severe hypoglycemia is potentially a marker for an excess of additional episodes and the observed effect can be interpreted as a measure of the cumulative effect of hypoglycemia.

Our reliance on ED and primary hospitalization diagnoses of hypoglycemia is a strength of the study, because these are clinically recognized exposures and not susceptible to recall bias and inaccurate self-reporting.[1,2] Moreover, our coding scheme for hypoglycemia was based on an established algorithm using *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnoses that has been validated in prior research.[3] In one study, this algorithm had 89% positive predictive value when compared with detailed medical record review.[3]

Regarding the possibility of confounding by educational level, individuals experiencing severe hypoglycemic episodes did not have lower educational levels than patients not experiencing such episodes. Sensitivity analyses demonstrated a similar association between hypoglycemic episodes and increased risk of dementia across all education levels and by stroke status.[1] If the association between hypoglycemia and dementia was spurious due to educational levels (or stroke), the findings would have been attenuated with adjustment.

The point that hospitalized cases of hypoglycemia may differ in etiology from episodes treated in the community and have causes such as serious underlying illness that could also be associated with dementia deserves attention. Two observations reduce this concern. First, the association was as strong for episodes treated in the ED as for hospitalized events. Second, the association persisted even with a 15-year lag between the hypoglycemic episode and first notation of dementia. This should eliminate most, if not all, confounding by serious illnesses associated with the hypoglycemia.

The data richness supporting this study was unique, including duration of diabetes, long-term glycemic control, ascertainment of diabetes pharmacotherapy, number of years using insulin, and a large number of comorbidities. Findings were stable despite adjustment for this wide range of factors. While we acknowledge that no observational study can completely eliminate unmeasured confounding, our findings suggest clinical caution in glucose-lowering treatments, particularly in older populations who have less to gain from tight glycemic control and are at the greatest risk for dementia.

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1. Cryer PE. The barrier of hypoglycemia in diabetes. *Diabetes*. 2008;57(12):3169-3176.
2. Tasker AP, Gibson L, Franklin V, Gregor P, Greene S. What is the frequency of symptomatic mild hypoglycemia in type 1 diabetes in the young? assessment by novel mobile phone technology and computer-based interviewing. *Pediatr Diabetes*. 2007;8(1):15-20.
3. Ginde AA, Blanc PG, Lieberman RM, Camargo CA Jr. Validation of ICD-9-CM coding algorithm for improved identification of hypoglycemia visits. *BMC Endocr Disord*. 2008;8:4.

Policies of Children's Hospitals on Donation After Cardiac Death

To the Editor: Dr Antommaria and colleagues[1] characterized donation after cardiac death (DCD) policies in children's hospitals and evaluated variation among policies. Western standards are that transplantation of organs is possible only if the patient complies with the dead donor rule.[2] Organ procurement is possible after the donor's death and must not cause death. Internationally, it is accepted as a norm that an individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions or (2) irreversible cessation of all functions of the entire brain, including brain stem, is dead.[3] *Irreversible* means that the function cannot be restored by anyone under any circumstances.[3]

Because DCD usually takes place after withdrawal of life support, the circulatory arrest might well be reversible by cardiopulmonary resuscitation within a certain period of time. In case of organ donation, the loss of brain functioning should always be the underlying criterion of death. In case of brain death, a patient with electroencephalographic activity is not legally dead and organs cannot be removed. According to Plum and Posner,[4] "Under clinical circumstances, total ischemic anoxia of the cerebral cortex lasting longer than about 4 minutes starts to kill brain cells, with the neurons of the cerebral cortex and cerebellum dying first." According to Table 3 in the article by Antommaria et al, in 7 hospitals pediatric patients are declared dead within 5 minutes, and in 1 hospital organs are removed within 2 minutes after circulatory arrest. These children were not (brain) dead when their organs were removed, and this is in conflict with the accepted dead donor rule in the Western world.[2]

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1. Antommaria AH, Trotochaud K, Kinlaw K, Hopkins PN, Frader J. Policies on donation after cardiac death at children's hospitals: a mixed-methods analysis of variation. *JAMA*. 2009;301(18):1902-1908.
2. Arnold RM, Youngner SJ. The dead donor rule: should we stretch it, bend it or abandon it? In: Arnold RM, Youngner SJ, Shapiro R, eds, et al. *Procuring Organs for Transplant.* London, England: John Hopkins University Press; 1985:219-234.
3. Guidelines for the determination of death: report of the medical consultants on the Diagnosis of Death to the President's Commission for the study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *JAMA*. 1981; 246(19):2184-2186.
4. Plum F, Posner JB. *The Diagnosis of Stupor and Coma.* 4th ed. New York, NY: Oxford University Press; 2007.

