Estimated global incidence of Japanese encephalitis: a systematic review

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Objective To update the estimated global incidence of Japanese encephalitis (JE) using recent data for the purpose of guiding prevention and control efforts.

Methods Thirty-two areas endemic for JE in 24 Asian and Western Pacific countries were sorted into 10 incidence groups on the basis of published data and expert opinion. Population-based surveillance studies using laboratory-confirmed cases were sought for each incidence group by a computerized search of the scientific literature. When no eligible studies existed for a particular incidence group, incidence data were extrapolated from related groups.

Findings A total of 12 eligible studies representing 7 of 10 incidence groups in 24 JE-endemic countries were identified. Approximately 67 900 JE cases typically occur annually (overall incidence: 1.8 per 100 000), of which only about 10% are reported to the World Health Organization. Approximately 33 900 (50%) of these cases occur in China (excluding Taiwan) and approximately 51 000 (75%) occur in children aged 0–14 years (incidence: 5.4 per 100 000). Approximately 55 000 (81%) cases occur in areas with well established or developing JE vaccination programmes, while approximately 12 900 (19%) occur in areas with minimal or no JE vaccination programmes.

Conclusion Recent data allowed us to refine the estimate of the global incidence of JE, which remains substantial despite improvements in vaccination coverage. More and better incidence studies in selected countries, particularly China and India, are needed to further refine these estimates.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

Japanese encephalitis (JE) is among the most important viral encephalitides in Asia, especially in rural and suburban areas where rice culture and pig farming coexist.[1–3] It has also occurred rarely and sporadically in northern Australia and parts of the Western Pacific.[4–6] JE is due to infection with the JE virus (JEV), a mosquito-borne flavivirus. The main JEV transmission cycle involves *Culex tritaeniorhynchus* mosquitoes and similar species that lay eggs in rice paddies and other open water sources, with pigs and aquatic birds as principal vertebrate amplifying hosts.[1,2,7] Humans are generally thought to be dead-end JEV hosts, i.e. they seldom develop enough viremia to infect feeding mosquitoes. Fewer than 1% of human JEV infections result in JE. Approximately 20–30% of JE cases are fatal and 30–50% of survivors have significant neurologic sequelae.[8] JE is primarily a disease of children and most adults in endemic countries have natural immunity after childhood infection, but all age groups are affected. In most temperate areas of Asia, JEV is transmitted mainly during the warm season, when large epidemics can occur. In the tropics and subtropics, transmission can occur year-round but often intensifies during the rainy season.[1–3]

The global incidence of JE is unknown because the intensity and quality of JE surveillance and the availability of diagnostic laboratory testing vary throughout the world. Countries that have implemented high-quality childhood JE vaccination programmes have seen a dramatic decline in JE incidence. Although JE is reportable to the World Health Organization (WHO) by its Member States, reporting is highly variable and incomplete. In the late 1980s, Burke and Leake estimated that 50 000 new cases of JE occurred annually among the 2.4 billion people living in the 16 Asian countries considered endemic at the time (approximate overall annual incidence: 2 per 100 000).[2] In the intervening two decades, despite major population growth, urbanization, changes in agricultural practices and increased use of the JE vaccine in many countries, this figure has been widely quoted, including very recently.[9–13] In 2000, assuming an annual, age-group-specific incidence of 25 cases per 100 000, Tsai estimated that in the absence of vaccination 175 000 cases of JE would occur annually among Asian children aged 0–14 years living in rural areas.[14] The current study used more recent, published, local or national incidence estimates and current population data to produce an updated estimate of the annual global incidence of JE.

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Methods

We approximated the JE-affected territory of each of the 24 countries endemic for JE using a recent update[15] of an earlier approximation by Tsai[16] with some modifications (Table 1, available at: http://www.who.int/bulletin/volumes/89/10/10-085233). Based on these same approximations,[15,16] we then stratified the JE-affected territory of some countries (e.g. China excluding Taiwan, India and Nepal) into two or more incidence strata. Because suitable studies of JE incidence were not available for every endemic country or incidence stratum, we sorted JE-endemic countries and incidence strata into 10 incidence groups (A, B, C1, C2 and D through I) based primarily on geographic proximity, ecologic similarity, vaccine programme similarity. Table 1 briefly describes the status of each endemic country's JE vaccination programme as of 2009, according to recent publications and unpublished sources.[8,17–20]

Incidence data

We identified studies that contained potentially useful data on the incidence of JE in Asia in a manner similar to the one used in a recent study of global typhoid fever incidence.[21] Whenever possible, this review followed the relevant guidelines for Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).[22] The review process is described as follows and no protocol is available. We conducted a MedLine search of papers in any language published between 1985 (arbitrarily chosen to emphasize recent data) and April 2010. We used the following search strategy and keywords: Japanese encephalitis *and* (incidence *or* prevalence *or* public health *or* surveillance *or* distribution *or* epidemiology). An initial set of 1374 unique citations was downloaded into a computerized database. The lead author then culled the set to approximately 255 citations by scanning titles and abstracts (if available) and discarding references that did not involve JE surveillance or epidemiology in humans (e.g. studies focused on non-human vertebrates or on entomology, molecular biology or virology). The lead author also obtained a full-text copy of each available reference for review and further culled the list to approximately 75 references by selecting only those that contained explicit human JE incidence data or data that could be used to calculate incidence. Additional references were sought from these papers' reference lists and from the collections of the authors (including several papers recently submitted or "in press"), and this yielded a total of 80 references of interest. Each of these papers (or the English translation of five Chinese-language papers) was then carefully reviewed by at least two authors to further cull the list, resulting in a final group of 12 studies that provided original, recent population-based and largely laboratory-confirmed incidence data (or hospital-based incidence data in a defined population).[13,20,23–32] These 12 studies consisted of one study each from Bangladesh, Cambodia, Indonesia, Malaysia and Thailand, two from China (excluding Taiwan) two from Japan and three from Nepal. They represented all but three (B, E and I) of the 10 incidence groups (Table 1). Fig. 1 shows the approximate locations of the study sites in each primary reference. Point estimates of the annual JE incidence in each primary reference are shown as cases per 100 000 persons (Table 2, http://www.who.int/bulletin/volumes/89/10/10-085233).

