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Dengue transmission risk maps of Argentina

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Summary Dengue is an emerging disease that has become important in Argentina because of its vector's presence (*Aedes aegypti*) and its endemicity in neighbouring countries. Thematic maps were built for Argentina considering four main factors: population susceptibility to dengue virus infection (population density); entrance of the virus from endemic countries (main roads and airports); conditions for the vector (urbanization, altitude, minimum, maximum and mean daily temperatures) and virus extrinsic incubation period (EIP) completion in the mosquito before its death. EIP duration was modelled with a temperature-dependent function and considering life expectancies of 10, 15 and 20 days for the adult mosquito. The results show maximum risk of dengue transmission in the northern and north-eastern part of the country year-round and in the centre during the summer. Although life expectancy of the adult mosquito has a considerable influence on EIP completion, the north-east to south-west decreasing gradient is maintained. Assuming 20-day life expectancy, the EIP would be completed in almost any region of the country; whereas with 15-day life expectancy it would be limited to vector distribution area, and at 10 days it would be restricted to the northern extreme of the country.

keywords *Aedes aegypti*, dengue, extrinsic incubation period, mosquito, risk maps, transmission risk, vector

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Introduction

Dengue is a viral disease maintained within a cycle that involves man and *Aedes* genus mosquitoes. The main vector is *Ae. aegypti*, a domestic day biting mosquito with preference for human blood (Horsfall 1955). After World War II, a global pandemic of dengue began in South-east Asia and has intensified during the last years. Epidemics are more frequent and dengue haemorragic fever (DHF) has emerged in the Pacific region and the Americas (Gubler & Clark 1995). In Argentina, isolated cases of dengue have been recorded between 1905 and 1911 (Kraus 1916; Otero 1916). An epidemic affecting five cities of Entre Ríos Province in 1916, had prevalences ranging from 15 to 85% (Gaudino 1916). During the first half of the century, *Ae. aegypti*, the main dengue vector, was present in the north and centre of the country (Bejarano 1979). Around 1960, the vector was eradicated from Argentina by the Panamerican campaign in response to the appearance of urban yellow fever epidemics. In 1987, the vector was detected in the northern region of the country (Campos 1993) and in subsequent years, in the rest of the northern and central provinces (Schweigmann & Boffi 1998). In 1987, Alonso *et al.* found a 10.6% (132/1248) prevalence of Den1 and Den2 antibodies in human sera in the provinces of Misiones, Formosa and Chaco. These authors suggested that the low levels of antibodies observed may be interpreted as 'negative for the actual infection and due to some previous infection by another flavivirus', and also that this condition would permit the epidemic spreading of the virus. After a long absence in the region, isolated cases of dengue were detected during the autumn of 1997 in Salta Province (Boffi 1998), in areas located near the Bolivian border. Brazil, Bolivia, Paraguay and neighbouring countries of the northern region of Argentina, are known to have endemic dengue (OPS 1997).

This situation led us to build a risk map of dengue in order to plan prevention strategies and better understand the transmission dynamics in the southern geographical distribution limit of the vector. The use of risk maps is still uncommon in Argentina, and risk is generally related to certain populations or referred as a factor, but not mapped.

Here we analyse the relationships between dengue transmission and environmental conditions at a geographical scale, based on the biology of both the vector and the virus. The objective of this study is to compare the risk of dengue virus transmission by *Ae. aegypti* in Argentine localities.

Methodology

Continental Argentina extends from 22° S to 55° S and 54° W to 74° W approximately (Figure 1). It encompasses several climatic regions from subtropical in the north to cold temperate in the south. According to Prothero (1989), four main factors play a role in studying the epidemic transmission of a vector-transmitted illness within a certain area: the existence of a human population susceptible to infection; arrival to the area of individuals carrying the pathogen; a vector density high enough to permit its transmission; and the development of the pathogen inside the vector, which must be accomplished before the death of the vector if transmission is to occur. We constructed

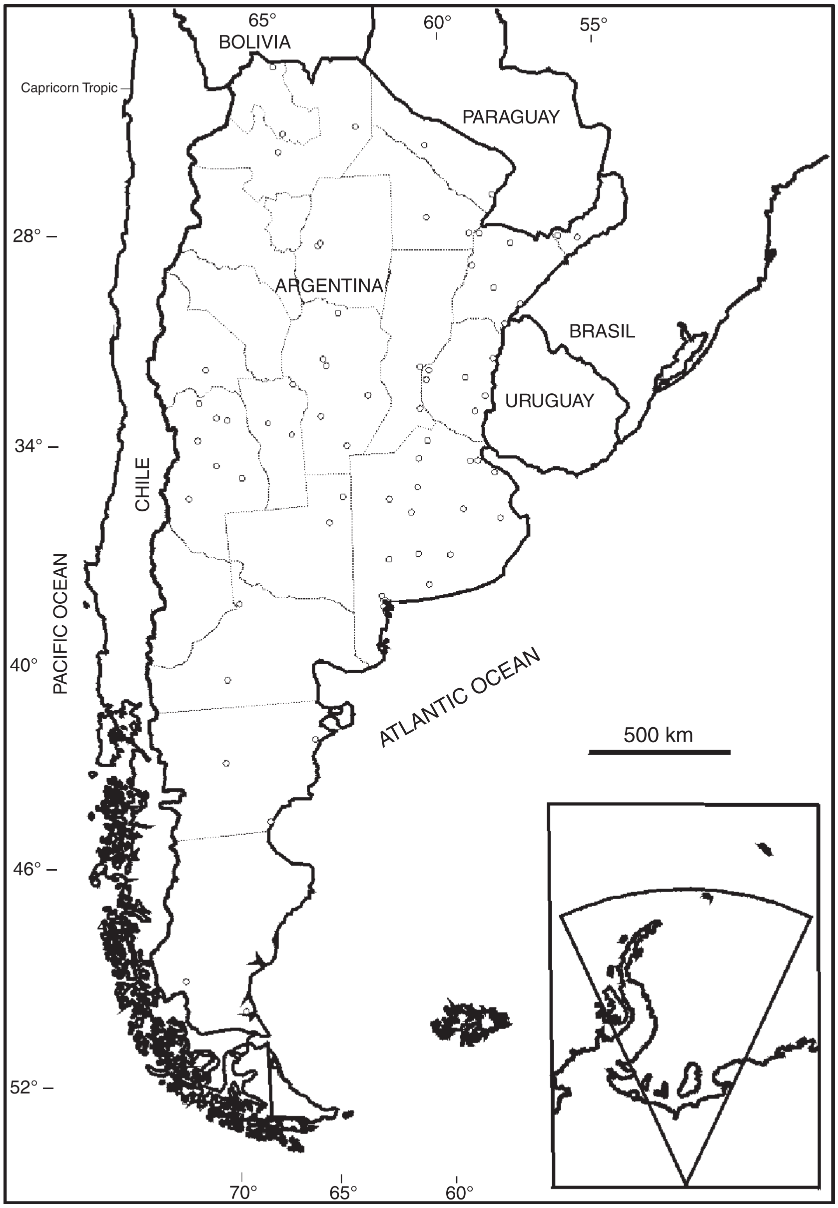

Figure 1 Argentina and its neighbouring countries. Full line: international limits; dashed line: Argentine provinces; circles: meteorological stations considered in the study.

thematic maps considering these four risk factors. The maps were then superimposed, and their areas and gradients used to determine risk areas.

