Global Mapping of Lymphatic Filariasis

E. Michael and D.A.P. Bundy

Disease maps are becoming increasingly important in infectious disease epidemiology and control. For lymphatic filariasis, the development of such maps has been hampered in the past by the lack of data on the geographical distribution of levels of infection or disease. Here, Edwin Michael and Don Bundy present an atlas for this parasitic disease derived from a recently compiled geographical database. Focusing on mapping and analysis of case prevalence data at the global and regional levels, the authors show how mapping the geographical distribution is integral not only to assessing spatial patterns in the infection and disease distribution but also to stratifying endemic areas by infection and/or disease rate.

Increasingly, disease atlases are becoming a basic epidemiological tool for the study and control of infectious disease[1–3] [see also Poster PTC 04 *Parasitol. Today* 13(11), 1997]. Mapping the geographical distribution of parasitic infection and disease rates is important not only for the accurate identification of areas of high risk[2–4], but also for the formulation and investigation of aetiological factors[1–3]. Recent developments in statistical methodology for deriving reliable estimates of variables to be mapped[2,5,6], coupled with the advent of desktop computer mapping systems, have made the construction of such maps considerably less complicated.

There have been several attempts to develop disease maps for lymphatic filariasis[7–9]. However, the major focus of this work has been restricted either to mapping the extent of the geographical spread of the infection[8,9] or, in limited cases, to displaying spatial variation in infection prevalences at local geographical scales[7]. A bigger constraint to the construction of a useful filariasis atlas in the past, however, has been the lack of data on the geographical distribution of the levels of infection or disease. Recently, we have been able to address this gap in spatial information from work initiated by the World Bank to estimate the current burden of filariasis in endemic countries[10,11]. This has yielded a uniquely large geographical database, which now allows us to construct a reliable atlas for this parasitic disease.

Here, we provide a brief review of the results of the first stage of this work, focusing on the mapping and analysis of infection and disease case variation at the global and regional levels. In particular, this article illustrates how mapping reveals spatial variation in filariasis prevalence across endemic areas and how, in turn, such variation affects attempts to identify areas and regions exhibiting significantly high infection/disease rates.

The global burden of disease estimates

The maps described here are based on the national prevalences of overall filariasis cases (both infection and chronic disease cases combined) estimated for 96 endemic countries in the 1993 World Bank Global Burden of Disease (GBD) study[10,11]. The methods used to derive these estimates have been described in detail previously[11] but, briefly, they entailed standardizing (for age and gender distributions), aggregating and projecting prevalence data from over 120 published papers, and documents held by the WHO, to the national level. Thus, although the assembled geographical database contains data on filariasis prevalence distribution at the 'within-country' level, here we address only the national estimates. Overall, the GBD estimates suggest a global filariasis case prevalence of 3.39% (arising from both *Wuchereria bancrofti* and *Brugia malayi* infections) in the exposed populations, with regional prevalences for bancroftian filariasis varying from 9.0% in sub-Saharan Africa to 0.1% in the Latin America and Caribbean regions (Table 1). Although these prevalences are low, it is clear from the numbers of individuals afflicted that lymphatic filariasis continues to be a major source of morbidity in endemic populations, with over 128 million people estimated currently to be infected or diseased.

Mapping the GBD estimates

The global geographical distribution of filariasis case prevalences based on the GBD estimates are shown for bancroftian and brugian filariasis in Fig. 1a and 1b, respectively. In general, countries with bancroftian filariasis in Asia and South America appear to have lower prevalences than the sub-Saharan African and Pacific Island regions. In Asia, prevalences range from 0.07% in Laos to 5.4% in India, and in South America they range from 0.03% in Brazil to 7.3% in Guyana (Fig. 1a); in contrast, 17/34 positive countries in Africa show prevalences of over 10%, with four countries having prevalences of over 20% [Guinea Bissau (37%), Comoros (27%), Seychelles (24%) and Nigeria (22%)] and the highest regional prevalence for filariasis (29%) occurs in the Pacific region, with the three highest prevalence rates in the world apparently occurring in Tonga (48%), Papua New Guinea (PNG; 39%) and the Cook Islands (39%). The highest geographical variation in the estimated national prevalences also occurs in the African and Pacific Island regions. This is most evident for Africa: there is no infection in the southern and northernmost regions, a low prevalence in the middle of the continent and high and very high prevalences along the eastern and western regions (Fig. 1a).