We used an Excel spreadsheet for all calculations in this study.

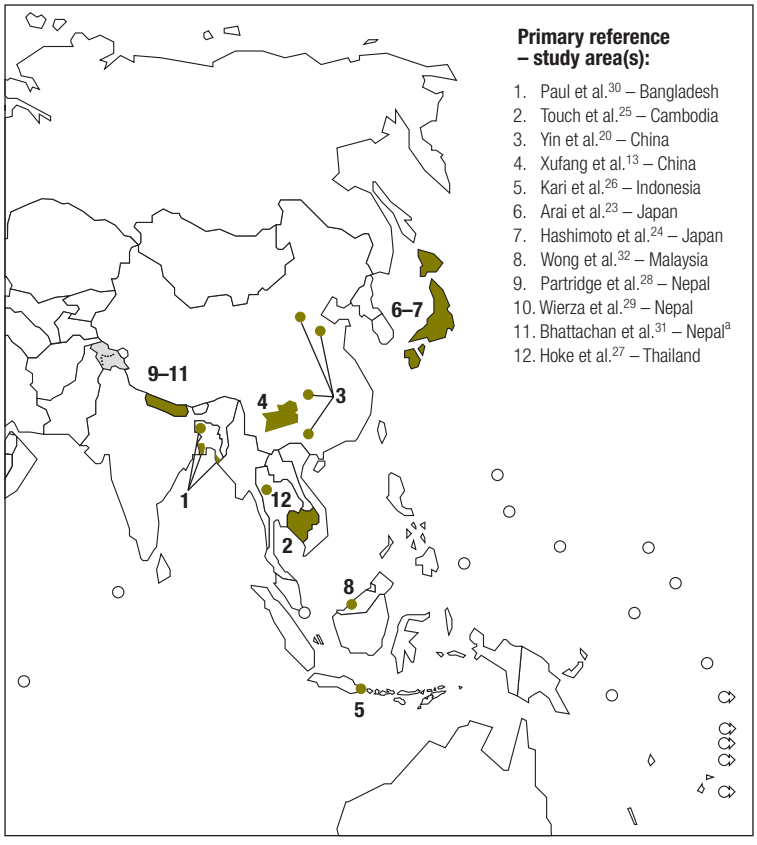
Population data

For each endemic country, we obtained the total population and that of the approximate JE-affected area from the country's official web site (as identified through www.GeoHive.com). We used the most recent census data (1998–2011) or official inter-census estimates (2000–2010) and dichotomized age as follows: children, aged 0–14 years; adults, aged ≥ 15 years (Table 1). For each country, the estimated total population aged 0–14 years was based on percentages for 2010 obtained from the United Nations[33] (for Taiwan, China, the percentage was obtained from *The world factbook*[34]). Because a concise source of such percentages for JE-endemic administrative divisions and subdivisions of countries was not available, we assumed that the age distribution within each country was homogeneous.

Assumptions by incidence group

In unvaccinated populations in endemic areas, JE is largely a paediatric disease and most people have acquired active

Fig. 1. **Primary reference study area(s)**



[a] Mountain and hill (non-Terai) districts only

immunity by adulthood. Conversely, in areas with long-standing, high-quality childhood vaccination programmes, JE is usually a rare disease of non-immune adults, especially the elderly. A transitional phase in which the incidence of JE in children and adults is about the same can also occur.[3] Because many of our primary references provided point estimates of JE incidence for all age groups combined or for children only (generally 0–14-year-olds), assumptions about age-specific JE incidence were often necessary. We had to make additional assumptions because of the absence of appropriate primary references for incidence groups B, E and I. We assumed that in some countries with a historically non-homogeneous distribution of JE risk (e.g. plain versus highland areas of Sri Lanka and northern versus southern portions of Thailand), the preferential use of vaccine in areas that were formerly higher-risk has homogenized the risk countrywide. Incidence groups are described in Table 1 and additional group-specific assumptions are summarized as follows:

- *Incidence Group A:* Overall incidence is 0.003 per 100 000; the child (aged ≤ 14 years) to adult (aged > 14 years) case frequency ratio is 7:1 (based on visual inspection of a figure in the report by Arai et al.[23]). Because this study[23] and the study by Hashimoto et al.[24] overlapped in time and because both were based on national surveillance, a weighted average of their respective results could not be used. Therefore, we used the incidence estimate by Arai et al. in our analysis but included the study by Hashimoto et al. in Table 2 for completeness and as general validation of the results obtained by Arai et al.
- *Incidence Group B:* JE is rare, with an overall incidence of 0.003 per 100 000, i.e. the authors assumed it to be the same as in historically high-incidence areas with long-standing, high-quality vaccination programmes (i.e. Incidence Group A); the child to adult case frequency ratio is 7:1.[23]
- *Incidence Group C1:* Overall incidence is 3.3 per 100 000 (weighted average of results from Yin et al.[20] and Xufang et al.[13]); the child to adult case frequency ratio is 3:1 (based on the ratio of 156 cases in 0–14-year-olds to 57 cases in persons aged > 14 years among combined residents and non-residents, as reported by Yin et al.[20]).
- *Incidence Group C2:* Overall incidence is 0.01 per 100 000; the child to adult case frequency ratio is 3:1 (as for Incidence Group C1).
- *Incidence Group D:* Incidence in children aged 12–14 years is the same as in children aged 0–11 years; incidence in children aged 0–14 years is 10.6 per 100 000 (weighted average of results from Touch et al.,[25] Kari et al.[26] and Hoke et al.[27]); the child to adult case frequency ratio is 7:1 (based on the ratio of 43 childhood cases to 6 adult cases detected from July 2001 through 2006 by Wong et al.[32]).
- *Incidence Group E:* Age-specific incidences in this group are assumed by the authors to be half as high as in incidence group D.
- *Incidence Group F:* Overall incidence is 2.8 per 100 000 (approximate weighted average of results from two studies from Nepal[28,29]); the child to adult case frequency ratio is 5:4 (based on the ratio of 532 cases in 0–14-year-olds to 419 cases in persons aged > 14 years, as reported by Wierzba et al.[29]).
- *Incidence Group G:* Overall incidence is 1.0 per 100 000 (approximate weighted average of results from three studies from Nepal[28,29,31] and one study from Bangladesh[30]); the child to adult case frequency ratio is 4:1 (based on the ratio of 73 cases in 0–14-year-olds to 17 cases in persons aged > 14 years, per the table in the report by Bhattachan and colleagues[31]).
- *Incidence Group H:* Overall incidence is 1.5 per 100 000 (based on 49 cases per 600 000 persons over a 5.5-year period in the study by Wong et al.); incidence in children aged 12–14 years is the same as in children aged 0–11 years; the child to adult case frequency ratio is 7:1.[32]
- *Incidence Group I:* Overall incidence is 3.3 per 100 000 (based on the average annual incidence of 6.5 per 100 000 in nearby Taiwan (China) during the immediate pre-vaccination era [1965–1967],[35] reduced by 50% following a national mass-vaccination campaign among children in 2009); the child to adult case frequency ratio is 7:1.[32]