Susceptible population

The brief history of dengue in Argentina suggests the existence of low levels of immunization, thus the population of the whole country was considered to be susceptible to the infection (Alonso *et al.* 1986, 1987). See below for population density maps.

Arrival of viraemic individuals

No endemic transmission of dengue is known in Argentina, therefore the entrance of the virus into a locality would originate from countries with dengue cases. As the viraemic period is about a week long, any air or land transport means may bring an infected person during the viraemic phase from endemic countries. Hence, we mapped the main roads connecting Argentina with neighbouring countries, some of which have endemic dengue, as well as the main national roads and the international airports (Figure 2).

Vector density

We analysed and mapped some environmental conditions for adult *Ae. aegypti* in different places to estimate their probability of yielding high mosquito densities (altitude, population density, urbanization and temperature). As no records of *Ae. aegypti* exist beyond 2200 m a.s.l. and only 2000 and 3000 m a.s.l. contour lines were plotted in the national charts, all localities at or above 3000 m a.s.l. were excluded from the analysis so as not to underestimate risk areas (Figure 3).

Aedes aegypti is a domestic mosquito, consequently urbanization might indicate the most suitable places for its development. About 87% of the Argentine population is concentrated in urban areas (INDEC 1991). We considered as favourable for the vector, those districts with more than 10 inhabitants per sq km or more than three cities per 10 000 sq km (a city being defined as having >2000 inhabitants). Therefore, >80% of the total population of the country inhabit areas with more suitable demographic conditions for the vector (Figure 2). The adult stage of *Ae. aegypti* is constrained by temperatures <0 and >40 °C. Under laboratory conditions, the lower thermal limit for the breeding of this species is 20 °C (Christophers 1960). The annual frequency of days 'with minimum temperature <0 °C', 'with maximum temperature >40 °C' and 'with mean temperature >20 °C' were calculated for 23 meteorological stations around the country. Contour lines were interpolated in three maps considering the mean of the annual frequencies for the 1959–1990 period (Figure 4). The Inverse Weighted Distance method with a power of two and a grid of 51 × 51 lines was used. The areas determined by the contour lines of the frequency maps were given relative values according to their favourableness for the vector, measured as the annual frequency of days presenting each of the above mentioned conditions. The best class of each map was given a relative value of '1'. The remaining classes were given values proportional to the maximum of each class (Figure 4a–c; Table 1). For example, in Figure 4a the frequency classes are: 0–10, 11–30, 31–60 and more than 60 days, and their respective values are 1, 3, 6 and 9. In the map representing the 'frequency of days with mean temperature >20 °C' this scale was reversed, as higher frequencies are in this case better for the mosquito.

These maps were superimposed and the resulting subareas were given values equal to the product of the relative values in each map. Adjacent subareas with equal inconvenience values were then merged. Figure 5 shows the final map for the thermal inconvenience index, where higher values of the index represent increasingly disadvantageous conditions for the mosquito. Figure 6 resumes all the environmental conditions for the vector.

Completion of the extrinsic incubation period

The pathogen in dengue transmission is a virus (serotypes 1, 2, 3 or 4) which can be spread by viraemic individuals through its main vector, the mosquito *Ae. aegypti*. The time elapsed between the entrance of the virus in the vector and the moment when it can be transmitted is known as

Table 1 Annual frequency classes

Relative Values given to map area	Number of days with Maximum temperature above 40 °C	Number of days with Minimum temperature below 0 °C	Number of days with Mean temperature above 20 °C
1	0–5	0–10	>180
2			90–180
3	5–15	11–30	<90
6	>15	31–60	
9		>60	

