most plausible small to moderate effects. In all observational studies, no matter how large and well designed, the amount of uncontrolled and unobservable confounding can be as large as the effect sizes being sought. Meta-analysis of small trials may introduce confounding as well as small to moderate biases due to differences in designs, adherence, follow-up, and outcomes. Thus, for small to moderate effects, observational studies and metaanalyses of small trials are useful primarily to formulate, not test, hypotheses.

With respect to costs, in trials complexity is rarely a virtue, whereas large simple trials are more feasible and can be done at relatively low cost per patient randomized. Establishing whether a statistically significant finding is clinically important is not unique to RCTs.

Industry sponsorship of trials creates a conundrum because of concern that industry scientists may be trying to prove that there is a valid statistical association to secure regulatory approval and widespread use of their drug, whereas independent academic scientists are trying to determine whether there is a valid statistical association. Nonetheless, during the last decade industry-sponsored trials have produced the majority of important advances in cardiovascular medicine. We support the widely used and increasingly accepted model of an academic scientific executive committee, an academic data and safety monitoring board, and an academic statistical data analysis center that are all independent and free from conflicts of interests with the sponsor. These checks and balances are crucial to the protection of human participants as well as the integrity of RCTs, whether industry or government sponsored.

Dr Sacristán states that randomized evidence concerns the average patient and may not apply to an individual patient. Recent breakthroughs, especially in genomics, have suggested the potential of tailoring a particular intervention to a particular patient. Nonetheless, the perfect should not be the enemy of the possible, so we believe that at present adopting a paradigm for individual patients based on reliable randomized evidence will do more good than harm, as well as the most good for the most patients.

Dr Bolland and colleagues suggest that large-scale randomized evidence may be impractical for exploring potential harm. A sufficient totality of evidence for concluding small to moderate benefit or harm must include large-scale randomized evidence. For example, for rosiglitazone the meta-analysis of small trials not designed a priori to test cardiovascular outcomes suggested harm and should have been considered a posteriori hypothesis formulat. The findings from the relatively large trial designed a priori to test the hypothesis did not support the hypothesis formulated from the meta-analysis. We agree that the meta-analysis of the small trials of rosiglitazone as well as the prespecified secondary subgroup analyses of their small randomized trial of calcium supplements, suggesting an increased risk of myocardial infarction, provide importantly relevant contributions to the overall body of evidence. Such analyses, however, should be followed by a trial designed a priori to test the hypothesis.

The guiding principle about benefit as well as harm of drugs should be that rational decisions for individual patients and the health of the general public should be based on a sufficient totality of evidence, which, for small to moderate effects, should include large-scale RCTs. Until the totality of evidence is sufficient, it is appropriate to remain uncertain about benefit and harm.

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Sudden Death During the Triathlon

RESEARCH LETTER

Dr Hennekens reported that he is funded by the Charles E. Schmidt College of Biomedical Science, Department of Clinical Science and Medical Education, and Center of Excellence at Florida Atlantic University (FAU) as principal investigator on 2 investigator-initiated research grants funded to FAU by Bayer; serves in an advisory role to investigators and sponsors as chair of the data and safety monitoring boards for Actelion, Amgen, Bristol-Myers Squibb, Dainippon Sumitomo, and Sanofi-Aventis, and as a member of the data and safety monitoring boards for Bayer and the Canadian Institutes of Health Research; serves in an advisory role to the US Food and Drug Administration, US National Institutes of Health, and UpToDate; serves as an independent scientist in an advisory role to legal counsel for General Electric, GlaxoSmithKline, and Stryker; serves as a speaker for the Association of Research in Vision and Ophthalmology, National Association for Continuing Education, PriMed, the International Atherosclerosis Society, AstraZeneca, and Pfizer; receives royalties for authorship or editorship of 3 textbooks and as co-inventor on patents for inflammatory markers and cardiovascular disease that are held by Brigham and Women’s Hospital; and has an investment management relationship with the West-Bacon Group within SunTrust Investment Services, which has discretionary investment authority. Dr DeMets reported that he is partially supported by a National Institutes of Health grant to the University of Wisconsin for the Clinical Translational Science Award for statistical consultation and collaboration and administrative leadership, as a leader of the Data Management and Biostatistics Core (Core C) of the Wisconsin Alzheimer’s Disease Research Center grant, by serving as a principal investigator on University of Wisconsin contracts with industry for statistical analysis center activity for multicenter trials, which are currently sponsored by Amgen, AstraZeneca, and Bristol-Myers Squibb; serves or has recently served as an independent biostatistician in an advisory role to investigators and sponsors as a member of the data and safety monitoring boards for Actelion, Amgen, Astellas, AstraZeneca, Biotronik, Boehringer-Ingelheim, CVRx, Genentech, GlaxoSmithKline, Novartis, Merck, Pfizer, Roche, Sanofi-Aventis, Takeda, the Duke Clinical Research Institute, the Population Health Research Institute of McMaster University, Canadian Institutes of Health Research, Harvard Clinical Research Institute, and Hamilton Clinical Research Institute; receives royalties from publishers of the 3 textbooks that he has authored and edited; has tax-sheltered retirement accounts in mutual funds with Fidelity and UBS; and has 2 small accounts of stock with Sun and Intel.