Results

Based on the assumptions noted above, we estimated that approximately 67 900 JE cases typically occur annually in the 24 JE-endemic countries, for an incidence of 1.8 per 100 000 overall (Table 3). Approximately 33 900 (50%) of these cases occur in China (excluding Taiwan) and approximately 55 000 (81%) occur in areas with well established or developing JE vaccination programmes, while approximately 12 900 (19%) occur in areas with minimal or no JE vaccination programmes. Approximately 51 000 (75%) of these cases occur in children aged 0–14 years, which gives an estimated overall annual incidence of 5.4 per 100 000 in this age group.

Discussion

In the pre-JE-vaccination era, tens of thousands of JE cases were often reported annually in Asia. During 1965–1975, more than 1 million cases were reported in China alone.[1] In Japan, the Republic of Korea and Taiwan (China) the introduction of routine childhood vaccination programmes against JE beginning 40 to 50 years ago, combined with increased urbanization and evolving agricultural practices, resulted in the virtual elimination of JE, despite continued enzootic JEV transmission.[2,14] Other Asian countries were slower to implement childhood JE vaccination programmes largely because of expenses and difficult logistics. Some of these countries now have well developed vaccination programmes, others have less developed programmes, and others still have no programmes at all.[8,17,19]

During 2006–2009, JE-endemic countries reported 27 059 cases of JE (annual range: 4502–9459; average: 6765) to WHO. Fully 86% of these (23 176 cases; average: 5794 cases per year) were reported from China and India; 16 countries reported a total of 3883 cases (annual average: 971); and 5 countries reported no cases.[36] While these data almost certainly include some non-JE cases that were clinically misclassified without the benefit of laboratory confirmation, they almost certainly also represent significant under-reporting of true cases.[1,14] The results of the current study suggest that the actual incidence of JE is nearly 10 times higher than reflected in recent reports to WHO. While we estimated that approximately 81% of JE cases presently occur in areas with well

Table 3. **Estimated annual incidence and case frequency of Japanese encephalitis (JE) by incidence group and age stratum[a]**

IG	Description	Countries/regions	0–14 years of age			≥15 years of age			All ages			
			Endemic area(s) population (millions)	Incidence[b]	Frequency	Endemic area(s) population (millions)	Incidence[b]	Frequency	Endemic area(s) population (millions)	Incidence[b]	Frequency	Percentage of total[c]
A	Historically high-incidence areas with long-standing, high-quality vaccination programmes	Japan, Republic of Korea, China (Taiwan)	28.5	0.003	1	170.0	0.003	5	198.5	0.003	6	<0.1
B	Extremely low-incidence areas; rare human cases; minimal or no vaccination programmes	Australia, India (lowest-incidence stratum), Pakistan, Russian Federation, Singapore	28.0	0.001	0	61.5	0.004	2	89.5	0.003	2	<0.1
C1	Historically high-incidence areas with expanding vaccination programmes	China (higher-incidence stratum)	200.0	12.7	25387	825.7	1.0	8462	1025.7	3.3	33849	49.9
C2	Historically medium-incidence areas with expanding vaccination programme	China (lower-incidence stratum)	53.9	0.04	21	222.7	0.003	7	276.6	0.01	28	<0.1
D	High-incidence areas with nascent or no vaccination programmes	Cambodia, Indonesia (higher-incidence stratum), Lao People's Democratic Republic, Malaysia (Borneo except Sarawak), Myanmar, Philippines, Timor-Leste	65.4	10.6	6927	146.4	0.7	990	211.8	3.7	7917	11.7

IG	Description	Countries/regions	0–14 years of age			≥15 years of age			All ages			
			Endemic area(s) population (millions)	Incidence[b]	Frequency	Endemic area(s) population (millions)	Incidence[b]	Frequency	Endemic area(s) population (millions)	Incidence[b]	Frequency	Percentage of total[c]
E	Medium-incidence areas with no vaccination programmes	Indonesia (lower-incidence stratum), Malaysia (peninsular), Papua New Guinea	58.9	5.3	3122	154.6	0.34	523	213.5	1.7	3645	5.4
F	Historically high-incidence areas with expanding vaccination programmes	Nepal (higher-incidence stratum); India (highest-incidence stratum)	135.7	5.1	6861	305.4	1.8	5489	441.1	2.8	12 350	18.2
G	Low-incidence areas with minimal or no vaccination programmes	Bangladesh, Bhutan, Brunei Darussalam, Nepal (lower-incidence stratum)	43.0	2.5	1086	92.8	0.3	272	135.8	1.0	1358	2.0
H	Historically medium-to-high-incidence areas with expanding vaccination programmes	India (medium-incidence stratum), Malaysia (Sarawak), Sri Lanka, Thailand, Viet Nam	151.1	4.7	7063	387.0	0.3	1009	538.1	1.5	8072	11.9
I	Historically medium-to-high-incidence area with expanding vaccination programme	Democratic People's Republic of Korea	4.6	12.6	586	15.7	0.5	84	20.3	3.3	670	1.0
Total (JE-endemic areas only)			**769.2**	**6.6**	**51 054**	**2381.7**	**0.7**	**16 843**	**3150.9**	**2.2**	**67 897**	**100**
Overall incidence (endemic + non-endemic areas)[b]			**–**	**5.4**	**–**	**–**	**0.6**	**–**	**–**	**1.8**	**–**	**–**

