Migraine is a neurovascular disorder that affects over 1 billion people worldwide. Its widespread prevalence, and associated disability, have a range of negative and substantial effects not only on those immediately affected but also on their families, colleagues, employers, and society. To reduce this global burden, concerted efforts are needed to implement and improve migraine care that is supported by informed health-care policies. In this Series paper, we summarise the data on migraine epidemiology, including estimates of its very considerable burden on the global economy. First, we present the challenges that continue to obstruct provision of adequate care worldwide. Second, we outline the advantages of integrated and coordinated systems of care, in which primary and specialist care complement and support each other; the use of comprehensive referral and linkage protocols should enable continuity of care between these systems levels. Finally, we describe challenges in low and middle-income countries, including countries with poor public health education, inadequate access to medication, and insufficient formal education and training of health-care professionals resulting in misdiagnosis, mismanagement, and wastage of resources.

Introduction

Migraine is a chronic and often lifelong disease that directly affects over 1 billion people across all world regions, cultures, and socioeconomic statuses.1,2 This prevalence is a largely avoidable burden to global health, since effective and cost-effective treatments exist for migraine.3,4 Evident deficiencies in systems of care require urgent correction, supported by informed health-care policies. In this context, epidemiological monitoring is a powerful tool to characterise the natural course of migraine and contextualise findings from clinic-based studies. Epidemiological studies are also key to quantifying the direct and indirect consequences of migraine, which enables us to understand the effect of migraine on people with the disorder and on their families, colleagues, employers, and society.

In this Series paper, we provide an overview of the epidemiology and global burden of migraine to increase awareness and understanding of them as a prerequisite for remedial action. We discuss the current structure and practices of migraine care, including specific challenges in low and middle-income countries. We also provide recommendations to standardise epidemiological monitoring, improve health-economic assessment, and tailor best practices within systems of care to local needs and resource availability.

Key messages

- Migraine is ubiquitous and prevalent, impairing the health and quality of life of many people, with profound effects on their families, colleagues, and society.
- Migraine is the leading cause of disability worldwide in people younger than 50 years (particularly in women) and a major cause of tremendous losses to the global economy.
- Despite these facts, serious deficiencies are reported worldwide in the professional and political awareness of migraine and resource allocation to its management.
- Primary-care professionals are the principal providers of health services for migraine; specialist referral can be needed for patients with treatment resistance, atypical features, or comorbidities.
- Epidemiological studies should continue to fill geographical and other knowledge gaps, using standardised consensus-based methodology to enable comparative assessments between countries.
- Methods to assess the range of indirect consequences of migraine (such as family effect, lost career potential) should be developed and yield a full account of migraine-attributed burden, to improve informed health-care policies.
- More research should identify best clinical practices and care strategies within structured headache services and assess their effectiveness, reach, and cost-effectiveness.
- In low and middle-income countries, concerted efforts should be made to find health-care solutions to migraine that are tailored according to local needs, infrastructure, and resources, of which training and education are key.

Search strategy and selection criteria

We searched MEDLINE (from database inception to Jan 1, 2020), and Embase (from database inception to Jan 1, 2020) for original research articles, systematic reviews, and meta-analyses. We used the search term “migraine” in combination with the terms “epidemiology”, “burden”, “health economics”, “systems of care”, “specialist care”, and “primary care”. We mainly selected publications in the past 5 years but did not exclude commonly referenced and highly regarded older publications. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant.
Epidemiology

Incidence of migraine

Epidemiological studies of migraine focus mainly on overall population prevalence. A few studies have estimated incidence rates. In a 12-year longitudinal Danish study, overall incidence was 8.1 per 1000 person-years in individuals without migraine initially. People aged 25–34 years (the youngest included) reported the highest incidence rates: 23 per 1000 person-years in women and 10 per 1000 person-years in men. Reported incidence rates declined with age thereafter. In a similar but dissenting 5-year longitudinal Turkish study, incidence was 23.8 per 1000 person-years overall, again higher in women than men.6