The map for brugian filariasis (Fig. 1b) appears to be relatively more homogeneous, although there is a slightly higher prevalence in the eastern regions.

Analysis of the mapped data

The geographical heterogeneity displayed in Fig. 1 may be misleading because the raw GBD prevalences also reflect variability induced by differences in the size of the underlying national populations[1,2,4], which range from a few thousand for some of the Pacific islands to hundreds of millions for some of the larger endemic nations. Prevalences from the smaller populations are likely to be much less stable than those from larger

Edwin Michael and Don Bundy are at The Wellcome Trust Centre for the Epidemiology of Infectious Disease, Department of Zoology, University of Oxford, South Parks Road, Oxford, UK OX1 3PS. **Tel: +44 1865 281233, Fax: +44 1865 281245, e-mail: edwin.michael@zoology.ox.ac.uk**

Copyright © 1997, Elsevier Science Ltd All rights reserved
0169-4758/97/$17.00 PII: S0169-4758(97)01151-4

Table 1. Global burden of disease (GBD) estimates of the number of cases and prevalence of filariasis (infection and chronic disease combined) by endemic regions[a]

Region	Population (millions)	Total no. of cases (millions) and [prevalence, %]			
		Wuchereria bancrofti		*Brugia malayi*	
Sub-Saharan Africa[b]	564	50.57	[8.97]	–	
Asia[c]	2770	62.35	[2.25]	12.91	[0.47]
Pacific Islands[d]	6.18	1.80	[29.11]	–	
Latin America[e]	441	0.40	[0.09]	–	
World	3781	115.12	[3.04][f]	12.91	[0.47][f]

[a] Data are modified from Ref. 11, and updated for sub-Saharan Africa by incorporating new estimates made for Ghana[17,18], Ethiopia[19–21], Sudan[12], Sierra Leone[12], Seychelles[22] and Zaire. Figures are for both sexes combined.
[b] Includes Egypt.
[c] Includes India and China.
[d] Includes Cook Islands, Fiji, French Polynesia, Guam, Kiribati, Marshall Islands, Micronesia, Nauru, New Caledonia, Niue, Palau Islands, Papua New Guinea, Solomon Islands, Tonga, Tuvalu, Vanuatu and Western Samoa.
[e] Includes the Caribbean nations.
[f] Represents the global prevalence for endemic populations only; for brugian filariasis this pertains only to the population of Asia.

