complement our findings from the Aerobics Center Longitudinal Study, as well as those from another recent report from the Netherlands of lower mortality risk among older adults reporting large, diverse social networks.[2] Taken together, these findings serve as a reminder that humans are innately social beings and that social functioning is as important as traditional biological and behavioral risk factors in determining health and well-being.

As epidemiological evidence continues to mount, efforts must shift to clinical assessment and intervention. As documented in both our article[1] and the letter by Loprinzi and El-Sayed, social relations can be assessed with a few simple questions (eg, "Can you count on anyone to provide you with emotional support such as talking over problems or helping you make a difficult decision?" and "How many close friends do you have?"). In order for individuals reporting low levels of support and/or few friends to receive evidence-based "treatment" options, individual-level interventions must be developed and tested. One novel approach that might simultaneously improve both perceptions of support and social integration could be the facilitation of pet adoption because pets can both provide companionship and serve as a catalyst for social interaction.[3,4] This may be one instance in which we can create (rather than improve) an intimate, supportive relationship for individuals with few existing family members or friends while also motivating additional social engagement in the community.

The findings reported by Loprinzi and El-Sayed in their letter to the editor complement our previous findings and contribute to the impressive evidence base on the importance of social relations to survival. We hope this discussion will motivate the establishment of clinical assessment procedures and the development of novel interventions to promote health and longevity.

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Risk of Disseminated Varicella Zoster in Immunosuppressed Patients Receiving Zoster Vaccination

To the Editor: The report by Cheetham et al[1] in the July 2015 issue of *Mayo Clinic Proceedings* uniquely addresses the risk of disseminated varicella zoster in patients taking immunosuppressant drugs at the time of zoster vaccination. For those of us providing care to immunosuppressed patients, 2 key questions are (1) whether immunosuppression reduces the efficacy of vaccination and (2) whether there are any risks specifically related to the use of a live attenuated vaccine. The first question is not addressed in the study by Cheetham et al, but the fact that there were no cases of disseminated zoster in this study's 4826 immunosuppressed patients who were vaccinated provides reassuring evidence that the risk of dissemination is low in this population. The results are valuable because prior reports of disseminated herpes zoster following vaccination of immunocompromised patients do not address causality or quantify risk.

The stated conclusion of the current study, however, is perplexing. These data are said to "support the current recommendations for zoster vaccination in that patients should withhold their immunosuppressant drugs for 4 weeks before immunization." Rather, the observation that there were no cases of disseminated zoster among immunosuppressed patients provides no rationale for stopping immunosuppressive therapy before vaccination. In fact, in combination with data presented confirming that immunosuppression increases the risk of herpes zoster even after stopping immunosuppressive therapy, these results arguably support the opposite conclusion—that it would be prudent to vaccinate immunosuppressed patients as soon as possible to minimize the time-dependent risk of herpes zoster. Moreover, the data reported no evidence to support a 4-week delay compared with any other arbitrarily chosen interval before vaccination.

The observation that there is increased risk of herpes zoster during a specific time frame following vaccination in *current* relative to *remote* users of immunosuppressants should not be misunderstood as a rationale for withholding therapy before vaccination. This reasoning is correct only if vaccination is the cause of the increased risk, a result that would be counterintuitive for an intervention intended to prevent herpes zoster, and indeed, there were significantly fewer zosterlike rashes in the vaccine arm relative to placebo arm in the Zostavax Efficacy and Safety Trial during the 42 days post-vaccination.[2] Rather, this observation[1] presumably reflects the difference in background incidence rates for each population,[3] again leading to the

conclusion that any delay in vaccination can only increase the risk of herpes zoster.

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In reply—Risk of Disseminated Varicella Zoster in Immunosuppressed Patients Receiving Zoster Vaccination

We thank Dr Bubb for his interest in our study and appreciate the opportunity to respond to his questions and concerns. Specifically, concern was raised about our conclusion that our findings "support the current recommendations for zoster vaccination in that patients should withhold their immunosuppressants for 4 weeks before immunization,"[1] even though we found no cases of disseminated varicella zoster among 4826 vaccinated individuals who were taking immunosuppressant medication. Additional concerns centered on our findings related to herpes zoster, specifically that (1) our data revealing a higher risk of herpes zoster in immunosuppressed patients who stopped immunosuppressive therapy argue that it would be prudent to vaccinate immunosuppressed patients as soon as possible, (2) the data do not support withholding immunosuppressant therapy for a minimum of 4 weeks before vaccination compared with any other arbitrarily chosen interval, and (3) vaccination is unlikely to be the cause of the increased risk of zoster during the 42 days postvaccination in the current vs remote immunosuppressant users.

Dr Bubb brings up good points, and we should have been clearer in our concluding remarks about withholding immunosuppressants. Current guidelines state that high-dose corticosteroids should be withheld for 4 weeks before administering the zoster vaccine, but the vaccine can be given to individuals taking low-dose corticosteroids without stopping therapy.[2,3] The results from our investigation suggest that there is a low risk of disseminated herpes zoster associated with the zoster vaccine when given to patients currently using immunosuppressant medications. However, it should be kept in mind that most of the patients in this study were receiving low-dose corticosteroids; too few patients were taking high-dose corticosteroids (n=550) at the time of vaccination to determine any associations or draw any inferences. Therefore, our results regarding disseminated varicella zoster support the recommendation to vaccinate patients taking low-dose corticosteroids without stopping therapy, but there is insufficient evidence to recommend vaccinating patients taking high-dose corticosteroids without stopping treatment. We recognize that our concluding statement could have been better stated.

According to Dr Bubb, the data confirm that "immunosuppression increases the risk of herpes zoster even after stopping immunosuppressive therapy" and suggest that "it would be prudent to vaccinate immunosuppressed patients as soon as possible to minimize the time-dependent risk of herpes zoster." The rate of herpes zoster for the remote immunosuppressant user group in our study was 15 cases per 1000 person-years, which is indeed higher than the rate of herpes zoster in nonimmunocompromised individuals (range, 6.0-8.6 cases per 1000 person-years among adults 60-79 years of age)[4] but is in fact consistent with rates of herpes zoster reported in patients with immune-mediated diseases, which range from as low as 6.4 to as high as 32.5 cases per 1000 patient-years.[5-9]

Regarding the choice of the 4-week interval for withholding therapy, the evidence supporting the recommendation to withhold immunosuppressants for 4 weeks before administering a live virus vaccine has never been strong. These recommendations, however, are not arbitrary but reflect the opinion of experts and are in part based on knowledge of the time it takes for the hypothalamic-pituitary-adrenal axis to recover from prolonged immunosuppression with corticosteroids. In our study, patients were classified as remote users if the immunosuppressant was stopped a minimum of 4 weeks before vaccination and as current users if the immunosuppressant was continued into this time frame. With lower rates of herpes zoster in the remote user group, our study results provide some evidence to support the recommendation to withhold immunosuppressants for 4 weeks before vaccination. Because most of the patients in this study were taking low-dose corticosteroids, the question then becomes whether low-dose corticosteroids should be stopped before vaccination. We do not believe that the results from this study, by themselves, support stopping low-dose corticosteroids before vaccination.

Our finding that the risk of herpes zoster was increased in the 42 days following vaccination in the current vs remote exposure group is complex because several factors are potentially at work. The study was designed to include a cohort of patients who, at baseline, have a higher risk of herpes zoster; the only observable difference between the comparison groups was current vs remote use of immunosuppressants. As