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### From the authors:

We read with interest the correspondence from J. Noeske and colleagues on the potential effect of cross-border migration on the multidrug-resistant tuberculosis (MDR-TB) treatment programme in Cameroon, elicited by our article on the framework for TB elimination in low TB incidence countries [1]. The manuscript highlights some of the consequences of cross-border migration for caring for people with TB and ending this epidemic, as well as relevant issues on clinical and public health management of MDR-TB in Cameroon.

Cross-border migration significantly contributes to TB epidemiology in many low incidence countries in Europe and elsewhere (figure 1) [3].

The effect is higher in countries that are close to the pre-elimination threshold, mainly since these countries are quite often attractive destinations due to a social environment more favourable to the needs of the migrants. In some low-incidence countries cross-border migration caused either by political, economic or environmental reasons is already becoming the main challenge to countries well advanced in the elimination of TB.

The vision of TB elimination is a global one: it should be immediately pursued in low TB incidence countries, and their experience should hopefully inspire action in countries with higher TB incidence.

As in the Cameroon example, people may migrate to access TB care of perceived higher quality or because in their original settings services are absent [4]. Others may voluntarily leave the host country during TB treatment, while some immigrants (in conflict with basic human rights and public health principles) are deported at the time of diagnosis or during treatment. In such cases, insufficient coordination of TB care services across borders or limited capacity at the receiving end can lead to a low quality of care (discontinuation of case holding), continued transmission and incomplete TB surveillance [5]. As pointed out by Noeske and colleagues, migration in search of quality healthcare may happen specifically to obtain second-line TB treatment which is not available in the country of origin. Programmes in the country where the diagnosis is made have the ethical imperative to treat patients until cure or to ensure that treatment is provided until the patient is cured [3]. Noeske and colleagues warn about the risk that a flow of migrants affected by drug-resistant TB would pose to the efforts of the host country to end TB and MDR-TB, although little evidence of transmission is available, particularly in Africa where more studies are needed. The authors advocate for joint measures across borders to contain the risk. Even in low incidence countries the influx of migrants with highly resistant forms of TB has already translated into challenges for contact investigation efforts, outbreak management and surveillance [6]. The same would



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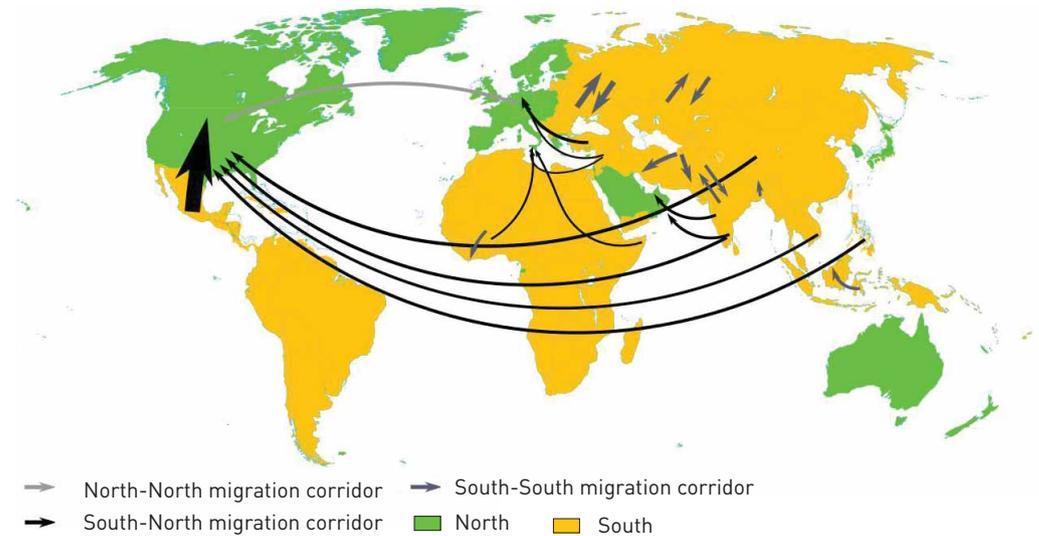


FIGURE 1 Map of global migration flows. Reproduced and modified from [2] with permission from the publisher.

apply to Cameroon, which offers an example of the deleterious consequences of the inability to ensure appropriate surveillance on drug resistance due to poorly coordinated cross-border migration.

