Climate change and infectious diseases in Europe: leishmaniasis and its vectors in Spain

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the results of this review; the revised tables are available in the webappendix.

In our reanalysis, we clarified definitions of the sample size used, including only those patients from each study with culture-confirmed multidrug-resistant tuberculosis who had started a second-line drug regimen. Characteristics of patients and treatment were established specifically for this subset of patients. In the paper by Munsiff and colleagues,[1] only 610 of 856 patients were treated with second-line drugs. Therefore, our recorded prevalence of HIV of 58% was on the basis of only the 352 patients infected with HIV from this smaller sample. Our misclassification of the proportion of patients in the cohort of Munsiff and colleagues that had previous treatment for tuberculosis has also been corrected in our revised tables.

Additionally, in our reanalysis we more precisely defined treatment programmes as having used "directly observed therapy (DOT) throughout treatment" if all patients received inpatient DOT and more than 50% received outpatient DOT. Our new definition includes the cohort of Munsiff and colleagues, in which 68% of patients started outpatient DOT (Munsiff SS, Alice Hyde Medical Center, personal communication).

Among all included patients with multidrug-resistant tuberculosis, the proportion achieving treatment success with second-line drugs was 64% (95% CI 58–68). Studies using individualised treatment regimens achieved 65% (95% CI 59–70) treatment success compared with 55% (95% CI 37–75) in studies using standardised treatment regimens. We assessed the effect of each study characteristic independently (webappendix, table 2). Overall, the proportion of patients treated successfully did not differ significantly on the basis of any individual study characteristic, as published previously. By contrast with our previous study, the pooled proportion of treatment success among the 12 studies that combined DOT throughout treatment with treatment duration over 18 months was substantially, but not significantly, greater (71%, 95% CI 62–79) than that in the 20 studies that did not have both features (59%, 95% CI 53–65). Our previous analysis suggested that there was a slightly smaller, but statistically significant, difference between these two groups.

The corrections of the data in our initial report highlight the importance of the use of predefined covariates and duplicate data abstraction when doing a meta-analysis. Our updated results remain consistent with those originally reported. Although the difference in treatment success achieved through the combination of treatment duration over 18 months and DOT throughout treatment is no longer statistically significant, the effect size remains substantial. The change in significance might be because of study heterogeneity, a less restrictive definition of what constitutes DOT throughout treatment, and insufficient power.

Meta-analyses provide more powerful conclusions by incorporating a greater sample size across more settings than can be done in a single study. However, heterogeneity in study populations, methods, and reporting techniques across studies limits the use of meta-analyses. Randomised clinical trials comparing programmatic and treatment regimen differences for patients with multidrug-resistant tuberculosis are needed and would provide a stronger evidence base for improving treatment outcomes in this population.

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We declare that we have no conflicts of interest.

1 Munsiff SS, Ahuja SD, Li J, Driver CR. Public-private collaboration for multidrug-resistant tuberculosis control in New York City. *Int J Tuberc Lung Dis* 2006; **10:** 639–48.

Climate change and infectious diseases in Europe: leishmaniasis and its vectors in Spain

It was with genuine interest that we read Jan C Semenza and Bettina Menne's article[1] published the June issue of *The Lancet Infectious Diseases*. We wish to acknowledge the authors' bravery for asserting that the "contribution of socioeconomic development, urbanisation, land-use, migration, or globalisation to infectious disease transmission is in some cases more important than climate change, but quantification

is intricate". We believe that too much importance is sometimes attributed to global warming in the context of vector-borne diseases, and other factors such as those highlighted by Semenza and Menne are too often overlooked.

On page 369 the authors express a similar idea, but we believe the assertion made on page 368 to be incorrect: "Sandfly distribution in Europe is south of latitude 45°N and less than 800 m above sea level, although it has recently shifted to a latitude of 49°N." Here we set out the data that shows why we disagree.

With respect to recent shifts in latitude, we do at least know that *Phlebotomus perniciosus* was captured on the Isle of Jersey in 1927[2] (located roughly at 49°N), and in various French territories located at similar latitudes in 1954 and 1985.[3,4]

It seems even more misguided to set an altitude limit for sandflies at 800 m. In Spain, Nájera-Angulo[5] listed captures of sandflies in Cercedilla (Madrid; 1214 m), Güejar Sierra (Granada; 1088 m), and Sigüenza (Guadalajara; 1005 m). In Sierra Nevada (southern Spain), *Sergentomyia minuta* and *Phlebotomus ariasi* were captured at 1750 m,[6] and these two species plus *Phlebotomus perniciosus* at 1600 m. Furthermore, the captures at elevations greater than 900 m above sea level made up 58·4% of the total captures.

Human cutaneous and visceral leishmaniasis have also been diagnosed in people (normally children) who live at elevations greater than 800 m above sea level. In Granada province,[7] cases of visceral leishmaniasis were recorded in Murtas (1114 m), Huetor Santillán (1015 m), Cadiar (916 m), and Alfacar (910 m); and in Almeria province[8] in Laujar de Andarax (918 m) and Felix (815 m). Cutaneous leishmaniasis was diagnosed in Murtas, Cádiar, and Orce (915 m), and Válor (900 m).[9] The leishmanin skin test recorded 3·4% positivity at elevations greater than 1100 m.[10]

With respect to the natural reservoir, 7·51% of the dogs from locations with altitudes of 750–1100 m above sea level had a titre of 1/160 or greater, and 1·03% of the dogs from places at higher than 1100 m.[10,11] Similar results were found in 2009.[12] In summary, in southern Spain there are numerous villages located at elevations greater than 800 m in which sandflies, cutaneous leishmaniasis, visceral leishmaniasis, and canine leishmaniasis are present.

It would seem that the errors come from the methods used in the article in question:[1] the data from PubMed and the period chosen. PubMed does not cover nationally published journals without impact factor, which allows useful data to be overlooked. Another cause of the errors is the period selected (1966–2009): an important period in the study of leishmaniasis is excluded that, in the case of Spain, would coincide with the maximum numbers of the disease in human beings (1912–1966).[13,14]

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