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To the Editor: With great interest I read the article by Byrne et al.1 assessing anti-restenotic efficacy of three different rapamycin-eluting stents with different coating strategies (biodegradable polymer, permanent polymer and polymer-free stents) at two time points after coronary stenting (6–8 months and 2 years). Although the authors suggested delayed late loss (the difference in in-stent late loss between 6 and 8 months and 2 years) was significantly different across the treatment groups, paired angiographic data were available for only 202 (50%) of 605 patients undergoing stenting. Missing was not at random; patients who underwent revascularisation or died were excluded for late follow-up analysis, which may lead to attribution bias.2 In fact, late luminal loss (of selected patients) was similar at 2 years (figure 4), although target lesion revascularisation rate (of all patients) seemed to differ at 2 years (figure 1). Therefore, it would be of great help if the authors would provide additional angiographic analysis such as multiple imputation and sensitivity analysis.3

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The author’s reply: We thank Dr Kaneda for raising an important issue in relation to the 2-year results of the ISAR-TEST-3 randomised trial.1 Missing data is a pervasive feature of angiographic follow-up studies in general as rates of surveillance angiography are always less than 100% in large clinical trials. This data is regarded as ‘missing not at random,‘ and the amount of error introduced is related to a number of factors including the sample size, the actual rate of angiographic follow-up and the absolute rate of restenosis.2 Notwithstanding this, angiographic markers of restenosis have proven to be robust surrogates of clinical stent efficacy and—within certain constraints—generally reliable endpoints in clinical trials of drug-eluting stents.3 4

A further layer of complexity is introduced by serial angiographic follow-up studies. The key distinction in this setting is that a proportion of patients will undergo target lesion revascularisation (TLR) at initial 6–8-month surveillance and are therefore not eligible for further angiographic analysis as time zero is considered reset. This occurrence is inextricably related to the question under study (namely comparative antirestenotic performance) and in our opinion is not adequately resolved by additional statistical analyses. The implications of this are well illustrated by our data set and are at the crux of the perceived discrepancy alluded to by Dr Kaneda.

Firstly, when we consider data on the subset of patients with paired angiographic follow-up, we must remember that patients with higher initial late loss at 6–8 months tend to be excluded as they are likely to have undergone initial TLR. In the results section, we can see that mean late luminal loss at 6–8 months for the entire study cohort is different from (considerably higher than) that in the subset with paired angiographic follow-up. Information on these excluded patients can be at least partially captured by reporting composite late luminal loss,5 which is the mean late loss at the latest valid angiographic follow-up—be that for example at 6–8 months (in patients undergoing TLR at this time point) or at 2 years (in TLR-free patients). For interest, this was 0.27±0.52 mm for the biodegradable polymer (BP) stent, 0.35±0.55 mm for the permanent polymer (PP) stent and 0.46±0.58 mm for the polymer-free (PF) stent (data available for 83.6% of BP, 80.63% of PP and 78.3% of PF stent respectively; figure 1). On the other hand, it is clear that due to its higher initial late loss, the overall rate of TLR remains highest with the PF stent at 2 years. This is in keeping with the trends in composite late loss reported above.

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