Re-assessing the global prevalence and distribution of lymphatic filariasis

E. MICHAEL[1], D. A. P. BUNDY[2] *and* B. T. GRENFELL[1]

[1] *Department of Zoology, University of Cambridge, Downing Street, Cambridge CB2 3EJ, UK*
[2] *Centre for the Epidemiology of Infectious Disease, University of Oxford, South Parks Road, Oxford OX1 3PS, UK*

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SUMMARY

This paper estimates the global burden of lymphatic filariasis based on a review of the published literature on infection and disease surveys. A method for aggregating and projecting prevalence data from individual studies to national, regional and global levels, which also facilitates the estimation of gender and age-specific burdens, is presented. The method weights in favour of the larger, and hence presumbably more reliable, studies and relies on estimated empirical relationships between gender, age, infection and disease in order to correct studies with incomplete data. The results presented here suggest that although the overall prevalence of filariasis cases is 2·0% globally (approximately totalling 119 million cases), the disease continues to be of considerable local importance, particularly in India and Sub-Saharan Africa. Estimates by age and gender clearly show that, unlike other helminth infections, filariasis is mainly a disease of the adult and older age-classes and appears to be more prevalent in males. This work suggests that the derivation of more accurate estimates of the burden of filariasis will require a better understanding of both the epidemiology and the spatial aspects of infection and disease. It also suggests that filariasis is preventable based on a geographically targeted strategy for control.

Key words: lymphatic filariasis, global burden, epidemiology.

INTRODUCTION

Reliable information about the distribution and prevalence of a parasitic disease is fundamental to the estimation of its public health significance (World Bank, 1993). For lymphatic filariasis, the distribution is thought to be confined to the tropics and sub-tropics while the most recent estimate of infection suggests the possibility of up to some 78·6 million individuals infected globally with the 3 major lymphatic filarial species – *Wuchereria bancrofti*, *Brugia malayi* and *B. timori* (WHO, 1992). These estimates are based largely on reports by Member States to the 1992 WHO Expert Committee on Filariasis, and have drawn attention to the fact that filariasis continues to be a sizeable problem in many parts of the world.

However, because these estimates do not differentiate between asymptomatic and clinical infection (WHO, 1984,1992), they provide little information on the magnitude of morbidity due to the infection. Reliable estimates of disability have become increasingly important to informing the debate on the public health importance of helminth infections (Warren *et al.* 1993; Evans, Gelband & Vlassoff, 1993; World Bank, 1993; Chan *et al.* 1994). This is despite the fact that the chronic disease manifestations of filariasis, such as hydroceles in men and lymphoedema, in contrast to most other helminthiasis (Guyatt & Bundy, 1991; Chan *et al.* 1994), are directly observable and is fairly well-documented in the literature.

These global estimates also do not provide data on the gender and age-distribution of infection (microfilaria-positive) and disease cases. Information on age and gender patterns are essential for attempts to quantify disease burden, especially those based on metrics, such as the Disability Adjusted Life Year (DALY), which measure the burden in terms of future stream of disability-free life lost, and used recently by the World Bank (1993) as a standardized approach to comparing the public health impact of different diseases and conditions.

Furthermore, the previous approaches to estimating infection (WHO, 1984, 1992) do not provide information on the technical bases of the reported estimates, which are likely to have varied between endemic countries. On the other hand, published literature on infection or disease surveys has been used successfully to estimate the burden of geohelminth infections (Crompton, 1988, 1989; Bundy & Cooper, 1989; Chan *et al.* 1994). Development of appropriate methods for calculating national, regional and global infection and disease prevalences, however, is integral to exploiting this data resource for estimating the disease burden of lymphatic filariasis.

The major aim of this study is therefore to reassess the current global and regional prevalence of lymphatic filariasis using published data of the

* Corresponding author.

Table 1. Sources of the estimates of prevalence (%) of lymphatic filariasis (infection plus disease) by country

Region[i] and country	Prevalence[ii] (%)	Sources
(A) Bancroftian filariasis		
Sub-Saharan Africa		
Angola	8·89	Azevedo, J. F. de, 1964[d] (423,234)[5]
Benin	11·90	Brengues, Subra & Bouchite, 1969[d,age,sex-specific; f,g] (2360)
Burkina Faso	12·88	Brengues *et al.* 1975[d] (72,206)[12]
Cameroon	11·11	Ripert *et al.* 1982[d,sex-specific; f,g,males,adults.] (626), Marceau *et al.* 1986[d] (1000)
Cape Verde	0·99	Azevedo, J. F. de *et al.* 1969[d] (607)
Central African Republic	1·29	Hawking, 1977[d] (100)
Chad	2·84	Hawking, 1977[d] (1681)[5]
Comoros	26·73	Blanchy & Galtier 1982[d,age,sex-specific] (353), Charafoudine & Pesson, 1986[d,age,sex-specific] (419)[7], Joire, Julivez & Galtier, 1988[c,sex-specific,adults.] (943)
Republic of Congo	0·70	Fain, Wery & Tilkin, 1969[d,sex-specific] (720)[8]
The Gambia	17·57	Knight, 1980[d,f,g. < and ⩾ 15yrs.] (2,309)[15]
Guinea	6·21	Hawking, 1977[d]
Guinea Bissau	36·50	Azevedo, J. F. de 1964[d,f] (1988)[3(sample size not given for one study)]
Ivory Coast	8·62	Brengues *et al.* 1975[a] (607)[d], (3555)[3]
Kenya	7·03	Wijers & Kinyanjui, 1977[a] (1794)[2], Wijers & Kaleli, 1984[d]
Liberia	11·11	Brinkmann 1976[d,age,sex-specific; f,g] (925), Kuhlow & Zielke, 1976[d] (6,695)[69], Zielke & Chlebowsky, 1979[d,age,sex-specific; g,age-specific] (1968)[17]
Madagascar	12·50	Brygoo, 1958[d] (468)
Malawi	17·35	Oram, 1958[f,g,sex-specific] (1642)[3], Oram, 1960[b]
Mali	11·50	Brengues *et al.* 1975[d] (4472)[6]
Mauritius	13·95	Huehns, 1953[d,age,sex-specific] (1930)
Mozambique	10·09	Pinhao, 1961[d. < and ⩾ 20yrs] (1420)[4]
Niger	4·90	Hawking, 1977[d]
Nigeria	22·11	Wijeyaratne *et al.* 1982[d,age-specific] (1561), Udonsi, 1986[d,age-specific] (1351)[4], Udonsi, 1988*b*[d,age,sex-specific] (1418)[7], Akogun, 1991[d,age-specific; f,g] (2552)[9]
Sao Tome and Principe	18·90	Azevedo J. F. de *et al.* 1969[d]
Senegal	12·37	Juminer, Diallo & Diagne, 1971[d,age-specific] (1841)[9]
Tanzania	11·74	McMahon *et al.* 1981[a] (2003)[4], Matola, 1985[a] (1947[inf], 2168[dis])
Togo	5·42	Brengues *et al.* 1969[d,age,sex-specific; f,g] (2360)[3]
Zambia	0·76	Hawking, 1977[d] (459)
Zimbabwe	4·63	Hawking, 1977[d] (109)
Latin America and Caribbean		
Brazil	0·03	Franco & Lima, 1966[d] (811,361)[24], Sherlock & Serafim, 1967[d,age,sex-specific] (22,174)[31]
Costa Rica	0·11	Weinstock *et al.* 1977[d,age-specific; f,g] (1196), Madrigal, *et al.* 1979[d] (119), Paniagua *et al.* 1983[d,age,sex-specific] (2879)[4]
Dominica Republic	1·55	Vincent, 1987[d,sex-specific; e]
Guyana	7·33	Nathan & Stroom, 1990[d,age,sex-specific] (2818)
Haiti	2·85	Raccurt, Mojon & Hodges, 1984[d,age,sex-specific] (1428), Raccurt, 1986[d] (6779), Raccurt *et al.* 1988[d,age,sex-specific; f,g] (421)
Surinam	0·42	Oostbrug, 1985[d,age,sex-specific; f,age,sex-specific] (107,415)
Trinidad	0·61	Nathan *et al.* 1982[d,f,age,sex-specific; g,age-specific] (562[inf], 326[dis])
Middle Eastern Crescent		
Egypt	0·65	Fahmy *et al.* 1977[d,age,sex-specific; f] (1998), Southgate, 1979[d], El-Ridi *et al.* 1984[d,f,g] (3215), Feinsod *et al.* 1987[d,f,sex-specific; g,age-specific] (191), Wahdan, 1991[d] (434,826)[30]
India	5·36	Rahman & Bhattacharya, 1971[d,age,sex-specific] (690)[2], Marwah, Rao & Gaur, 1972[d,e,age,sex-specific; e,f,sex-specific; g] (7194)[15], Chandra *et al.* 1973[d] (531)[3], Bhattacharya & Gubler, 1973[d,age,sex-specific] (1338)[2], Russel *et al.* 1975[a] (6781)[5], Dondero *et al.* 1976[a] (660), Rao *et al.* 1980[a] (11,300), Rajagopalan *et al.* 1981[d,age,sex-specific] (10,522), Rath *et al.* 1984[d,e,age,sex-specific; f,sex-specific; g] (9323), Sharma *et al.* 1984[d,e], Sarma *et al.* 1987[d,age,sex-specific; e,age-specific; f,sex-specific; g] (2921), Biswas *et al.* 1989[d,e], Jain *et al.* 1989[d,age,sex-specif; e,age-specific] (11,105), Rajagopalan *et al.* 1989[d,age,sex-specific] (24,946), Hyma, Ramesh & Gunasekharan, 1989[d,age,sex-specific; e,f,sex-specific; g] (93,402), Ramaiah *et al.* 1989[d,age,sex-specific; e,f,sex-specific; g] (7976), Kumar & Chand, 1990[d,age,sex-specific] (13,918), Pani *et al.* 1991[a] (34,615[inf],6493[dis])
China	0·48	Self, 1991[d]
Other Asia and Islands		
Bangladesh	2·19	Barry *et al.* 1971[a,f,sex-specific; g] (9624), Wolfe & Aslamkhan, 1971[d,sex-specific; institutions] (4190)[39], Wolfe & Aslamkhan, 1972[a,f,sex-specific; g] (1443)[2]
Burma	0·10	Hawking, 1976[d] (880,258)[14]
Other Polynesia	22·77	Ciferri *et al.* 1969[d,f,g] (826[4,inf],1008[4,dis], Hawking & Denham, 1971[d(Nauru,Tokelau(326),Wallisislands)], Weller *et al.* 1982[d,e,age-specific] (459)