Another approach to estimating incidence uses reported age of migraine onset. This methodology was applied in the American Migraine Prevalence and Prevention Study,7 which found peak incidence rates at age 20–24 years in women (18.2 per 1000 person-years) and 15–19 years in men (6.2 per 1000 person-years). Nevertheless, median age of onset was marginally lower in women (23.2 years) than in men (25.5 years). Of both sexes, 75% reported onset of migraine before the age of 35 years.7

Prevalence of migraine

1-year period prevalence

For migraine, 1-year period prevalence is frequently reported. However, it is important to recognise that a single migraine day per year is sufficient to define an active headache disorder.8 Standardised methodologies have been developed for use in population studies worldwide.9

1-year prevalence is estimated at 15% worldwide, highest in southeast Asia (25–35%) and lowest in China (9%).10,11 The Eurolight project,12 collecting data from nine European countries, reported a 1-year prevalence of 35% after sex adjustment. By contrast, US-based estimates have reported a 1-year prevalence of 12–13%, remaining stable over time.13 Thus, estimates from the USA and Europe are discordant.4

Despite this substantial global burden of migraine, knowledge of it remains far from complete, with data missing from some regions of the world, especially regarding children and adolescents. Additionally, variable methodology with differences in study populations, selection criteria, and case definition has affected findings and made comparisons difficult. For example, European and US estimates are discordant, most probably for two reasons. The first reason is that the Eurolight project considered both definite and probable migraine (probable migraine fulfilled all but one of the criteria formally required for migraine),8,14 after first excluding tension-type headache as the diagnosis. The rationale was that a common headache disorder was unlikely to be any other disorder but migraine, if not tension-type headache. The US studies did not adopt this approach, including only definite migraine, whereas probable migraine accounted for approximately 40% of ascertained cases in the Eurolight project.12,13 The second reason is that many US studies required that participants report severe headache, which would reduce the likelihood of headache being reported.

Production of consensus-based methodological guidelines for cross-sectional studies has been one of the most important initiatives of the Global Campaign Against Headache, led by the non-governmental organisation Lifting The Burden (LTB) who have official relations with WHO.9 These detailed recommendations, developed by an expert consensus group with experience and competence in headache or general epidemiology and drawn from all six WHO world regions, are for anyone with an interest in designing, implementing, understanding, or assessing studies that measure or describe the burden of headache in populations. Their purpose is to improve and standardise methods in use, minimising differences in studies worldwide, thereby unmasking true variations attributed to factors such as geography, ethnicity, culture, and proportions of urban versus rural dwellers.

Migraine in children, adolescents, and older people

Similar to incidence, prevalence of migraine is clearly age-related and sex-related (figure 1). Its prevalence peaks in those aged 35–39 years,15 being lower at each end of the lifespan (ie, relatively low prevalence in children or adolescents, and older people).15,15,16,17 In school-aged children (aged 6–17 years), a nationwide Turkish study reported a 1-year migraine prevalence of 26% (7% definite, 19% probable),18 whereas one US study found a 1-year prevalence of 6% in adolescents, not including those with probable migraine.19 The US study estimate was reduced to 4% in adolescents without parental history of migraine.19 In older people (aged 60 years or older), prevalence rates are reported in the range of 3–6%.19,20

Figure 1: The global age-standardised prevalence and the global prevalence of migraine by age and sex Reproduced from the GBD 2016 Headache Collaborators’ systematic analysis for the Global Burden of Disease Study 2016.15 Global age-standardised prevalence is 14.4% (95% CI 13.8–15.0).
Prevalence by geographical region and race

The prevalence of migraine varies across geographical regions (figure 2). According to the 2016 *Lancet* Global Burden of Disease (GBD) study, prevalence is highest in Nepal and lowest in China. The high prevalence in Nepal has been attributed to a strong association with living at high altitudes. Regarding race, one US-based study found a relatively higher prevalence in White people than in Black people. However, comparisons of published prevalence estimates between geographical regions and races are confounded by the previously noted methodological variations. Even with standardised and rigorous methodology, it is not easy to separate biological racial differences from geographical differences and those arising from cultural, lifestyle, and environmental factors.

