Editor's Note

This invited correspondence, by Dr Vasilios Kotsis, was originally intended to appear as a critique at the time of publication of its subject article (Gilles Chironi, Alain Simon, Jérôme Gariepy, Maria Balice, Muriel Del-Pino, Jaime Levenson. Differential Associations of Statin and Fibrate Treatment with Carotid Arterial Remodeling. Am J Hypertension 2005;18:1476—1481.) The Editors apologize for our error, and the regrettable delay in publication that has resulted.

Were Patients With Unfavorable Outcomes Deleted in a Covert Duplicate Publication Reporting Effect of Placebo on Hypertension?

To the Editor:

In 2001 the *Journal* published a report of a cross-over trial by Roland Asmar and colleagues on the effect of placebo in hypertension.[1] We included this trial when we updated our systematic review of effects of placebo in 2004[2,3] and asked Prof. Asmar whether he would share with us the results from the first period of his cross-over trial and whether he knew of any similar trials. He declined our request for these data and wrote that to his knowledge his 2001 trial was the only such hypertension cross-over trial.

We subsequently identified a trial report from 1996, also with Asmar as first author.[4] The two reports describe trials of nearly identical designs and very similar patients (eg, their mean height and weight and their standard deviations were identical). The 1996 paper reported a non-significant effect of placebo on 24-h ambulatory diastolic blood pressure in 34 patients, whereas the 2001 paper reported a significant effect in 26 patients.

The 2001 paper did not mention or refer to the 1996 paper. We therefore e-mailed Asmar again, asking whether the two trial reports describe overlapping populations of patients, but received no answer.

As a consequence we submitted a letter to the *Journal* in which we described our findings and suggested that Asmar and colleagues were given the opportunity to reply and that their reply was documented by submitting individual patient data to the editorial office of the *Journal*.

We then received a copy of a correspondence between the editor and Asmar, as well as two spreadsheets with individual patient data provided by Asmar. The number of patients in the first spreadsheet was 34, and 26 in the second. The age, weight and height of the 26 patients in the second spreadsheet were identical to the age, weight and height of 26 of the 34 patients listed in the first spreadsheet.

This indicates that Asmar and colleagues' 2001 publication was a covert duplicate publication where a number of patients with unfavorable outcomes had been deleted.

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Reply:

Thank you for your interest to our article.[1] Our study was designed as a crossover study in order to distinguish between the regression over the mean phenomena due to time from the real placebo effect due to the placebo intake. Therefore, following your request in 2003 to analyze only the first period of the study, I mentioned that such analysis will be inappropriate.

Regarding your request to look in our archive for these data, I did not reply simply because I was overburdened with work. In fact, at that moment (2003) the Broussais Hospital, where the study was coordinated, was closing down; and because at the same period, the Cardiovascular Institute, where I am practising, was being relocated. Shortly after, in May 2004 and for clearness reasons, we provided the editor with the full individual data of our database.

Concerning the study and the two related publications, there was an overlapping population but the two articles are complementary and both present crucial original and different findings.

The 1996 publication[2] deals with the 34 patients included in a multicentric study. The publication results were focused on the placebo effect on the systolic and diastolic blood pressure (BP), through clinic and ambulatory measurement.

Pulse pressure became of growing interest after 1996.Therefore, my co-investigators in the 2001 publication, wished to analyze the placebo effect on pulse pressure, and not only on systolic and diastolic BP. This is why the 2001 publication has been carried out. The 2001 publication includes 26 patients from the global population after a stricter ambulatory BP measurement (ABPM) quality control. Some of the patients did not fill the quality criteria as described in the "Procedures" paragraph of the article. The patient selection was not performed to "comply with the favored conclusion of the investigators."

Concerning the results, according to our interpretation, both studies showed a placebo effect. In the 1996 publi-

cation,[2] placebo effect was not significant on ABPM data of the full population but significant on the ABPM data of the placebo responders in clinic: "Placebo decreased the clinic BP and reduced systolic and diastolic ambulatory BP." The second publication[1] showed significant reduction with placebo of both systolic and diastolic BP but the "placebo effect was not observed for pulse pressure and heart rate." In both publications we insist on the fact that placebo presents a proper effect and may decrease BP both in clinic and ABPM in similar population.

Hope that this gives you satisfaction.

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Re: Hawkins RG, Houston MC Is population-wide diuretic use directly associated with the incidence of end-stage renal disease in the United States? A hypothesis. Am J Hypertens. 2005 Jun;18(6):744-9.

To the Editor:

We read with interest the article by Hawkins and Houston[1] invoking a relationship between use of thiazide diuretics and end stage renal disease (ESRD). We agree with the concerns expressed in the accompanying editorials about the inherent pitfalls in inferences the investigators drew from their ecologic study.[2,3] Hawkins and Houston failed to address another major problem with their study, namely "indication bias." In fact, diuretics have a role in the management of chronic kidney disease, especially the loop diuretics, which they suggested may comprise as much as 46% of all diuretics prescribed. Therefore individuals diagnosed with chronic kidney disease, an antecedent to ESRD, may be prescribed diuretics for clinical management, hence the indication bias. In addition, although the investigators correctly point out that estimated glomerular filtration rate (GFR) was lower in the thiazide group compared to amlodipine in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), this parameter may be difficult to interpret due to acute hemodynamic changes associated with initiation of amlodipine therapy.[4] They fail to report that the incidence of ESRD in ALLHAT was not different between the angiotensin-converting enzyme (ACE) inhibitor and the diuretic groups (relative risk lisinopril versus chlorthalidone 1.12; 95% confidence interval [CI] .89–1.04, $P = .33$) and the calcium channel blocker versus diuretic groups (relative risk amlodipine versus chlorthalidone 1.11, 95% CI 0.88–1.38, $P = 0.38$). This was consistent when stratified by baseline GFR and the presence of diabetes at baseline.[5] The composite end point of a 50% decline in GFR or ESRD was also not different between thiazide diuretic compared to amlodipine and lisinopril in patients with moderate/severe reduction in GFR.[5] Renal outcomes were prespecified secondary end points in ALLHAT, and the data are robust with large numbers of patients, and a total of 448 ESRD events (total of 1049 renal end points including ≥50% decline in GFR events), clearly sufficient to refute the notion that diuretic therapy is associated with increased risk of ESRD. The question studied by the investigators is of clinical interest but the question is better answered by treatment comparisons in randomized controlled trials such as ALLHAT.

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