Table 1. (*cont.*)

Region[i] and country	Prevalence[ii] (%)	Sources
Fiji	10·69	Hawking & Denham, 1971[g], Mataika *et al.* 1971*b*[d,age,sex-specific] (4483), Mataika *et al.* 1971*a*[f,age,sex-specific]
French Polynesia	12·62	Laigret, 1984[d,f,g], Perolat *et al.* 1986[d]
Indonesia	1·77	van Djik, 1961[a] (1206), Self *et al.* 1978[a] (536), Joesef & Cross, 1978[d] (14,219)[18], Harbut, 1983[d,age,sex-specific] (358)[2]
Laos	0·07	Tawil, 1979[c] (2339)
Malaysia	0·40	Hii *et al.* 1985[d,age,sex-specific; f,sex-specific; g] (1680)
Nepal	0·84	Jung, 1973[a] (5302)
New Caledonia	18·72	Hawking & Denham, 1971[d,f]
Other Micronesia	3·07	Hawking & Denham, 1971[d]
Micronesia	11·12	Hawking & Denham, 1971[d]
Papua New guinea	72·02	Knight *et al.* 1979[a] (233), Kazura *et al.* 1984[a] (99)
Philippines	4·12	Rozeboom & Cabrera, 1964[d,age,sex-specific] (280), Cabrera & Jueco, 1972[d,age,sex-specific] (248), Wenclesloa *et al.* 1972[d,age,sex-specific] (7,222), Grove *et al.* 1978[a] (555), Enarson & Enarson, 1982[a] (590), Ishii *et al.* 1983[d,age,sex-specific] (267), Schultz, 1988[d,age,sex-specific] (1546)[8]
Western Samoa	7·73	Kimura, Penaia & Spears, 1985[a] (8385)[28]
Seychelles	10·02	Lambrecht, 1971[d,age-specific] (2474)[6]
Sri Lanka	1·62	Hawking, 1976[d], Dissayanake, 1989[d,age,sex-specific; f,sex-specific] (4004)[2]
Thailand	2·82	Harinasuta *et al.* 1970[d,age,sex-specific; f,sex-specific; g,age-specific] (1549)
Republic of Tongo	48·04	Desowitz & Hitchcock 1974[d,f,age,sex-specific;] (296), Desowitz, Berman & Puloka, 1976[d,f,g,age-specific] (606)[2]
Vanuatu	11·99	Bouree, Sauvagnac & Montaville, 1987[d,f] (7137)[13]
Vietnam	1·35	Hawking, 1976[d]
(B) Brugian filariasis		
India	0·30	Russel *et al.* 1980[c] (2542), Chandrasekharan, Balaraman & Rao, 1981[d,f,age-specific.] (533), Rath, Mohapatra & Das, 1989[d] (529), Raina *et al.* 1990[d,age,sex-specific] (2186), Pani *et al.* 1990[f,age,sex-specific] (7766), Srividya *et al.* 1991*a*[d,age,sex-specific] (22,579)
China	0·37	Anti-epidemic station, Zhejiang Province 1981[d], Ling, 1985[d] (2100), Liu, Liu & Chen, 1989[d] (494,000)
Other Asia and Pacific Islands		
Indonesia	2·58	Partono *et al.* 1972[a] (635)[3], Partono *et al.* 1977*a*[d,age,sex-specific; f] (3658)[7], Partono *et al.* 1977*b*[d,age,sex-specific; f,sex-specific] (2764)[7], Joesef & Cross, 1978[d] (125,312)[110], Sudomo *et al.* 1982[d,age,sex-specific] (197)[2]
Malaysia	1·88	Mak *et al.* 1977[d,age,sex-specific; f,sex-specific] (858), Hii 1978[d,sex-specific] (1305)[17], Rubis *et al.* 1981[d,age,sex-specific] (1613)[7]
Thailand	0·39	Guptavanji *et al.* 1977[a] (5021)[2],[c] (36,457)[8], Harinasuta & Sucharit, 1977[d,age,sex-specific; f,sex-specific] (4291)[11]
Philippines	0·82	Wencleslao *et al.* 1972[d,age,sex-specific] (14,543)[39], Cabrera & Jueco, 1972[d,age,sex-specific] (248)[2]
Republic of Korea	0·03	Kim, No & Lee, 1987[d] (1863)[2]
Vietnam	0·77	Hawking, 1976[d]

[i] As defined for the Global Burden of Disease Study (World Bank, 1993).

[ii] Estimates of disease prevalence are for both sexes combined following the methods described in the text.

Superscripts in literature citations

[a] Study provides age-sex stratified data for both infection and disease.

[b] Study provides age-stratified data on infection and disease.

[c] Study provides overall prevalence of infection and disease.

[d] Study contains prevalence data on infection.

[e] Study contains prevalence data on overall disease. This pertains to the case in bancroftian filariasis when disease prevalence figures refer to hydrocele and lymphoedema combined.

[f] Study contains prevalence data on lymphoedema.

[g] Study contains prevalence data on hydrocele.

When the supersripted letters are followed by suffixes, age and/or sex-specific, they refer to the availability of the corresponding age/sex stratified data. Thus, [d,age,sex-specific] specifies the availability of infection prevalence data stratified by age and sex.

Numbers with brackets denote the number of subjects surveyed and examined. Note that some studies do not provide sample sizes. Superscripted numbers (> 1) following bracketed figures represent the number of separate surveys reported in the citation. The sample sizes listed are simply the sum of the separate samples examined. Note that in some studies, sample sizes of infection and clinical or disease surveys differed. Thus (562[inf],326[dis]) means that 562 individuals were examined for infection status, while 326 individuals were examined for the presence of disease conditions.

Countries in Africa potentially at-risk of infection for which there are either no data or recent information (Hawking, 1977) include: Ascension, Botswana, Burundi, Djibouti, Equatorial Guinea, Gabon, Ghana (but see Gyapong *et al.* 1993), Lesotho, Reunion, Rwanda, St Helena, Somalia, Tristan da Cunha, Uganda and Zaire.

