between off-pump and on-pump CABG, which is contradictory compared with Kuss and colleagues' results from nonrandomized studies.

Late mortality in off-pump CABG is another concern. In the meta-analysis by Wijesundera and coworkers,⁴ only 2 observational studies reporting risk-adjusted effects on long-term (≥ 1 year) outcomes showed essentially no change in mortality (odds ratio 1.01; 95% CI, 0.74–1.40; $P = .93$). In the ROOBY trial,³ although no significant difference was found for the rate of death from any cause within 1 year (4.1% vs 2.9%; RR 1.41; 95% CI, 0.90–2.24; $P = .15$), the rate of death from cardiac causes within 1 year was higher in the off-pump group than in the on-pump group (2.7% vs 1.3%; RR 2.05; 95% CI, 1.09–3.86; $P = .03$). Our recent meta-analysis⁵ of 12 randomized trials (4326 patients enrolled) including the ROOBY trial demonstrated a statistically significant increase in late (≥ 1 year) all-cause mortality by a factor of 1.37 with off-pump relative to on-pump CABG (RR 1.373; 95% CI, 1.043–1.808; $P = .024$).

Despite the superiority of off-pump CABG to on-pump CABG in short-term mortality found in Kuss and associates' meta-analysis¹ of propensity score analyses, on-pump rather than off-pump CABG should be considered at least for patients who meet the criteria for enrollment in randomized trials (typically for low- to moderate-risk patients) because late, not short-term, mortality reduction must imply the greatest clinical benefit among patients undergoing CABG.

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References

1. Kuss O, von Salviati B, Börgermann J. Off-pump versus on-pump coronary artery bypass grafting:

a systematic review and meta-analysis of propensity score analyses. *J Thorac Cardiovasc Surg*. 2010 Feb 16 [Epub ahead of print].

2. Møller CH, Penninga L, Wetterslev J, Steinbrüchel DA, Glud C. Clinical outcomes in randomized trials of off- vs. on-pump coronary artery bypass surgery: systematic review with meta-analyses and trial sequential analyses. *Eur Heart J*. 2008;29:2601-16.
3. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med*. 2009;361:1827-37.
4. Wijesundera DN, Beattie WS, Djaiani G, Rao V, Borger MA, Karkouti K, et al. Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. *J Am Coll Cardiol*. 2005;46:872-82.
5. Takagi H, Matusi M, Umemoto T. Off-pump coronary artery bypass may increase late mortality: a meta-analysis of randomized trials. *Ann Thorac Surg*. 2010;89:1881-8.

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Reply to the Editor:

We thank Takagi and Umemoto¹ for their interest in our recent systematic review of propensity score (PS) analyses in off-pump versus on-pump coronary artery bypass grafting.² As Takagi and Umemoto correctly point out, our estimate for the effect of off-pump coronary artery bypass grafting on short-term mortality (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.60–0.75) differs from the corresponding estimate from randomized controlled trials (RCTs). In their large meta-analysis, Møller and colleagues³ found a relative risk of 0.98 (95% CI, 0.66–1.44). Takagi and Umemoto¹ calculated a relative risk of 1.06 (95% CI, 0.67–1.67) by adding the results of the ROOBY trial⁴ to Møller and colleagues' results.

Setting aside the subtlety of equating ORs with relative risks, we would like to point out 2 facts. First, even after including the ROOBY results to the data of Møller and colleagues,³ the CI for the effect still includes our PS effect estimate of 0.69. That means that even data from nearly 100 randomized trials on the off-pump/on-pump issue still leave considerable uncertainty (as reflected by the large CI) on the size of the true effect. In particular, were still far from achieving *equivalent* short-

term mortality, which Takagi and Umemoto¹ deduce from the current data. This lack of information is also emphasized by Møller and colleagues³ in their trial sequential analysis: The authors state that demonstrating equivalence or a minimal clinically relevant effect of the off-pump technique on mortality would require more than 240,000 patients.

Second, and this is also pointed out correctly by Takagi and Umemoto,¹ we do not expect the effect estimates from PS analyses and RCTs to be equal because the underlying study populations usually differ. Patients in RCTs are, in general, younger and healthier than the average patient. In a study currently under review, we reviewed 28 PS analyses and 51 RCTs that compared off-pump and on-pump coronary artery bypass grafting.⁵ We found an average age of 65.8 years and an average left ventricular ejection fraction of 58.8% in the PS analyses, compared with an average age of 63.1 years and a mean left ventricular ejection fraction of 62.7% in the RCTs, confirming that patients in the PS analyses are older and in poorer health. After generating similar study populations from PS analyses and RCTs by a meta-matching algorithm (resulting in a meta-matched sample of 10 PS analyses and 29 RCTs), we found an OR for short-term mortality of 0.53 (95% CI, 0.43–0.66) in the PS analyses and 0.58 (95% CI, 0.24–1.39) from the RCTs, resulting in an OR difference of –0.05 (95% CI, –0.56 to 0.47). Unfortunately, this difference is also associated with a large CI, but there is some evidence (supported by other clinical outcome data not shown) that the treatments effects are similar, provided the underlying populations in PS analyses and RCTs are similar.

