CASE STUDY

Parameterising the kinetics of early disease in tuberculosis

WHY DID WE DO IT?

The course of TB disease is not the same for everyone. Some progress rapidly, others slowly, while others may have a fluctuating disease path. The kinetics of early (including subclinical) disease are not usually apparent, occurring prior to the development of significant symptoms. Until recently little attention has been paid to this in TB models or policy. However, it has important implications for TB transmission and estimates for global disease burden. Parameterising the kinetics of early disease requires longitudinal studies with radiographic and bacteriological follow-up, not feasible if treatment is available. We therefore conducted a systematic review focusing on pre-chemotherapy literature to inform key estimates for progression and regression of early disease in a model. These results can then be used to address various questions, including the expected incidence of clinical disease from those detected in prevalence surveys.

WHO

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WHERE

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WHEN

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WHAT

Systematic review of the natural history of untreated pulmonary tuberculosis in adults

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HOW DID WE DO IT?

Few systematic reviews of historical literature have been conducted. In developing the protocol we sought input from others that had undertaken similar reviews and gained access to reference libraries of former WHO epidemiologists. We focussed on English and German literature reflecting the major studies of this period. In addition to electronic databases, manual searches of bibliographic indexes was undertaken. 10,621 titles were screened and 1,792 full texts reviewed, 48 studies were identified with extractable data. The data was used to parameterise a 5-state model including minimal TB (bacteriologically negative, evident disease) and subclinical TB (bacteriologically positive, without symptoms). We used this work as the basis for symposia at the 50th and 51st Union World Conference on Lung Health, initiating debate on the importance of the subclinical disease state.

SO WHAT?

This work has potential to influence the approach to estimating the global burden of disease from national prevalence surveys. These surveys utilise chest x-ray and symptom screening followed by sputum culture to estimate disease prevalence, identifying largely subclinical disease. Models that relate this to disease incidence incorporate the regression from culture positive to negative but these parameters have been derived from a limited data set. Our work will provide greater confidence in the parameters used.

WHAT DID WE LEARN?

A systematic review of this historical literature has been an enormous undertaking, a team effort involving a multinational, multi-lingual team. We learnt that the historical literature is rich and has much relevant insight to offer, but much of it is still not easily and electronically accessible to contemporary TB researchers and policymakers. Methodology is varied and variable which provided challenges for data synthesis.