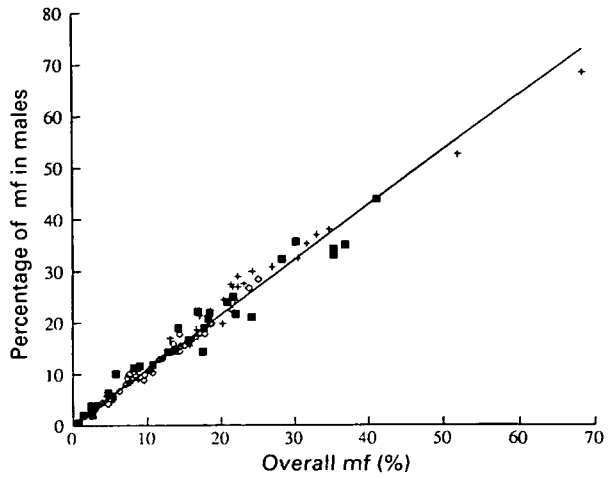

Fig. 1. The relationship between overall microfilarial prevalence (both sexes combined) and male infection proportion. The line represents the weighted best least squares fit ($t = 100{\cdot}39$, D.F. = 95, $P < 0{\cdot}0001$) of the linear regression model through the origin (equation (2) in the text) with coefficients: $E(Y_t) = 1{\cdot}07\ X_t$. The data are from 96 separate studies from Sub-Saharan Africa, (■), Other Asia and Islands (+) and India regions (◇). Analysis of co-variance indicated no significant regional differences in the observed relationship ($F = 1{\cdot}503$, D.F. = 2,93, $P > 0{\cdot}5$), as can also be seen clearly from the graph (see however Hedges & Olkin (1985) for discussion on the validity of the F-test in meta-regression). Note that the estimated relationship suggests significantly higher infection in males (slope significantly greater than 1, $t = 7{\cdot}00$, D.F. = 95, $P < 0{\cdot}001$). *Data sources*: SSA (30 data points): Blanchy & Galtier, 1982: Akogun, 1991; Udonsi 1988*a*, *b*; Matola, 1985; Wijeyaratne *et al.* 1982; Ripert *et al.* 1982; Kuhlow & Zielke, 1976; Zielke & Chlebowsky, 1979; Brunhes, 1975; Gyapong *et al.* 1993; Brengues, 1975; McMahon *et al.* 1981; Wijers & Kinyanjui, 1977; OAI (33 data points): Ciferri *et al.* 1969; Mataika *et al.* 1971*b*; Rosen, 1955; Beye *et al.* 1953; van Djik, 1961; Cartel *et al.* 1992; Self *et al.* 1978; Barry *et al.* 1971; Schultz, 1988; Wolfe & Aslamkhan, 1972; Rozebroom & Cabrera, 1964, 1965; Enarson & Enarson, 1982; Harinasuta *et al.* 1970; Jachowski & Otto, 1955; David & Edeson, 1965; Kazura *et al.* 1984; Tanaka *et al.* 1980; Mahfuddin *et al.* 1977; Ishii *et al.* 1983; McCarthy & Fitzgerald, 1955; Knight *et al.* 1979; Lie, Hudajo & Amaliah, 1960; Symes, 1960; Iyengar *et al.* 1959; IND (33 data points): Bhattacharya & Gubler, 1973; Dondero *et al.* 1976, Jain *et al.* 1989; Nair, 1960; Basu *et al.* 1965; Jain *et al.* 1987; Rajagopalan, Shetty & Arunachalam, 1981; Rajagopalan *et al.* 1989, 1971; Joseph & Peethambaran, 1963; Kant, Sen & Puri, 1956; Krishnaswami, 1955; Kumar & Chand, 1990; Nair, 1962, Rahman & Bhattacharya, 1971; Rath *et al.* 1984; Singh, Raghavan & Krishnaswami, 1956; Singh *et al.* 1963, 1964; Varma *et al.* 1960; Varma, Dass & Sinha, 1961*a*, *b*, *c*; Ramaiah *et al.* 1989; Chand *et al.* 1961, 1962; Russel, Das & Rao, 1975; Sarma *et al.* 1987.

occurrence of infection (defined as positive for microfilaria) and chronic disease (restricted to hydrocele and lymphoedema). The secondary aim is to address the methodological issues of rate projections and aggregations arising from using the published data on community infection and disease prevalences in endemic countries. This work forms part of the Global Burden of Disease study, a World Bank initiative to develop indices of disability for the purposes of comparison between different diseases and illnesses (World Bank, 1993). It also forms part of a WHO initiative to update the existing estimates of the global prevalence of infection (WHO, 1984, 1992).

MATERIALS AND METHODS

Data sources

The estimates derived here are for 6 out of the 8 regions defined for the Global Burden of Disease study (see World Bank, 1993). The Established Market Economies and Formerly Socialist Economies of Europe are excluded as infection is not considered endemic in these regions (WHO, 1984, 1992). The data used for the estimates are prevalence values of microfilaraemia and chronic disease derived from published community-based studies in each country. They are based on extensive computer literature searches complemented with reference tracing and scrutiny of reports held by the WHO. As far as possible, the most recent data published for each country were used, older data (largely restricted to the 1960s) were used only when no recent data were available for a particular country.

The above searches located some 118 publications (published between 1953 and 1991) with relevant data for disease estimation. A complete bibliography, including the data content of each study, is given in Table 1, and highlights the considerable variation in the information content of published studies. Only 20 studies provide complete information on the age–sex distribution for both microfilaraemia and the 2 forms of chronic disease in the community, the majority of studies tending to give only partial (with a greater bias for infection than disease) or no age–data (see Table 1). The studies also varied considerably in reporting infection and disease prevalences by gender, with most studies presenting only combined results for the sexes. Most studies provide results for 'combined' disease, or give results for either lymphoedema or hydrocele but not for both. Most publications were concerned with one survey only; however, a few dealt with several surveys either within the same country or within a group of countries. The number of studies available for each country also varied (Table 1).

Methodological approach

Overview. The methodology developed is primarily founded on the need to extrapolate individual study prevalences to larger populations at the national and

