group were 582 (30%) of 1920 and 380 (39%) of 973. There were no major differences when comparing each individual component of established cardiovascular disease. The minimal difference in the on-treatment and ITT analyses strongly suggests that any differential drop-out did not explain the findings of our study.

Finally, Singh comments that reducing urate might confer cardiovascular benefit. In our view, establishing the benefits of allopurinol or urate-lowering therapy beyond all reasonable doubt must await the outcome of other studies, including the ALL-HEART study,[2] an ongoing randomised trial of allopurinol versus usual care in patients with ischaemic heart disease.

Xu states that one of the main differences between the FAST[1] and CARES[3] trials is the use of a lead-in phase and, therefore, lower rates of treatment discontinuation in FAST. This is not totally correct. CARES also up-titrated allopurinol doses in those randomly assigned to allopurinol and up-titrated febuxostat in those randomly assigned to febuxostat. However, about 56% of those randomly assigned to each group had previously been taking allopurinol and about 4% had been taking febuxostat. As about 60% of each group had been taking urate-lowering therapy before randomisation and only 34% were treatment-naive, we do not think that FAST and CARES differed much in this respect.

Our interpretation of the differential increase in early withdrawal from randomised therapy is simply that any switch to a new therapy from one that has been well tolerated might be predicted to cause more withdrawals. All participants were taking baseline allopurinol; half continued this and the other half were changed to febuxostat. There were 470 more withdrawals from febuxostat than from allopurinol (appendix). As all patients were receiving allopurinol at baseline, it is not surprising that there were fewer adverse events in the allopurinol group.

See Online for appendix

In addition, Xu asks about hospitalisation for arrhythmia and deaths. After withdrawal from randomised treatment, 19 patients (0·751 per 100 patient-years) in the febuxostat group were hospitalised for arrhythmia compared with four patients (0·557 per 100 patient-years) in the allopurinol group. Only one event (in the febuxostat group) occurred within 30 days of withdrawal from randomised treatment.

The low number of hospitalisations for arrhythmia after withdrawal from treatment and the fact that only one occurred within 30 days of withdrawal from treatment do not suggest an adverse effect associated with withdrawal from febuxostat treatment.

The figures for deaths after withdrawal from treatment are 114 deaths (4·506 per 100 patient-years) in the febuxostat group and 89 deaths (12·395 per 100 patient-years) in the allopurinol group. A total of 27 deaths occurred within 30 days of withdrawal from treatment in the febuxostat group compared with 25 in the allopurinol group.

There was no evidence of an increase in mortality after febuxostat withdrawal in FAST.

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Global Burden of Disease Health Financing Collaborator Network. Past, present, and future of global health financing: a review of development assistance, government, out-of-pocket, and other private spending on health for 195 countries, 1995–2050. Lancet *2019;* **393:** *2233–60*—In this Article, the Global Burden of Disease Health Financing Collaborator Network has been updated to include Maciej Banach, Sarah Friedman, and Raghavendra Guru Srinivasan. The affiliations of Maciej Banach, Sarah Friedman, and Raghavendra Guru Srinivasan have also been added, and the affiliations of Martin Amogre Ayanore and Masood Sepehrimanesh have been updated. These corrections have been made to the online version as of Sept 9, 2021.

Burkart KG, Brauer M, Aravkin AY, et al. Estimating the cause-specific relative risks of non-optimal temperature on daily mortality: a two-part modelling approach applied to the Global Burden of Disease Study. Lancet *2021;* **398:** *685–97*—In this Article, the spelling of author Jiawei He's name was incorrect. This correction has been made to the online version as of Sept 9, 2021.