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THE AUTHORS AND A COLLEAGUE REPLY

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In reply to Johnson: after taking into account the subjects who were assigned to treatment but did not receive a study drug, the overall frequency of discontinuation was 27.3% in the isoniazid-only group and 13.0% in the combination-therapy group. The difference between the two groups in permanent drug discontinuation owing to adverse events was small, but this outcome is an important measure of drug tolerability. The reasons for drug discontinuation other than adverse events are shown in Figure 1 in the Supplementary Appendix of our article (available at NEJM.org) and are summarized in Table 1. The numbers and percentages for many of the reasons for discontinuation are approximately two to three times as high in the isoniazid-only group as in the combination-therapy group; this is consistent with a duration of treatment that was three times as long in the isoniazid-only group as in the combination-therapy group.

Our study primarily assessed close contacts of persons with tuberculosis who were susceptible to isoniazid and rifampin; the trial did not provide data relevant to populations with an increased risk of resistance. Drug-resistance rates among immigrants in the United States may be lower than in their country of origin (Centers for Disease Control and Prevention data). Latent *Mycobacterium tuberculosis* infection is a paucibacillary state, and treatment of latent *M. tuberculosis* infection has not been associated with increased drug resistance among persons in whom tuberculosis develops despite preventive therapy.[1] However, as in our study, it is important that clinicians rule out active tuberculosis before initiating treatment of latent *M. tuberculosis* infection.

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References

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Table 1.

Reason for Study-Drug Discontinuation among Subjects in the Modified Intention-to-Treat Population.*

Reason for Discontinuation	Isoniazid Only (N = 3745)	Combination Therapy (N = 3986)
	number (percent)	
Received treatment for incorrect duration or received incorrect no. of doses	129 (3.4)	69 (1.7)
Died before 75% of doses received	2 (0.1)	0
Withdrew consent	43 (1.1)	28 (0.7)
Was lost to follow-up during study phase	265 (7.1)	52 (1.3)
Had treatment discontinued by clinician	45 (1.2)	18 (0.5)
Declined treatment	199 (5.3)	174 (4.4)
Became pregnant	48 (1.3)	19 (0.5)
Had other or unknown reason	195 (5.2)	67 (1.7)

*Data shown are for all enrolled subjects who were eligible to participate in the study. In the modified intention-to-treat study population, 95 subjects in the isoniazid-only group (2.5%) and 90 subjects in the combination-therapy group (2.3%) were assigned to treatment but did not receive a study drug.