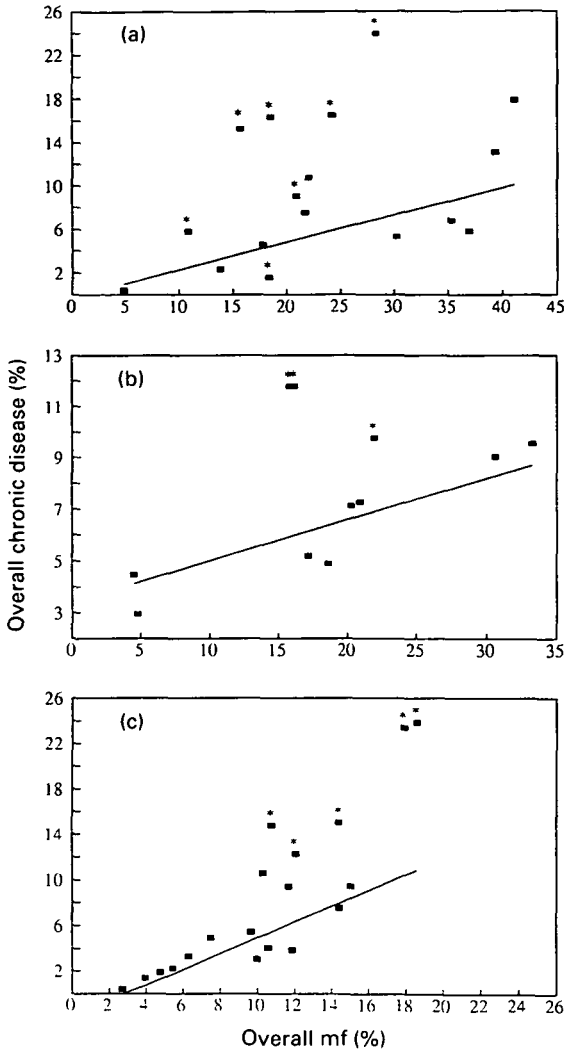

Fig. 2. The relationship between overall infection prevalence (combined sexes) and overall disease proportion (combined sexes) for (A) Sub-Saharan Africa (17 studies), (B) Other Asia and Islands (15 studies) and (C) India (19 studies) regions. Lines show the best fit linear regression models (equation (1)) for each region yielding the following equations: SSA = $E(Y_i)$ = $-0{\cdot}20+0{\cdot}25X_i$ (t = 25·00, D.F. = 15, $P < 0{\cdot}0001$), OAI = $E(Y_i)$ = $3{\cdot}4+0{\cdot}16X_i$ (t = 4·85, D.F. = 13, $P < 0{\cdot}001$), IND = $E(Y_i)$ = $-02{\cdot}1+0{\cdot}60X_i$ (t = 7·00, D.F. = 17, $P <$ 0·001). Note the high degree of between-study variability observed for the relationship in each region. The asterisks mark those studies that contribute more than 5% each to the overall heterogeneity about the regression line, and hence have the least weights in the regression. The fitted lines clearly show that the influence of these studies is heavily discounted during the weighted least squares fit of the models. The estimated relationships indicate slight regional differences (F = 10·806, D.F. = 2,43, $P < 0{\cdot}01$, steeper rise in disease with infection in the India and Sub-Saharan Africa regions but higher disease prevalence at lower infection in the Other Asia and Islands region), facilitating the incorporation of some geographical variation in the estimation of disease prevalences. *Data sources*: Akogun, 1991; Matola, 1985; Brunhes, 1975; Gyapong *et al.* 1993; Brengues, 1975; McMahon *et al.* 1981; Wijers & Kinyanjui, 1976; van Djik, 1961; Wolfe & Aslamkhan, 1972; Mahfuddin *et al.* 1977; McCarthy & Fitzgerald, 1955; Weller *et al.* 1982; de Rook, 1959; Knight *et al.* 1979; Kazura *et al.* 1984; Enarson & Enarson, 1982; Barry *et al.* 1971; Self *et al.* 1978; Ciferri *et al.* 1969; Iyengar *et al.* 1959; Galliard, Mille & Robinson, 1949; Dondero *et al.* 1976; Nair, 1960, 1962; Joseph & Peethambaran, 1963; Krishnaswami, 1955; Rath *et al.* 1984; Varma *et al.* 1960; Ramaiah *et al.* 1989; Chand *et al.* 1961, 1962; Iyengar, 1952; Srivastava & Prasad, 1962; Singh *et al.* 1963, 1964; Sarma *et al.* 1987; Rahman, Singh & Srivastava, 1959.

regional levels, and the need to deal with the incomplete age–gender–disease information of published studies (see Table 1). These considerations required the development of the following 3-phased approach to burden estimation. First, to incorporate gender and disease-specific (hydrocele and lymphoedema) distributions into those studies lacking this information. Second, to derive age-specific prevalences for each condition in each study and, third, to sum these individual study prevalences within age groups to provide age-specific prevalences at the country, regional and global levels, or across age-groups to provide a summary age-adjusted figure. The approach is described in detail in the following 3 sections.

Incorporation of gender and disease-specific distributions. This primarily required the estimation of (a) the relationship between overall point prevalences of infection and chronic disease, (b) the sex ratios of infection and disease prevalences and (c) in the case of bancroftian filariasis, the ratio of hydrocele to lymphoedema for a given overall male disease prevalence. We derive simple linear regression models to estimate these relationships taking appropriate account, however, of the considerable between-study variation in sample size (Table 1, see Hedges & Olkin, 1985). Specifically, given the non-constant error variance, we used a weighted least-squares regression model of the form :

$$E(Y_i) = \beta_0+\beta_1 X_i+e_i \qquad i = 1, \ldots, N, \tag{1}$$

where E(·) denotes expected value; Y_i is the prevalence of overall infection or disease, the prevalence of male infection or disease, or the prevalence of hydrocele as a proportion of overall male disease for study i; X_i is the overall microfilarial or infection prevalence, the prevalence of overall disease (undifferentiated by gender), or the prevalence of male disease (both hydrocele and lymphoedema) observed in each study; N is the number of studies; and $\text{var}(e_i) = \sigma^2/w_i$, where σ^2 represents the error variance or residual mean square of the model (Weisberg, 1985; Hedges & Olkin, 1985). Thus,

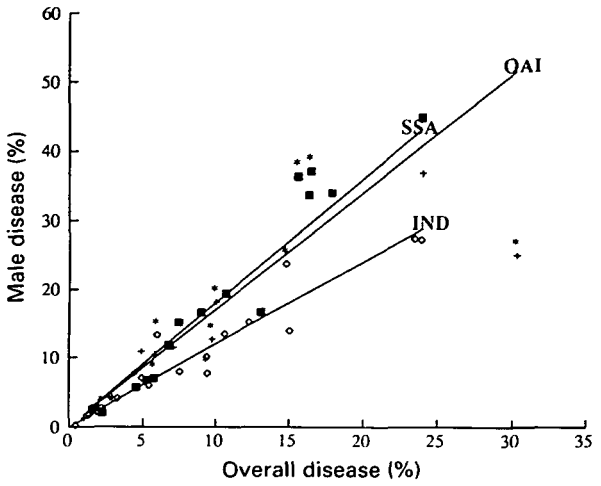

Fig. 3. The relationship between overall disease prevalence (combined sexes) and male disease proportion. Data from studies in Sub-Saharan Africa (■), data from studies in Other Asia and Islands (+), data from India (◇). Lines indicate the best fit linear model (equation (2)) in each region: SSA = $E(Y_i)$ = $1{\cdot}8X_i$ ($t = 36{\cdot}38$, D.F. = 15, $P < 0{\cdot}0001$), OAI = $E(Y_i)$ = $1{\cdot}7X_i$ ($t = 39{\cdot}22$, D.F. = 9, $P < 0{\cdot}0001$), IND = $E(Y_i)$ = $1{\cdot}2X_i$ D.F. = 16, $P < 0{\cdot}0001$). As in Fig. 3, the asterisks mark studies contributing to > 5% of the total variance about the regression line. Male disease in the community appears to be significantly lower in India for a given overall disease prevalence (F = 13·827, D.F. = 2,40, $P < 0{\cdot}0001$). *Data sources*: SSA: Ufomadu *et al.* 1991; Matola, 1985; Brunhes, 1975; Gyapong *et al.* 1993; Brengues, 1975; McMahon *et al.* 1981; Wijers & Kinyanjui, 1977; Estambale *et al.* 1994; OAI: Ciferri *et al.* 1969; van Djik, 1961; Self *et al.* 1978; Barry *et al.* 1971; Enarson & Enarson, 1982: Kazura *et al.* 1984; Mahfuddin *et al.* 1977; McCarthy & Fitzgerald, 1955; Knight *et al.* 1979; Iyengar *et al.* 1959; IND: Pani *et al.* 1991; Dondero *et al.* 1976; Nair, 1960; Joseph & Peethambaran, 1963; Krishnaswami, 1955; Nair, 1962; Rath *et al.* 1984; Varma *et al.* 1960; Ramaiah *et al.* 1989; Chand *et al.* 1961, 1962; Iyengar, 1952; Singh *et al.* 1963, 1964; Russel *et al.* 1975; Sarma *et al.* 1987.

given the binomial response variable Y_i, approximate weights w_i are readily given by

$$w_i = \frac{1}{p_i(1-p_i)/n_i} \tag{2}$$

where $p_i(1-p_i)/n_i$ gives the binomial variance of p_i, and $p_i \doteq Y_i$ is the studied prevalence or proportion, and n_i is the study sample size. The intuitive rationale for these weights is that reliable estimates (small variance) have relatively large weight and unreliable estimates (large variance) have relatively small weights in the respective regressions (Hedges & Olkin, 1985).

Analysis of geographical variation in the relationships was limited by restriction of available data to Sub-Saharan Africa, Other Asia and Pacific Islands and India. This was a particular problem for brugian filariasis, as we were able to locate only 11 studies with concomitant information on overall infection and disease prevalences, and only 10 studies giving gender data on lymphoedema prevalences. This precludes the analysis of geographical variation for this disease, and we apply the estimated relationships globally to all relevant *Brugia* studies regardless of study region.