IG, incidence group.

[a] Total population (endemic + non-endemic areas) aged 0–14 years is 1000.9 million; aged ≥ 15 years, 2692.7 million; and combined, 3693.6 million (country-specific data not shown).

[b] Per 100 000.

[c] Total frequency divided by 67 897 times 100.

Note: See text for assumptions.

established or developing JE vaccination programmes, this probably reflects the epidemiological distribution of JE, since vaccination programmes are more likely to exist in areas with the highest risk of JEV transmission. It may also reflect better surveillance and case-reporting in such areas. Vaccination programmes in many of these areas should be expanded and strengthened. Endemic countries without programmes or with programmes in early development should be fully supported in their efforts to implement and strengthen JE vaccination programmes.

Because we studied JE incidence, not mortality or morbidity (e.g. in terms of disability-adjusted life years [DALY]), we did not attempt to estimate the global burden of JE.[37,38] Nevertheless, our results could contribute to efforts to refine estimates of this burden. Based on an earlier estimated frequency of 44 000 new JE cases per year, including 14 000 deaths (32%) and 24 000 cases with sequelae (55%, or 71% of survivors), and an average disability weight of 0.616, Mathers et al. estimated the global burden of JE to be 709 000 DALY (by comparison, the estimated global burden of acute malaria was 46 000 000 DALY).[37] If we assume a case fatality rate of 20–30% and long-term neuropsychological morbidity among 30–50% of survivors,[8] the results of the current study similarly suggest that approximately 13 600 to 20 400 acutely fatal JE cases occur and that 14 300 to 27 200 JE survivors develop long-term neuropsychological sequelae each year. Although several studies characterizing long-term outcomes in JE survivors have been published,[39–42] additional studies are needed to allow for refined estimates of the global burden of JE.

The methods we used in the current study resembled the methods that have been employed to estimate the global incidence of other infectious diseases, including typhoid fever, *Haemophilus influenzae* type b disease and streptococcal disease.[21,43,44] Our study is therefore subject to many of the same limitations. First, we derived estimates from sparse data of variable quality, with some notable exceptions (e.g. data from Japan). Furthermore, useful data were lacking from several important countries or parts of countries. The absence of data from India is particularly worrisome because the country has a very large population and several diverse JE-endemic regions Although we did not feel that a formal sensitivity analysis was essential to enable us to appropriately interpret our results, these results would obviously be highly sensitive to relatively small changes in some input data, especially for China and India, which together contain approximately two thirds of the world's population at risk for JE. This is particularly true for Incidence Group C1 (the higher-incidence stratum of China), which accounted for half of our estimated global total of annual JE cases, and, to a lesser extent, for incidence groups D, F and H (much of India and south-eastern Asia). In contrast, our results would be far less sensitive to changes in input data for incidence groups A, B, C2 and I. Another limitation of our approach is that some of the 12 key references for JE incidence involved hospital-based surveillance in imperfectly defined catchment areas. Such studies tend to underestimate true incidence because they depend on all true cases being hospitalized (as opposed to being treated as outpatients) and within their residential catchment area. Other studies relied on an incomplete network of sentinel hospitals and are similarly subject to an underreporting bias, although such a bias is not readily quantifiable. The following are also potential sources of error that are difficult to quantify: (i) a lack of standardized laboratory testing methods (e.g. the use of various commercially available or in-house test kits for the detection of anti-JEV immunoglobulin M antibody); (ii) incomplete collection of clinical samples (e.g. failure to collect and test both acute- and convalescent-phase samples in all suspected cases, resulting in some degree of underdiagnosis); and (iii) the co-circulation of other cross-reactive flaviviruses (especially dengue viruses) in some JE-endemic areas

We did not attempt to distinguish between urban and rural incidence because few, if any, of the studies on which our results were based broke down incidence in this way. They involved surveillance in whole countries or in areas that included a mix of urban and rural populations. Nevertheless, the risk of JE continues to be strongly associated with exposure in rural and, to a lesser extent, suburban areas.[3] Another limitation of our approach is that JE is an ecologically complex epidemic as well as endemic disease and therefore does not exist in a steady-state, even when incidence is reduced by means of increased vaccine usage. Thus, to state that a set number of new JE cases occurs globally each year (e.g. 50 000, 67 900 or 175 000) is overly simplistic, however convenient it may be for some purposes, because the situation is clearly more dynamic. It was recently discovered, for example, that the JEV is circulating in Tibet (China), formerly believed to be non-endemic.[45] More accurate estimates of the global incidence of JE, including its natural fluctuations over time, will await the development of better surveillance and laboratory capability throughout the endemic region, as well as the publication of additional population-based surveillance studies of laboratory-confirmed cases. To this end, agencies funding vaccine programmes should consider concurrently funding well designed, population-based surveillance studies of laboratory-confirmed cases, particularly in JE-endemic countries for which no reliable incidence data currently exist. ■

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ملخص

معدل الانتشار التقديري العالمي لالتهاب الدماغ الياباني: مراجعة منهجية

الغرض تحديث معدل الانتشار التقديري العالمي لالتهاب الدماغ الياباني باستخدام المعطيات الحديثة بهدف توجيه جهود الوقاية والمكافحة.