Prevalence by socioeconomic status

Several studies across income classes (low, middle, and high) have found no apparent association of migraine prevalence with socioeconomic status. However, two US population-based studies found a higher prevalence in those with low household income by comparison with people on high incomes. Additionally, poverty was associated with disorders characterised by 15 headache days or more per month in Russia and Georgia. It can be speculated that low socioeconomic status is associated with increased migraine prevalence when income is a predictor of access to health care. Indeed, this has been the conclusion of LTB studies in low-income countries, in which relative poverty is associated with poor access to health-care and rural dwelling.

Global burden

Disability and years of life lost

Despite considerable advances in diagnosis and treatment, migraine remains the second leading cause of disability worldwide, exceeded only by low back pain. The latter comprises a multiplicity of disorders with varying aetiology, unlike migraine. To put this in perspective, migraine contributes 45·1 million years lived with disability (YLDs), accounting for 5·6% of the global disease burden and more than all other neurological disorders combined. As this burden peaks between the ages of 35–39 years (figure 3), migraine constitutes the leading cause of disability worldwide in people younger than 50 years, particularly women. Consequently, migraine primarily affects people in their productive peak, contrasting with most other disorders, which are increasingly associated with YLDs in later life.
The burden of migraine on the family

Epidemiological studies of migraine have mostly focused on the affected individual, whereas the burden on the family is rarely mentioned (figure 4). The Eurolight project found that migraine not only affected child care but also strained partner relationships. In fact, partners of those with migraine can themselves suffer losses related to work productivity and social activities. As might be expected, the burden of migraine on the family becomes greater with increased migraine frequency. In the US-based Chronic Migraine Epidemiology and Outcomes (CaMEO) study, data were collected from partners and children of those individuals with high-frequency migraine. The migraine burden was most evidently reflected in negative emotional consequences and inability to participate in family and social activities. This effect was further magnified in single-parent homes, where partner-support was not available.

Comorbidities of migraine

Migraine, and even more so chronic migraine, is comorbid with a range of conditions and diseases. There is a strong association between migraine and both depression and anxiety disorders, with depression also increasing the risk of transformation to chronic migraine. Additionally, migraine is associated with other chronic pain conditions, such as neck and low back pain. Regarding cardiovascular events (eg, ischaemic heart disease or stroke), risks are more pronounced in migraine with aura than in migraine without aura. Other migraine-related comorbidities include epilepsy and obesity in those with chronic migraine. Generally, comorbidities are more frequently associated with chronic migraine than with episodic migraine, and can act as risk factors for migraine becoming chronic. The importance of this observation is that, if risk factors for migraine progression can be identified, this can provide a basis for preventive intervention, modifying the clinical course of migraine by addressing modifiable risk factors, such as depression and obesity. However, reliability of association estimates is impaired by variable data quality, particularly by inconsistencies in the criteria used for defining chronic migraine.

Improving epidemiological studies of migraine

Much insight has been acquired from the extensive body of epidemiological studies on migraine. Although many previous shortcomings have affected data quality, concerted efforts have been made to address these problems by standardising methodology and data reporting. Thus, LTB’s international consensus-based guidelines cover sampling, engagement with participants, and case ascertainment, all of which are crucial factors to data quality. International Classification of Headache Disorders criteria should always be the basis of diagnosis, with the inclusion of probable migraine (with definite migraine and probable migraine reported separately). This implies simultaneous application of diagnostic criteria for tension-type headache, since the diagnosis of probable migraine is mainly based on exclusion of definite tension-type headache. Enquiries into attributable burden should accompany those into prevalence, since prevalence alone does not provide enough information to be of public-health value.
All of these factors, which affect case ascertainment, enable consistent measurements and comparative assessments to identify true differences between populations rather than those due to methodological variations. However, although cross-sectional studies following these guidelines can reveal factors associated with high disease burden, longitudinal studies are also needed to ascertain causation and identify interventions that affect risk factors. The public-health challenge of migraine warrants substantial investment in optimisation of epidemiological studies.

