careers.<sup>37</sup> In Nepal, people with headache of all types

reported impairment of QoL, which was greatest among those with pMOH.<sup>38</sup> Anxiety and depression were both associated with pMOH and migraine, but not with TTH.<sup>39</sup> Participants with headache and a comorbid psychiatric disorder had even poorer QoL than those with headache alone.

### African Region

LTB has conducted two population-based studies with standardized methodology in sub-Saharan Africa: in Ethiopia<sup>26</sup> and Zambia<sup>25</sup> (►Table 1). One-year headache prevalence of all headaches was only 45% in Ethiopia compared with 62% in Zambia, but migraine (18 vs. 23%) and TTH (21 vs. 23%) were similar in the two countries. The major difference was in headache on  $\geq 15$  days per month, much more prevalent in Zambia (12%) than in Ethiopia (3.2%), largely because of pMOH (7.1 vs. 0.7%). In both countries, pMOH was a mainly urban problem, and Zambia is far more urbanized than Ethiopia. One-day prevalence of headache in Zambia was 19%,<sup>25</sup> much higher than that in China or India, again largely because of pMOH (by definition occurring on  $\geq 15$  days per month). Impact on productivity was very similar in the two countries for all headache types except pMOH: Ethiopians with pMOH reported much higher individual levels of missed paid work and household work<sup>40</sup> than their Zambian counterparts,<sup>41</sup> greatly countering the lower prevalence of pMOH in Ethiopia (►Table 2). Indirect costs of headache were estimated to translate into 1.6% lost GDP in Ethiopia<sup>40</sup> and a similar 1.9% loss in Zambia.<sup>41</sup>

### Americas

No LTB studies have yet been completed in this region, but a wealth of population-based data from the United States is available from other surveys. These studies have used somewhat different sampling methods and case definitions (especially for headache on  $\geq 15$  days per month, including MOH), generating prevalence estimates generally below those found by LTB in Europe. The American Migraine Study, for example, has found a rather lower 1-year prevalence of migraine, although it has consistently been in the range of 12 to 13% over multiple years.<sup>42</sup> TTH is estimated to occur in approximately 40% of the US population but is more common in those aged under 40 years, in Caucasians, in women, and in those with higher educational levels.<sup>43</sup> Headache on  $\geq 15$  days per month is found in approximately 4% of the population, more in Caucasians, in women, and in those less well educated.<sup>44</sup> Societal impact is again high, with an estimated mean annual cost of >US\$2,600 per person with episodic migraine. For those diagnosed with chronic migraine (probably including many who would be diagnosed elsewhere with MOH), this cost rises to >US\$8,000 per person annually.<sup>45</sup>

### Conclusions on Epidemiology

LTB studies have reliably demonstrated that, worldwide, headache disorders are highly prevalent and burdensome in all world regions. Except in China, all national studies have found the prevalence of migraine, and, less so, that of TTH, to be higher than GBD estimates of global averages.<sup>4,46</sup> This suggests that GBD estimates of both prevalence and burden,

which take account of all available data—many of them generated by older studies with questionable methodology, case definitions or case ascertainment—are too low and will be revised upward as further LTB studies are completed.

Regional variations are not large, although China, with relatively less headache in a population of 1.3 billion, depresses regional estimates in the Western Pacific. Headache on  $\geq 15$  days per month appears to be particularly problematic in countries of the former Union of Soviet Socialist Republics (USSR), which has not been explained. In Zambia, the very high urban (but not rural) prevalence of pMOH stems from a combination of factors: a high underlying prevalence of migraine (the principal precursor of MOH), limited availability of and poor access to health care, total lack of public health care education, and, in contradistinction, ready access in urban (but not rural) areas to over-the-counter analgesics.<sup>25</sup>

The need for interventions is very apparent, an issue we now address.

## Interventions to Reduce the Burden of Headache

### Health Care Utilization Patterns

Despite the unquestionably high burden of headache worldwide, health care provision for headache, the quality of care delivered, and rates of utilization are consistently poor across regions, countries, cultures, and settings.<sup>29</sup> For example, a survey of migraine patients from the United Kingdom, France, Germany, Italy, and United States found that not only consultation rates with physicians were unexpectedly low, but also that, of patients who did consult for their migraines, fewer than 10% were prescribed triptans, the standard treatment for disabling migraine.<sup>47</sup> Yet, more than half in each country reported moderate or greater disability during their migraine attacks, and fewer than one-third of survey respondents believed that their current migraine therapy was consistently effective.

LTB studies have enquired into this issue as well. In India, fewer than one-quarter of those with headache had consulted a physician for their disorder in the preceding year.<sup>36</sup> In China, barely half of those with migraine or headache on  $\geq 15$  days per month, and only 40% of those with TTH, had done so.<sup>48</sup> In China, underdiagnosis and misdiagnosis were common: more than half of those with migraine or headache on  $\geq 15$  days per month, and almost two-thirds with TTH, reported no previous diagnosis. Those with migraine were as likely to have been diagnosed with “nervous headache” as with migraine, and “nervous headache” and “vascular headache” were the most likely diagnoses in those with TTH or headache on  $\geq 15$  days per month.