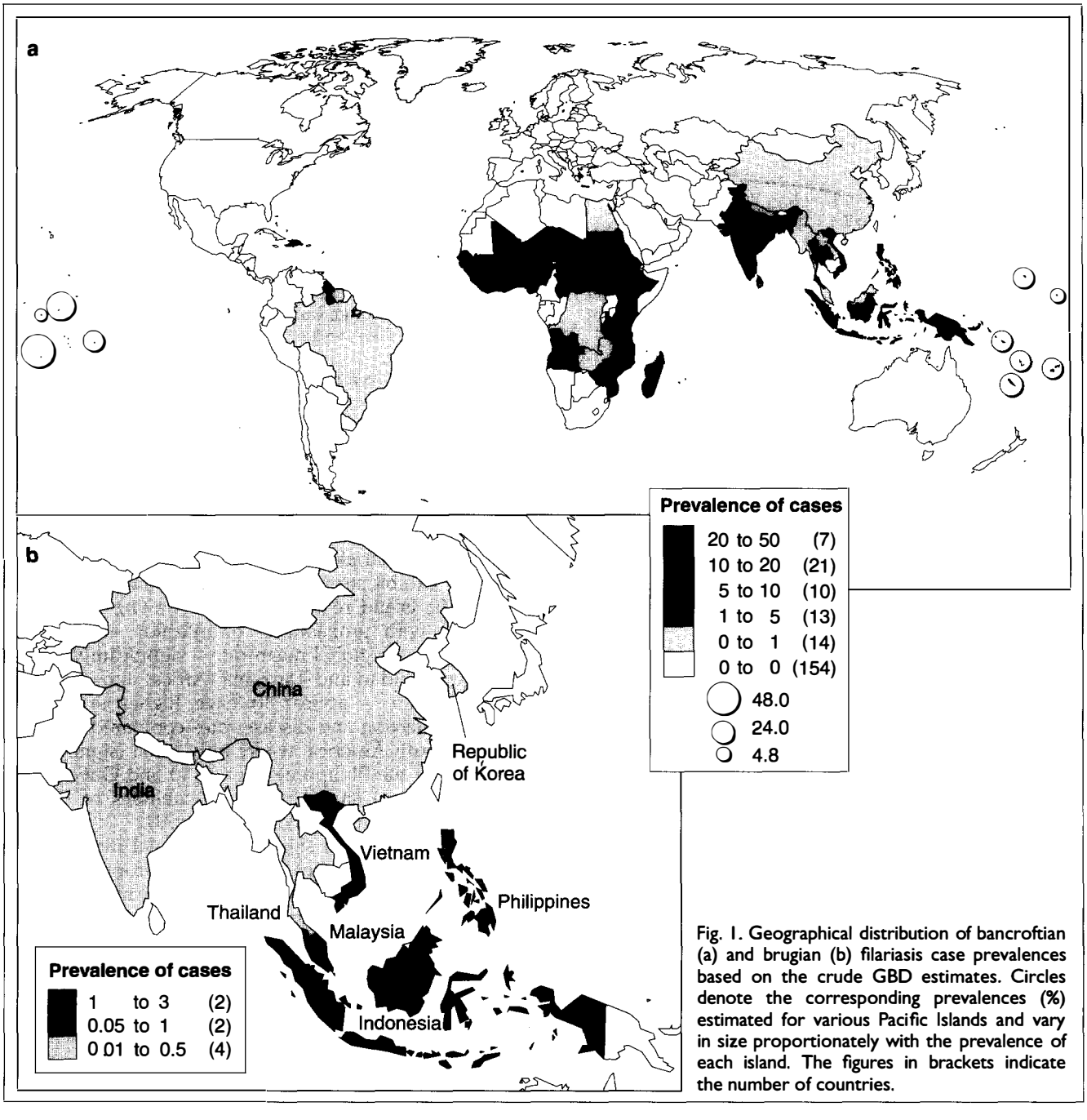


Fig. 1. Geographical distribution of bancroftian (a) and brugian (b) filariasis case prevalences based on the crude GBD estimates. Circles denote the corresponding prevalences (%) estimated for various Pacific Islands and vary in size proportionately with the prevalence of each island. The figures in brackets indicate the number of countries.

Box 1. Probability Mapping

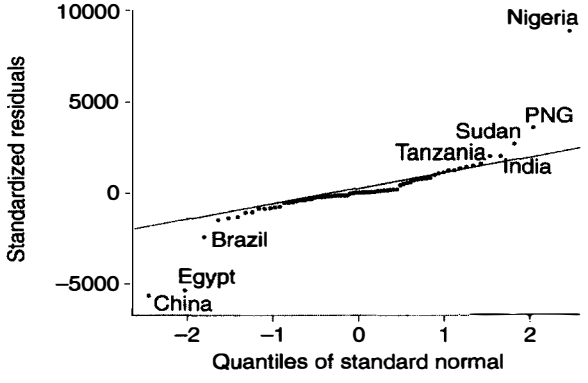
Probability maps have long been used in spatial epidemiology as a tool for assessing the significance of the mapped rates[1,4]. In essence, the method involves transforming the given areal prevalences or rates on to a probability scale of observing each individual rate under some theoretical model of the infection or disease process. It has been usual to map the probability of getting a level of cases at least as big (or small) as that recorded if the process generating the infection or disease distribution is spatially random[1,4]. Formally, this constitutes a simple Poisson model for the infection or disease process on the map, in which the observed events or counts, y_i, in each area i are considered to be observations on independent Poisson random variables with expected values μ_i. A sensible estimate of the mean (expected) count in each area, μ_i, is then given by:

$$\hat{\mu}_i = n_i \left(\frac{\Sigma y_i}{\Sigma n_i} \right) \quad (1)$$

Then we map:

$$p_i = \sum_{x>y_i} \frac{\mu_i^x e^{-\mu_i}}{x!} \quad (2)$$

Note that when μ_i is large, as is clearly the case here, a Poisson distribution approximates to a Normal distribution with the same mean and variance[1]. Thus, assessments of the significance of y_i can be made using Normal inference. In particular, standardized residuals (see details of derivation in Ref. 1) from the fit of $\hat{\mu}_i$ to y_i can then be plotted against the quantiles of the standard Normal distribution to determine the probability of observing each y_i. For example, in the Fig., countries with standardized residuals ≥1.96 of the values on the x axis may be considered to have significantly higher infection or disease cases, while countries with residuals ≤−1.96 may be considered to have significantly lower cases at the 5% probability level[1]. The Normal distribution for the residuals also implies that a good fit to the Poisson model is indicated if the standardized residuals lie on the Normal probability line plotted in the Fig. (left) (Ref. 1). It is readily seen that there is a marked spread in the extreme quantiles, indicating a significant departure from Poissonian randomness for the data.



Although the idea of the probability map is to standardize rates on to a probability scale for proper comparison, it should be noted that it is only an exploratory device. In particular, because it weights in favour of larger populations, extreme p_i values for such populations may represent only modest increases of risk[2,5,6]. As mentioned above, another limitation is that Poisson maps do not take account of spatial dependence in the data, although a way forward here may be to construct maps at a more local or regional level[5]. Other methods based on Bayesian formulations[2,6] and generalized linear mixed models[16] may provide more suitable approaches to analysing mapped data, but computational difficulties have so far hampered their wider use. Clearly, further work is required in this area.

The Fig. (above) shows a normal probability plot of the standardized residuals derived from the fit of the Poisson global mean number of cases to the observed number of bancroftian cases in the various endemic countries. The results show a departure from the Poisson assumption for the global data. The identification of the countries exhibiting the anomalous residuals portrays the regional bias in the data. By contrast, similar plots at the regional levels indicated closer agreements with the Poisson assumption (data not shown).

countries simply because of the greater variance of the prevalence estimate when derived from smaller denominators[1,2,4]. Therefore, the assessment of spatial heterogeneity requires that this impact of population size be addressed effectively[2,4].

Here, we attempt a preliminary analysis of this problem using the approach of probability mapping[1,4]. Probability mapping (Box 1) stabilizes the individual prevalence rates for population size variations and, thereby, also provides a tool for highlighting anomalous areas. Note that while Poisson probability mapping is most appropriate for smoothing incidences or rates of rare conditions, the Normal approximation to the Poisson distribution may be used to produce the corresponding (approximate) probability maps for non-rare events, such as the present infection and disease prevalences[1] (Box 1).