**Health economics**

The economic consequences of migraine emphasise the need for improved health policies that are informed by evidence. In Europe, financial costs attributed to migraine were estimated at €50 billion to €111 billion in 2011, of which direct costs accounted for 7% and indirect costs for 93%. In the USA, direct costs were estimated at US$11 billion and indirect costs at $12 billion in 2007. The European and US estimates thus differ considerably in the ratio of indirect to direct costs. Treatment costs are generally higher in the USA by comparison with Europe, but this difference is probably due to methodological differences. Some US estimates excluded productivity losses and might not account for the indirect costs related to presenteeism (ie, working while having migraine). Notably, in 1999, US estimates found these indirect costs related to loss of productivity amounted to approximately $5 billion. Additionally, the US studies used fee-for-service, paid by individuals or insurers, as a surrogate for unit prices to estimate direct costs. Such calculations underestimate direct costs by excluding those related to individuals with migraine who do not seek medical care, or use uncovered medical services, such as complementary or alternative treatments. By contrast, European studies used a bottom-up approach (ie, summing the costs of each item of treatment or service used reported by each surveyed individual), thus generating more comprehensive cost estimates by comparison with the US estimates. Additionally, the higher prevalence estimates in Europe contribute to higher cost estimates.

**Direct costs of migraine**

Direct costs are an important measure that inform health-care policy and allow for forecasts of expenses incurred by health-care services. In Europe, direct health-care costs attributed to migraine were €1222 per person in 2011. In the USA and Canada, these costs were calculated separately for episodic and chronic migraine: $383 over 3 months for episodic migraine and $1036 for chronic migraine. Although these data suggest that direct costs are driven by migraine frequency, total direct costs are higher for episodic than for chronic migraine because of the much higher prevalence of episodic migraine.

**Indirect costs of migraine**

Indirect costs constitute most of the economic burden in Europe, of which productivity losses account for two-thirds. Similarly, productivity losses account for most indirect costs of migraine in the USA, although estimated productivity losses are lower than in Europe. In the USA, individuals with migraine missed about 9 more days of work per year than those without migraine, an additional estimated cost of $2350 per affected person in 2019. This time off work corresponds to about 4% of total work time for average full-time workers. However, it must be emphasised that productivity losses at work incur greater total costs than absences from work.

More research is needed to understand fully all indirect costs of migraine, especially in low and middle-income countries (LMICs), where policy decisions to invest in headache services might be more sensitive to cost–benefit analyses. Nonetheless, as shown in estimates from many different countries, indirect costs are clearly very high, with gross domestic product losses of up to 2%.

**Other indirect consequences of migraine**

Indirect consequences of migraine vary between individuals and are rarely fully accounted for in estimating total costs. These consequences are wide-ranging and include lifestyle compromises, family impact (impairment of personal relationships, abdication of family responsibilities, and imposition on others of carer burdens), damaged career potential, and increased risks of disorders secondary to treatment (eg, medication-overuse headache or opioid addiction). Although these have been quantified to some extent in Eurolight and CaMEO, it has not been possible to estimate their financial effect. Consequently, health-economic studies largely ignore these intangible but nonetheless important factors; therefore, the true economic burden of migraine is underestimated. Putting this right is a challenging task; we recommend an expert consensus approach, seeking to formulate further guidelines on how these indirect consequences might be measured and interpreted.

**Implications for health-care policy**

Since migraine is a prominent driver of losses to global and national economies, sensible health-care policies would allocate more resources to implementing effective headache services. The predictable benefits are potentially large, both economically and in addressing unmet needs of a billion affected people. Indeed, economic analyses have found that delivery of basic evidence-based migraine care within structured headache services will be highly cost-effective and perhaps cost-saving, including in LMICs.

**Systems of care**

Systems of care vary considerably between and within countries, with differing availability of human and
of care: structured services (in which primary and specialist care complement and support each other) and comprehensive referral and linkage systems that enable continuity of care between these levels. However, these care systems exist in few countries, and are nowhere organised optimally (ie, efficiently, equitably and with full reach in accordance with locally assessed needs); thus, challenges in primary and specialist care remain in many countries worldwide.

