genome sequencing shows a low proportion of tuberculosis disease is attributable to known close contacts in rural Malawi. *PLoS One* 2015;10(7):e0132840.

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THE AUTHORS REPLY: We agree with Jain et al. that the low rates of case detection among child contacts in our study contrast sharply with the findings of studies in other countries.¹ However, we think it is unlikely that many cases of tuberculosis in children were missed, since we observed that mortality among children younger than 15 years of age was 0.5% at 2 years. This rate is substantially lower than would be expected if the incidence of undetected, untreated tuberculosis were high. We have also found low rates of infection among child contacts in households of patients with newly diagnosed tuberculosis.² Epidemiologic and social factors may be responsible for this finding, since more than 75% of tuberculosis in Vietnam occurs among men,³ whereas women traditionally have had responsibility for the care of young children in that country. Nevertheless, these findings warrant further exploration. Given the serious consequences of tuberculosis for children, early case detection in children remains an important priority.⁴ However, our findings show the importance of also targeting older populations in active case-finding efforts and indicate that screening is likely to be most efficient when guided by knowledge of the characteristics of the local populations affected by tuberculosis.

We agree with Yates that household exposure to tuberculosis constitutes just a part of the explanation for the increased risk of tuberculosis among household contacts. Not only do house-

hold members share proximity to the known index case, but they may also share other exposures outside the household, as well as other biologic and socioeconomic risk factors. Consequently, household-contact investigation provides an ideal opportunity to identify and address coexisting conditions and support populations affected by socioeconomic deprivation. Clearly, advocacy for tuberculosis care must promote not only access to screening and treatment, but also mitigation of the socioeconomic circumstances in which the disease is able to arise.⁵

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Since publication of their article, the authors report no further potential conflict of interest.

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Venetoclax–Rituximab in Chronic Lymphocytic Leukemia

TO THE EDITOR: In the phase 3 MURANO trial, Seymour et al. (March 22 issue)¹ compared the efficacy of venetoclax plus rituximab with that of bendamustine plus rituximab in patients with relapsed or refractory chronic lymphocytic leukemia. Patients were stratified according to the presence or absence of chromosome 17p deletion, which was present in 46 of 173 patients

(26.6%) in the venetoclax–rituximab group and 46 of 169 patients (27.2%) in the bendamustine–rituximab group.

In the multicenter phase 2 trial of the German Chronic Lymphocytic Leukemia Study Group, chromosome 17p deletion was the only established risk factor that negatively affected the response in the bendamustine–rituximab group.

The authors concluded that bendamustine plus rituximab was an effective option for patients with chronic lymphocytic leukemia who had not received treatment, except for those with chromosome 17p deletion.²

In light of this information, in the CLL10 (First-line Chemoimmunotherapy with Bendamustine and Rituximab versus Fludarabine, Cyclophosphamide, and Rituximab in Patients with Advanced Chronic Lymphocytic Leukaemia)³ and HELIOS (Ibrutinib Combined with Bendamustine and Rituximab Compared with Placebo, Bendamustine, and Rituximab for Previously Treated Chronic Lymphocytic Leukaemia or Small Lymphocytic Lymphoma)⁴ trials comparing bendamustine plus rituximab with ibrutinib plus bendamustine, patients with chromosome 17p deletion were excluded because of known poor response rates with bendamustine plus rituximab. However, in another study, venetoclax resulted in an overall response rate of 75.5% and a 12-month progression-free survival of 69% among patients with relapsed or refractory chronic lymphocytic leukemia and chromosome 17p deletion.⁵ Why was it thought to be appropriate to randomly assign patients with chromosome 17p deletion to bendamustine plus rituximab in the MURANO trial?

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TO THE EDITOR: Seymour et al. report that venetoclax plus rituximab was superior to bendamustine plus rituximab in relapsed or refractory chronic lymphocytic leukemia. In this trial, which was designed by the trial investigators and the sponsors (Genentech and AbbVie), the comparator group (bendamustine plus rituximab) is noticeably inferior; this is reminiscent of chlorambucil control groups in previous trials involving patients with chronic lymphocytic leukemia.^{1,2} In addition, the duration of treatment in the two groups was not balanced, patients in the control group were not allowed to cross over to the experimental group after disease progression, and previous treatment with bendamustine was allowed. It comes as no surprise that the experimental group profoundly outperformed the control group.

In an era of changing clinical trials, with new approaches to trial design,³⁻⁵ and with various new effective treatment options that have good safety profiles in chronic lymphocytic leukemia, a better choice of trial design and control group would have used limited resources more effectively. Also, we would like to know what percentage of patients in each group received bendamustine previously. What was the median time to clearance of minimal residual disease? Finally, what was the scientific rationale for choosing the 2-year duration for venetoclax treatment?

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