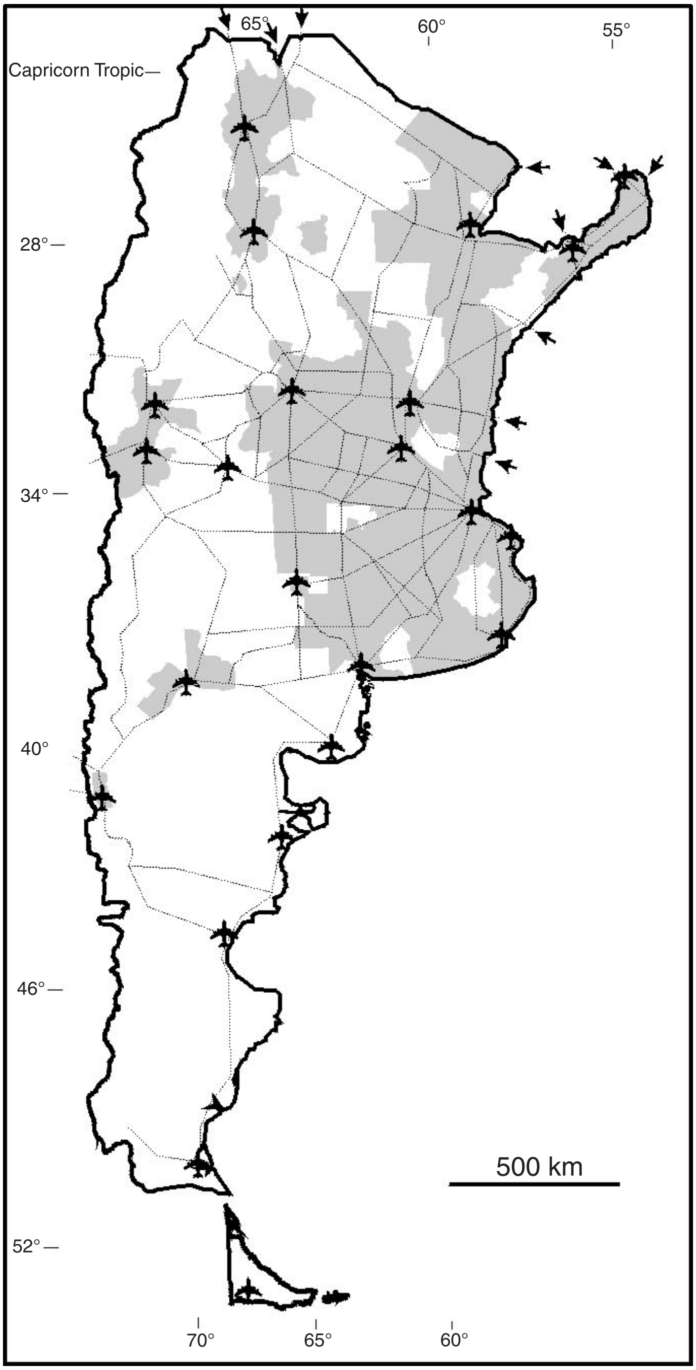

Figure 2 Demography and transportation. Dashed lines: main roads; aeroplane icons: main airports; shaded areas: more densely populated and urbanized political districts (areas having more than 10 inhabitants/km^2 or more than three cities/10 000 km^2); arrows: international paths. The two southern most arrows on the eastern limit of the country indicate the roads that concentrate the heaviest traffic burden between Brazil and Argentina. These roads go across Uruguay, which is free from endemic dengue.

extrinsic incubation period (EIP). This period is known to vary as a function of temperature (McLean *et al.* 1974; Watts *et al.* 1987), and a mathematical model describing the behaviour of the EIP as a function of temperature was developed by Focks *et al.* (1993a,b, 1995). Field studies on *Ae. aegypti* in tropical areas rendered survivals of 8.5 days (14° N, Sheppard *et al.* 1969); >9 days (4° S, Trpis *et al.* 1995), and 6–10.3 days (20° S, Muir & Kay 1998). At the northern limit of the vector distribution (Odessa 45° N), Korovitskii and Artemenko (Christophers 1960) reported

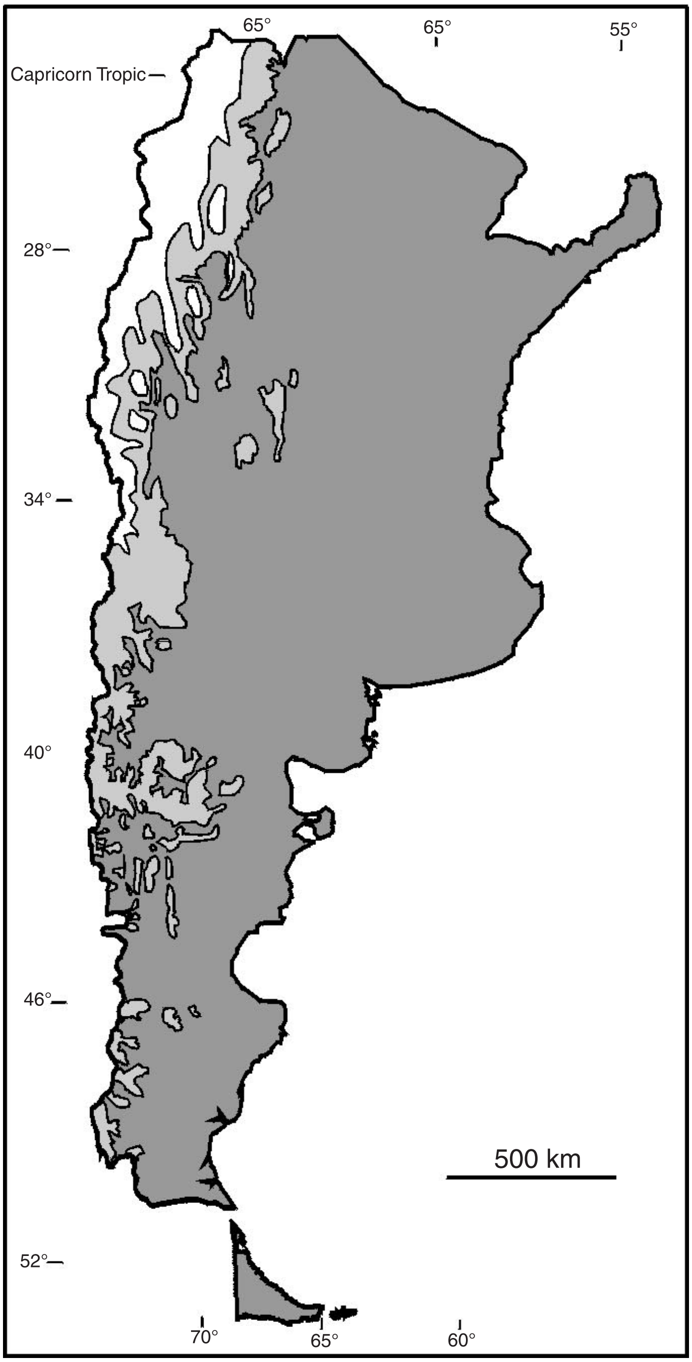

Figure 3 Altitude above sea level. White: areas excluded from the transmission risk (above 3000 m a.s.l.); light grey: between 1000 and 3000 m a.s.l.; dark grey: below 1000 m a.s.l.

survival periods of 10 days in warm rooms, 15 days outdoors and 18 days in basements. As Argentina represents the southern limit of the distribution of *Ae. aegypti* (ranging from 35° to 22° S) and its survival has not been studied, we chose 10, 15 and 20 days in order to cover a broad spectrum of life expectancies. The chosen values are higher than those mentioned in the literature so as not to underestimate the transmission risk.

The duration of the EIP in Argentina was estimated according to the model by Focks *et al.* (1993a,b, 1995)