Cross-border migration is a major phenomenon in this century and the related consequences on the health of both migrant and native populations cannot be ignored [7]. The current immigration emergency observed in the Mediterranean basin is a signal: in the first 8 months of 2015 322 500 refugees and asylum seekers landed on European shores (115 500 in Italy; 204 954 in Greece; 1953 in Spain; and 94 in Malta) escaping war, political unrest, economic crisis, and the imbalance between population growth and job opportunities in the countries of origin. This contrasts with 219 000 recorded in 2014 [8]. Today, coordinated public health mechanisms to guarantee TB prevention, diagnosis, treatment and care across borders are not in place in most settings, despite resolutions and statements by bodies such as the World Health Organization (WHO) and the European Union [9]. Several potentially effective interventions have been identified and recommended starting from the political action required to ensure the essential regulatory health policies are implemented, including those related to containment of transmission of infectious diseases that must be founded on sound ethical principles and respect of human rights [3]. Furthermore, specific regulations are necessary to guarantee access to healthcare for undocumented immigrants, compounded with cross-border collaboration and the establishment of referral systems with contact-tracing and information sharing systems. Platforms to exchange countries' experience, best practices and challenges will help countries to address regional and cross-border problems by standardised and compatible mechanisms [10].

Disentangling the puzzle of cross-border migration is first of all a political issue: national governments, TB programmes, international agencies and other stakeholders are urged to find the way of building a joint effective response. As described in the correspondence from Cameroon, migration flows from Equatorial Guinea pose challenges to the programme in Cameroon and threatened the effectiveness of the short-course MDR-TB regimens being operationally tested in the country with success. However, the authors wrongly imply in their letter that the WHO ignores evidence and unnecessarily recommends a MDR-TB treatment regimen that is less effective, longer, more costly and more toxic. This is misleading, and until sufficient evidence is collected and properly evaluated, the WHO will continue supporting countries to use a short MDR-TB treatment regimen only under operational research conditions, as it has done in the case of Cameroon. A proper assessment of shorter regimens, their advantages and risks is necessary before new recommendations are made and disseminated.

In an era of global movements where transmissible diseases do not respect borders, national programmes need to equip themselves to cope with migrants and their health problems, and identify additional national and international support to fund this extraordinary effort.



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**Cross-border migration: migrant and native populations' health cannot be ignored by national TB programmes** <http://ow.ly/U7TO4>

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# Is there hope of improving the prognosis of pulmonary tumour thrombotic microangiopathy?



*To the Editor:*

We read with interest the letter by KUMAR *et al.* [1] reporting two new cases of fatal pulmonary tumour thrombotic microangiopathy (PTTM). As discussed by the authors, *ante mortem* diagnosis of PTTM is difficult to confirm because of a rapid progression of the disease. The disease is characterised histopathologically by microscopic tumour emboli and remodelling of the pulmonary vasculature, leading to right heart failure, severe hypoxaemia and, ultimately, death in the very short term, within a few hours or days following admission.

However, some cases have also been reported in the literature with higher survival of a few months that were not analysed in detail by KUMAR *et al.* [1], who cited only one of these cases [2]. After reviewing all cases published in PubMed-indexed journals, since the original description by VON HERBAY *et al.* [3], we found six additional observations of such prolonged survival after a diagnosis of PTTM (table 1) [4–9]. These cases drew our attention because they could also be interesting to highlight the physiopathological mechanisms of PTTM and identify potential targeted therapies for this fatal condition.

One of these cases reported prolonged survival of a patient treated for a colorectal cancer with chemotherapy including bevacizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody [7]. VEGF is known to have a specific role in angiogenic endothelial cells and, thereby, in promoting the proliferation of endothelium involved in embryonic development and tumour angiogenesis. A recent clinical analysis of 30 autopsy cases observed that the immunohistochemistry of tumour cells