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Sudden Death During the Triathlon

To the Editor: Triathlon is among the most vigorous amateur athletic disciplines, requiring expertise in swimming, biking, and running.13 Although sudden death risk has been
assessed for the amateur marathon,\(^4\) it has not been systematically investigated for triathlon.

**Methods.** Participants who completed 2971 USA Triathlon (USAT) sanctioned events from January 2006 through September 2008 were tabulated using online race results (approximately 95% of event results).\(^5\) Participants in nonsanctioned races, relay races, or triathlons without full swim-bike-run sequence were excluded. Deaths were identified in the US Registry of Sudden Deaths in Athletes\(^6\) and USAT records,\(^5\) which have tabulated these events over 30 and 5 years, respectively; autopsy reports were obtained from medical examiners. The Abbott Northwestern Hospital institutional review board determined this study was exempt. Confidence intervals (CIs) were calculated using Poisson analysis (JMP version 7; SAS Institute Inc, Cary, North Carolina).

**Results.** A total of 959,214 participants were analyzed (mean [SD], 323 [444] per race); 59% were men. Forty-five percent completed in short (swim <750 m), 40% in intermediate (swim 750-1500 m), and 15% in long (swim >1500 m) triathlon races (TABLE).

Fourteen participants died during 14 triathlons (rate, 1.5 per 100,000 participants; 95% CI, 0.9-2.5), including 13 while swimming and 1 biking (Table). Athletes who died were 28 to 65 years old (mean [SD] age, 44 [10] years). Triathlons with deaths included more participants (n = 1319; 95% CI, 1084-1584) than races without deaths (n = 318; 95% CI, 302-334). Of the swimming deaths, 11 were men and 2 were women.

Six deaths occurred in short, 4 in intermediate, and 3 in long races (2 in an Ironman triathlon). Eight swimmers were in distress and called for assistance, and 5 were found motionless on the water. Deaths occurred in the open ocean (n = 6), lakes (n = 4), reservoirs (n = 2), or a river (n = 1). The bicycle fatality resulted from a fall causing cervical injuries.

Drowning was the declared cause of each swimming death, but 7 of 9 athletes with autopsy had cardiovascular abnormalities identified. Six had mild left ventricular hypertrophy with maximum wall thickness of 15 to 17 mm and mean (SD) heart weight of 403 (77) g, including 1 with a clinical history of Wolff-Parkinson-White syndrome. One other athlete had a congenital coronary arterial anomaly, and 2 had structurally normal hearts.

**Comment.** Although the contribution of cardiovascular abnormalities cannot be definitively excluded in some cases,\(^2\) logistical factors and adverse environmental conditions may have been responsible for these events, given that about 95% of triathlon fatalities occurred during the swimming segment. Furthermore, deaths were more common in triathlons involving greater numbers of competitors. Because triathlons begin with chaotic, highly dense mass starts, involving up to 2000 largely novice competitors entering the water simultaneously, there is an opportunity for bodily contact and exposure to cold turbulent water.\(^7\) Triathlons also pose inherent obstacles to identifying distressed athletes and initiating timely resuscitation on open water. Compared with these triathlon findings, marathon racing analyzed for more than 3 million runners over 30 years reported a mortality rate of 0.8 per 100,000 participants (95% CI, 0.5-1.1).\(^4\)

Study limitations include the possibility that all sudden deaths may not have been identified, as neither of the registries is based on mandatory reporting. Although it is not possible to determine the precise number of US triathlons annually, USAT events likely represent a large proportion. This study was designed to explore risk per participation; an unknown number of athletes competed more than once within the data set.

Although mass screening before competition may be impractical, awareness of cardiovascular risks may motivate athletes to seek preparticipation evaluations on an individual basis. Efforts to improve triathlon safety could include establishing minimum achievement standards for participating, including swimming proficiency.