Primary care

Most migraine care should be initiated and maintained in primary care (figure 5). In Europe, evidence suggests that primary care can, if given the resources, meet the needs of 90% of patients consulting for headache (the majority having migraine, setting aside the 50% with either migraine or tension-type headache who can self-manage). Thus, primary care is the first and principal setting in which improvements in migraine diagnosis and treatment should be made.

Headache is the most common presenting neurological symptom in primary care. General practitioners, as front-line caregivers, should have the necessary basic skills for migraine diagnosis (which is almost always based on medical history without investigations), exclude secondary causes, and use evidence-based treatment algorithms. However, diagnostic delay, misdiagnosis, and inadequate care continue to be major problems. In one transcontinental study of patients with migraine referred to specialised headache centres, general practitioners had improperly diagnosed 72%. In three European countries (Austria, France, and the UK), general practitioners used migraine preventive medications in fewer than 10% of patients eligible for them. Primary care clinicians are often not aware of practice guidelines and therefore cannot implement them, even in high-income countries.

Over the past 3 years, LTB has entered the final stages of its Global Campaign to improve headache care, with education identified as key to implementing and sustaining effective headache services. LTB has shown that basic training for primary-care professionals will improve confidence and competence in diagnosis and clinical management of migraine, coupling better clinical outcomes with reductions in costs through wastage-avoidance. A single structured educational programme on headache disorders delivered in primary care in Estonia had beneficial effects lasting up to 3 years. The European Headache Federation has outlined key principles of postgraduate training for efficient management of headache disorders in primary care. The International Headache Society likewise prioritise education and promote knowledge-sharing through regional and online courses.

Readily available clinical tools also support management in primary care. A headache diary, completed by newly presenting patients for at least 1 month, provides information on characteristics and burden of headache. The headache diary is validated for diagnosis and treatment evaluation, can be easily translated into local languages, and can be available as e-diaries. Treatment of migraine is based on the principle of stepped management, and in most cases is simple, with non-opioid analgesics (ie, non-steroidal anti-inflammatory drugs [NSAIDs] and paracetamol) as a first treatment and, if these drugs are insufficient, triptans. These acute treatments are usually adequate and preventive medications are properly reserved for (and should be offered to) the minority of patients remaining adversely affected despite their optimal use of acute therapies.

A genuine problem among general practitioners is not having the time needed to address headache management. Other health-care professionals have obvious roles. Nurses trained in migraine management are effective and can reduce referrals to specialists with no overall increase of costs. In countries, such as many in sub-Saharan Africa, where front-line services are delivered by clinical officers, they too have the skills to diagnose and manage most headaches, requiring only...
some further basic training. Pharmacists can offer advice and treatment, with acute migraine medications such as NSAIDs being already available over the counter, and triptans increasingly so.\textsuperscript{70,75} Removing the requirement for a prescription dismantles a substantial barrier to care and reduces the number of consultations in primary care.

**Specialist care**

With educated primary care able to meet the needs of most patients with migraine, some will nonetheless require specialist referral. Eurolight\textsuperscript{79} found that patients who had consulted a specialist received better care than did those treated by general practitioners,\textsuperscript{75} which was probably attributed to the greater expertise of the specialist and access to a multidisciplinary team of caregivers for the patient. However, specialist services are in short supply, even in high-income countries, and often hampered by long waiting lists.\textsuperscript{77} Within structured services, one of the purposes of primary care is to ensure that only those individuals who require specialist referral are duly referred. People who require specialist referral include patients with atypical features who might be diagnostically challenging, treatment-resistant, or affected by particular comorbidities such as major depressive disorder or cardiovascular risk factors.

Despite the widely accepted benefits of specialist care, formal assessments of its use and system-level effectiveness are few and limited in scope, meaning there is a crucial evidence gap. In fact, data suggest that improvements need to be made in both specialist-care and primary-care services. According to a global survey of neurologists, explicit diagnostic criteria are used to support headache diagnosis in only 56% of countries that responded.\textsuperscript{51} In Europe, preventive medications were used in only 26% of those individuals who were eligible for this treatment.\textsuperscript{77} Improvements in specialist services, along with primary care, could yield further substantial gains. These improvements should include regular quality assessments (following published guidelines) and, importantly, assurance that repatriation to primary care is timely and coordinated with the general practitioner to ensure continuity of care.