Figures 1–3 and Table 2 summarize the results of the linear regression analyses used to derive the relationships, together with the details of the studies used in the estimation. The results for bancroftian filariasis (Figs 2 and 3) indicate some variation in the infection–disease–gender relationships by region. Disease estimates for Latin America and the Caribbean, the Middle Eastern Crescent and China, for which no or incomplete data were available were extrapolated simply by using the mean overall global relationships in each case (data not shown).

Hydrocele cases as a proportion of male disease appeared independent of the overall prevalence of male disease in each region (none of the regressions were significant). Hence, the weighted mean proportion of hydrocele (as a proportion of male disease) was calculated from the studies in each region using the formula:

$$\hat{p}_{hj} = \frac{\sum_i^k w_i p_{hi}}{\sum_i^k w_i} \tag{3}$$

where $\hat{p}_{hj}$ is the weighted mean proportion, p_{hi} is the proportion in each study i and w_i represent the study weights following equation (2). The results indicated that 94% (S.E = 0·017, $n = 14$, *data sources*: Brengues, 1975; Brunhes, 1975; Wijers & Kinyanyui, 1977; Wijers, 1977; McMahon *et al.* 1981; Matola, 1985; Ufomadu *et al.* 1991; Gyapong *et al.* 1993) and 93% (S.E. = 0·03, $n = 10$, *data sources*: Beye *et al.* 1952; McCarthy & Fitzgerald, 1955; Iyengar, de Rook & van Djik, 1959; van Djik, 1961; Ciferri *et al.* 1969; Barry, Ahmed & Khan, 1971; Wolfe & Aslamkhan, 1972; Mahfuddin *et al.* 1977; Self *et al.* 1978; Knight *et al.* 1979; Enarson & Enarson, 1982) of observed male disease prevalence may be attributed to hydrocele in Sub-Saharan Africa and Other Asia and Islands regions. In India, the corresponding proportion was significantly lower (Analysis of co-variance: F = 32·60, D.F. = 2·35 $P <$ 0·0001) at 80% (S.E. = 0·026, $n = 14$, *data sources*: Iyengar, 1952; Nair, 1960; Varma, Sinha & Dass, 1960; Chand *et al.* 1961; Chand, Singh & Vyas, 1959; Singh *et al.* 1963, 1964; Dondero *et al.* 1976; Rath *et al.* 1984; Sarma *et al.* 1987; Ramaiah *et al.* 1989).

Specific prevalence estimates were extrapolated from the empirical data using the above relationships in the following manner. Overall community infection or disease prevalences s_i, and male infection

Table 2. Results of weighted linear regressions used for estimating infection and disease prevalences from individual studies in brugian filariasis providing only overall infection and/or partial disease data[a]

(i) Relationship between overall community infection prevalence X_t and male infection prevalence Y_t[b]
$Y_t = 1{\cdot}2X_t$, $t = 37{\cdot}33$ D.F. $= 14$ $P < 0{\cdot}0001$
(ii) Relationship between community infection X_t and disease prevalence Y_t[c]
$Y_t = 0{\cdot}5 + 0{\cdot}11X_t$, $t = 2{\cdot}220$ D.F. $= 16$ $P = = 0{\cdot}05$
(iii) Relationship between overall lymphoedema X_t and male lymphoedema Y_t[d]
$Y_t = 1{\cdot}13X_t$, $t = 13{\cdot}07$ D.F. $= 9$ $P < 0{\cdot}0001$

[a] Data are from studies from all *Brugia* endemic regions (OAI, CHN and IND).
[b] Regression (through the origin) of male infection prevalence on overall (combined sexes) infection prevalence; used to derive sex-specific estimates of infection from overall community infection prevalence. Note that the slope indicates significant higher infection in males. *Data sources*: Ramachandran *et al.* 1971; Barclay, 1969; Partono *et al.* 1972, 1977*a*, *b*, 1978; Kapojos *et al.* 1976; Guptavanij *et al.* 1971, 1977; Harinasuta *et al.* 1970; Raina *et al.* 1990; Srividya *et al.* 1991*a*; Wenceslao *et al.* 1972; Mak *et al.* 1977; Rubis *et al.* 1981.
[c] Regression of disease prevalence on infection prevalence; used to derive disease estimates from studies giving only overall infection prevalence (see text). *Data sources*: Barclay, 1969; Partono *et al.* 1972, 1977*b*; Guptavanij *et al.* 1971, 1977; Harinasuta *et al.* 1970; Dondero & Menon, 1972; Mak *et al.* 1977.
[d] Regression of male lymphoedema prevalence on overall lymphoedema prevalence. Slope value indicates significant higher disease in males. *Data sources*: Barclay, 1969; Partono *et al.* 1972, 1978; Guptavanij *et al.* 1971, 1977; Harinasuta *et al.* 1970; Dennis *et al.* 1976; Pani *et al.* 1990; Estambale *et al.* 1994.

or disease prevalences s_{tm}, are obtained from the corresponding regression equations ($Y_t \doteq s_t, s_{tm}$,) for the particular region (*i.e.* equation coefficients in Figs 1–3 and the corresponding mean global regression relationships). Similarly, hydrocele prevalence for a given male disease prevalence is calculated by direct multiplication with the mean proportions estimated for each region (equation (3)), and in the case of regions with incomplete data (Latin America and the Caribbean, China and Middle Eastern Crescent) by the global mean of 0·89 (S.E. = 0·025, n = 38). Overall female infection or disease prevalences, s_{tf}, for study i are derived from estimated male disease prevalences, s_{tm}, as follows

$$s_{tf} = \hat{p}_t + (\hat{p}_t - s_{tm}) \tag{4}$$

where $\hat{p}_t \doteq X_t$ is the observed overall disease prevalence for the study. Equation (3) is similarly adapted to calculate male lymphoedema prevalences from estimated hydrocele prevalences.

Generation of age-specific prevalences for each study. These were directly recorded to the nearest age-class of interest (0–4, 5–14, 15–44, 45–59 and 60+ yrs) for studies providing such data. Age-prevalences for studies that provided only crude overall infection and/or disease (point) prevalences were derived as follows. First, a search for studies with age-specific details of infection and disease was made for each region. Sufficient numbers of studies for bancroftian filariasis (see Table 3 for details) were found only for Sub-Saharan Africa , Other Asia and Pacific Islands and India. The age-specific prevalences from these studies, s_{tj}, where j denotes the age groups 0–4, 5–14, 15–44, 45–59 and 60+ for each study i, were then combined (see method below) to produce reference age–prevalence curves for each region. Age–weights, a_j, calculated from these curves were then applied to the crude overall community prevalences, s_t, of studies in the corresponding region to derive infection and disease age-specific prevalences. Given s_t, the community prevalence, the age-specific prevalence for each condition is then given by

$$s_{tj} = s_t . a_j \tag{5}$$

where the age-weights a_j are as shown in Table 3. Note that global weights were calculated (not shown) and applied to studies in Middle Eastern Crescent, China and Latin American and the Caribbean.

For brugian filariasis, there were insufficient studies to derive separate reference curves for Other Asia and Pacific Islands, India and China, the 3 endemic regions for this infection (WHO, 1992). In total, we were able to locate 5 studies with complete disease age–prevalence data for females and only 4 with similar disease (lymphoedema) age–details for males, all from Other Asia and Pacific Islands (Table 3). Thus, a common reference curve was derived and used for all 3 endemic regions.

