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UK FASHIoN—how clinically relevant are the results?

We have read with great interest the UK FASHIoN study by Damian Griffin and colleagues.[1] In this randomised controlled trial of 348 patients from 23 centres, the authors conclude that patients with femoroacetabular impingement syndrome have better hip-related quality of life at 12 months after hip arthroscopy than after conservative care.

The pragmatic approach, in which orthopaedic surgeons from various backgrounds could recruit and operate on patients, not only deserves appreciation, but serves as an example for future trials. However, because the minimum clinically important difference of 6·1 points on the iHOT-33 was exceeded by only 0·7 points, we felt that a close look at the trial's results was warranted.

The lower limit of the CI of the adjusted treatment effect (6·8 points; 95% CI 1·7–12·0) does not exceed the minimum clinically important difference of 6·1 points on the iHOT-33 used by the authors,[1] nor the minimum clinically important difference of 12·1 points described by Nwachukwu and colleagues.[2] This is also true for all the subanalyses (appendix). If this is the case, is it legitimate to conclude that there is a clinically significant difference?

We believe that the FASHIoN trial is extremely relevant in a field in which hardly any level 1 evidence exists so far. However, the conclusion of the FASHIoN trial might be better formulated by mentioning that there is a small effect of hip arthroscopy compared with conservative care in patients with femoroacetabular impingement syndrome, but whether this effect is clinically significant remains an open question.

We declare no competing interests.

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Alcohol consumption and vascular disease: other points to consider

Iona Millwood and colleagues[1] assessed the associations between cardiovascular risk and genotype-predicted mean alcohol intake in men and women in China. The results suggested that the apparently protective effects of moderate alcohol intake against stroke are largely non-causal.

Some problems with this study have caught our attention. First, the authors recorded alcohol use and other characteristics at baseline, but they did not obtain information about the changing patterns of alcohol consumption during follow-up, which should be considered. Second, this study followed participants for about 10 years, but population mobility has seen a substantial increase over this period, particularly in rural areas. Increased mobility could result in a certain percentage of missed visits. Third, the information from the 4781 missing participants should be removed because the information about their health is unclear.

Additionally, a study has reported an immediately higher cardiovascular risk following any alcohol consumption,[2] whereas another study showed that heterogeneous associations exist between the amount of alcohol consumed and the initial presentation of cardiovascular diseases.[3] Nevertheless, Millwood and colleagues'[1] study suggested that reductions in alcohol consumption should provide overall health benefits. Interpretation of their conclusion needs to be done with caution because of the above uncertainties.

We declare no competing interests.

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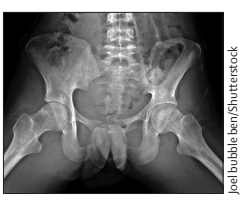
As suggested by Iona Millwood and colleagues[1] in their Article, and by an accompanying Comment,[2] a better understanding is needed of how genetics will redefine the risks associated with alcohol consumption. Screening methods for alcohol-associated risk, such as AUDIT and AUDIT-C are dependent upon the number of standard drinks consumed, but they might not be the relevant tools to determine the risks associated with alcohol consumption globally.[3] Because 8% of the global population have a genetic variant of *ALDH2* rs671 (known as *ALDH2**2), which causes an accumulation of acetaldehyde after alcohol consumption, guidelines taking into consideration this genetic



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See **Online** for appendix

For **AUDIT and AUDIT-C screening tests** see https://www.gov.uk/government/publications/alcohol-use-screening-tests

variant could lay the groundwork for precision medicine strategies.

Furthermore, when developing recommendations, acknowledgment that additional environmental sources of acetaldehyde exposure exist, including acetaldehyde present in tobacco cigarettes, is important. Frequently, people use tobacco and alcohol together—as reported by Millwood and colleagues (61% of all men are smokers and 71% of current drinkers are smokers).[1] Smoking tobacco cigarettes while consuming alcohol transiently increases acetaldehyde concentrations in the saliva 6-times higher than the concentrations when consuming alcohol alone.[4] In a small clinical study, genetic variations that cause acetaldehyde accumulation (rs671 and rs1229984) paired with lifestyle choices of drinking alcohol and smoking tobacco cigarettes identified a 189-times higher risk for developing oesophageal cancer.[5] Because combining alcohol and tobacco use are known to result in a greater accumulation of acetaldehyde, determining whether the risk of cerebrovascular disease for people who smoke cigarettes and drink alcohol is increased relative to those who only consume alcohol is important.

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Authors' reply

We thank Qiang Liu and colleagues and Eric Gross and colleagues for their comments on our Article.[1]

Liu and colleagues raised queries about changing patterns of alcohol consumption during the follow-up period and the handling of participants who were lost to follow-up. As described in the Article,[1] we asked again about alcohol intake in subsets of about 5% of participants in two resurveys approximately 3 years and 8 years after the median baseline survey year. As described in the appendix,[1] these repeat measures were used to estimate the participants' usual alcohol intake over the study period, to account for regression dilution bias in the associations assessed. Fewer than 1% of participants were considered lost to follow-up during the study period.[1] These participants' data were censored at the point at which they were lost.[1]

Gross and colleagues suggest a need to consider the *ALDH2* rs671 variant genotype, which is present in about 35–40% of east Asians, as well as cigarette smoking, when developing guidelines for alcohol use, given that both these factors can increase acetaldehyde exposure in certain tissues following alcohol use, which might affect cancer risk because acetaldehyde can damage chromosomes.[2,3] The pathological mechanisms by which alcohol can affect disease incidence might vary for stroke and myocardial infarction and particular types of cancer, but it is not yet clear how much they affect overall risk. However, they might mean that different diseases should be considered separately, as in our report, when interpreting mendelian randomisation studies of potentially causal effects.[1]

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Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet 2019; **394:** 1638–50—In this Article, in Procedures, the correct dose of mometasone furoate is 100 µg. This correction has been made to the online version as of Sept 26, 2019, and the printed version is correct.

Waksman R, Di Mario C, Torguson R, et al. Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study. Lancet 2019; **394:** 1629–37—The appendix of this Article has been corrected as of Oct 7, 2019.