Supplementary Online Content


**eFigure.** (Figure 1) A table of all reversal in the *NEJM* in 2009 and how they contradicted existing medical practice

**eReferences**

This supplementary material has been provided by the authors to give readers additional information about their work
## Figure 1:

<table>
<thead>
<tr>
<th>Article</th>
<th>Date of Publication</th>
<th>How it contradicted existing medical practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Prednisolone for Preschool Children with Acute Virus-Induced Wheezing</td>
<td>1/22/2009</td>
<td>Several sets of national guidelines recommend that oral corticosteroids be given to preschool aged children who present to a hospital with virus-induced wheezing (1,2,3). However, the data for steroids use in this population is unclear. This large randomized, double-blind, placebo-controlled trial found no benefit of steroids among preschool children presenting to the hospital with acute, mild-to-moderate virus-induced wheezing.</td>
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<tr>
<td>Quality of Life after Late Invasive Therapy for Occluded Arteries</td>
<td>2/19/2009</td>
<td>Late opening (3-28 days after myocardial infarction) of a completely occluded coronary artery is a common practice, particularly in the United States (4,5,6,7). Such late opening is thought to improve mortality, ventricular function, and quality of life. Previously, the Occluded Artery Trial (OAT), a large randomized study, found no benefit in major cardiovascular events for this therapy (8). This study reexamined OAT with respect to economic and quality of life outcomes. Late opening of occluded infarct-related arteries provided a marginal advantage for physical function at 4 months that was not sustained for the 3 year trial duration. Late opening resulted in higher total medical costs and lower quality-adjusted life expectancy at 2 years.</td>
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<tr>
<td>Intensive versus Conventional Glucose Control in Critically Ill Patients</td>
<td>3/25/2009</td>
<td>The mortality benefit of routine prostate cancer specific antigen (PSA) screening continues to be debated. This large, randomized trial failed to detect any mortality benefit of routine screening among American men.</td>
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<td>Mortality Results from a Randomized Prostate-Cancer Screening Trial</td>
<td></td>
<td>Since 2001, tight glycemic control (81 to 108 mg per deciliter) has been widely recommended and practiced in intensive care units (9,10). The Nornoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial showed that tight control, as compared with conventional glucose control, increased the absolute risk of death at 90 days by 2.5 percentage points.</td>
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<td>Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis</td>
<td>4/2/2009</td>
<td>Because of their significant cardiovascular risk, hemodialysis users are recommended to take statins according to clinical guidelines worldwide (11,12). A Study to Evaluate the Use of Rosuvastatin in Subjects on Regular Hemodialysis: An Assessment of Survival and Cardiovascular Events (AURORA) found no benefit in the combined end point of myocardial infarction, stroke, or death from cardiovascular causes among these patients, despite significant improvements in LDL cholesterol.</td>
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<tr>
<td>Efficacy of Esomeprazole for Treatment of Poorly Controlled Asthma</td>
<td>4/9/2009</td>
<td>Acid reflux is thought to exacerbate wheezing among asthmatic patients. Current guidelines recommend that patients with poorly controlled asthma, particularly those with nighttime symptoms, be tested for gastroesophageal reflux disease, even in the absence of heart burn symptoms. If detected, proton-pump inhibitors (PPI) are recommended in these patients (13). This study found that, despite a substantial incidence of GERD in this population, the addition of a PPI did not confer benefit.</td>
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<td>Cognitive Function at 3 Years of Age after Fetal Exposure to Antiepileptic Drugs</td>
<td>4/15/2009</td>
<td>Several sets of consensus guidelines (the American Academy of Neurology (14) the American College of Obstetricians and Gynecologists (15) and the International League against Epilepsy (16) do not distinguish among antiepileptic drugs used during pregnancy with respect to teratogenic risks. The Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study found that valproic acid, as compared with other commonly used drugs, was associated with poorer cognitive function at 3 years of age.</td>
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<tr>
<td>Early versus Delayed, Provisional Eptifibatide in Acute Coronary Syndromes</td>
<td>5/21/2009</td>
<td>2007 guidelines from the American College of Cardiology and the American Heart Association (17) recommend that among patients with NSTE/MI and high-risk features aspirin and either clopidogrel or a glycoprotein IIb/IIIa inhibitor be given before angiography (i.e., early therapy) (class I recommendation). This study, the EARLY ACS trial, showed that contrary to this recommendation, the early use of eptifibatide was not superior to eptifibatide post angiography, and likely resulted in higher rates of bleeding.</td>
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<tr>
<td>Endoscopic versus Open Vein-Graft Harvesting in Coronary-Artery Bypass Surgery</td>
<td>7/15/2010</td>
<td>Endoscopic harvesting of the saphenous vein for coronary artery bypass surgery has swelled in popularity. It is a procedure which eliminates the need for the long incisions associated with open harvesting, reduces wound infections, decreases postoperative pain, and shortens length of stay in the hospital (18-20). In fact, in 2005 the International Society for Minimally Invasive Cardiothoracic Surgery recommended that it should replace open harvesting as standard of care (21). This study showed that endoscopic harvesting resulted in higher rates of vein-graft failure at 12 to 18 months, and, at 3 years, higher rates of death, myocardial infarction, or repeat revascularization.</td>
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</table>
Vertebroplasty is a medical procedure where cement is injected into fractured spinal bone, in theory, restoring the original shape, diminishing pain, and stabilizing the fragments. Interventional neuroradiologists pioneered its use in the United States in the 1990s. By the late 1990s, case series were published, and technical details were shared (22). Proponents of vertebroplasty lobbied Medicare to fund the procedure, and in 2001, their request was granted. In that year, more than 14,000 vertebroplasties were performed in the United States, and by 2004, that number was 27,000 (23). Vertebroplasty quickly became a multi-million dollar a year industry. In these paired articles, the procedure was shown to be no better than a sham procedure.