Data aggregation to produce nation and regional age–prevalence estimates. National and regional age–prevalence estimates were obtained by combining the observed and derived age-specific data of individual studies. First, age–prevalences from each study in a particular country are averaged to obtain the corresponding national gender–disease specific prevalences by age-class, c_{tj}. For each age group, and for each sex and condition, this is given by

$$c_{tj} = \frac{\sum_t^k w_{tj} s_{tj}}{\sum_t^k w_{tj}} \tag{6}$$

where w_{tj} is the weight associated with age group j for study i and is given by equation (2); s_{tj} is the prevalence for age group j and study; and k denotes

Table 3. Age weights to generate age-specific disease prevalences from overall community prevalences

Species and region	Age class	Age-weight				
		Male			Female	
		Inf[1]	Hyd[2]	Lymph[3]	Inf[1]	Lymph[3]
(A) *Wuchereria bancrofti*						
Sub-Saharan Africa	0–4	0·30	0·01	0·01	0·50	0·05
	5–14	0·50	0·10	0·02	0·60	0·10
	15–44	1·1	0·80	0·50	1·2	1·1
	45–59	1·4	1·9	1·9	1·6	3·7
	60+	1·8	2·4	3·4	1·6	3·9
Other Asia and Pacific Islands	0–4	0·30	0·01	0·01	0·50	0·10
	5–14	0·50	0·15	0·25	0·70	0·16
	15–44	1·2	1·2	1·1	1·2	1·1
	45–59	1·7	2·7	3·0	1·5	3·5
	60+	1·5	3·5	3·7	1·6	3·1
India	0–4	0·50	0·05	0·10	0·65	0·15
	5–14	0·75	0·20	0·30	0·90	0·35
	15–44	1·2	1·1	1·0	1·0	1·1
	45–59	1·3	2·1	2·3	1·3	2·2
	60+	1·2	2·5	2·9	1·7	2·7
(B) *Brugia malayi*						
(all regions)	0–4	0·20		0·0	0·35	0·0
	5–14	0·65		0·01	0·70	0·01
	15–44	1·2		0·90	1·3	0·70
	45–59	1·5		3·2	1·2	4·1
	60+	1·7		5·3	2·4	5·5

[1] Microfilarae + ves.
[2] Hydrocele cases.
[3] Lymphoedema cases.
Data sources: SSA: McMahon *et al.* 1981; Brunhes, 1975; Gyapong *et al.* 1993; Udonsi, 1986; Zielke & Chlebowsky, 1979; Brengues *et al.* 1969; Brengues, 1975; Oram, 1960; Akogun, 1991; Wijers, 1977; Wijers & Kinyanjui, 1977; OAI: Ciferri *et al.* 1969; Mataika *et al.* 1971*a*, *b*; Rosen, 1955 Beye *et al.* 1952, 1953; van Djik, 1961; Cartel *et al.* 1992; Self *et al.* 1978; Barry *et al.* 1971; Schultz, 1988; Wolfe & Aslamkhan, 1972; Rozeboom & Cabrera, 1964, 1965; Enarson & Enarson, 1982; Harinasuta *et al.* 1970; Jachowski & Otto, 1955; David & Edeson, 1965; Kazura *et al.* 1984; Tanaka *et al.* 1980; Mahfuddin *et al.* 1977; Ishii *et al.* 1983; McCarthy & Fitzgerald, 1955, 1956; Abdulcader & Padley, 1960; Knight *et al.* 1979; Lie *et al.* 1960; Symes, 1960; IND: Bhattacharya & Gubler, 1972; Pani *et al.* 1991; Dondero *et al.* 1976; Jain *et al.* 1987, 1989; Nair, 1960, 1962; Basu *et al.* 1967; Rajagopalan, Kazmi & Mani, 1977; Rajagopalan *et al.* 1981, 1989; Joseph & Peethambaran, 1963; Kant *et al.* 1956; Krishnaswami, 1955; Kumar & Chand, 1990; Rahman & Bhattacharya, 1971; Rath *et al.* 1984; Singh *et al.* 1956; Varma *et al.* 1961*a*, *b*, *c*.

the number of studies. As before, this weighting scheme is used to discount the impact of small (and hence less reliable) studies (Hedges & Olkin, 1985).

The next step involved the estimation of the number of affected individuals in a particular country by gender and age-class from the estimated age–prevalences and demographic data. For each sex and disease, the numbers affected in each age-class is calculated from

$$T_{+ij} = c_{ij} . T_{ij} \quad (7)$$

where T_{+ij} is the number of estimated infected or diseased individuals in age group j in country i, and T_{ij} is the age group population size. Where available, information on the size of the population at-risk of infection were used in these calculations (Table 4). In calculating the population at risk in China, it has been customary to ignore the populations of provinces having infection prevalences below 1% (Self, 1991). Here, we have considered the population of any province with endemic infection to be potentially at risk.

Regional prevalences were calculated by summing the number of cases across the endemic countries of the region and dividing by the total regional population. Thus for each sex and disease condition, the age-specific regional prevalences R_{ij} are given by

$$R_{ij} = \frac{\sum_{i}^{N_+} T_{+ij}}{P_{ij}} . 100 \quad (8)$$

where T_{+ij} is the number of affected individuals in each age group j for each endemic country i; N_+ is the total number of endemic countries in the region; and P_{ij} is the total regional population in age-class j. This method provides a crude weighting for national population size differences.

Table 4. Estimates of at-risk population size for lymphatic filariasis by country

(Modified from information held by the Filariasis Expert Committee, WHO.)

Country	Population in millions[1]	At-risk population size (millions)
Bangladesh	106·656	68·316
Brazil	150·367	3·00
China	1133·693	805·111
		(55·562)
Costa Rica	2·807	0·041
Dominican Republic	7·074	1·500
Egypt	52·063	3·700
Fiji	0·745	0·413
Guyana	0·799	0·650
Haiti	6·471	1·000
India	849·514	394·067
		(152·110)
Indonesia	178·228	22·000
		(22·000)
Kenya	24·158	9·856[2]
Malaysia	17·860	1·994
		(1·994)
Myanmar	41·607	3·120
Nepal	18·916	1·018
Philippines	61·481	15·803
		(15·803)
Sri Lanka	17·003	4·400
Tanzania	24·516	10·000
Thailand	55·854	9·000
		(6·950)
Trinidad	1·237	0·004
Vietnam	66·311	10·007

[1] Population statistics from the World Bank (1993).
[2] Proportion of population at-risk assumed to be similar to that of Tanzania.
Numbers in brackets denote the estimated at-risk population size for brugian filariasis. The total national population is assumed to be the at-risk population for all other countries.

The estimation of overall filariasis cases. The procedures described above allow the extrapolation of separate estimates for each of the disease conditions observed in filariasis. To obtain an estimate of the overall number of filariasis cases (*i.e.* microfilarial and diseased cases combined), however, required the development of methods to control for the number of individuals with both types of condition (infection with disease symptoms) in order to avoid double counting. We address this by analysing available data for hydrocele (h_{mf+}) and lymphoedema (l_{mf+}) cases who are also microfilaraemic in order to estimate the weighted proportions of such cases (see equation (3)), and use these to predict the proportion of individuals with simultaneous disease and infection, h_{mf+i}, l_{mf+i}. (data sources: *hydrocele*: de Rook, 1957, 1959; Nair, 1960; van Djik, 1961; Barry *et al.* 1971; Wolfe & Aslamkhan, 1972; Brengues, 1975; Dondero *et al.* 1976; Wijers & Kinyanyui, 1977; Abaru *et al.* 1980; McMahon *et al.* 1981; *lymphoedema*: Causey *et al.* 1945; de Rook, 1959; Nair, 1960; van Djik, 1961; Barry *et al.* 1971; Brengues, 1975; Dondero *et al.* 1976; Wijers & Kinyanjui, 1977; McMahon *et al.* 1981; Weller *et al.* 1982). The analysis indicated that on average 22% of hydrocele patients are microfilaraemic, while up to 8·9% of lymphoedema patients may be microfilaraemic. Overall filariasis cases in each study are then given for males, say, by :

$$T_{ijm} = s_{ijmf} + s_{ijh} + s_{ijl} - s_{ijmf}\,(s_{ijhmf+} + s_{ijlmf+}) \qquad (9)$$

where T_{ijm} is total male filariasis cases in study i and age-group j; s_{ijmf} is the observed age-specific male microfilarial prevalence; s_{ijh} is the hydrocele prevalence; s_{ijl} is the male lymphoedema prevalence; and s_{ijhmf+} and s_{ijlmf+} are the corresponding expected proportions of male microfilaraemic hydrocele and lymphoedema cases. Note that the proportion of infected individuals for both disease conditions is assumed to be independent of age-group, gender and the community prevalence of infection, as a first approximation (see Michael, Grenfell & Bundy, 1994). The overall filariasis cases at the country, regional and global levels are then calculated employing the same methodology as outlined for the separate infection and disease conditions.

Table 5. Global estimate of the number of cases and prevalence of filariasis (infection and chronic disease) due to *Wuchereria bancofti* by region

(Estimates of the number of cases are given in millions while prevalences are in percentages (%). Figures are for both sexes combined.)