In lower-income countries, health care availability and utilization are even poorer, but low consultation rates do not necessarily equate to lack of willingness to pay for headache care. In Georgia, 93% of survey respondents with headache would reportedly pay an average of US\$8 per month for effective headache care, which would cover medical costs in that country and is an indication that headache services

are potentially sustainable even in a poor country.<sup>30</sup> Cost, it appears, is not the primary barrier to care. Rather, lack of awareness among politicians obstructs adequate provision of services, among providers leads to misdiagnosis and mismanagement of even common headache disorders, and among patients results in low uptake which is reinforced by unsatisfying outcomes. The remedy for all is educational interventions, which are desperately needed.

### Health Care Delivery Systems

Structured headache services are best able to provide nationwide headache care efficiently, cost-effectively, and equitably, and are central to any national health care solution for headache.<sup>29</sup> LTB and the European Headache Federation have advocated a three-tier system.<sup>49</sup> It assumes that approximately 50% of all those with headache—generally those with episodic TTH but also some with less frequent and disabling migraine—ought to be able to manage themselves, an assumption calling for public education in support of the health care intervention. Of the other 50% who need professional care, level 1 health care providers, that is, primary care physicians (or, in many countries, clinical officers or nurses), should manage the great majority (~90%). Level 1 providers, with the clinical skills expected in primary care supplemented by basic training, are entirely capable of diagnosing and managing common primary headache disorders while recognizing secondary headaches that require management of the underlying condition. Level 2 providers, that is, physicians with an interest in headache and additional theoretical and practical training in headache medicine (often but not necessarily general neurologists), should manage a further 8 to 10%, including more complex primary headache disorders as well as some secondary headaches. Finally, level 3 providers, that is, fully trained specialist physicians in academic medical centers, should manage 1 to 2% with highly complex or rare primary headaches and the full range of secondary headache disorders. The purpose behind this hierarchical structure, which requires lower levels to act as gatekeepers to higher, is to reserve higher levels for those who need them; otherwise, higher level providers are soon inundated by large numbers of people whose needs could and should be efficiently met elsewhere.<sup>49</sup>

Aspects of this model have been piloted in various locations. In the Netherlands, a study of the cost-effectiveness of migraine-trained nurses for follow-up of patients in primary care practices found that while practice-specific costs increased, total costs at a societal level were likely to decrease.<sup>50</sup> At the same time, use of nurses would improve service capacity at level 1. In Russia, the Yekaterinburg Headache Initiative was established in 2012 with three goals: (1) creating government awareness of headache as a public health concern, and, as a consequence, gaining political support for better health care provision; (2) implementing the three-tier model of headache care; and (3) developing the requisite educational initiatives for primary care providers, nonspecialist neurologists, pharmacists, and the general public.<sup>51</sup> Its evaluation is still in progress. Although the initiative has struggled with the first goal despite clear evidence of the high burden of headache in Russia,<sup>31</sup>

optimism remains that it may serve in Russia as a scalable model of improved headache health care regionally and nationally. In Georgia, a country previously with no health care provision for headache, LTB supported the opening of two specialty headache clinics providing level 3 services. The goal, with these clinics established, was to put in place the requisite support of better levels 1 and 2.<sup>52</sup> Early results, not quite as expected, included the opening by other nonstate agencies of several other headache clinics in the country, which have altered the landscape for people whose needs were previously wholly unmet.<sup>29</sup> In addition, lobbying of drug manufacturers brought substantial reductions in the cost of triptans and therefore these essential drugs, previously barely used, became widely affordable.<sup>30</sup>

### Educational Interventions

A WHO worldwide survey of health care providers identified lack of training in diagnosing and managing headache disorders as a key reason for inadequate headache health care; better professional education was reported as the most needed change.<sup>29</sup> Educational initiatives, supported by the development and provision of clinical tools to aid nonspecialists in headache care, are an integral part of structured service implementation to reduce the burden of headache.

Recent research into educational interventions, supported by LTB, has demonstrated tangible positive effects. In Estonia, general practitioners who attended an educational program delivered as two 6-hour courses on headache medicine referred fewer patients to specialists, used more specific headache diagnoses, ordered fewer (unnecessary) diagnostic tests for headache, and were more likely to initiate headache treatment than they did prior to the intervention.<sup>53</sup> Thus, a relatively small investment in education aimed at level 1 providers can significantly and beneficially change their practice. A follow-up study showed these benefits to be durable, requiring reinforcement only every 2 to 3 years.<sup>54</sup>

In China, a continuing medical education program (headache schools) has trained more than 600 rural and urban neurologists with an interest in headache management.<sup>55</sup> A cornerstone of this program is the introduction of a systematic disease management model called “SMART” (Screen, Migraine, Aura, Red flags, and Treatment), which standardizes the neurologists’ approaches to screening, diagnosing, and managing migraine. A second pillar of the program is the “train-the-trainer” model: neurologists who have received the training return to their regions of practice and offer training to other local health care providers, thereby promoting knowledge of headache at level 1. Similar educational campaigns and train-the-trainer models can easily be adapted for implementation in a variety of settings, including low-income countries.