Breast-cancer survivors with lymphedema may limit the use of the affected arm based upon guidance from the American Cancer Society (24). This randomized trial showed, that contrary to this position, weight lifting improves the symptoms of lymphedema.

Renal failure is associated with substantial morbidity and mortality and is common among patients requiring intensive care. In recent years, there has been a widespread increase in the use of higher-intensity continuous renal-replacement therapy compared to lower intensity replacement therapy among critically ill patients (25,26). This large, multicenter, randomized, controlled trial of intensity of renal support in acute kidney injury (RENAI) indicates that such practice is not justified, as high intensity therapy did not improve mortality at 90 days.

Renal artery stenosis is associated with hypertension and kidney disease, but it is unclear if the relationship is causal (27). Despite this uncertainty, data from studies in the United States indicate that revascularization is performed in 16% of patients with newly diagnosed atherosclerotic renovascular disease and hypertension (28). This large randomized trial (ASTRAL) of revascularization with medical management versus medical management alone found substantial risks but no evidence of benefit from revascularization in this population.

The use of erythropoiesis stimulating agents among patients with anemia and chronic kidney disease is widespread. The belief that this therapy confers benefit is so strong that major clinical trials have considered the use of placebo unnecessary or even unethical. (29-31) The Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) showed that the use of these agents did not reduce the risk of either death or a cardiovascular event or death or a renal event and was associated with an increased risk of stroke.

Zetia or Ezetimibe was licensed by the Food and Drug Administration in 2002 based upon its ability to reduce the LDL cholesterol level without major short term side effects. Since that time, Zetia has been prescribed widely to improve cardiovascular risk. A number of other studies have suggested that the net effect of Zetia may not be beneficial. This current study shows that for one surrogate of atherosclerotic disease the Zetia does not result in the regression of carotid artery intimal medial thickness, while niacin (another cardiovascular drug) does. This study further undermines the purported benefit of Zetia with respect to cardiovascular risk.

**Figure 1 - A table of all reversal in the NEJM in 2009 and how they contradicted existing medical practice**
Figure 1 citations:

2) British guideline on the management of asthma. Thorax 2003;58:Suppl 1:i1-i94
16) Commission on Genetics, Pregnancy and the Child, International League against Epilepsy. Guidelines for the care of women of childbearing age with epilepsy. Epilepsia 1993;34:588-589

20) Seabolt PB, Reardon MJ. Endoscopic vein harvesting in cardiac surgery. Curr Opin Cardiol 2003;18:444-446