Region[a]	Population	Infections[b]	Lymphoedema	Hydrocele	Total no. of cases[c]	Percentage of total global cases
SSA	512	27·87	4·64	10·20	40·02 **7·81**	37·69
OAI	793	11·33	1·79	1·90	14·46 **1·83**	13·62
IND	849	29·46	6·58	12·88	45·53 **5·36**	42·88
CHN	1134	4·05	0·11	1·68	5·46 **0·48**	5·14
LAC	441	0·32	0·031	0·057	0·395 **0·09**	0·37
MEC	391	0·24	0·056	0·060	0·34 **0·09**	0·32
World	4119	73·27	13·21	26·79	106·19 **2·58**[d]	

[a] Regions as defined in the Global Burden of Disease study (World Bank, 1993). SSA = Sub-Saharan Africa, OAI = Other Asia and Islands, IND = India, CHN = China, LAC = Latin America and Caribbean, MEC = Middle Eastern Crescent.
[b] Microfilaraemia cases.
[c] Denotes infection and chronic disease cases, including hydrocele in males, combined as described in the text. Lower numbers denote the prevalence in each region.
[d] Represents the global prevalence for endemic populations only.

Table 6. Global estimate of the number of cases and prevalence of filariasis (infection and chronic disease) due to *Wuchereria bancofti* by age group

(Estimates of the number of cases are given in millions, prevalences are in percentages (%). Figures are for both sexes combined.)

Age class	Population[a]	Infections[b]	Lymphoedema	Hydrocele	Total no. of cases[c]	Percentage of total global cases
0–4	552	2·71	0·13	0·06	2·88 **0·52**	2·72
5–14	918	11·44	0·94	1·82	13·63 **1·48**	12·84
15–44	1932	42·76	6·45	15·62	60·72 **3·14**	57·18
45–59	432	10·70	2·57	5·65	18·13 **4·20**	17·07
60+	285	5·74	2·44	3·64	10·83 **3·80**	10·20
Total	4119	73·27	13·21	26·79	106·19 **2·58**[d]	

[a] Population in endemic regions only (see Table 5).
[b] Microfilaraemia cases.
[c] Denotes infection and disease cases, including hydrocele in males, combined as described in the text. Lower numbers represent the prevalence in each age group.
[d] Represents the global prevalence for endemic populations only.

RESULTS

The estimates of number of cases and prevalence of infection, lymphoedema and hydrocele in males are given in Tables 5–10. The results are in terms of the endemic populations only, i.e. those living in the regions where significant risk of infection exists. For each parasite species, these estimates are given for different age classes, by gender and for different endemic regions.

The estimated total number of *W. bancrofti* infections is 73 million, while the numbers of lymphoedema and hydrocele cases are estimated to be 13 and 27 million respectively (Tables 5 and 6).

Table 7. Global estimate of the number of cases and prevalence of filariasis (infection and chronic disease) due to *Brugia malayi* by endemic region

(Estimates of the number of cases are given in millions while prevalences are in percentages (%). Figures are for both sexes combined.)

Region[a]	Population	Infections[b]	Lymphoedema	Total no. of cases[c]	Percentage of total global cases
OAI	793	5·07	1·21	6·18 **0·78**	47·84
IND	849	1·80	0·86	2·58 **0·30**	20·01
CHN	1134	3·49	0·73	4·15 **0·37**	32·16
World	2776	10·36	2·81	12·91 **0·47**[d]	

[a] Regions as defined in Table 5.
[b] Microfilaraemia cases.
[c] Denotes infection and chronic disease cases, including hydrocele in males, combined as described in the text. Lower numbers denote the prevalence in each region.
[d] Represents the global prevalence for endemic populations only.

Table 8. Global estimate of the number of cases and prevalence of filariasis (infection and lymphoedema) due to *Brugia malayi* by age group

(Estimates of the number of cases are given in millions, prevalences are in percentages (%). Figures are for both sexes combined.)

Age class	Population[a]	Infections[b]	Lymphoedema	Total no. of cases[c]	Percentage of total global cases
0–4	340	0·40	0·02	0·42 **0·12**	0·71
5–14	578	1·45	0·07	1·52 **0·26**	2·63
15–44	1342	6·32	1·11	7·33 **0·55**	39·50
45–59	309	1·34	0·81	2·08 **0·67**	28·17
60+	207	0·83	0·80	1·56 **0·75**	28·51
Total	2776	10·36	2·81	12·91 **0·46**[d]	

[a] Population in endemic regions only (see Table 7).
[b] Microfilaraemia cases.
[c] Denotes infection and chronic disease cases, including hydrocele in males, combined as described in the text. Lower numbers denote the prevalence in each age group.
[d] Represents the global prevalence for endemic populations only.

The total number of cases (infection and chronic disease) arising from *W. bancrofti* infection, however, is estimated at 106 million. The estimates for *B. malayi* (Tables 7 and 8) indicate a global total of some 10 million cases of infection with a further 3 million cases suffering from lymphoedema. The total number of *B. malayi* filariasis cases (infection and chronic disease) is estimated to be around 13 million, yeilding a total filariasis burden from both species combined of 119 million cases. The overall prevalence of filariasis cases is thus low: 2·6% in the exposed population or 2·0% globally for bancroftian filariasis, and 0·5% and 0·25% respectively for brugian filariasis.

The regional distribution of cases is shown in Tables 5 and 7 for bancroftian and brugian filariasis respectively. For bancroftian filariasis, India, with 45·5 million cases, and Sub-Saharan Africa, with 40 million cases, have similar burdens (Table 5). These regions account for 43% and 38% of the world burden. The highest prevalence of cases occurs in Sub-Saharan Africa (8% compared to 5% in India). The region with the third highest number of cases and prevalence for bancroftian filariasis is 'Other Asia and Islands' (Asia, excluding China, India and Pakistan and including Pacific islands) (Table 5). China, with a total burden of 5·5 million cases, comes next in order of importance, while lower burdens of

Table 9. Estimates of the number of cases, in millions, of filariasis infection and lymphoedema due to *Wuchereria bancrofti* by gender and region

	Population		Infections[b]		Lymphoedema		Total no. of cases[c]	
Region[a]	Males	Females	Males	Females	Males	Females	Males	Females
SSA	253	259	14·74	13·13	1·78	2·86	24·28	15·74
OAI	401	392	6·54	4·79	0·92	0·87	8·87	5·59
IND	440	410	17·00	12·46	2·60	3·98	29·43	16·10
CHN	585	549	2·25	1·80	0·06	0·05	3·62	1·84
LAC	220	221	0·19	0·13	0·014	0·017	0·25	0·15
MEC	198	193	0·13	0·11	0·027	0·029	0·21	0·13
World[d]	2096	2023	40·86	32·41	5·36	7·81	66·65	39·54
			1·95[e]	**1·60**	**0·26**	**0·39**	**3·18**	**1·95**

[a] Regions as defined in Table 5.
[b] Microfilaraemia cases.
[c] Infection and chronic disease cases, including hydrocele in males, combined as described in the text.
[d] Population in endemic regions only.
[e] This and other figures in bold represent the gender prevalences for endemic populations only.

Table 10. Estimates of the number of cases, in millions, of filariasis infection and lymphoedema due to *Brugia malayi* by gender and region

	Population		Infections[b]		Lymphoedema		Total no. of cases[c]	
Region[a]	Males	Females	Males	Females	Males	Females	Males	Females
OAI	401	392	3·17	1·90	0·76	0·45	3·87	2·30
IND	440	410	1·11	0·69	0·58	0·28	1·63	0·95
CHN	585	549	2·24	1·25	0·46	0·27	2·65	1·50
World[d]	1426	1351	6·52	3·84	1·81	1·00	8·16	4·75
			0·45[e]	**0·28**	**0·13**	**0·07**	0·57	**0·35**

[a] Regions as defined in Table 5.
[b] Microfilaraemia cases.
[c] Infection and chronic disease cases combined as described in the text.
[d] Population in endemic regions only.
[e] This and other figures in bold represent the gender prevalences for endemic populations only.

infection and disease are observed for 'Latin America and Caribbean' and 'Middle Eastern Crescent' regions. Note that the entire burden (some 340 thousand cases) attributed to the 'Middle Eastern Crescent' region occurs in Egypt (Table 1).

