## RESPONSE TO ALICI

*To the Editor*: In response to our study on the diagnostic challenges of distinguishing protracted from new-onset delirium,[1] Alici raises two important questions for research on the persistence of delirium: use of the Confusion Assessment Method (CAM) for assessing the presence of persistent delirium and frequency of reassessments.[2] As for the CAM, use of the question "Is there evidence of an acute change in mental status from baseline" is potentially problematic for two reasons. First, the question does not specify which baseline the interviewer is referring to, the original baseline before admission (weeks or months earlier) or a more-recent baseline since admission. Second, it does not distinguish new-onset delirium from a fluctuation in mental state in the context of persistent delirium.

The original baseline was used as the reference;[1] most informants told the interviewer that the patient's mental state had not been the same since admission to the hospital. Admittedly, this is an additional potential limitation of the study. There is a need to develop and validate a CAM modified to assess the persistence of delirium.

As to the frequency of reassessments for persistent delirium, daily face-to-face reassessments may be feasible in hospital and postacute care settings,[3,4] but they are not feasible after discharge in most healthcare systems (including our system), where patients may be dispersed over a large metropolitan area and may move to different settings during the follow-up period. It was challenging to complete even the two face-to-face reassessments described in the present study. The limited number of reassessments was, nonetheless, an acknowledged limitation of the study. Future studies of the persistence of delirium conducted in special healthcare contexts (e.g., managed care programs) may be able to conduct more-frequent reassessments over longer follow-up periods.

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## CAN WE EQUATE ALL PROTON PUMP INHIBITORS WITH ONE ANOTHER?

*To the Editor*: The article of Hinson and colleagues[1] is important in that they show that long-term use of proton pump inhibitors can affect parathyroid hormone (PTH) levels independent of bisphosphonate use, which may be an important risk factor for fractures in elderly adults. However, there are some points that should be addressed.

First, the greater risk of osteoporosis and fracture with PPIs such as esomeprazole, omeprazole, pantoprazole, and rabeprazole has been shown in many studies,[2,3] although this effect may not be generalized to all PPIs. Moreover, the type of each PPI molecule may affect PTH levels differently. PTH levels may not be attributable to a group effect of PPIs. It would be better if the authors could provide information about the individual effects of each PPI type on PTH levels.

Second, the authors mention that the inclusion criteria included measurement of calcium, vitamin D, and PTH levels, but seeing as it is a retrospective study, there is no information about levels of these parameters before starting a PPI or bisphosphonates prescription. Therefore, the possibility cannot be excluded that the calcium levels of subjects in the PPI group were lower before the use of the medication.

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## RESPONSE TO SUMER AND COLLEAGUES

*To the Editor*: We thank Sumer and colleagues[1] for their interest in our research.[2] We agree that different types of proton pump inhibitors (PPIs) may affect parathyroid hormone (PTH) levels differently. Future studies may also find that PTH levels vary according to different PPI dosing, drug formulation (immediate vs delayed release), and routes of administration (oral, intravenous, gastrostomy tube). Our study also assumed a group effect for bisphosphonates (alendronate, ibandronate, zoledronate, risedronate). Thus, one could alternatively ask, "Can we equate all bisphosphonates with each other?" In summary, although we agree that greater efforts are needed to answer these important questions in the context of PTH levels and bone health, our study design and population size were not sufficient to speculate on such matters.

Sumer and colleagues correctly highlight that the possibility cannot be excluded that calcium levels of subjects in the PPI group were already lower before starting PPIs. We agree and indirectly address this point in the Discussion section (in the context of higher PTH levels rather than lower calcium levels): "The present study was unable to differentiate whether PPIs (directly or indirectly) increase PTH or, alternatively, whether high PTH increases the likelihood of PPI exposure. Indigestion and other gastrointestinal complaints are classic symptoms and signs associated with hyperparathyroidism (abdominal groans). It should not be surprising then that people with higher PTH commonly require medications that treat PTH-associated symptoms."[2] There is also evidence that PPIs play a more-physiological and -immediate role in lowering calcium and increasing PTH.[3,4] These roles were considered in more depth in the Discussion section.[2] In any case, we agree that prospective studies are now needed to determine whether our findings are of any clinical utility with regard to PPI-induced bone fragility or can be attributed to confounding comorbidities more common in individuals chronically exposed to PPIs.

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