The global probability map for bancroftian filariasis is displayed in Fig. 2 and, as expected, the transformation of the country prevalences to a probability scale replaces the high spatial variation of the earlier map (Fig. 1) with a more homogeneous pattern in the 'between-country' distribution of infection and disease. However, the results in the figure (and the more formal results shown in Box 1) also confirm the impression gained from Fig. 1 that the underlying infection and disease rate for filariasis is not constant across the world, but may exhibit strong regional variations. Africa, and the Pacific Island region (data not shown), with more countries with probabilities of infection and disease higher than the global mean rate – significantly higher in Nigeria, Sudan and Tanzania (Africa) and PNG (the Pacific region) – appear to have higher underlying regional infection and disease rates compared to either Asia or South America, where only India (significantly higher) and the Philippines (for Asia) and Guyana (for South America) show higher probabilities of disease rate compared to the global mean (Fig. 2).

The existence of a significant regional influence on spatial variation implies that it is inappropriate to use global approaches to Poisson probability mapping as a tool for stratifying countries by disease risk[2,5,6], because such a scheme assumes equal probability for the occurrence of infection and disease in all areas of the map, ie. the procedure is spatially invariant. The result would be to overemphasize the significance of extreme values on the map[1,4], thereby distorting the stratifying scheme. This suggests that separate probability maps based on local regional mean rates may be required to identify anomalous countries in each endemic region[2,5,6].

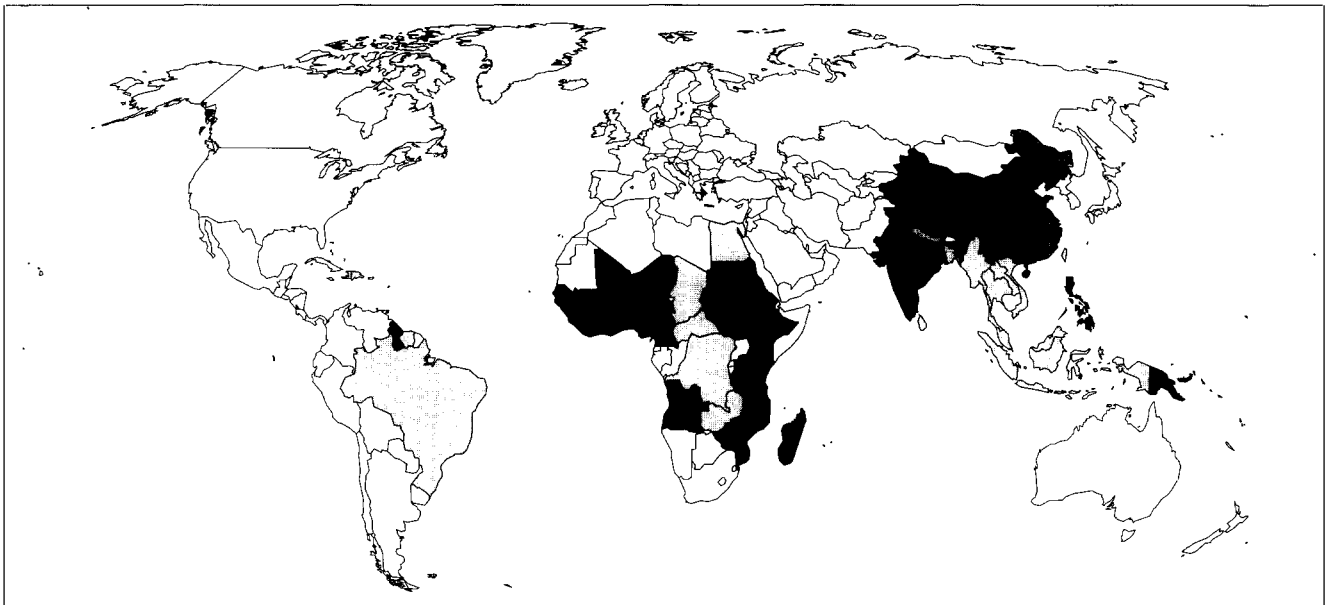


Fig. 2. Global Poisson probability map for bancroftian filariasis case prevalences. The map shows $P_{i>mean}$ values calculated using the methods described in Box 1, and may be interpreted by considering that there is a 'high probability' ($p>0.90$) that the prevalence estimated in each black area is higher than the mean global value (MGV); there is 'equivocal evidence' that the risk of each dark shaded area is higher than the MGV ($p = 0.50$–0.90) and that of each light shaded area is lower than the MGV ($p = 0.10$–0.50); and, finally, there is a 'high probability' that the risk of each medium shaded area is lower than the MGV ($p<0.10$). (NB Case probabilities for all the other endemic Pacific Island countries lay between 0.50 and 0.90.)