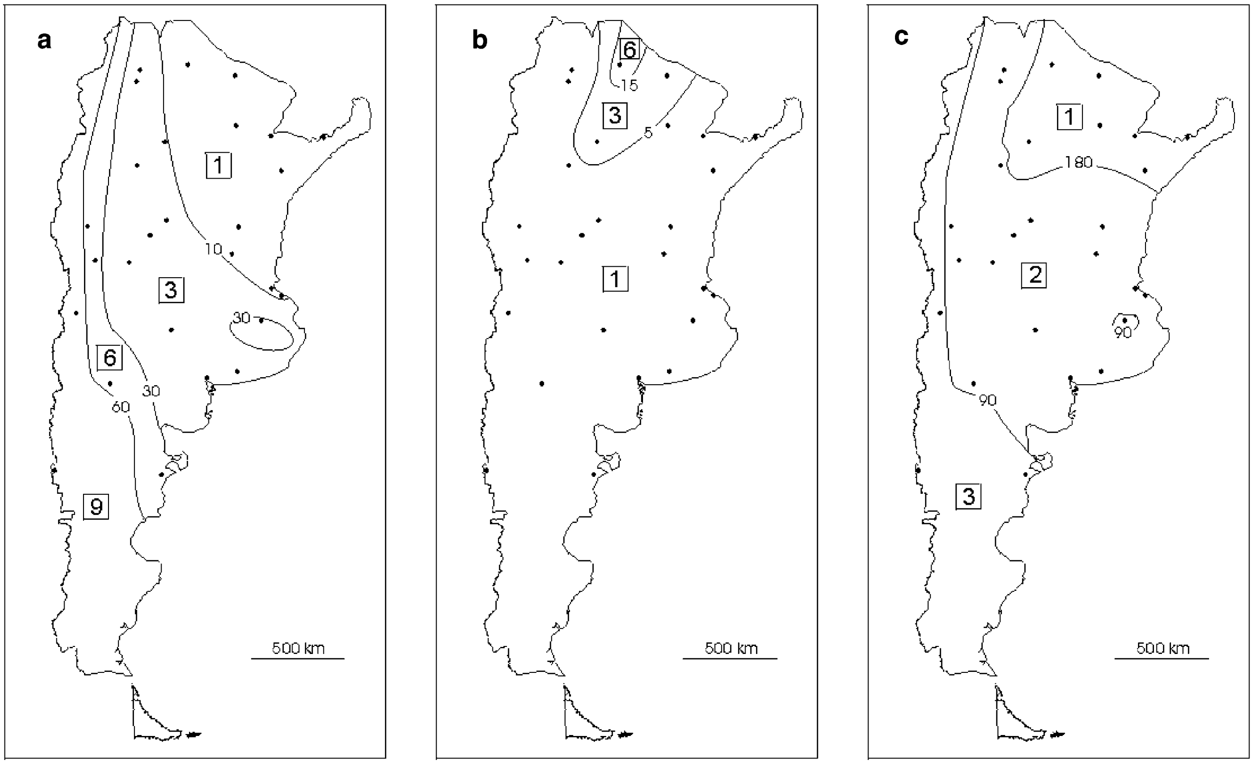

Figure 4 Extreme and mean temperature maps. Circles: meteorological stations; boxed numbers: relative values (inconvenience); contour lines: annual frequency of days with: (a) minimum temperature below 0 °C; (b) maximum temperature above 40 °C; (c) mean temperature above 20 °C.

using the parameters from Jetten and Focks (1996). Daily mean temperatures (calculated as the mean value between the maximum and minimum daily temperatures) from 1974 to 1990 were used to compute the proportion of EIP completed within each day, in 84 meteorological stations throughout the Argentine territory (data provided by the National Meteorological Service). Three scenarios with mosquito life expectancies of 10, 15 and 20 days were considered to assess the EIP completion during the mosquito life span. We assumed that the vector was potentially present in all localities, that it had bitten a viraemic person and carried the virus, and that its life expectancy was constant through the years and all over the country. For each one of the proposed scenarios, we calculated the corresponding potential EIP completion at each locality. For that purpose, the proportions of the EIP completed daily were added for periods of subsequent days equivalent to the mosquito life expectancy. If the result was >0.99, a value of '1' was given to the starting day of that period, otherwise a '0' value was assigned. The days on which the initiated EIPs can be completed before mosquito death were considered as days of possible transmission (DPT). For example: on 21 July 1975, in locality 'XX', considering a 10-day mosquito life expectancy, the proportions of the EIP completed on the 21st, 22nd, … 29th and 30th of July were added. If this sum was >0.99, we calculated that transmission would have been possible on 7/21/75 (that day represents 1 DPT). The number of DPT was added for each year between 1974 and 1990, for each one of the 84 meteorological stations. The median of each station during the 16-year period was used to interpolate contour lines (interpolating methodology as above mentioned, Figure 7a–c). Seasonal maps were built in a similar manner, but considering only a 20-day life expectancy scenario (Figure 8).

Results

Potential entrance of the virus

Figure 2 shows that the main roads and airports concentrate in the central and northern regions of the country. On

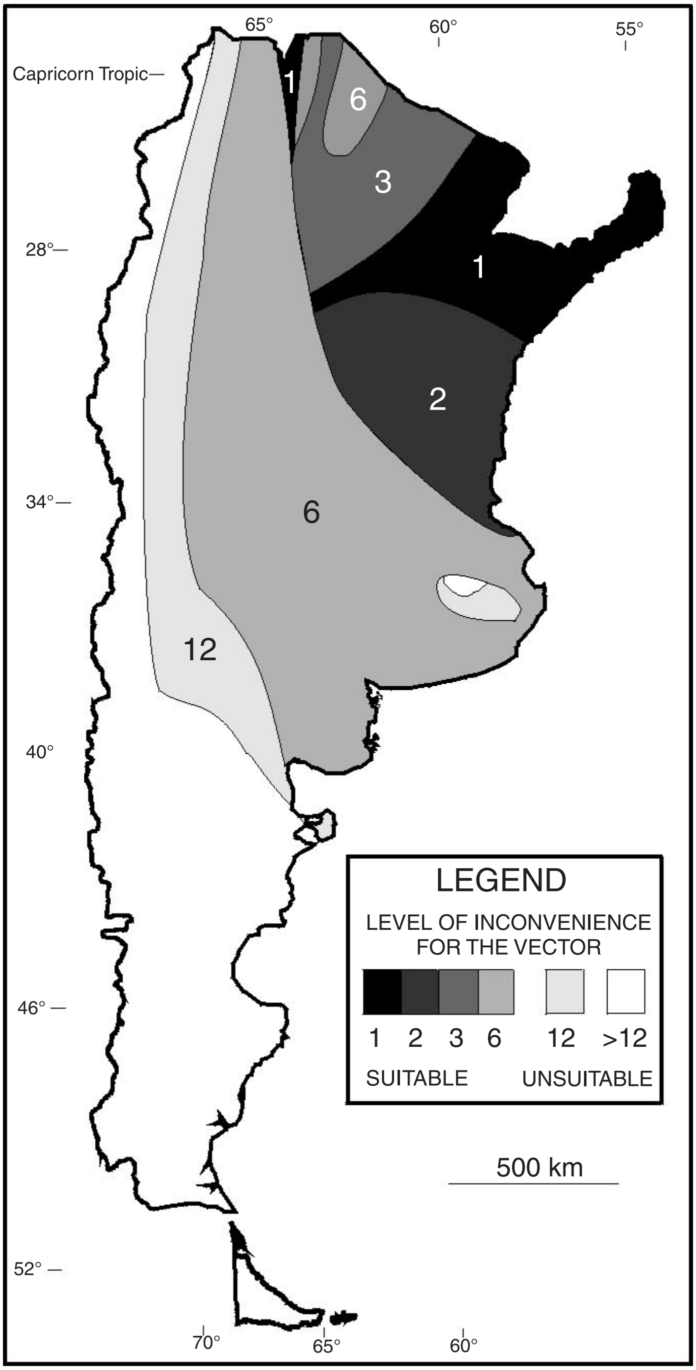

Figure 5 Thermal inconvenience index map. Higher values indicate increasing levels of inconvenience for the vector. Values of 12 and above are considered to be unsuitable for *Ae. aegypti.*

the other hand, the roads connecting Argentina with neighbouring countries (some of them having endemic dengue) are located at its northern and eastern borders. This suggests that the virus would mainly be introduced in those areas.