In Reply: Drs de Groot and Kompanje identify important ongoing issues regarding the declaration of death and DCD. However, they fail to acknowledge ongoing criticism of current neurological criteria of death, insufficiently characterize the duration of ischemia needed for irreversible cessation of all functions of the entire brain, and hold DCD to a higher standard of irreversibility than is used in other clinical contexts.

In their letter, de Groot and Kompanje focus on loss of brain function as the fundamental criterion of death. There has been, however, substantial criticism of this approach. Critics argue that individuals fulfilling neurological criteria may retain integrative function of the posterior pituitary and do not inevitably progress to cardiac arrest quickly.[1] Thus, the premise stated by de Groot and Kompanje may be equally problematic as what they criticize.

They note that anoxia begins to kill brain cells after 4 minutes and that 7 institutions require total waiting periods of less than 5 minutes. However, medical literature suggests that functional survival is possible after 10 to 20 minutes of normothermia without blood flow.[2] The longest combined waiting period specified in the policies we reviewed was 10 minutes, required by only 2 institutions. If one takes the writers' argument seriously, none of the policies have sufficient waiting periods.

As to overall criteria for death, they argue that irreversible "means that the function cannot be restored by anyone under any circumstances." This is a higher standard than is used in other clinical contexts. Individuals with do-not-attempt-resuscitation orders who are not potential organ donors may be declared dead well before the time that cardiopulmonary resuscitation would never work. Advocates of DCD argue that it is sufficient to wait long enough that spontaneous recovery of cardiorespiratory function or "autoresuscitation" is sufficiently unlikely.[3]

Ongoing conceptual clarification is needed regarding these topics, as well as further empirical study regarding the effect the evolving criteria for death may have on public trust in organ retrieval from deceased donors.

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1. Truog RD, Robinson WM. Role of brain death and the dead-donor rule in the ethics of organ transplantation. *Crit Care Med*. 2003;31(9):2391-2396.
2. Safar P. Cerebral resuscitation after cardiac arrest: a review. *Circulation*. 1986; 74(6 pt 2):IV138-IV153.
3. Bernat JL. Are organ donors after cardiac death really dead? *J Clin Ethics*. 2006; 17(2):122-132.

Functional Outcomes of Older Overweight Cancer Survivors After Diet and Exercise

To the Editor: In their randomized controlled trial, Dr Morey and colleagues[1] reported that among older, long-term (≥5 years) survivors of colorectal, breast, and prostate cancer, a diet and exercise intervention reduced the rate of self-reported functional decline. The body mass index (BMI) of the participants ranged from 25 to 40 (calculated as weight in kilograms divided by height in meters squared).

Approximately 41% of men and 53% of women in the United States have levels of serum 25-hydroxyvitamin D below 28 ng/mL.[2] An indicator of vitamin D status, serum 25-hydroxyvitamin D may be low in obese adults and has an inverse relationship with BMI.[3] Epidemiologic studies indicate that low levels of serum 25-hydroxyvitamin D are associated with an increased risk of colon, prostate, and breast cancer, along with higher mortality from these cancers.[4] Evidence also suggests that in older persons a mean serum concentration greater than 65 nmol/L of vitamin D may improve muscle performance.[5]

Therefore, it would be useful to examine the vitamin D status or vitamin D supplementation of the study population and its relationship with functional outcome.

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1. Morey MC, Snyder DC, Sloane R, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors. *JAMA*. 2009;301(18):1883-1891.
2. Zadshir A, Tareen N, Pan D, Norris K, Martins D. The prevalence of hypovitaminosis D among US adults: data from the NHANES III. *Ethn Dis*. 2005;15 (4 suppl 5):S5-97-S5-101.
3. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357(3):266-281.
4. Giovannucci E, Liu Y, Rimm EB, et al. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. *J Natl Cancer Inst*. 2006; 98(7):451-459.
5. Dawson-Hughes B. Serum 25-hydroxyvitamin D and functional outcomes in the elderly. *Am J Clin Nutr*. 2008;88(2)(suppl):537S-540S.

In Reply: Given the recent attention surrounding vitamin D, the request by Dr Shil and colleagues to explore intake in relation to physical function is a compelling question. In response, we conducted a cross-sectional analysis of our baseline data (n=641).[1] As described in the main outcomes article, telephone interviews were used to gather data on diet and supplement use, through 2 unannounced 24-hour recalls (multipass method with the Nutrition Data System for Research software, version 2006; Nutrition Coordinating Center, Minneapolis, Minnesota), and to assess physical function, which was captured using 3 instruments: physical function subscales of the Medical Outcomes Study Short-Form 36 (SF-36) and the basic and advanced lower extremity function subscales of the Late Life Function and Disability Index, with