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Reply

to comment on "Indirect comparisons of new oral anticoagulant drugs for efficacy and safety when used for stroke prevention in atrial fibrillation" AND "Lack of stroke subtype information may hinder indirect comparison between the ROCKET-AF and other trials of new oral anticoagulants"

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Reply

We thank Drs. Li and Zhao for their interest in our paper (1). They are correct that indirect comparisons cannot address all the heterogeneity between trials, as well as the underlying pathogenic mechanisms that they allude to. However, it is not very likely that there would be major differences in stroke subtypes among the 3 studies. Also, the inclusion and exclusion criteria are broadly the same in the 3 trials, except for the ROCKET-AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) trial, wherein more patients may possibly have a different stroke type than thromboembolism-related, because of the higher-risk profile.

The only way to definitively address this issue would be to perform a large head-to-head randomized trial, and with the current agents, this would need to be a 4-arm noninferiority randomized trial of dabigatran (2 doses), apixaban, and rivaroxaban, which would probably require a massive number of atrial fibrillation patients (probably >50,000) and require >5 years of follow-up.

In the absence of head-to-head comparisons, indirect comparisons allow the opportunity to have some insight into how these novel anticoagulants would perform against each other for the main efficacy and safety endpoints (2). To that end, our analysis (1) concludes that there are no profound differences in the major efficacy and safety endpoints between the novel oral anticoagulants. This is consistent with other recent papers on the same topic (3,4), although 1 analysis by Kansal et al. (5) did highlight some differences with fewer incidents of ischaemic stroke and intracranial hemorrhage, as well as cost effectiveness, when dabigatran was compared against rivaroxaban.

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Please note: Dr. Lip has served as a consultant for Bayer, Astellas, Merck, AstraZeneca, Sanofi, BMS/Pfizer, and Boehringer Ingelheim and has served on the Speakers' Bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, and Sanofi. Dr. Larsen and Dr. Rasmussen have served on the Speakers' Bureau for BMS/Pfizer and Boehringer Ingelheim. Dr. Skjøth has reported that he has no relationships relevant to the contents of this paper to disclose.

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Not All Fat Is Equal

We read with interest the paper by Gupta et al. (1). Adipose tissue is a major source of hormones and cytokines implicated in systemic inflammatory reactions, metabolic abnormalities, hypertension, and insulin resistance (2,3). The investigators use body mass index (BMI) to classify adiposity status. However, it is useful to re-evaluate how body fat is determined. Numerous studies have produced evidence that BMI has limited ability to accurately predict body composition.

So how fat is fat? BMI is the most commonly used measure to determine adiposity status in everyday clinical practice. It is a safe, convenient, and popular method. However, the index is an indirect surrogate of body fat, which is not able to distinguish lean body mass from fat mass. There is growing body of evidence that BMI may misclassify weight status in many patients (4–6). It tends to overestimate normal weight and underestimate overweight or obesity.

Dual-energy X-ray (DXA) absorptiometry is considered by many to be a gold standard for assessing body composition (direct measurement of total body fat and lean soft tissue mass). It provides a more accurate indication of body fat percentage, which is one of the fundamental links between obesity and its associated disease risk.