mained noninferior to the standard biopsy strategy with respect to the detection of clinically significant prostate cancer (absolute difference, 0.5 percentage points; 95% confidence interval [CI], −3 to 4), and the detection probability of clinically insignificant cancers remained markedly lower in the experimental biopsy group than in the standard biopsy group, with a relative between-group difference of 42% (95% CI, 21 to 58).

To definitively answer the question of whether MRI-detected and systematic biopsy–detected prostate cancer are equivalent with regard to relevant cancer end points, long-term follow-up data from well-designed prospective and adequately powered trials are needed. Such data are currently not available (and may never be). The results presented here suggest that the evidence of noninferiority of combined biopsy (performed only in men with visible lesions on MRI) with respect to the detection of clinically significant prostate cancer is robust to adjustment for potential inflation of the Gleason score and strengthen the indication that any difference in long-term outcomes is likely to be small. However, more research is needed to fully elucidate the effect of MRI on appropriate risk stratification in patients with prostate cancer and on reduction in mortality from early detection.

While we agree with Yoshida and Fujii that men with a negative MRI need further surveillance, in light of the high negative predictive value of MRI,[1] we argue that such men can be followed within a screening program and undergo biopsy at future screenings if indicated by MRI or by a high predicted prostate cancer risk. To subject men with a negative MRI to standard biopsy would forgo the potential of MRI to reduce the number of unnecessary biopsies and diagnoses of clinically insignificant disease.

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

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Fetal Surgery for Severe Left Diaphragmatic Hernia

TO THE EDITOR: The lower mortality reported by Deprest et al. (July 8 issue)[1] among infants with severe congenital diaphragmatic hernia who were assigned to fetoscopic intervention than among those who were assigned to expectant care should not be interpreted as endorsing broad application outside well-designed trials at experienced centers. Despite the standardized protocol, the report does not include information regarding adherence to standardized care[2] during a trial period of more than 10 years at 10 fetal centers and 26 neonatal centers with variable experience treating infants with congenital diaphragmatic hernia. The low use of extracorporeal life support appears inconsistent with "best practices," perhaps limited by availability, center experience, and bias related to the lack of blinding.

Higher mortality in the control group than that at U.S. centers with experience using permissive hypercapnia or spontaneous ventilation[3-5] raises the question of whether consistent improvement in nonfetal intervention might similarly improve outcomes and decrease the rationale for fetal intervention. Neonatal advances must consider long-term morbidity, especially among premature neonates, but, as acknowledged by the authors, the trial was not powered for and cannot effectively inform associated coexisting conditions in these premature infants. These issues require discretion in counseling vulnerable parents when congenital diaphragmatic hernia is diagnosed prenatally.

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THE AUTHORS REPLY: We thank Stolar et al. for their comments, and we agree with some of their concerns. We recommended that fetoscopic endoluminal tracheal occlusion (FETO) be offered only by centers with extensive experience in fetoscopy and balloon insertion and removal. With respect to long-term outcomes, we are collecting such data from the trial cohort and advocate prospective registration of future cases of congenital diaphragmatic hernia for which FETO would be appropriate as a second-best option to a randomized, controlled trial.[1,2]

Mortality in our control group was indeed higher than in the cited studies. Data from neonatal management centers typically overestimate survival because they do not include intrauterine deaths, terminations, and fetal abnormalities.[3] In addition, the single previous randomized, controlled trial included fetuses with moderate hypoplasia, which inevitably contributed to the higher survival.[4]

We agree that in our trial, adherence to the standardized neonatal management protocol may have varied, but the same strategy and protocol were previously used successfully in another randomized, controlled trial.[5] Extracorporeal life support may not have been offered by some centers because of its unproven benefit in congenital diaphragmatic hernia and its potential complications.

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

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