The regional distribution of the estimates for brugian filariasis (Table 7) indicates that almost half of the global burden (48%) is confined to the 'Other Asia and Pacific islands' region, mainly the South-East Asian countries of Indonesia, Thailand, Malaysia and Philippines (Table 1). China and India account for the remaining 32% and 20% of the global burden respectively.

The national prevalence figures given in Table 1 need to be interpreted cautiously as they are likely to be considerably more imprecise than regional figures. In part, this reflects the smaller number of studies of varying sample sizes used in their estimation. However, since they also reflect extrapolations from specific study areas, a fuller treatment of precision would require more detailed information than currently available on the spatial distribution of the disease within each country. Nonetheless, the present figures show that although there is wide variation, Sub-Saharan Africa proportionately possess the largest number of countries with moderate to high prevalence of bancroftian filariasis cases, with 16/28 countries indicating prevalences over 10%. Countries belonging to 'Other Asia and Pacific islands' seem to exhibit even greater variation, with some of the highest prevalences in the world apparently occuring in Papua New Guinea and Republic of Tongo (Table 1). By contrast, the endemic countries of 'Latin America and Caribbean' and 'Middle Eastern Crescent' (Egypt) all tend towards low prevalence values. In general, national prevalences of brugian filariasis are low, irrespective of region (Table 1).

The age-specific estimates clearly show the marked age-dependency of infection and disease (Tables 6 and 8). For both species, infection prevalence tends to rise asymptotically with age, while chronic disease rises linearly. Numerically, the largest number of cases occur in the 15 to 44 year

age-groups, but this partially reflects their much larger sampling sizes since prevalences, especially of disease, tend to increase with age (Tables 6 and 8). About 57% of the total burden for bancroftian filariasis and 40% of the total brugian filariasis burden occur in the 15 to 44 year age-group. Similar age-patterns were also observed at the regional level (data not shown), with only slight differences in the degree of age dependency occurring between regions. There was also no gender-specific difference in this pattern.

The prevalence and number of total cases are significantly higher among males for both parasite species (Tables 9 and 10). On average, there are about 25% more cases of bancroftian infection among males and nearly twice as many males as females with *B. malayi* infections. Chronic disease due to bancroftian filariasis is also more prevalent among males. However, this is largely due to the incidence of hydroceles, since when the numbers of cases of lymphoedema are compared the bias appears to be in the opposite direction, with a significantly greater (1·5 times more) amount of disease among females (Table 9). This female bias for lymphoedema is largely the result of the estimates for Sub-Saharan Africa and India, the 2 regions with the highest infection and disease prevalences. All the other regions indicate either a male or only a slight (Middle Eastern Crescent) female bias. By contrast, both infection and lymphoedema cases are more prevalent among males in all endemic regions in the case of brugian filariasis (Table 10).

DISCUSSION

The present estimates suggest that a total of some 119 million individuals may be currently afflicted with lymphatic filariasis. This figure is higher than the most recent estimate by WHO suggesting a global total of 78·6 million cases (WHO, 1992). Two possibilities may account for this discrepancy. First, the increase in number of cases may be an inevitable result of the continuing increase in world population even when case prevalences remain unchanged. Second, the present estimates may be an over-estimation of the 'true' prevalence despite being based on a broader (and hence more representative) database.

Ascribing some level of statistical certainty to the present estimates, however, has proved difficult. The approach adopted here essentially involves data aggregation at different population levels and the use of empirical relationships between key parameters to estimate case prevalences when no local information exists. Both these procedures were adjusted for only one type of bias, namely sample size differences between studies. Although weighting positively in favour of larger and presumably more reliable studies, this adjustment does not control for other biases in individual studies, such as the reliability of the sampling or diagnostic method used (Southgate, 1974; Sasa, 1976; Grenfell *et al.* 1990), demographic differences (Brabin, 1990; Pani *et al.* 1991), socio-economic status (Wijers & Kinyanjui, 1977; Grove, Valeza & Cabrera, 1978; Jain *et al.* 1989; Evans *et al.* 1993), and spatio-environmental factors (Grove, 1983; Southgate, 1992). Statistical adjustment for these factors, however, is hampered by the lack of relevant information on such biases in many of the published studies, and is also difficult to justify because of inadequate understanding of the epidemiology of infection and disease (Grove, 1983; Srividya *et al.* 1991*b*; Bundy, Grenfell & Rajagopalan, 1991; Grenfell & Michael, 1992; Michael *et al.* 1994).

It is clear that at least 2 areas warrant particular attention for the development of more reliable methods for extrapolating from published data. The first concerns the need for more accurate estimations of the epidemiological relationships between key variables, used to derive indirect estimates when local data are unavailable, and the second relates to the need to address the effects of spatial heterogeneity in infection and disease. Spatial heterogeneity in lymphatic filariasis and other helminth infections is a relatively neglected area of study (Booth & Bundy, 1992) but its resolution is not only important for more accurate estimations of global means but also for understanding the population risk factors underlying disease clustering. The resolution of both these questions, however, requires the collection of detailed, standardized data, and current attempts by the WHO to develop Rapid Assessment methods for determining community infection and disease prevalences can only aid this process.

Nonetheless, the present estimates have proved valuable in extending and in identifying areas of continuing weakness in our knowledge of the distribution, epidemiology and public health significance of lymphatic filariasis (WHO, 1994; World Bank, 1993). The estimates suggest that the prevalence of infection and disease is relatively low when considered at a global or regional scale, although it is clear that great variation may occur between endemic countries. Although this spatial heterogeneity may reflect the effect of sampling variation, it could also, on the other hand, suggest that the disease may be of considerable local importance, particularly in India, Africa and among the Pacific islands, where country-specific prevalences range from near 0% up to the very high rates of > 20% estimated for some African and Pacific island nations. Support for new national disease surveys, perhaps through the development and deployment of Rapid Assessments methods, will be crucial in addressing this problem.

A finding of potential importance regarding the distribution of bancroftian filariasis at the regional scale is that Sub-Saharan Africa has the highest over-

all prevalence, has proportionately more countries with high prevalences, and with 40 million cases, almost as many cases of infection and disease as India (45·5 million). This contrasts with previous estimates (WHO, 1984, 1992), which suggested that a significant majority of filarial infection and disease cases occured in India. Given the potential public health significance of this result for Africa, it is clear that there is a particular need for more precise information on infection incidence in this region, including information to quantify current at-risk population sizes or, at the very least, to determine remaining endemic countries.

This work also provides, for the first time, some information on the age and gender distribution of infection and disease cases at the global, regional and national scales. This has proved vital for assessing the public health impact of the disease using metrics, such as the DALY (World Bank, 1993), which measures burden due to disease in terms of future stream of disability-free life lost (more details on disability derivation given in Michael *et al.* (1995)). The age-distributions show that, unlike most other nematode infections (Chan *et al.* 1994), lymphatic filariasis is an affliction of the adult and older age classes, particularly in the case of chronic disease. Furthermore, this age-pattern was consistent for both species, across regions, and for both sexes. This implies a relatively low disease impact for lymphatic filariasis.

The current estimates of disease necessarily, through lack of data, focus on the more gross manifestations of lymphoedema and hydrocele. How justified this limited focus may be is debatable given that other forms of disease, particularly 'acute' disease, such as adenolymphangitis (ADL) (WHO, 1994; Pani *et al.* 1991, 1995) and 'subclinical' pathology in microfilaraemics (Dreyer *et al.* 1992; Witte *et al.* 1993; Freedman *et al.* 1994), are thought to be significant additional sources of disability. The implications of these disease manifestations for calculating filariasis burden is discussed in detail by Michael *et al.* (1995), but it is clear that their inclusion will have a significant effect on estimates of disease burden, particularly as they are likely to appear earlier in life than chronic manifestations, are likely to be at least as prevalent (Pani *et al.* 1991), and appear to occur similarly in both genders (Pani *et al.* 1991, 1995).

A final implication of the estimates is that filarial disease, because of the general low prevalence, may be preventable using simple, low cost approaches to control (WHO, 1994). The local importance of disease, however, argues for a geographically targeted strategy for control.

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