### Pharmacological Interventions

While triptans and other newer acute treatments for migraine may be cost-prohibitive in low-resource settings, cost-effective interventions for headache disorders exist. Aspirin, for example, is universally available worldwide. In

a WHO model of cost-effectiveness applied to Russia, China, India, and Zambia, aspirin used for acute migraine within the context of structured headache services supported by professional and public education was highly cost-effective in all settings at less than US\$100 per healthy life year (HLY) gained.<sup>56</sup> Very few health care interventions offer such low-cost benefit. Sumatriptan, 50 mg, in the same context would cost nearly US\$4,000 per HLY gained—still cost-effective in most settings if reserved, in a stepped-care management paradigm, for people who need it. Amitriptyline was the most cost-effective prophylactic medication, with a cost in a stepped-care management paradigm of less than US \$1000 per HLY gained.

### Conclusions on Interventions

With unquestionable evidence of need for them, interventional models have been proposed and some evidence adduced of their feasibility, effectiveness, and cost-effectiveness. This is work in progress, representing the final stage of LTB’s Global Campaign against Headache.<sup>6,7</sup>

### Remaining Challenges

Education at multiple levels is an essential pillar of intervention, providing support to any service implementation, but it is logistically challenging. Training specialists are not the greatest of problems; far more difficult is the provision of even basic training to health care providers throughout a country’s primary care. How and by whom is this to be done? Otherwise, against all economic reasoning, the major and enduring challenge in implementing interventions for headache appears to be an obdurate lack of political will.<sup>29</sup>

### Secondary Headaches

While most of the public health burden of headache is due to primary headache disorders, secondary headaches are common, some are serious, and a few are life-threatening. These are headaches with another underlying causative disorder, which, rather than the symptom of headache, requires treatment.

Secondary headaches may be especially troublesome in low-resource settings where acute infectious diseases—many associated with headache—are more common than in the developed world. For example, in a recent study of patients with neurologic symptoms presenting to a rural hospital in the Democratic Republic of Congo, more than half (57%) did so with headache, mostly due to acute infections of the central nervous system (CNS).<sup>57</sup> It may not fall to headache services to manage such patients, but, where these services exist, such patients (experiencing headache) will present to them. Frontline providers (level 1), usually non-headache specialists and, in low-income countries, often nonphysician health care workers, must be able to differentiate between primary and secondary headache disorders and immediately recognize those among the latter that are serious. Accurate diagnostic algorithms that require little neurologic training and minimal technology are needed for this purpose and still require development and testing.

The HIV epidemic poses a huge challenge to health care providers who care for headache, especially in sub-Saharan Africa where 70% of the global HIV-infected (HIV+) population reside.<sup>58</sup> Headache is common and the most frequent cause of pain among HIV+ people.<sup>59–61</sup> But, while headache in an HIV+ person may herald an underlying CNS opportunistic infection, primary headache disorders are still the most common cause of headache in HIV+ populations.

Guidelines for the diagnosis of primary headache disorders always include a list of “red flag” symptoms, signs, and comorbidities that should prompt further and often searching inquiry.<sup>62–64</sup> A history of HIV infection is included in this list, with the consequence that investigations such as brain imaging and lumbar puncture are recommended for nearly every HIV+ patient presenting with headache. In low-income countries, this is simply not feasible: access to computed tomography (CT) and magnetic resonance imaging (MRI) is limited and/or prohibitively expensive, and lumbar puncture is rarely performed for multiple reasons including lack of provider training and patients’ refusals.<sup>65</sup> Furthermore, the utility of other red flags in predicting secondary etiologies of headache has not been well studied in HIV-uninfected populations and not studied at all in HIV+ populations.<sup>66–69</sup> The few studies that have been conducted indicate that abnormal findings on neurologic examination are the strongest predictor of intracranial pathology,<sup>68,69</sup> but this, too, poses challenges in low-income countries. Neurologists are scarce, and frontline health care providers with minimal training in neurology may not be able, or have the equipment, to reliably detect subtle abnormalities such as a visual field deficit, or even critical signs such as papilledema. Research is urgently needed to support the development of evidence-based practical guidelines for evaluating and managing HIV+ patients presenting with headache in low-income countries, where referring all such patients for diagnostic investigations and specialist care is not an option.

## Conclusions

Mounting epidemiological data show that headache disorders, especially migraine, TTH, and MOH, are common and cause substantial disability worldwide, impairing QoL, harming productivity, significantly diminishing GDP, and imposing considerable burdens of financial cost on people and societies. Thus these disorders represent a major public health problem in countries of all economic strata. Cost-effective interventions exist, but, if they are ever to be implemented, educational campaigns are needed to improve awareness of the problem among politicians, the public, and health care providers. A three-tier system of structured headache services, emphasizing care by primary care providers for the majority of headache sufferers, is a proposed solution and is adaptable for implementation across a variety of settings, if government and institutional support can be provided. However, significant challenges remain, especially in low-income countries, and research continues to overcome these.<sup>70</sup>

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