Environmental conditions for the vector

Figure 3 shows that altitude restrictions are limited to the western region of the country. Figure 2 shows that the districts with the highest densities of population and cities

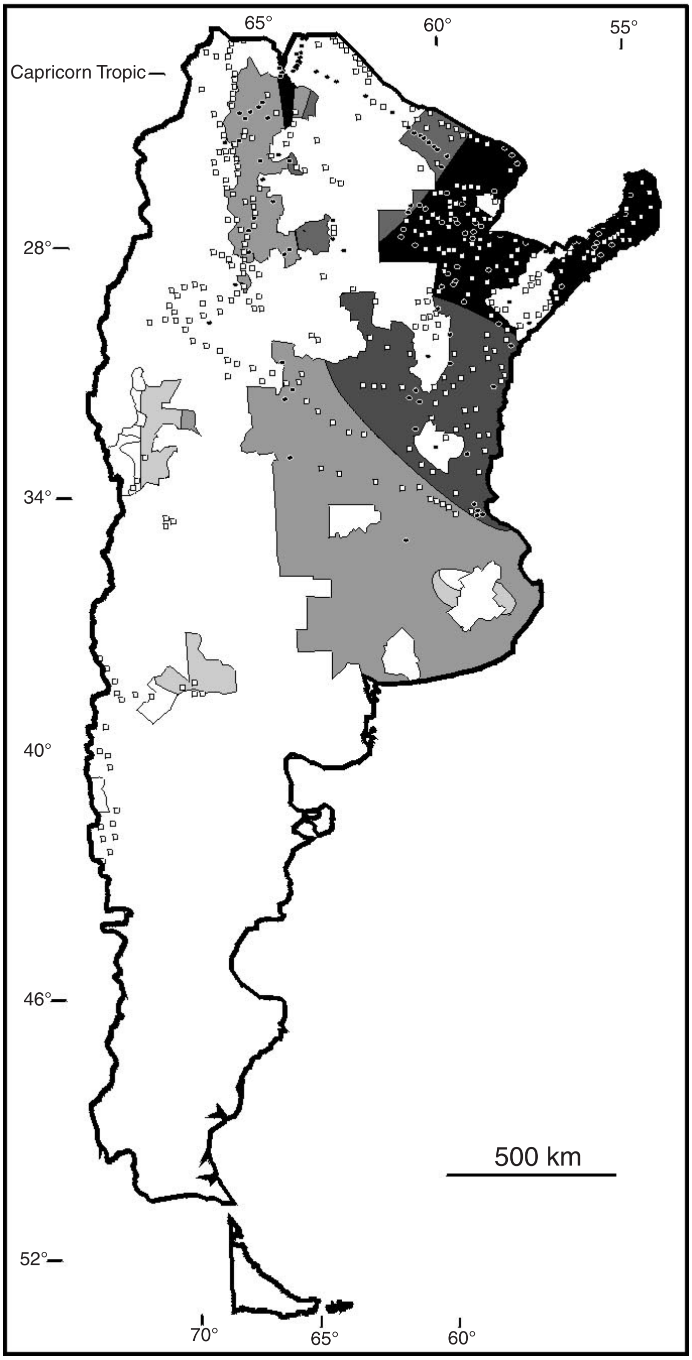

Figure 6 Environmental conditions for the vector. Black filled circles: positive localities; white filled squares: negative localities; shaded areas: conditions for the vector (darker areas being more suitable).

are mainly located in the central-eastern and north-eastern portions of the country. Minimum temperatures seem to be restrictive towards the south-west (Figure 4a). While favourable to the north-east, maximum temperatures appear to be restrictive in the northern end of the country (Figure 4b). Mean temperatures show a gradient of increasing favourableness from south-west to north-east (Figure 4c). The combined map of extreme and mean temperatures reveals that the most favourable thermal conditions for the development of the vector might be

