

1 Latent tuberculosis infection care

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1 Dear Editor,

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3 We note with interest the article from Holzman et al (1), which is an important and
4 clinically useful piece not only for the USA but also many other countries with low TB
5 incidence and latent TB infection (LTBI) screening programs. We applaud their
6 endeavours using large scale, 'real world' public health LTBI data collection,
7 collation, and analysis, and believe this needs to be replicated elsewhere.

8

9 We would be interested to have the authors comment on the following:

10

11 Though the stated study objective was to quantify the 'LTBI care cascade...and
12 identify factors associated with failure to complete each cascade step' only limited
13 data were presented on those associated with loss at every step. We appreciate,
14 and the authors acknowledged, the difficulty of assessing the impact of more than
15 demographic and clinical factors, such as potentially modifiable within-system
16 factors, yet they could report these from one site with a particularly high proportion of
17 pre-employment assessments. Might it be possible to obtain these for other
18 populations and study sites, and so improve the applicability of their findings for
19 other public health services elsewhere? This would be particularly helpful in regard
20 to their data on the homeless who had very low levels of treatment initiation and
21 completion.

22

23 Adherence measured by clinic-recorded initiation of LTBI treatment will inherently
24 overestimate true adherence. Thus, despite the authors' useful analysis by drug
25 regimen, it is difficult to draw conclusions from the current data on treatment
26 effectiveness.

27

28 Is LTBI treatment free for all populations studied? A fee barrier amongst some
29 groups would clearly affect the LTBI cascade and alter interpretation of these results.

30

31 In the presented methods the split of prospective to retrospective data collection and
32 source-site distribution is unclear but important. Interpretation would alter
33 significantly if, for example, all the employment screening data were retrospectively
34 collected.

35

36 Finally, a reported 7,228 of 10,962 included US-born patients had no indication for
37 testing and, as we would expect, had a lower rate of LTBI (2% versus 6%). Pre-
38 employment screening, which the authors acknowledge is in low-risk individuals,
39 comprises 59% of US-born and 26% of the non-US born patients included. We
40 would be interested to see a subgroup analysis that excludes low-risk populations,
41 primarily those from pre-employment screening. The current grouping may
42 misrepresent the treatment cascade for high-risk populations that clinicians are most
43 likely to consider when using this publication to assess and improve their
44 programmes.

45 The data presented by Holzman *et al* add to our understanding of the
46 implementation of TB preventive therapy. Future work should explore specific
47 barriers to uptake of LTBI treatment and how resources can be more effectively
48 focussed on high-risk groups. In addition, there is a need for high-quality prospective
49 data on adherence to LTBI therapy and how this affects future risk of TB disease.

1 Notes

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3 Funding

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5 Authors report no funding related to this work.

6

7 Potential conflicts

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1 References

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31. Holzman SB, Perry A, Saleeb P, Pyan A, Keh C, Salcedo K, et al. Evaluation of the Latent
4 Tuberculosis Care Cascade Among Public Health Clinics in the United States. Clin Infect
5 Dis. 2022 Apr 1;ciac248.

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