**Cost-effectiveness of systems-level management strategies**

The number of headache centres within countries should be optimised: too few would not adequately meet needs, whereas too many would not be cost-effective.\textsuperscript{77} Although the clinical benefit and cost-effectiveness of specific interventions are reasonably well documented, there are few formal assessments of the cost-effectiveness of systems-level headache services. In one Danish study,\textsuperscript{79} the number of missed workdays was reduced by about half (from a starting point of ~6 days per month) following treatment at a specialised headache centre. With an average Danish daily wage of US$166 in 2005, this represented a potential net gain of approximately $500 per month per person.\textsuperscript{79} However, this simple estimate did not include other measures of cost or benefit, such as those arising from impaired or improved work performance; presenteeism, in many studies,\textsuperscript{8,40} has accounted for the largest economic burden attributed to migraine. Additionally, since the Danish patients were recruited from a specialised headache centre,\textsuperscript{79} many would have been difficult-to-treat cases. The benefits at systems level accruing from better treatment in primary care are expected to be far greater (higher numbers of patients, who are generally more responsive to treatment than those needing specialist care). Further cost-effectiveness studies are needed to confirm this empirically, informing health policy and generating a sound evidence base for greater investment in systems-level management of migraine.

**Challenges in LMICs**

ITB and the Global Campaign against Headache have spent more than 15 years studying the prevalence and burden of headache in LMICs,\textsuperscript{80} and clearly confirmed that migraine substantially impairs health of people worldwide, regardless of geography and income.\textsuperscript{1} Migraine is either the second or third highest contributor to YLDs in every world region, regardless of its sociodemographic development, according to GBD studies.\textsuperscript{1} Indeed, migraine disability is magnified by low allocation of resources to its mitigation, the consequence of limited resources overall coupled often with an even greater deficiency of information to guide policy.\textsuperscript{85} Moreover, in many LMICs, other major pressing health issues (such as tuberculosis, malaria, and HIV) take priority, even though migraine in these countries remains a leading contributor to disability,\textsuperscript{7} burdening their economies with reduced productivity and lost earnings. Yet, even in LMICs, people with headache are willing to pay out of their own pockets for effective treatment, regardless of its frequency,\textsuperscript{85} showing that diagnosis and treatment of headache disorders are feasible in all economies.\textsuperscript{8,79}

In all countries, the multiple causes of suboptimal care include inadequate awareness among health professionals and politicians. However, in some countries, migraine is not recognised as a disorder with a neurobiological basis.\textsuperscript{85} For example, in India, migraine is not regarded as a treatable disorder that qualifies for reimbursement by insurance agencies.\textsuperscript{81} The fact that simple evidence-based treatment strategies for migraine are a highly cost-effective use of health resources, even in LMICs, is a political message that needs constant repetition.\textsuperscript{8,79}

**Access to medication and reimbursement**

Medications are an essential component of optimal migraine care. In countries with established headache services, approximately 50% of people with migraine rely
Panel: Migraine care in Brazil, Russia, India, and China

Brazil
Brazil has a population of 210 million people, with migraine affecting approximately one-seventh of the adult population. Care is provided by either a public health sector (free of charge) or a private health sector. The public health sector is very under-resourced, which often leads to misdiagnosis and substandard patient care. Additionally, the public health sector has limited access to tertiary centres and multidisciplinary care units. Quality of care is better in the private health sector, with more accurate diagnosis and improved treatment strategies. Nonetheless, evidence-based practices for migraine care remain inadequate across both the public and private health sectors.

Russia
Russia has a population of 147 million people, with migraine affecting approximately one-fifth of the adult population. The health-care system includes both a public sector (free of charge) and a private sector. In the public sector, approximately 25-50% of affected individuals consult a physician (mostly neurologists) because of their migraine. Misdiagnosis is a challenge, since only 12% of individuals with migraine are correctly diagnosed. The prevalence of misdiagnosis is probably because the International Classification of Headache Disorders (ICHD) criteria for migraine are inconsistently used by physicians. However, considerable progress has been made since 2011, and more than 50 tertiary headache centres have been established in over 30 cities. Most of these (80%) are private headache centres that offer a multidisciplinary approach to migraine care. Furthermore, in 2013, the ICHD criteria have been translated into Russian to increase awareness and educate caregivers. National guidelines for migraine care were introduced by the Ministry of Health in 2016 and headache disorders have now become a mandatory part of the curriculum in medical schools.