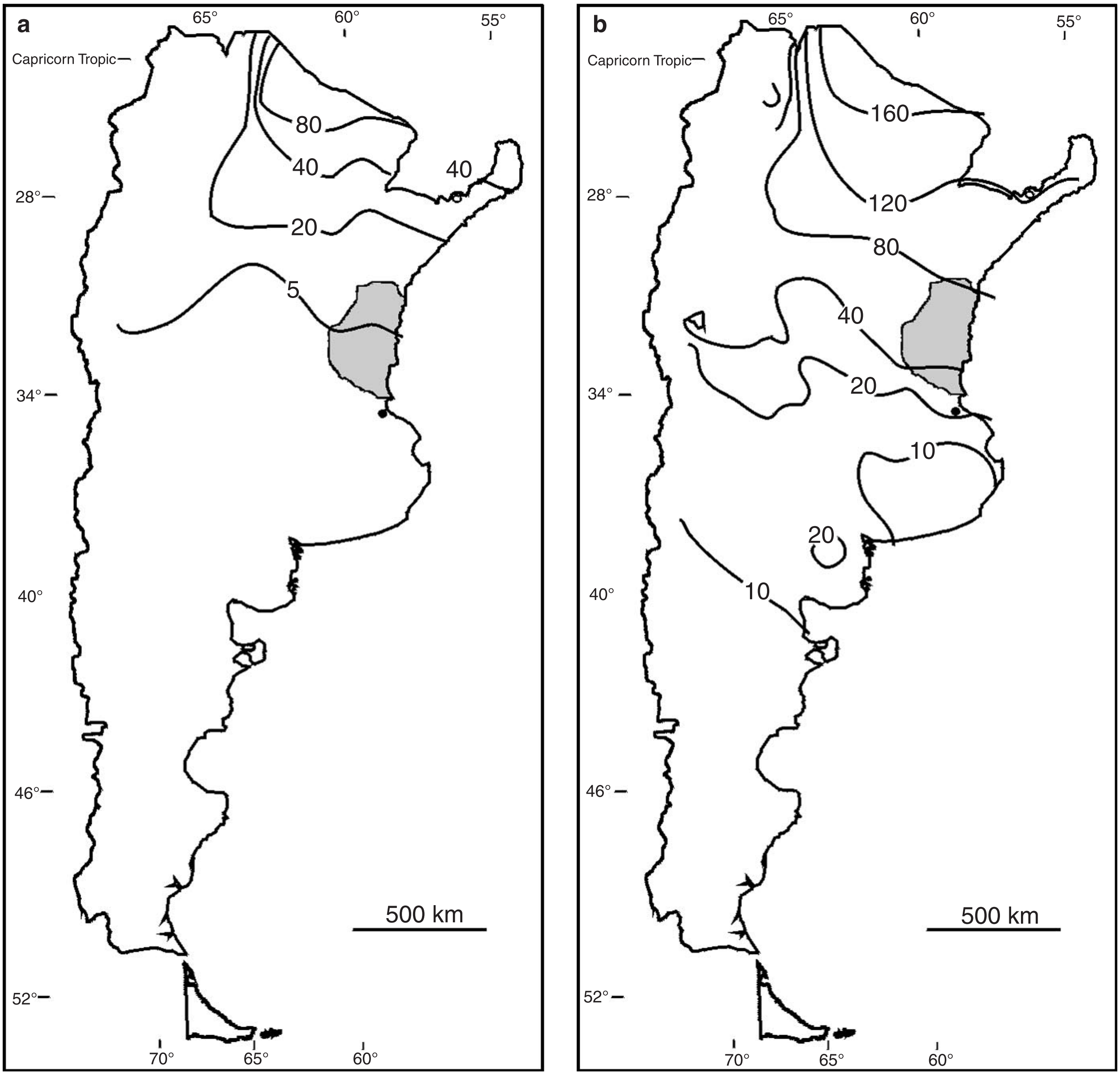

Figure 7 Annual frequency of DPT: number of days in which complete EIP iniciate (median for 1974–1990). (a) 10-day mosquito life expectancy scenario; (b) 15-day mosquito life expectancy scenario; (c) 20-day mosquito life expectancy scenario. Black filled circle: Buenos Aires City; blank circle: Posadas City; shaded area: Entre Ríos Province.

found in north-eastern Argentina and also in a wedge in the north-west (Figure 5). Figure 6 summarizes the environmental conditions for the vector. Historical information indicates that *Ae. aegypti* has never been found in areas of thermal inconvenience levels above 12. Thus, areas with levels exceeding this limit value were excluded from the potential transmission areas.

EIP completion

The number of days a year on which initiated EIPs could be completed (DPT) is shown in Figure 7(a–c) for 10, 15 and 20 expected days of life, respectively. Although the number of DPT varies considerably for the different life expectancies, the direction of the gradient remains constant (south-west to north-east). The EIP completion might be possible

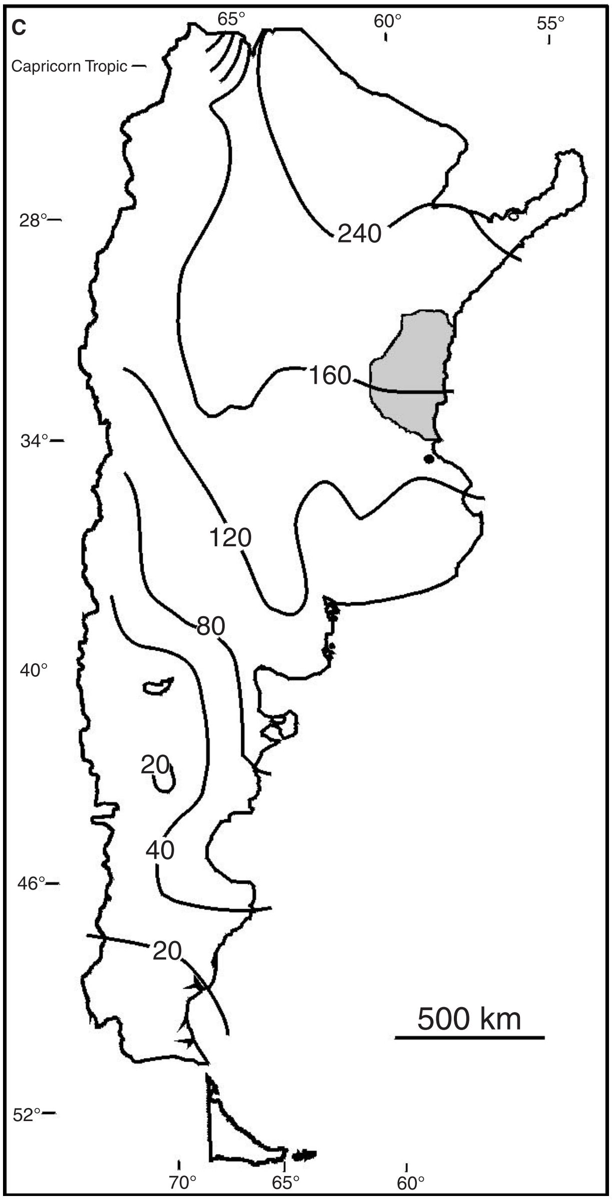

Figure 7 (*Continued*).

in the northern part of the country under any of the three scenarios, in the northern and centre under the second one (15 days), and almost anywhere, except the Andes Cordillera and southern Patagonia, under the third one (20 days) (Figure 7a–c).

Assuming 15-day life expectancy, Posadas City would have four times the DPT of Buenos Aires City (120 *vs.* 25 DPT; Figure 7b), whereas under a 20-day scenario it would only be double (240 *vs.* 120 DPT; Figure 7c). The best areas for EIP completion in Argentina (more DPT) would be near the centre of Formosa Province (northern part of the country) (Figure 7a–c). This is to the west of the areas with best thermal conditions for the vector (Figure 5). Under a 10–15-day scenario (Figure 7a,b), the zones of possible EIP completion are included in the vector suitable areas (Figure 6). Assuming 20-day mosquito life expectancy (Figure 7c), suitable areas for the vector might have more than 80 days a year of potential virus transmission. During all four seasons, the EIP would be completed in those areas most favourable to the mosquito. In autumn and winter, the EIP would only be completed in the northern part of the country, whereas in summer and spring, that would be the case in almost any region (Figure 8).

Discussion

Of the few attempts to map risk of dengue, the most noteworthy is the description of risk factors in individual localities in Puerto Rico by Rodriguez-Figueroa *et al.* (1995). The Ministry of Health in Argentina has made available only a map constructed by expert opinion (Figure 10; R. Boffi, personal communication). This classifies the country into three zones (priority 1–3, with priority 1 having the highest risk), based on the historical distribution of *Ae. aegypti* and possible routes of entry of virus.