**LETTERS**

**Table.** Sudden Deaths in USA Triathlon Sanctioned Events, 2006-2008

<table>
<thead>
<tr>
<th>Race segment</th>
<th>Participations, No.</th>
<th>Deaths, No. (% of Total Deaths)</th>
<th>Deaths Per 100,000 Participants, No. (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swim</td>
<td>13 (93)</td>
<td>1.4 (0.8-2.3)</td>
<td></td>
</tr>
<tr>
<td>Bike</td>
<td>1 (7)</td>
<td>0.1 (0.01-0.7)</td>
<td></td>
</tr>
<tr>
<td>Run</td>
<td>0</td>
<td>0.0 (0.0-0.3)</td>
<td></td>
</tr>
<tr>
<td>Event length</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short (swim &lt;750 m)</td>
<td>435,049 6 (42)</td>
<td>1.4 (1.1-3.1)</td>
<td></td>
</tr>
<tr>
<td>Intermediate (swim 750-1500 m)</td>
<td>381,817 4 (29)</td>
<td>1.0 (0.4-2.8)</td>
<td></td>
</tr>
<tr>
<td>Long (swim &gt;1500 m)</td>
<td>142,348 4 (29)</td>
<td>2.8 (1.0-7.5)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>569,864</td>
<td>11 (80)</td>
<td>1.9 (1.1-3.5)</td>
</tr>
<tr>
<td>Female</td>
<td>389,350</td>
<td>3 (20)</td>
<td>0.8 (0.3-2.4)</td>
</tr>
<tr>
<td>Year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>276,458</td>
<td>2 (14)</td>
<td>0.7 (0.2-2.9)</td>
</tr>
<tr>
<td>2007</td>
<td>342,612</td>
<td>4 (29)</td>
<td>1.2 (0.4-3.1)</td>
</tr>
<tr>
<td>2008</td>
<td>340,144</td>
<td>8 (57)</td>
<td>2.4 (1.2-4.7)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

\(^a\)The same number of participations was assumed for each of the 3 triathlon segments.

\(^b\)Triathlon event lengths are categorized by the length of the swimming segment.

\(^c\)Includes the Ironman event, in which the swim portion is 2.4 miles, biking is 112 miles, and running is the marathon distance (26.2 miles).

\(^d\)January 1 through September 14, 2008, only.

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CORRECTIONS

Data Error and Incorrect Table Headings: In the Original Contribution entitled “Patient-Reported Long-term Outcomes After Conventional and High-Dose Combined Proton and Photon Radiation for Early Prostate Cancer” published in the March 17, 2010, issue of JAMA (2010;303[11]:1046-1053), a number and corresponding percent were incorrectly stated in the text. On page 1051, center column, second paragraph, the second sentence should have read, “Of the original 393 participants in PROG 9509, 55 (14%) died and an additional 58 patients (14.8%) did not participate in the survey, reducing study power and raising the possibility of bias.” This article was corrected online for typographical errors on March 17, 2010.

In the same article, headings were incorrectly printed in Table 6 on page 1051. Column 1 should have read “Dysfunction,” column 2 should have read “PROG 9509 All Patients,” and column 3 should have read “Boston Area Cohort Study.”

Table 6. Comparison of Mean Urinary, Bowel, and Sexual Function Scores

<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>PROG 9509 All Patients</th>
<th>Boston Area Cohort Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>280</td>
<td>97</td>
</tr>
<tr>
<td>Time of follow-up, median, y</td>
<td>9.4</td>
<td>5.9</td>
</tr>
</tbody>
</table>

Error in Text: In the Original Contribution entitled “Characteristics of Published Comparative-Effectiveness Studies of Medications” published in the March 10, 2010, issue of JAMA (2010;303[10]:951-958), a wording error appeared in the Comment section on page 956, third column, first full paragraph, first sentence. The sentence should have read, “Inactive-comparator trials were more likely than active-comparator trials to report positive results, presumably because active comparators are more effective than inactive controls.”

Misspelling Changing Meaning: In the Literatim entitled “Abraham Flexner and His Remarkable Report on Medical Education: A Century Later” published in the February 3, 2010, issue of JAMA (2010;303[9]:888-890), “contract” was misspelled as “contact,” changing the meaning of a sentence. The last sentence of the second paragraph in the left column on page 888 should have read “Less well recalled was Flexner’s emphasis on the physician’s social contract—a commitment to helping others and the prevention of disease in the population rather than merely the cure of the individual.”

Incorrect P Value: In the Original Contribution entitled “Comparison of Platelet Function Tests in Predicting Clinical Outcome in Patients Undergoing Coronary Stent Implantation” published in the February 24, 2010, issue of JAMA (2010;303[8]:754-762), a P value was displayed incorrectly. In Figure 2, the P value for Plateletworks should be “P for model = .054.”

Incorrect Reporting: In the Commentary entitled “Perioperative β-Blockers for Cardiac Risk Reduction: Time for Clarity” published in the February 10, 2010, issue of JAMA (2010;303[8]:551-552), the text and table incorrectly reported the type of surgical procedures undergone by patients in one study. On page 551, the sentence “The POISE study included patients undergoing vascular surgery who had varied risk factors including peripheral vascular disease, congestive heart failure, or need for emergency surgery.” should have read “The POISE study was a trial of noncardiac surgery that included patients undergoing vascular or nonvascular surgery and who had varied risk factors, including peripheral vascular disease, congestive heart failure, or need for emergency surgery.” In the Table on page 552, the text in the POISE “Surgical Procedure” column should have read “Variable.”

Vascular (41.9%), intra-abdominal/intraperitoneal (21.3%), orthopedic (20.9%), other (15.9%).”

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