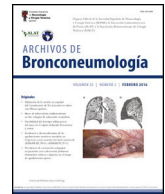




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## Editorial

### MSCA-RISE: EUSAT-RCS TB Research Consortium: Challenges and Opportunities in Tuberculosis Research

Tuberculosis (TB) remains one of the deadliest infectious diseases, with a growing need for innovative approaches to tackle its persistent threat, especially in underserved and high-risk populations. Joining the effort to END TB by 2030, proposed by the World Health Organization (WHO),<sup>1</sup> the EUSAT-RCS consortium initiated in 2019, and was funded by the Marie Skłodowska-Curie Actions (MSCA) Research and Innovation Staff Exchange (RISE) program (grant number: 823890) until March 2024.<sup>2</sup> The consortium fostered a collaborative network between academia and the private sector from Europe, Paraguay and South Africa and has built TB research capacity through multidisciplinary studies and impactful initiatives focussing on the most vulnerable, high risk groups in society.

The establishment of the EUSAT-RCS research hub in Paraguay exemplifies the consortium's commitment to durable, and most importantly, locally driven TB research. This collaboration is more than just another TB research site; it is a long-term asset for the Latin America region, designed to support TB research and healthcare initiatives long after the project funding concludes. The consortium connected local researchers with global experts, fostered knowledge exchange and provided advanced training. Over 190 exchange months with early stage – and experienced researchers from 9 different institutes were accomplished in 5 years. Public Paraguayan institutions such as the National TB program, the National Reference hospital (INERAM) and Laboratory and the National University's Research Institute have all gained knowledge, skills, and established important networks for troubleshooting and collaborations.<sup>3</sup> Finally, as an example of career development, 6 PhD projects were linked to EUSAT-RCS, articulating the consortium with specific competitive funding sources. The EUSAT-RCS network continues its career support actions with ongoing PhDs and postdoc positions.

The TB epidemic in Latin American prisons is a major public health concern, with a rapidly increasing TB incidence in the past decade in contrast with the decline in other areas.<sup>4</sup> Poor living conditions and limited access to screening and healthcare come after a steady increase in incarceration rates, making the population deprived of liberty a particularly vulnerable group. The consortium focused on innovative approaches for mass screening in prisons. The PriNose study (NCT04407325)<sup>5</sup> evaluated the performance of an electronic nose to enhance TB screening, compared to a solid clinical and microbiological evaluation and AI-powered chest X-ray. The study did reveal a staggering prevalence of TB within these prison populations – so high that it signals an impending public health catastrophe. We expect to make the results available by

Q2 2025. Another innovation in this study was the use of a video film to support the written informed consent for those with limited literacy.<sup>6</sup> This novel approach was evaluated with a nested qualitative study on a subgroup of participants (Schippers et al., manuscript under review). Finally, a third study evaluated the 'cascade of care' for our PriNose study participants that were diagnosed with TB to make sure they started and finished treatment, as we handed these patients over to the National TB program after establishing the diagnosis (manuscript under preparation). Overall, the PriNose study provides a comprehensive analysis of the situation of TB in Paraguayan prisons. This will serve as basis for the urgently needed interventions to start improving the harsh reality of TB in vulnerable, confined communities. The preliminary results and possible strategies were discussed in the Alliance Meeting in March 2024 held in Asuncion and synthesized in a white paper. This is a call for action urging the health authorities to prioritize TB screening, prevention and (prophylactic) treatment, as recommended by the WHO.<sup>7</sup> The consortium will work with local health authorities to design and implement strategies to combat this looming catastrophe.

Another area of focus of the consortium was to improve the outcomes of difficult-to-treat TB by optimising rifampicin doses. Summarising previous evidence, we performed a systematic review and network meta-analysis showed that the optimal rifampicin dose, a 2.5–3.5 times higher than that used in current first-line standard of care, is safe.<sup>8</sup> However, most trials focused on young people with low comorbidities and moderately severe pulmonary TB. This gap of evidence informed the design of the RIAItra trial, an international phase 2b/c open-label clinical trial, evaluating safety and efficacy of optimized doses of rifampicin in people with a higher risk of treatment failure and relapse (EudraCT: 2020-003146-36).<sup>9</sup> The setup of this study was an excellent opportunity to improve the clinical trial capacity across several Paraguayan institutions. The results of this trial may have far reaching implications by demonstrating that an optimized dose of rifampicin is both safe and effective across the most vulnerable patients. Future phase III clinical trials with optimized rifampicin dose might then have a short list of exclusion criteria for potential study participants, achieving the WHO adagio: "leave no one behind".

Through the durable research hub and innovative studies like PriNose and RIAItra, the EUSAT-RCS consortium is addressing the urgent need for targeted, effective interventions in TB endemic regions. By focusing on high-risk populations and prioritizing inclusivity in treatment trials, EUSAT-RCS exemplifies how international research collaborations, supported by programs like MSCA-RISE,

<https://doi.org/10.1016/j.arbres.2025.03.004>

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Please cite this article as: C. Magis-Escurra, J. Espinosa-Pereiro, L. Gomez Paciello et al., MSCA-RISE: EUSAT-RCS TB Research Consortium: Challenges and Opportunities in Tuberculosis Research, Archivos de Bronconeumología, <https://doi.org/10.1016/j.arbres.2025.03.004>

can make strides toward tackling the world's most pressing health issues.

In conclusion, the EUSAT-RCS consortium has been more than just a coincidental network of researchers; it is a testament to the power of resilient, sustainable partnerships. The consortium will continue trying to drive TB research toward a future where effective diagnostics, treatments and preventive measures are accessible to all, no matter how marginalized or vulnerable a person may be. As the consortium moves forward, it continues to embody the commitment to equitable healthcare solutions that will, ultimately, bring the world closer to ending TB.

### Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work the author(s) used ChatGPT in order to check grammar. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

### Funding

Marie Skłodowska-Curie Actions (MSCA) Research and Innovation Staff Exchange (RISE) program (grant number: 823890).

### Conflicts of Interest

None to declare.

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