A risk map based on actual cases cannot be constructed as Argentina is not endemic for dengue. However, as demonstrated by the mathematical models of Focks *et al.* (1993a), key factors determining transmission risk for dengue are the duration of the virus' transmission cycle and survival of the vectors. This insight made it possible for us to produce maps of relative transmission risk for the entire country using data on daily temperatures and a range of plausible vector survival rates to estimate the number of DPT.

The epidemic in Entre Ríos Province during February–March 1916, provides some indirect evidence of what might be the most appropriate vector life span. Assuming similar climatic conditions to those of 1974–1990 and a 10-day mosquito life expectancy, there would have been only five DPT in Entre Rios, so an epidemic of the scale recorded would have been unlikely. If the mosquito life expectancy had been 15 days, 40–80 DPT would be expected (Figure 7b), with transmission declining at the beginning of autumn (April) (compare Figures 7b and 8). The end of the epidemic could then be attributed to the fall in temperatures preventing completion of the EIP. Alternatively, if the life expectancy were 20 days, 140–200 DPT would be expected (Figure 7c) and EIP completion would

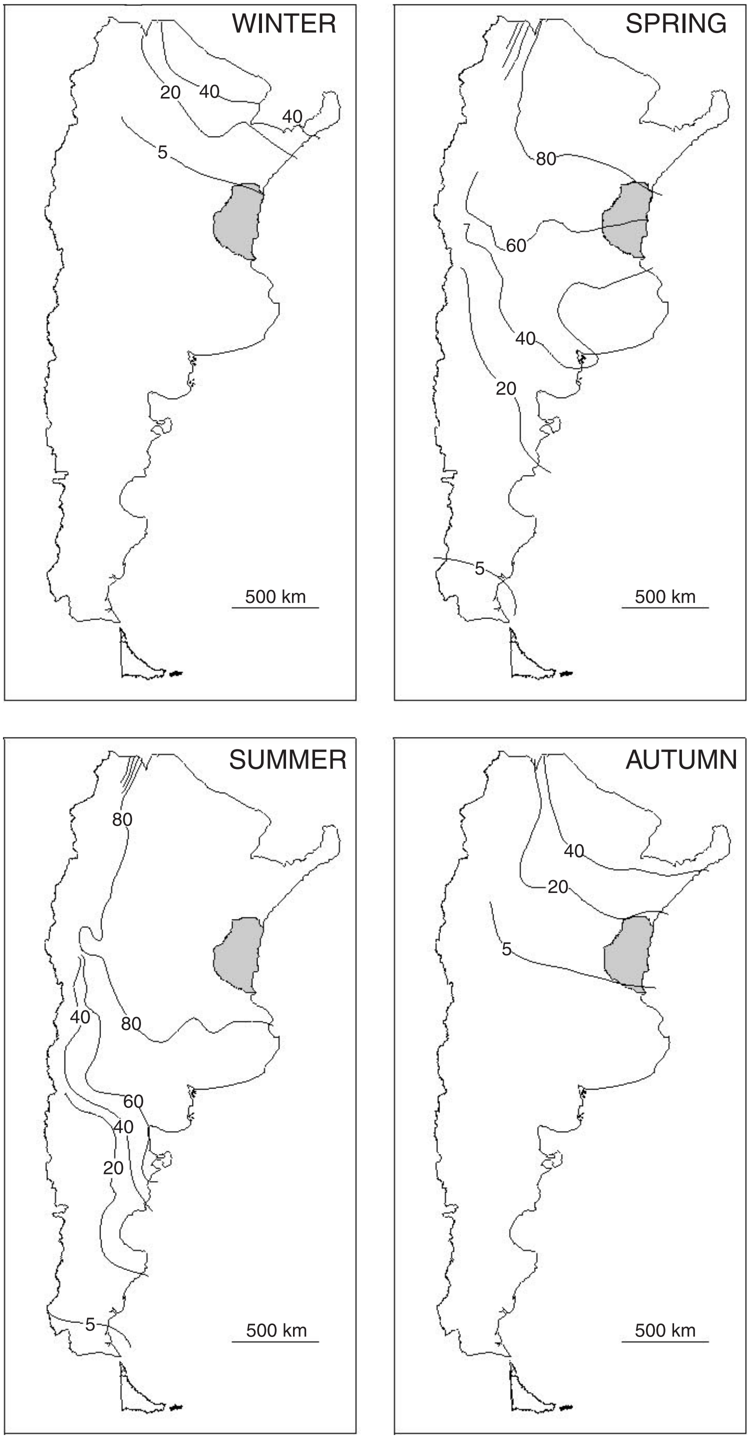

Figure 8 Seasonal DPT considering a 20-day mosquito life expectancy (median for 1974–1990). Shaded area: Entre Ríos Province.

continue in autumn. If this was the case, the epidemic probably ended because of a seasonal decline in the *Ae. aegypti* population, as has been observed during the autumn in Buenos Aires (Schweigmann *et al.* 1997). The 1916 epidemic certainly did not end because the human population acquired immunity, since the cities affected first