Finally, we completely agree with Takagi and Umemoto¹ on the importance of long-term mortality. Sufficient long-term mortality figures were available in 7 PS analyses in our data set, initially accounting for 6813 patients.

By restricting the analysis to information provided only in the text (and not, eg, extracted from Kaplan–Meier curves) and considering only the effect of the longest time of follow-up from each study, we calculated an OR of 0.82 (95% CI, 0.67–1.02; $P = .07$). This shows that in PS analyses the superiority of the off-pump approach applies not only to short-term mortality but also to long-term mortality, albeit to a smaller degree.

Eventually, the results of current randomized studies on risk groups that mirror today's typical patient populations will elucidate the truth about the differences between the on- and off-pump approaches.

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References

1. Takagi H, Umemoto T. To pump, or not to pump, that is the question. *J Thorac Cardiovasc Surg.* 2010;140:485-6.
2. Kuss O, von Salviati B, Börgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. *J Thorac Cardiovasc Surg.* 2010 Feb 16 [Epub ahead of print].
3. Möller CH, Penninga L, Wetterslev J, Steinbrüchel DA, Gluud C. Clinical outcomes in randomized trials of off- vs. on-pump coronary artery bypass surgery: systematic review with meta-analyses and trial sequential analyses. *Eur Heart J.* 2008;29:2601-16.
4. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med.* 2009;361:1827-37.
5. Kuss O, Legler T, Börgermann J. Do treatments effects differ between randomized trials and propensity score analyses in similar populations? Evidence from a meta-propensity score analysis in off-pump versus on-pump coronary artery bypass surgery. 2010 (submitted).

doi:10.1016/j.jtcvs.2010.04.020

THEORETICAL COST BENEFITS OF CRYOBIOPSY To the Editor:

I commend the study by Schumann and colleagues¹ that demonstrated the clear superiority of cryobiopsy over standard forceps biopsy for endoluminal tumor, showing a 36% relative increase and 24% absolute increase in yield as the result of larger and less fragmented samples.¹ Unfortunately, the acquisition of new equipment and technology is hampered by resource rationing in health care systems. Because tariff-base health care systems require demonstration of cost benefit, this article provides useful evidence with which to develop cryobiopsy in bronchoscopy units. At Glenfield Hospital, Leicester, which includes an annual number of 531 fiberoptic bronchoscopies annually, we have audited our own diagnostic yield with forceps biopsy for endoluminal tumor and found this to be only 77% overall for 132 cases over 1 year with evidence of tumor (with some variation between trainees and consultants).²

By assuming a similar number of bronchoscopies per year with endoluminal tumor with a similar yield with forceps biopsy, this equates to 30 non-diagnostic bronchoscopies (Table 1). Under the National Tariffs for 2010 and 2011,³ the total extra annual cost is calculated to be more than £15,000

per year to the Primary Care Trust 9 (Table 1). By assuming a relative increase in performance with cryobiopsy similar to that reported by Schumann and colleagues,¹ this would translate to a cost savings of more than £15,000 per year (Table 1). The capital cost of the cryobiopsy equipment (£7500, ERBE Medical UK, personal communication, May 2010) could be covered by saving 15 repeat bronchoscopies, which would take an estimated 6 months (at 30 saved per year; Table 1). After 1 year, residual cost savings would total more than £6500 despite deductions for capital, maintenance, and consumable costs (Table 1). For subsequent years, residual funds would be in excess of £14,000 (Table 1).

The data provided by Schumann and colleagues¹ give respiratory physicians the opportunity to provide a robust financial case for adding cryobiopsy to their bronchoscopy unit on the basis it will fund itself in 6 months, according to our own calculations and experiences. In addition, better quality biopsies will provide better material for bronchoscopic tissue research studies and molecular markers.⁴

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TABLE 1. Breakdown of extrapolated cost benefits of cryoprobe

Diagnostic yield with forceps biopsy at Glenfield Hospital, Leicester (%)	77%
Repeat bronchoscopy rate (%)	23%
No. of bronchoscopies with macroscopic tumor/year	132
No. of repeat bronchoscopies needed/year (132 × 23%)	30
Cost of standard bronchoscopy (2010 tariff)	£504
Published improved relative increase in yield with cryobiopsy (%)	36%
Estimated diagnostic yield with cryobiopsy at Glenfield Hospital, Leicester (36% relative increase on 77%) (%)	100%
Cost saving of cryobiopsy to Primary Care Trust (£504 × 30)	£15,120
Cost of cryobiopsy equipment (cryosurgery unit and cable, adapter, probes, gas tube, footswitch)	£7,500
No. of bronchoscopies to prevent to cover costs (7500/504)	15
Total annual costs (service contract+consumables)	£955
Residual cost savings after capital costs (15,120 – 7500)	£7,620
Residual cost savings after annual costs (7620 – 955)	£6,665
Residual cost savings, year 2 onward (15,120 – 955)	£14,165