We illustrate such a map for Africa in Fig. 3, which further reduces the heterogeneity observed in Figs 1a and 2 for this region and identifies only Nigeria (with a prevalence of 22.1%) and Egypt (with a prevalence of 0.65%) as the countries with significantly high and low infection/disease rates, respectively. The significance of the observed rates for all other endemic countries in relation to the mean regional prevalence for Africa (10.3% for positive nations) is equivocal, suggesting that the underlying infection/disease rates of these countries are similar to the mean case rate for this region. Similar bancroftian filariasis maps constructed for Asia and the Pacific Island region (not shown) also indicated that only the prevalences exhibited by India (5.4%), China (0.5%) and PNG (39%) differed significantly from their respective mean regional rates (2.4% for positive countries in Asia and 29% for the Pacific region). In contrast, the analysis for South America (data not shown) identified the Dominican Republic (1.55%), Haiti (2.85%) and Guyana (7.33%) to have high infection/disease prevalences, and Brazil (0.03%) to have a significantly low case prevalence compared with the low regional mean rate (0.2% for positive countries).

Concluding remarks

The most important contribution of our global mapping of filariasis is the detection of strong regional differences in the prevalence of bancroftian filariasis. The maps of this parasitic disease show that, in general, infection and disease prevalences are higher and more varied in the sub-Saharan African and Pacific Islands regions compared with Asia and South America. This new finding is fundamentally different from the traditional view, which considered

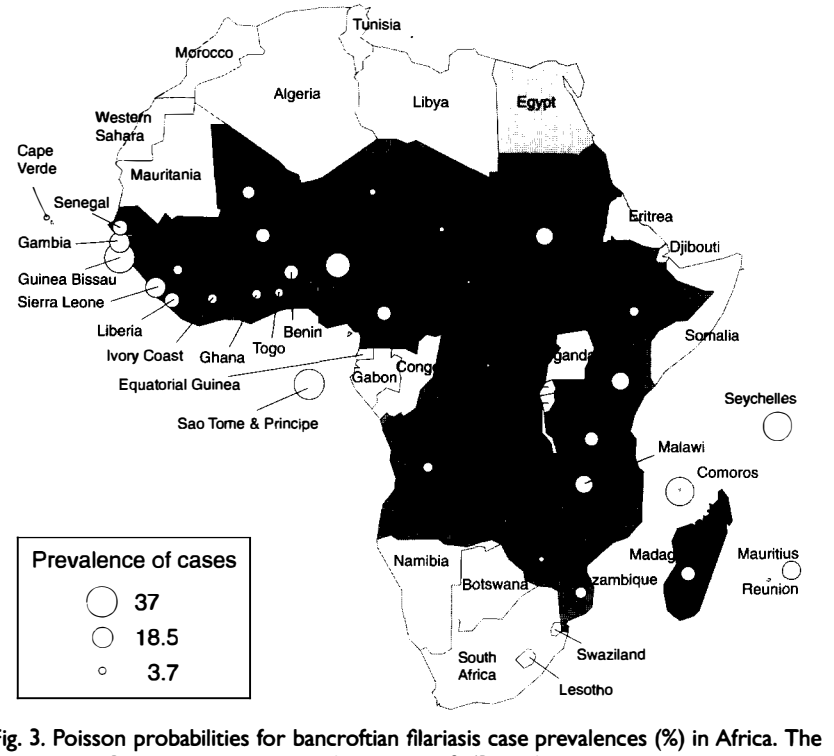


Fig. 3. Poisson probabilities for bancroftian filariasis case prevalences (%) in Africa. The map shows $P_{i>mean}$ values calculated using Eqn 2 (Box 1) but in relation to the mean regional value (MRV) for Africa (10.3% for positive nations). Interpretation of the probabilities is similar to that for Fig. 2, but is based on the estimated African MRV. The proportional circles denote the observed raw prevalences of each country.