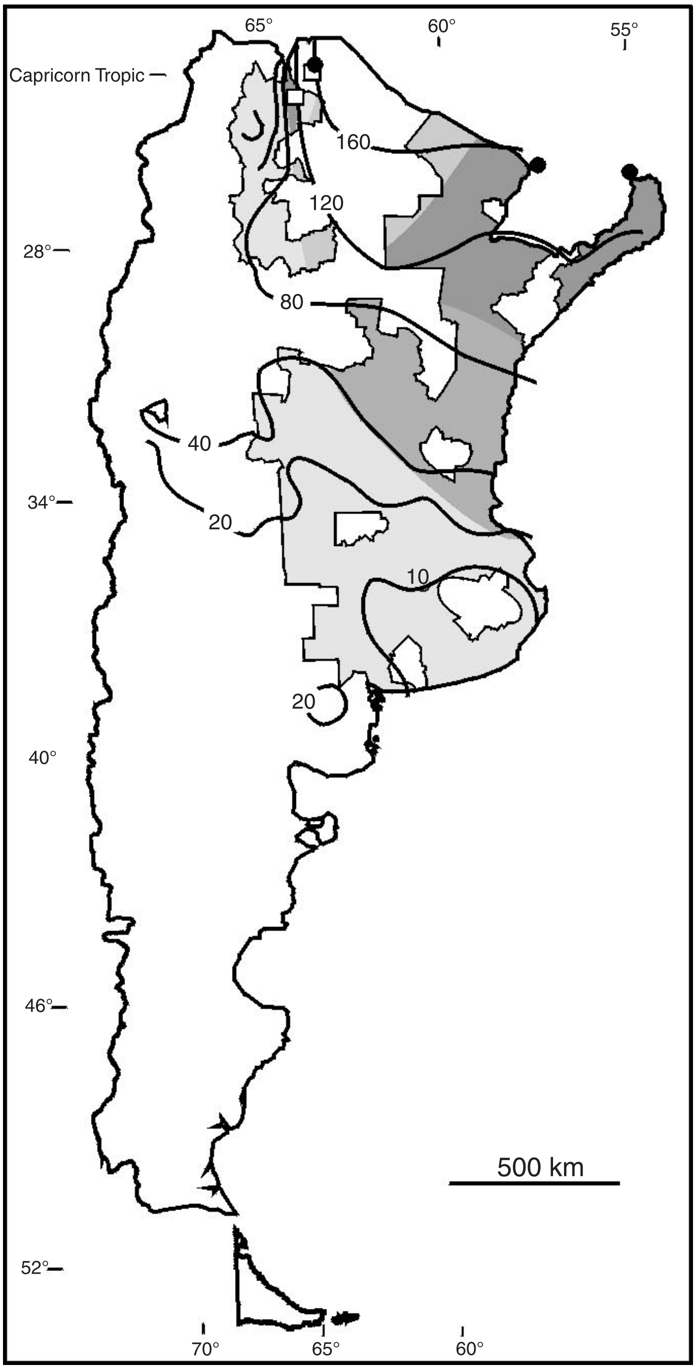

Figure 9 Dengue transmission risk map. Shaded areas: conditions for the vector (darker areas being more suitable); contour lines: number of DPT (higher values indicate better conditions for the EIP completion); black filled circles: localities with recently detected dengue epidemics; white squares: localities with recently isolated cases.

had much higher incidences than those affected last (only 15%).

Based on this argument, we chose Figure 9 as dengue transmission risk map for Argentina. The isolated cases of the disease detected in 1997 in the north-west (Avilés *et al.* 1999), and the epidemics of Tartagal in 1998, Foz do Iguazú (Brasil), and Asunción (Paraguay) in 1999 (R. Boffi, personal communication), occurred within or close to the high-risk zones defined in this map, thus supporting the validity of our model.

The construction of a national-level model using easily accessible data on a coarse geographical scale implicitly

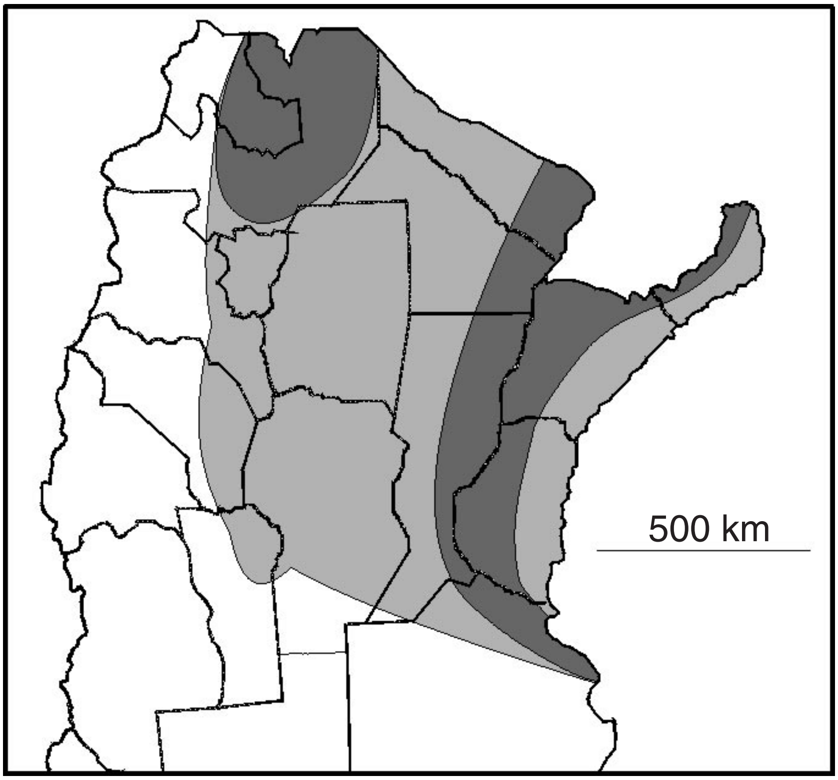

Figure 10 Dengue risk map of the National Health Ministry. Dark grey: priority 1 (higher risk); light grey: priority 2; white: priority 3. (R. Boffi 1997, personal communication).

assumes that the effects of microclimatic variation are uniform over the whole country. This assumption of homogeneity may be incorrect. For instance, *Ae. aegypti* tends to seek out humidity and to shelter from excessive heat so high temperatures may not limit its distribution if resting places can be found (Christophers 1960). While we estimated that there are nearly 15 days per year with temperatures above the upper limit for the mosquito in northern Argentina, it may be that these temperatures reduce the mosquito population without completely precluding transmission. We plan finer-scale studies of effects of microclimatic and microhabitat variation using GIS for those cities with high data densities.

Moreover, the new maps do not improve on the model of Figure 10 as regards arrival of the virus. The risk of importing the virus is increased by urbanization and high human population density, as is that of transmission, because *Ae. aegypti* is a domestic mosquito. However, we were only able to make superficial use of demographic data because there are no suitable publications on which to base a quantitative model of the relationship between transmission risk and human population density.

It would also be possible to elaborate our model in several other ways. We did not consider the number of days for which mosquitoes survive in the infective state after completing the EIP; this would give a better estimate of relative transmission potential. Moreover, we chose to assign a fixed life expectancy to the vector rather than modelling the survival of the mosquito as a function of environment conditions. Mosquito survival in the laboratory is optimal at 2 or 3° below the optimal activity temperature (Christophers 1960) and it is probable that the virus development is correlated with the metabolic rate and thus activity of the mosquito. In accordance with this, the areas with the best conditions for mosquito survival in our model do not match exactly with those areas where virus development is shorter. Regarding the role of the EIP in dengue transmission, differences in the EIP completion among the best areas for its completion and the best areas for the vector would be two to four times higher for a 10-day life expectancy, up to two times higher for 15 days and <0.5 times higher for 20 days.

Although Sheppard *et al.* (1969) found that there was no seasonal variation in life expectancy of *Ae. aegypti* in Thailand, its survival is temperature-dependent in the laboratory and probably also in Argentina, where variation in temperature is considerable. The most densely populated areas in the centre-east have a markedly seasonal temperate climate. Buenos Aires is almost at the southern edge of the distribution of *Ae. aegypti* and adults are not detected during the winter (Schweigmann *et al*. 1997).

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