

The ethics of including PDL in TB vaccine trials

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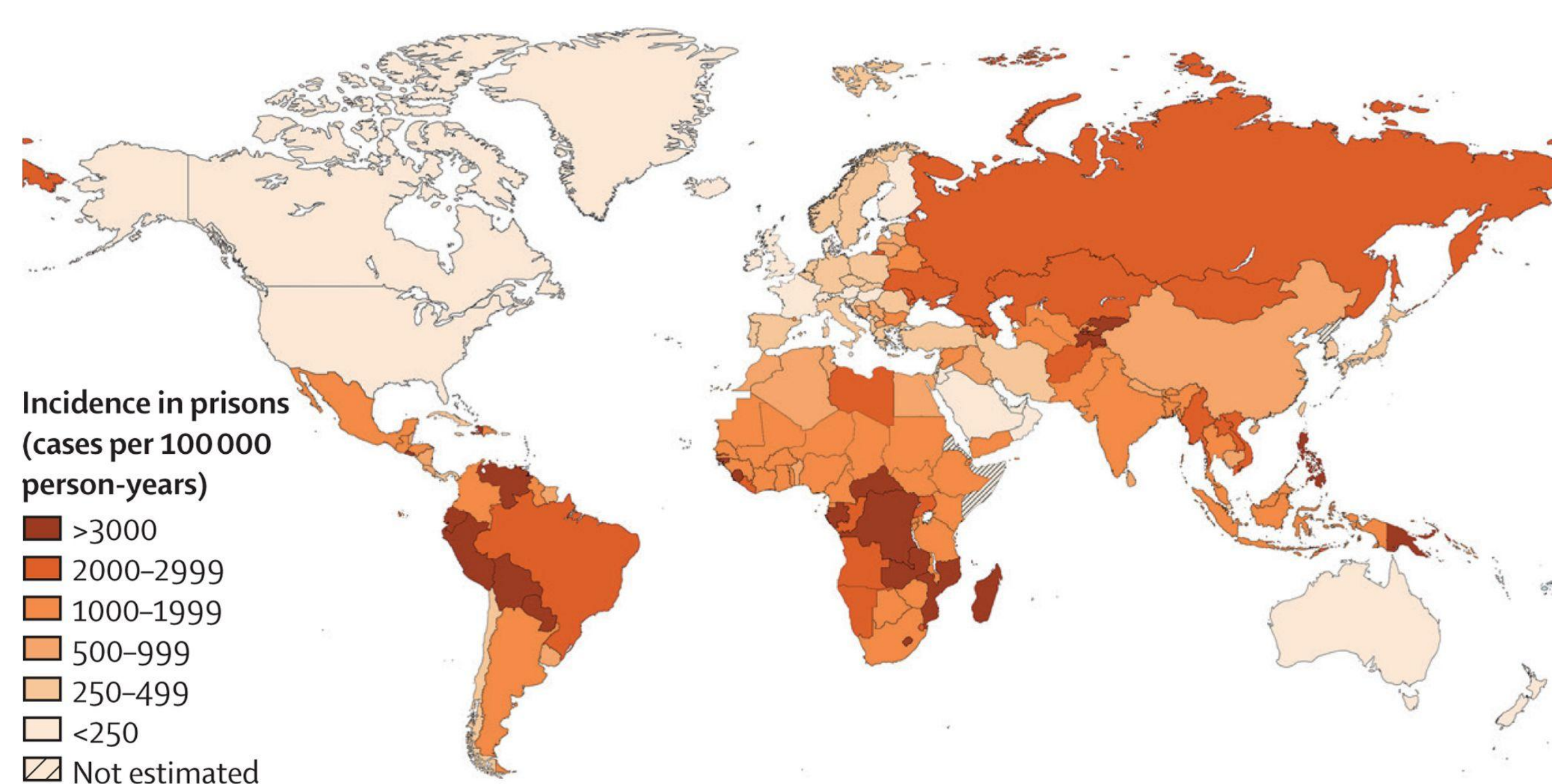
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Background

Developing a safe and effective vaccine against tuberculosis (TB) for adolescents and adults could have a major impact on the global TB burden. In some countries, e.g. Brazil, prisons concentrate >50 times the TB case burden as the general population and would be an epidemiologically favorable setting for testing TB vaccines.

Due to a history of abusive treatment of persons deprived of their liberty (PDL) in medical research, and many countries' wrongful treatment of PDL, there is a reluctance to include PDL in research.

Yet, advocates argue that systematic exclusion of PDL from research, especially vaccine trials for TB, unduly restricts PDL from exercising their autonomy and taking part in research that holds special promise of being beneficial to them.



Estimated tuberculosis incidence in prisons (cases per 100 000 person-years) by country in 2019. Reproduced with permission from Martinez, Leonardo et al. "Global, regional, and national estimates of tuberculosis incidence and case detection among incarcerated individuals from 2000 to 2019: a systematic analysis." *The Lancet. Public health* vol. 8,7 (2023): e511-e519.

Methods

To identify potential motivations for reluctance to include PDL in research, we examine existing human subjects protection documents, including ones specific to research involving PDL: the Nuremberg Code, the Helsinki Declaration, the Belmont Report, US 45 CFR Part 46 (including Subpart C), and the Institute of Medicine's report on research involving PDL.

We abstract pertinent ethical considerations underlying these principles and regulations, and review additional potential concerns. We recommend ways to preempt or mitigate all of these ethical concerns.

Acknowledgements

This work is funded by Open Philanthropy.

Results

Main ethical considerations:

1. Perceived coercion
2. Trial participation that appeals to PDL due to unjustly low access to prevention, diagnosis and care
3. Unfair distribution of burdens and benefits of the research
4. Lack of privacy
5. Misunderstanding of risks due to lower education levels among PDL (e.g. therapeutic misconception)

Recommendations:

➡ Provide standards of **TB diagnosis, treatment and prevention** closer to the level available outside prison, or to international recommended policies, whichever is greater or more relevant, not conditional on trial participation.

➡ **Addresses concerns 1 and 2**

➡ Provide enhanced **privacy protections** to reduce disclosure of trial participation to staff or other PDL.

➡ **Addresses concerns 1 and 4**

➡ **In-depth engagement** of PDL, advocates/former PDL, and correctional institutions throughout planning, design and implementation of trials.

➡ **Addresses concerns 1, 2, 3, 4 and 5**

➡ Prioritize PDL in **post-trial access** to approved vaccines.

➡ **Addresses concerns 2 and 3**

Discussion/Conclusion

Restrictions on PDL participating in research exist for important reasons, but should not reduce PDLs' ability to exercise personal autonomy by participating in research that is morally permissible and complies with US regulations.

TB vaccine research including PDL can meet US regulatory requirements, e.g. non-coercion, focus on diseases endemic in prisons, and benefits to participating PDL. With these measures, TB vaccine can include PDL while protecting their interests and their autonomy to decide whether to participate as much as possible.

These measures would help ensure that phase 3 trials of TB vaccines including PDL promote global health and PDLs' health, and treat participating PDL as ethically as possible, exceeding regulatory requirements.

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