sub-continent India to be the most important region for filariasis[8,9], although it is clear that India, with the largest number of cases for a single country (48.1 million cases of both *W. bancrofti* and *B. malayi* infections)[11], and at highest risk to bancroftian filariasis in the Asian region, remains an equally important endemic area.

Although the GBD estimates upon which the present analyses are based derive from the most detailed database available currently on the distribution of filariasis[11], it is notable that much of the data, particularly for Africa and the Pacific Islands (the two potentially most important regions apart from India detected here), are either from older surveys (conducted in the 1950s and 1960s) or are derived from single surveys within countries (see Table 1 in Ref. 11). The maps depicted in Fig. 1 also indicate continuing gaps in knowledge on infection and disease incidence for several potentially endemic African countries including Eritrea, Djibouti, Somalia, Uganda, Rwanda, Burundi, Republic of Congo, Gabon and Equatorial Guinea, where filariasis is known to occur but for which currently data are unavailable[12]. Similarly, in the Asian region, new information on infection and disease distribution is required for Cambodia and indeed for Myanmar, Vietnam and Laos where the data are derived from older and limited surveys[11]. Also, a special effort should be made to update the information on the distribution in the Pacific region, given that the importance detected for this region in the present study is based mainly on old data (largely conducted between the 1950s and 1960s for most of the islands)[13]. This variability in the base data, both in terms of survey numbers per country and the date of the study (later studies would be expected to use newer and more reliable techniques of blood sampling), may explain in part the equivocal significance of many of the observed national prevalences that are detected on the probability maps of Fig. 2. These considerations indicate that there is a current need for research aimed at obtaining more precise basic information on infection and disease distributions for this parasitic infection. Although this is most pertinent for the distributions in Africa and the Pacific Islands foci, it is clear that the situation also applies equally to Southeast Asia.

The significance of the existence of a regional pattern in parasitic disease distributions is that it may imply the likely operation of genuine geographical variation in the underlying infection rate. This has important implications for planning control strategies as it argues for a geographically targeted strategy for control. This conclusion would be strengthened further by the detection of systematic geographical covariations of the infection and disease patterns with specific aetiological factors. The resolution of such questions, however, would require information on infection, disease and risk factor distributions on a finer geographical scale, perhaps down to province or district levels, than was used in this study. Current attempts to develop and deploy rapid assessment methods (RAP) based on both lay and focus group reporting[14] and new simple-to-use diagnostic tools[15] will prove crucial to the success of this endeavour, and deserve support. Present work in collaboration with the WHO aims to initiate the first stage in this process via the setting up of a geographical information systems (GIS) platform describing the spatial distribution of infection and disease at within-country levels. Further progress will also require the development of easy-to-use statistical methodology that allows the investigation of non-rare conditions across large areas. By contrast, most currently available methods address variation in rates or proportions either across small areas or of rare disease events[1,2,5,6].

The present results suggest that these developments are likely to play an increasingly valuable role not only in the analysis of filariasis and other parasitic distribution patterns but also ultimately in planning and monitoring parasite control.

Acknowledgements

C.P. Ramachandran (former Chief, Filariasis Control, WHO) was instrumental in initiating our interest in pursuing the mapping approach to filariasis distribution. We thank P.K. Rajagopalan and P.K. Das for stimulating our interest in investigating the geographical patterns of filariasis. This work was executed through a WHO Special Programme for Research and Training in Tropical Diseases (TDR) grant.