الطريقة جري ترتيب اثنين وثلاثين منطقة وبائية ينتشر فيها التهاب الدماغ الياباني، في 24 بلداً أسيوياً وفي غرب المحيط الهادي، إلى 10 مجموعات وفقاً لمعدل الانتشار على أساس المعطيات المنشورة ورأي الخبراء. وقد بُحِثَ عن الدراسات الاستقصائية السكانية التي استخدمت حالات مؤكدة مختبرياً عن طريق البحث الحاسوبي في النشريات العلمية لكل مجموعة من مجموعات معدل الانتشار. وإذا لم توجد دراسات عن معدل الانتشار تصلح لمجموعة محددة من مجموعات معدل الانتشار، يجري استيفاء معطيات الانتشار من المجموعات ذات العلاقة.

النتائج تم إجمالاً تحديد 12 دراسة تصلح للإدراج في البحث، وقد مثلت 7 إلى 10 مجموعات وفقاً لمعدل الانتشار في 24 بلداً متوطناً فيها التهاب الدماغ الياباني. وتبين أنه تقع سنوياً 67900 حالة نموذجية من التهاب الدماغ الياباني (معدل الانتشار الإجمالي: 1.8 لكل 100000)، ولا يُبلغ منها إلى منظمة الصحة العالمية إلا 10% فقط. وتقع حوالي 33900 (50%) من هذه الحالات في الصين (باستثناء تايوان، الصين) وتقع حوالي 51000 حالة (75%) في الأطفال في عمر 0-14 سنة (معدل الوقوع: 5.4 لكل 100000). وحوالي 55000 حالة (81%) تقع في مناطق يستقر فيها برامج التمنيع ضد التهاب الدماغ الياباني أو يجري تطوير البرامج فيها، بينما تقع حوالي 12900 حالة (19%) في مناطق لا يوجد فيها برامج التمنيع أو أنها توجد على نطاق محدود.

الاستنتاج تتيح المعطيات الحديثة لنا تصحيح معدل الانتشار التقديري العالمي لالتهاب الدماغ الياباني، والذي مازال منتشراً على نطاق واسع بالرغم من التحسن الذي شهدته برامج التمنيع. وهناك حاجة إلى مزيد من دراسات أفضل حول معدل الانتشار في بلاد منتقاة، ولاسيما الهند والصين، من أجل تصحيح هذه التقديرات.

摘要

日本脑炎的全球发病率评估：系统综述

目的 旨在运用最新数据更新日本脑炎（JE）的全球发病率评估，从而为预防和控制工作提供指导。

方法 基于已发布的数据和专家意见，24个亚洲和西太平洋国家的32个日本脑炎流行地区被分为10个发病率组。检索相关科学文献，为每个发病率组检索出基于人群监测研究并采用实验室检查确诊的病例数据。当某个特定发病率组没有有效的研究数据时，其发病率数据从相关组推测得出。

结果 共确定了24个日本脑炎流行国家中10个发病率组中的7个代表组的12项合格研究。每年都会发生约67 900例日本脑炎（总发病率：1.8/100 000），然而其中仅10%报备世界卫生组织。其中33 900（50%）例发生在中国（中国台湾除外），并且近51 000（75%）发生在0-14岁的儿童中（发病率：5.4/100 000）。约55 000（81%）例发生在拥有完善的日本脑炎疫苗接种计划的地区或日本脑炎疫苗接种计划处于发展中的地区，而约12 900（19%）例发生在只有很少或没有该疫苗接种计划的地区。

结论 最新数据使我们得以完善对日本脑炎全球发病率的评估，尽管疫苗接种率不断提高，但发病率依然很高。还需要收集选定国家特别是印度和中国更多更好的研究数据，以进一步完善这些评估。

Résumé

Estimation de l'incidence mondiale de l'encéphalite japonaise: une évaluation systématique

Objectif Mettre à jour l'estimation de l'incidence mondiale de l'encéphalite japonaise (EJ) à l'aide des données récentes afin de guider les efforts de prévention et de contrôle.

Méthodes Trente-deux régions endémiques de l'EJ dans 24 pays de l'Asie et du Pacifique occidental ont été classées en 10 groupes d'incidence sur la base des données publiées et d'expertises. Des études de surveillance basées sur la population, utilisant des cas confirmés en laboratoire, ont été investiguées pour chaque groupe d'incidence par une recherche informatisée de documentation scientifique. Lorsqu'aucune étude éligible n'existait pour un groupe d'incidence particulier, les données d'incidence étaient extrapolées à partir des groupes associés.

Résultats Un total de 12 études éligibles, représentant 7 des 10 groupes d'incidence dans 24 pays endémiques de l'EJ, a été identifié. Approximativement 67 900 cas d'EJ sont enregistrés chaque année (incidence totale: 1,8 pour 100 000), dont seulement 10% environ sont signalés à l'Organisation mondiale de la Santé. Approximativement 33 900 (50%) de ces cas apparaissent en Chine (à l'exclusion de Taïwan, Chine) et environ 51 000 (75%) cas touchent des enfants de 0 à 14 ans (incidence: 5,4 pour 100 000). Approximativement 55 000 (81%) cas sont enregistrés dans des régions offrant des programmes de vaccination de l'EJ en voie de développement ou bien établis, alors qu'approximativement 12 900 (19%) cas apparaissent dans des régions proposant des programmes de vaccination de l'EJ minimum ou inexistants.

Conclusion Les données récentes nous ont permis d'affiner l'estimation de l'incidence mondiale de l'EJ, qui reste importante malgré les améliorations apportées par la couverture de la vaccination. Des études de l'incidence plus nombreuses et plus précises dans des pays sélectionnés, en particulier la Chine et l'Inde, sont nécessaires pour affiner davantage ces estimations.