India
India has a population of 1.3 billion people, with a 1-year prevalence of migraine (ie, individuals with a minimum of one migraine day per year) of 25% in South India (data from other regions are unavailable). The health-care system includes a public sector (free of charge), a self-paid private sector, and an insurance-funded health-care provision. In the public sector, clinics are overcrowded and there is limited allocation of resources for headache care. Access to headache care is further restricted in rural areas (where 75% of the population live) as 70% of physicians are based in urban areas. About one-third of affected individuals have sought medical care for migraine at least once within the past year, with most consultations taking place in primary-care settings. By contrast, the private sector is not easily affordable and used by fewer than 5% of the overall population.

China
China has a population of 1.4 billion people, with a 1-year prevalence of migraine of 9%. Migraine is the cause of 331 years lived with disability (YLDs) per 100,000 people per year accounting to a total of 5.5 million YLDs. Furthermore, annual costs attributed to migraine in China surpass US$47 billion. Care is provided by clinics and a level-based hospital system (level 1: community or district hospitals, level 2: municipal hospital, and level 3: provincial hospitals). The public health sector is generally not free of charge but often covered by medical insurance. In some instances, insurance might also cover expenses related to services provided by the private health sector (clinics and hospitals). Although more than half of affected individuals seeking care for migraine contact physicians at clinics (rather than hospitals), only around 14% are correctly diagnosed. 33% are misdiagnosed, and 53% remain undiagnosed. Additionally, migraine-specific acute medications and evidence-based preventive medications are underused. Over the past decade, efforts have yielded great progress: approximately 135 headache clinics have been established across China and diagnostic and clinical management guidelines (introduced in 2015) have already yielded benefits in clinical practice.

on self-treatment, managing their headaches with over-the-counter drugs such as NSAIDs. The proportion is, inevitably, much higher in countries without these services, but the adequacy of self-treatment is questionable. NSAIDs are widely available, with ample evidence supporting their use as highly cost-effective treatment for migraine, even in LMICs.

Triptans and effective preventive migraine medications (eg, propranolol, amitriptyline, and topiramate) are also available in many LMICs, but not all, and usually off-label in the case of preventive medicines. However, the persistence of insufficient awareness and understanding continues to limit equitable access to these medications, even in specialist care. According to WHO, inadequate reimbursement is a problem frequently encountered by neurologists providing care for migraine.

Medications for migraine are chosen according to availability and cost rather than efficacy and safety profile. An excellent example is the continuing and common use of ergotamine in low-income countries, despite triptans being more effective and safer.

Health-care underuse and mismanagement
It seems intuitive that best use should be made of the limited resources available for migraine care; however,
available health services for migraine are underused in LMICs. Estimates suggest that only 13% of people with migraine in low-income countries are diagnosed by a health-care professional. Even among those most severely affected (≥15 headache days per month), fewer than 50% had used health services in a Chinese population-based survey. The same study also reported that individuals with migraine were as likely to be diagnosed with “nervous headache”—a non-existent diagnosis—as with migraine. Aside from misdiagnosis, undertreatment is also a matter of concern, and not only in low-income countries. In Russia, preventive medication is used by fewer than 1% of people with migraine, despite an estimated need of 17% in the population with migraine (panel). Collectively, these data underscore the inequities in provision of basic information to individuals with migraine and inadequate training of health-care professionals.

Education and training of health-care professionals
Optimal migraine care demands formal education and training of health-care professionals. Neurologists worldwide highlight insufficient education (at all levels) as the problem most needing to be rectified in the clinical management of headache disorders. Typically, worldwide, only 4–6 hours of undergraduate medical curricula are dedicated to headache disorders, and headache is a minor topic within the crowded agenda of postgraduate neurology specialist training.