References

1 Cliff, A.D. and Haggett, P. (1988) *Atlas of Disease Distributions. Analytical Approaches to Epidemiological Data*, Blackwell Publishers
2 Mollie, A. (1996) in *Markov Chain Monte Carlo in Practice* (Gilks, W.R., Richardson, S. and Spiegelhalter, D.J., eds), pp 359–379, Chapman & Hall
3 Snow, R.W., Marsh, K. and le Sueur, D. (1996) **The need for maps of transmission intensity to guide malaria control in Africa.** *Parasitol. Today* 12, 455–457
4 Bailey, T.C. and Gatrell, A.C. (1995) *Interactive Spatial Data Analysis*, Longman Scientific & Technical
5 Marshall, R.J. (1991) **Mapping disease and mortality rates using empirical Bayes estimators.** *Appl. Stat.* 40, 283–294
6 Bernardinelli, L. and Montomoli, C. (1992) **Empirical Bayes versus fully Bayesian analysis of geographical variation in disease risk.** *Stat. Med.* 11, 983–1007
7 Sasa, M. (1976) *Human Filariasis – A Global Survey of Epidemiology and Control*, University Park Press
8 World Health Organization (1984) **Lymphatic Filariasis. Fourth Report of the WHO Expert Committee on Filariasis.** *WHO Tech. Rep. Ser.* 702, WHO
9 World Health Organization (1992) **Lymphatic Filariasis: The Disease and its Control.** *WHO Tech. Rep. Ser.* 821, WHO
10 World Bank (1993) *World Development Report 1993. Investing in Health*, Oxford University Press
11 Michael, E., Bundy, D.A.P. and Grenfell, B.T. (1996) **Re-assessing the global prevalence and distribution of lymphatic filariasis.** *Parasitology* 112, 409–428
12 Hawking, F. (1977) **The distribution of human filariasis throughout the world. Part III. Africa.** *Trop. Dis. Bull.* 74, 649–679
13 Hawking, F. and Denham, D.A. (1971) **The distribution of human filariasis throughout the world. Part I. The Pacific region, including New Guinea.** *WHO/FIL/71.94*, 31 pp (mimeogr.)
14 Gyapong, J.O., Dollimore, N., Binka, F.N. and Ross, D.A. (1995) **Lay reporting of elephantiasis of the leg in northern Ghana.** *Trans. R. Soc. Trop. Med. Hyg.* 89, 616–618
15 Weil, G.J., Lammie, P.J. and Weiss, N. (1997) **The ICT filariasis test for diagnosis of bancroftian filariasis.** *Parasitol. Today* 13, 398–401
16 Breslow, N.E. and Clayton, D.G. (1993) **Approximate inference in linear mixed models.** *J. Am. Stat. Assoc.* 88, 9–25
17 Gyapong, J.O., Magnussen, P. and Binka, F.N. (1994) **Parasitological and clinical aspects of bancroftian filariasis in Kassena-Nankana District, Upper East Region, Ghana.** *Trans. R. Soc Trop. Med. Hyg.* 88, 555–557
18 Gyapong, J.O., Adjei, S. and Sackey, S.O. (1996) **Descriptive epidemiology of lymphatic filariasis in Ghana.** *Trans. R. Soc. Trop. Med. Hyg.* 90, 26–30
19 McConnel, E. and Schmidt, M.L. (1973) **Bancroftian filariasis in Gambela, Illubabor Province, Ethiopia.** *Trop. Geogr. Med.* 25, 300–303
20 McConnel, E. and Asfaha, W. (1976) **A survey for *Wuchereria bancrofti* in Ethiopia.** *Ethiopian Med. J.* 14, 31–36
21 Jemaneh, L. and Kebede, D. (1995) **Clinico-epidemiological study of lymphatic filariasis in southwestern Ethiopia.** *Ethiopian Med. J.* 33, 143–153
22 Lambrecht, F.L. (1971) **Preliminary report on the distribution and epidemiology of filariasis in the Seychelles islands, Indian Ocean.** *Southeast Asian J. Trop. Med. Public Health* 2, 222–232