Резюме

Оценка заболеваемости японским энцефалитом в мире: систематическое исследование

Цель Используя новейшие данные, внести изменения в оценку заболеваемости японским энцефалитом (ЯЭ) в целях руководства мероприятиями по профилактике этого заболевания и борьбе с ним.

Методы Тридцать два района, эндемичных по ЯЭ, в 24 странах Азии и западной части Тихоокеанского региона были разделены по показателю заболеваемости на 10 групп на основе опубликованных данных и мнений экспертов. По каждой группе был проведен компьютеризированный поиск по научной литературе с целью выявления исследований в области эпидемиологического надзора на базе популяций с использованием лабораторно подтвержденных случаев заболевания. В случае отсутствия исследований, соответствующих требованиям поиска, по какой-либо группе заболеваемости данные о заболеваемости экстраполировались на основе показателей родственных групп.

Результаты Всего было выявлено 12 исследований, отвечающих критериям поиска, которые представляли семь из 10 групп заболеваемости в 24 странах, эндемичных по ЯЭ. Как правило, ежегодно происходит примерно 67 900 случаев заболевания ЯЭ (средняя заболеваемость: 1,8 на 100 тыс. человек населения), из которых только о 10% направляются уведомления во Всемирную организацию здравоохранения. Приблизительно 33 900 (50%) из этих случаев происходят в Китае (кроме Тайваня) и примерно 51 тыс. (75%) – среди детей в возрасте до 14 лет (заболеваемость: 5,4 на 100 тыс. человек населения). Приблизительно 55 тыс. случаев (81%) происходят в районах, в которых постоянно проводятся или начали осуществляться программы вакцинации от ЯЭ, а примерно 12 900 (19%) – в районах, где программы вакцинации от ЯЭ имеют минимальный охват или не проводятся.

Вывод Новейшие данные позволили нам уточнить оценку заболеваемости ЯЭ в мире. Она остается значительной, несмотря на расширение охвата вакцинацией. Для более полного уточнения этих оценок необходимы более широкие и глубокие исследования заболеваемости в некоторых странах, в частности, в Индии и Китае.

Resumen

Incidencia global estimada de la encefalitis japonesa: una revisión sistemática

Objetivo Actualizar la incidencia global estimada de la encefalitis japonesa (EJ) utilizando datos recientes para orientar los esfuerzos de prevención y control.

Métodos En base a los datos publicados y a la opinión de profesionales especializados, treinta y dos áreas endémicas de EJ en 24 países de Asia y el Pacífico Occidental se clasificaron en 10 grupos de incidencia. Mediante una búsqueda informatizada de la literatura científica, se buscaron estudios de vigilancia basados en la población utilizando casos confirmados en laboratorio para cada grupo de incidencia. Cuando no se encontraron estudios aptos para un grupo de incidencia específico, se procedió a la extrapolación de los datos de incidencia de los grupos en cuestión.

Resultados Se identificaron un total de 12 estudios aptos que representaban 7 de los 10 grupos de incidencia en 24 países con EJ endémica. Aproximadamente, al año se solían producir 67 900 casos de EJ (incidencia global: 1,8 por cada 100 000 habitantes), de los cuales solo el 10% se notificaron a la Organización Mundial de la Salud. De estos casos, aproximadamente 33 900 (el 50%) se producen en China (excluyendo Taiwán, China) y aproximadamente 51 000 (el 75%) se producen en niños con edades comprendidas entre los 0 y los 14 años (incidencia: 5,4 por cada 100 000 habitantes). Aproximadamente 55 000 (el 81%) casos se producen en áreas en las que existen programas de vacunación de EJ oficialmente establecidos o en desarrollo, mientras que aproximadamente 12 900 (el 19%) se producen en áreas con pocos o con ningún programa de vacunación de EJ.

Conclusión Los recientes datos nos permitieron perfeccionar la estimación de incidencia global de la EJ, que sigue siendo importante, a pesar de las mejoras en la cobertura de vacunación. Es necesario disponer de mejores estudios de incidencia en determinados países, específicamente en China y India, para seguir perfeccionando estas estimaciones.

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Table 1. **Japanese encephalitis (JE) incidence group, endemic areas, current vaccine programme description (as of 2009) and population data, by country**

IG	Description	Country	Endemic area(s)	Vaccination programme	Population, endemic area(s) only				
					Year	Data type	Total (millions)	Age (years)	
								0–14	≥15
A	Historically high-incidence areas with long-standing, high-quality vaccination programmes	China (Taiwan)	Countrywide	Mass vaccination of children was begun in 1968, followed by routine childhood vaccination	2010	Inter-census estimate	23.1	3.6	19.5
		Japan	Countrywide	Vaccine first introduced in 1954; widespread childhood vaccination conducted from 1967 to 2004; recommendation for vaccination withdrawn in 2005 and coverage declined; recommendation reinstated in 2009, but coverage remains low	2010	Census	128.1	17.2	110.9
		Republic of Korea	Countrywide	Routine childhood vaccination programme began in the 1970s	2005	Census	47.3	7.8	39.5
B	Extremely low-incidence areas; rare human cases; minimal or no vaccination programmes	Australia	Torres Strait Islands and Far North Statistical Division, Queensland State	Mass vaccination was conducted on outer Torres Straits Islands only in 1995, followed by routine vaccination programme	2009	Inter-census estimate	0.25	0.05	0.2
		India	Lowest-incidence stratum (north-west –Haryana, Punjab)	Generally none, but mass-vaccination campaigns conducted in a portion of Haryana state in 2007–2009	2008	Inter-census estimate	53.1	16.2	36.8
		Pakistan	Sindh province	None	1998	Census	30.4	10.8	19.7
		Russian Federation	Primorsky Krai	None	2010	Census	2.0	0.3	1.7
		Singapore	Countrywide	None	2010	Census	3.8	0.7	3.1
C1	Historically high-incidence areas with expanding vaccination programmes	China	Higher-incidence stratum (Anhui, Chongqing, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, and Zhejiang provinces)	From 1981 to 2007, vaccine used extensively but non-uniformly in children; beginning in 2008, incorporated into Expanded Programme on Immunization in all endemic provinces	2010	Census	1025.7	200.0	825.7
C2	Historically medium-incidence areas with expanding vaccination programme	China	Lower-incidence stratum (Beijing, Hainan, Hebei, Heilongjiang, Jilin, Liaoning, Nei Mongol, Ningxia, Shanghai, and Tianjin provinces; Hong Kong Special Administrative Region and Macau Special Administrative Region)	As above, except for Hong Kong SAR and Macau SAR, which have no vaccination programmes	2007	Inter-census estimate	276.6	53.9	222.7