Strategic educational initiatives driven by the international headache organisations should supplement formal educational programmes provided locally, but these programmes require political will to replace the current inertia. Since primary care is the point of entry into headache services for most people with migraine, local educational programmes should target undergraduate medical curricula. Subsequently, continuing medical education should maintain and develop the basic expertise needed by primary-care professionals, keeping their knowledge updated. Specialist training is within the role of the international headache organisations, to be supplemented by national professional headache societies, which all countries should establish.

Conclusion
Global action is needed to tackle the public-health burden attributed to migraine. Consensus guidelines should improve epidemiological studies to ascertain the burden of migraine beyond the individual patient, reflecting also on the effects on family, friends, colleagues, employers, and society. As diagnosis and clinical management continue to be suboptimal worldwide, more research should be high on the agenda to identify best clinical practices, tailored to local needs and resource availability. A commitment to global collaboration should be the first major step towards putting migraine near the top of the global health-policy agenda.

Contributors
MA, TJS, and RBL initiated the concept and designed the scope of this Series paper. SA, DCB, RBL, and SaY wrote the first draft of the epidemiology section. DCB, TPD, and TJS wrote the first draft of the health economics section. MA, TPD, and ZK wrote the first draft of the systems of care section. MA, TPD, and ZK wrote the first draft of the challenges in LMICs section. MA, AVK, and AO wrote the first draft of the section on Brazil. MA, ERL, and PP R wrote the first draft of the section on Russia. MA, TPD, KR, and SS wrote the first draft of the section on India. MA and ShY wrote the first draft of the section on China. All authors reviewed and approved the final version.

Declaration of interests
MA is a consultant, speaker or scientific advisor for AbbVie, Allergan, Amgen, Alder, Biohaven, Eli Lilly, Lundbeck, Novartis, and Teva; primary investigator for Alder, Amgen, Eli Lilly, Lundbeck, Novartis and Teva trials; MA has no ownership interest and does not own stocks of any pharmaceutical company. MA serves as associate editor of Cephalalgia, and associate editor of the Journal of Headache and Pain. MA is president of the International Headache Society. DCB has served as a consultant to and received research funding from Amgen–Novartis, Allergan, Avanir, Biohaven, Eli Lilly, Promius–Dr Reddy’s, and Teva. DCB is on the editorial board of Current Pain and Headache Reports. PP-R has received honoraria for participation in clinical trials and contribution to advisory boards or medical education from Allergan, Almirall, Amgen, Biohaven, Chiesi, Electrocore, Eli Lilly, Medscape, Novartis, and Teva. PP-R’s headache research is supported by La Caixa Foundation, AGAUR, Instituto Investigacion Carlos III, Migraine Research Foundation, PERIS, EraNet Neuron, FEDER RIS3CAT, and Novartis. AO is on consultant or advisory boards for Allergan, Eli Lilly, Novartis, Teva–Amgen, and Abdi Ibrahim Ilac. SS reports consultant, advisory board, or speaker fees for Abbott, Allergan, Eli Lilly, Medscape, Novartis, and Teva. SA reports personal fees from Allergan, Percept, Novartis, Teva, Satsuma, Amgen, Eli Lilly, Supernus, Theranica, Biohaven, and Promius, outside the submitted work. TJS is co-editor of the Journal of Headache and Pain, a director and trustee of Lifting The Burden, and reports personal fees from Eli Lilly, outside the submitted work. RBL serves on the editorial boards of Neurology and Cephalalgia and as senior advisor to Headache, has received research support from the National Institutes of Health, and receives support from the Migraine Research Foundation and the National Headache Foundation. RBL has reviewed for the National Institute on Aging and the National Institute of Neurological Disorders and Stroke, serves as consultant, advisory board member, or has received honoraria from Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Boston Scientific, Dr Reddy’s, Electrocore, Eli Lilly, eNeuraTherapeutics, GlaukSmithKline, Merck, Novartis, Teva, and Vedanta. RBL has received royalties from Wolf’s Headache and Infosys; and holds stock options in eNeura Therapeutics and Biohaven. All other authors declare no competing interests.

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