Concerns about report suggesting glucosamine and chondroitin protect against cartilage loss

We wish to raise several concerns about the validity and conclusions of the recent report from Martel-Pelletier and coauthors¹ regarding potential effects of glucosamine and chondroitin (G+C) on cartilage loss over time. The report used data from the Osteoarthritis Initiative (OAI), a large observational study from which the authors attempted to draw inferences about the effects of these treatments.

First, it is not clear why the authors chose to divide subjects into those on analgesics/nonsteroidal anti-inflammatory drugs (NSAIDs) versus those not on analgesics/NSAIDs before examining the effects of G+C. We are unaware of any data and none is cited that would suggest that G+C would have different effects on cartilage in those taking versus those not taking analgesics/ NSAIDs. We note that the use of analgesics/NSAIDs in most persons in OAI was intermittent, not continuous. If analgesic/ NSAID users had lower cartilage volumes than non-users, they could have adjusted for analgesic/NSAID use in analyses. If the authors believed that the effects of G+C would be different by analgesic/NSAID use, they should have tested for a difference using an interaction term. If the effects were not different, they should have analysed all subjects on G+C versus all those not on G+C adjusting for differences between the groups. Based on the extensive data presented in their paper, we strongly suspect that such an analysis would have yielded no significant findings—no association of G+C with protection against cartilage loss.

Also, in examining the effects of a treatment on outcomes in an observational study, one generally attempts to either match those on treatment with those not on treatment so that both treated and non-treated groups are similar in terms of their risk of outcomes (in this case cartilage loss) or adjust for differences between groups using multivariable analyses. Table 2 in their study shows considerable evidence that the G+C group was different from the non-G+C group in ways that might well have affected their rate of cartilage loss, yet the authors present a univariate analysis of the effect of G+C on cartilage loss in their tables. In the text, they acknowledge that a multivariable analysis showed no significant effect of G+C on cartilage loss. The authors should have presented adjusted analyses and made primary conclusions based on these.

Lastly, the authors highlight the effects on lateral cartilage loss of G+C, suggesting it is clinically meaningful. Since most patients in the OAI progression cohort have medial disease, why is any effect on lateral cartilage loss relevant? In the one subset finding suggesting an effect on one medial subregion, we note that four medial subregions were tested and only one of these showed an effect and this effect was only in one subgroup, the analgesic/NSAID group and not in the other. It might have been appropriate to adjust for the large number of comparisons carried out. A glance at the p values produced in the analyses presented suggests that significant results would not have survived such an adjustment.

In conclusion, we disagree with the conclusions put forward by Martel-Pelletier *et al* in their recent paper and suggest that there is no convincing evidence presented that G+C have any effect on cartilage.

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Martel-Pelletier J, Roubille C, Abram F, et al. First-line analysis of the effects of treatment on progression of structural changes in knee osteoarthritis over 24 months: data from the osteoarthritis initiative progression cohort. Ann Rheum Dis 2015;74:547–56.