IG	Description	Country	Endemic area(s)	Vaccination programme	Population, endemic area(s) only				
					Year	Data type	Total (millions)	Age (years)	
								0–14	≥15
D	High-incidence areas with nascent or no vaccination programmes	Cambodia	Countrywide	National programme started in three provinces in late 2009	2008	Census	13.4	4.3	9.1
		Indonesia	Higher-incidence stratum (Bali, Nusa Tenggara, all provinces on Borneo and Sulawesi, and the Moluccas)	None	2010	Census	50.4	13.6	36.8
		Lao People's Democratic Republic	Countrywide	None	2009	Inter-census estimate	6.1	2.1	4.0
		Malaysia	Sabah and Labuan (all of Malaysian Borneo except Sarawak)	None	2000	Census	3.2	1.0	2.2
		Myanmar	Countrywide	None	2000	Inter-census estimate	49.0	12.5	36.5
		Philippines	Countrywide	None	2007	Census	88.6	31.4	57.2
		Timor-Leste	Countrywide	None	2010	Census	1.1	0.5	0.6
E	Medium-incidence areas with no vaccination programmes	Indonesia	Lower-incidence stratum (all provinces on Sumatra, Java and Papua, plus Kepulauan Bangka Belitung and Riau)	None	2005	Inter-census estimate	187.2	50.5	136.6
		Malaysia	Peninsular Malaysia	None	2000	Census	21.9	6.6	15.3
		Papua New Guinea	All provinces on the main island	None	2000	Census	4.4	1.7	2.7
F	Historically high-incidence areas with expanding vaccination programmes	India	Highest-incidence stratum (north-central and north-eastern – Assam, Bangla [West Bengal], Bihar, Manipur, Uttar Pradesh)	National programme started in 2006; previously, very limited state-based use as outbreak response	2008	Inter-census estimate	428.6	131.2	297.5
		Nepal	Higher-incidence stratum (24 Terai and Inner Terai districts)	Vaccine introduced in 2006	2001	Census	12.5	4.5	8.0
G	Low-incidence areas with minimal or no vaccination programmes	Bangladesh	Countrywide	None	2001	Census	124.4	38.9	85.4
		Bhutan	Southern foothillls (Chhukha, Dagana, Monggar, Pemagatshel, Samdrupjongkhar, Samtse, Sarpang, Trashigang, Tsirang, Zhemgang districts)	None	2005	Census	0.4	0.1	0.3
		Brunei Darussalam	Countrywide	None	2010	Census	0.4	0.1	0.3
		Nepal	Lower-incidence stratum (51 mountain and hill districts)	Vaccine campaigns conducted in three hill districts in 2008–2009	2001	Census	10.7	3.9	6.8

IG	Description	Country	Endemic area(s)	Vaccination programme	Population, endemic area(s) only				
					Year	Data type	Total (millions)	Age (years)	
								0–14	≥15
H	Historically medium-to-high-incidence areas with expanding vaccination programmes	India	Medium-incidence stratum (south – Andhra Pradesh, Goa, Kerala, Karnataka, Maharashtra, Pondicherry, Tamil Nadu)	National programme started in 2006; previously, very limited state-based use as outbreak response	2008	Inter-census estimate	366.4	112.1	254.3
		Malaysia	Sarawak	Vaccine introduced in 2001 nationwide, but subsequently scaled-back to Sarawak only	2000	Census	2.4	0.7	1.7
		Sri Lanka	Countrywide	Vaccine introduced in 1988, with initial use in high-risk areas	2010	Inter-census estimate	20.7	5.1	15.5
		Thailand	Countrywide	Routine childhood vaccination began in 1990, initially in higher-risk provinces	2006	Inter-census estimate	62.8	12.9	49.9
		Viet Nam	Countrywide	Vaccine introduced in 1997, with initial use in high-risk areas	2009	Census	85.8	20.3	65.6
I	Historically medium-to-high-incidence area with expanding vaccination programme	Democratic People's Republic of Korea	All provinces except Ryanggang and North Hamyong	Minimal vaccine coverage from 1994 to 2008; in 2009, a mass campaign vaccinated nearly half a million children in five provinces and Pyongyang	2008	Census	20.3	4.6	15.7
	–	–	**Subtotal (JE-endemic areas only)[a]**	–	–	–	**3150.9**	**769.2**	**2381.7**

IG, incidence group.

[a] The total population (endemic + non-endemic areas) aged 0–14 years is 1000.9 million, aged 15+ years is 2692.7 million, and combined is 3693.6 million (country-specific data not shown).

Table 2. **Summary of the 12 primary references used to estimate the incidence of Japanese encephalitis (JE) in Asia, by incidence group**

IG	Country	Reference	Study type	Laboratory-confirmed		Study period	Study area	Study age group	Estimated study population	Estimated annual incidence[a]	Relative quality of study data
				No.	%						
A	Japan	Arai et al. (2008)[23]	Routine (passive) national surveillance	53	100	1992–2004 (13 years)	Entire country	All	126.4 million (approx. mid-interval population)	0.003	Medium-quality data from national surveillance system based on physician reports of laboratory-confirmed cases; caveats include that laboratory methods used have evolved over time.
		Hashimoto et al. (2007)[24]	Routine (passive) national surveillance	33	100	2000–2005 (6 years)	Entire country	All	126.55 million	0.004	Medium-quality data from national surveillance, based on laboratory confirmation of physician-reported, clinically suspected cases.
C1	China	Yin et al. (2010)[20]	Multiple hospital-based surveillance	121	100	Apr. 2007 to Sept. 2008 (17 months) or Sept. 2006 to Sept. 2008 (25 months), depending on prefecture	Guigang prefecture, Guangxi province; Yichang prefecture, Hubei province; Jinan prefecture, Shandong province	All	14.13 million	0.6[b]	Medium-quality data from 6 carefully selected sentinel hospitals in each prefecture; caveats include that not all hospitals in each prefecture were included.
		Xufang et al. (2010)[13]	Multiple hospital-based surveillance	1609	75	2006 (1 year)[c]	Guizhou province	All	37.6 million	4.3	Medium-quality data; all hospitals in the province were included in surveillance, but samples were unavailable for testing in 25% (455/1837) of clinically suspected cases, so incidence estimate was adjusted upward, based on seropositivity rate among those tested.
C2	China	Yin et al. (2010)[20]	Multiple hospital-based surveillance	18	100	Apr. 2007 to Sept. 2008 (17 months)	Shijiazhuang prefecture, Hebei province	All	5.06 million	0.01[d]	See above.
D	Cambodia	Touch et al. (2009)[25]	Multiple hospital-based surveillance	583[e]	19	2007 (1 year)	Entire country	0–14 years	5.25 million	11.1	Medium-quality data from 6 carefully selected sentinel hospitals distributed throughout the country.
	Indonesia	Kari et al. (2006)[26]	Multiple hospital- and clinic-based enhanced (active) surveillance	90	100	July 2001 to Dec. 2003 (2.5 years)	Bali province	0–11 years	599120	6.0	High-quality data; all health care facilities in the province providing care for the study population were included in active surveillance system.
	Thailand	Hoke et al. (1988)[27,f]	Vaccine trial; enhanced (active) local public health surveillance	11	100	1985–1986 (2 years)	Kampangphet province	1–14 years	21516	25.6	High-quality data; all health care facilities in the province providing care for the study population were included in active surveillance system.

IG	Country	Reference	Study type	Laboratory-confirmed		Study period	Study area	Study age group	Estimated study population	Estimated annual incidence[a]	Relative quality of study data
				No.	%						
F	Nepal	Partridge et al. (2007)[28]	Multiple hospital-based surveillance	225	(100)	2006 (1 year)	Terai & Inner Terai districts (n=24)	All	12.46 million[g]	1.8	Medium-quality data from national surveillance system, based on laboratory confirmation of clinically suspected cases using an incomplete network of 93 hospitals and clinics; caveats include that specimens for laboratory testing were unavailable in 16% of clinically suspected cases, with no adjustment for this potential source of underdiagnosis.
		Wierzba et al. (2008)[29]	Multiple hospital-based surveillance	951	100	May 2004 to Apr. 2006 (2 years)	Terai & Inner Terai districts (n=24)	All	12.46 million[g]	3.8	Medium-quality data from national surveillance system, based on laboratory confirmation of clinically suspected cases using an incomplete network of 64 hospitals; caveats include that specimens for laboratory testing were unavailable in 31% of clinically suspected cases, with no adjustment for this potential source of underdiagnosis.
G	Bangladesh	Paul et al. (in press)[30]	Multiple hospital-based surveillance	472[d]	8	Oct. 2007 to Dec. 2008 (15 months)	Bagerhat, Chittagong, Cox's Bazar, Jessore, Jhenaidah, Khulna, Naogaon, Narail, Nawabganj, Rajshahi, & Satkhira districts	All	27.5 million	1.4[d]	Relatively lower quality data because incidence was not directly measured, but rather extrapolated retrospectively from hospitalized, laboratory-confirmed cases to non-hospitalized, clinically suspected but laboratory-untested patients.
	Nepal	Partridge et al. (2007)[28]	Multiple hospital-based surveillance	67	100	2006 (1 year)	Mountain and hill (non-Terai) districts (n=51)	All	10.69 million[g]	0.6	See above.
		Wierzba et al. (2008)[29]	Multiple hospital-based surveillance	84	100	May 2004 to Apr. 2006 (2 years)	Mountain and hill (non-Terai) districts (n=51)	All	10.69 million[g]	0.4	See above.
		Bhattachan et al. (2009)[31]	Multiple hospital-based surveillance	90	100	2007 (1 year)	Mountain and hill (non-Terai) districts (n=51)	All	10.69 million[g]	0.8	Medium-quality data from national surveillance system, based on laboratory confirmation of clinically suspected cases using an incomplete network of hospitals; specimens for laboratory testing were available in 96% of clinically suspected cases.
H	Malaysia	Wong et al. (2008)[32]	Single hospital-based surveillance	49	100	July 2001–2006 (post-vaccine programme) (5.5 years)	Sibu Hospital, Sarawak state	All	600 000 (in catchment area)	1.5	Medium-quality data from a single, central, large, sentinel hospital; caveats include that incidence estimates were apparently based on the assumption that 100% of JE cases in this hospital's catchment area would present to this hospital, and that none from outside the catchment area would do so.

IG. incidence group.

[a] Per 100 000.

[b] Weighted average of results from all three prefectures (using raw incidence data, as data used in their adjustment of incidence rates were not provided).

[c] April to November, but because this timeframe brackets the JE transmission season in the region, 1 year was used.

[d] Using raw incidence data, as data used in their adjustment of incidence rates were not provided.

[e] 100% of study cases were laboratory-confirmed; the study's authors then extrapolated their results to a larger geographic area, proportionate to the total number of acute encephalitis syndrome cases reported.

[f] These historical, pre-vaccination-era data from Thailand were used, in part, to estimate incidence in Incidence Group D, but present-day Thailand was included in Incidence Group H.

[g] 2001 census data.