not a primary or secondary outcome of the study and may not have been systematically collected or reported, raising issues of ascertainment bias. This issue is even more challenging because all patients had cognitive impairment. Second, study discontinuation rates were high and there was not a planned, rigorously conducted period of off-drug follow-up. In addition, our analysis updates the published findings from study 078, since a subsequent investigation suggested that these were incomplete.3

Implications for individuals who used rofecoxib are unclear, since it was withdrawn from the market nearly 5 years ago. To our knowledge, no studies have been conducted to determine for how long the increased cardiovascular risk associated with rofecoxib use persists, to elucidate the mechanism, or to examine whether there are long-term risks after discontinuation of other non-steroidal anti-inflamatory drugs, selective or nonselective. To improve drug safety evaluation within clinical trials, periods of off-drug surveillance should be used when appropriate to ensure observation of long-term effects.

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Cognitive decline is a major public health care issue, and a well-recognized clinical manifestation of cognitive decline is falls. Seniors with cognitive impairment fall at twice the rate of peers without cognitive impairment.1,2

Exercise training may be an effective strategy against cognitive decline,1,3 and it is recommended for prevention of falls. We recently reported that 12 months of once-weekly (1×RT) or twice-weekly (2×RT) resistance training improved selective attention and conflict resolution compared with a balance and tone program (BAT; control) among 155 community-dwelling senior women (ie, Brain Power resistance training study).3 We also found that both resistance training programs provided better...
value for falls prevented compared with the BAT program. To our knowledge, no study has examined whether both cognitive and economic benefits of exercise persist after formal cessation. Hence, we examined whether improved selective attention and conflict resolution as well as economic benefits were sustained 12 months after formal cessation of the Brain Power resistance training study.

**Methods.** We conducted a 12-month follow-up study from May 2008 to April 2009. Of the original 155 participants, 123 consented to the follow-up study. Ethics approval was obtained from the Vancouver Coastal Health Research Institute and the University of British Columbia’s Clinical Research Ethics Board.

Our primary outcome measure was the specific executive cognitive function of selective attention and conflict resolution, as measured by the Stroop Test. Secondary measures included set shifting, working memory, and current physical activity level.

Between-group differences in executive cognitive functions were compared by multiple linear regression analyses as in our original trial. For current physical activity level, baseline score and experimental group were used as covariates. Two planned simple contrasts were performed to assess differences between (1) the 1×RT group and the BAT group and (2) the 2×RT group and the BAT group. The overall α level was set at P < .05.

For the economic evaluation, we calculated the incremental cost per fall prevented for both 1×RT and 2×RT groups compared with the BAT group from a Canadian Health Care System perspective using a 21-month time horizon (2009 prices). All hospital admission–related costs were based on a fully allocated cost model of a tertiary care setting as in our original trial. For current physical activity level, baseline score and experimental group were used as covariates. Two planned simple contrasts were performed to assess differences between (1) the 1×RT group and the BAT group and (2) the 2×RT group and the BAT group. The overall α level was set at P < .05.

**Results.** Of the 123 who consented, 109 completed the assessment at the end of the 12-month follow-up (37 from the 1×RT group, 41 from the 2×RT group, and 31 from the BAT group). The mean (SD) age of the cohort was 71.6 (3.0) years.

There was a significant between-group difference in selective attention and conflict resolution at the end of the 12-month follow-up study (P = .04). Specifically, the 1×RT group sustained improved Stroop test performance compared with the BAT group (P = .04) (Table). There were no significant between-group differences in set shifting, working memory, and current physical activity level.

The unadjusted incidence rate ratio over the 2-year period for the 1×RT group indicated a 30% (incidence rate ratio, 0.70; 95% confidence interval, 0.37-1.33) nonsignificant reduction in falls and an 8% (incidence rate ratio, 1.08; 95% confidence interval, 0.79-1.47) nonsignificant increase in the 2×RT group.

On the basis of the point estimates from our base case analysis, we found that the 1×RT group incurred fewer health care resource utilization costs and had fewer falls than the BAT group; thus, 1×RT was less costly and more effective than BAT. Although the 2×RT group also incurred fewer care utilization costs than BAT, the 2×RT group sustained more falls. Thus, 2×RT was less effective than BAT.

**Comment.** We provide novel data suggesting that both the cognitive and economic benefits of once-weekly resistance training can be sustained 12 months after its formal cessation. Specifically, 12 months after trial completion, former participants of the 1×RT group demonstrated a 15% improvement in their performance on the Stroop test compared with those in the BAT group. This novel finding supports the emerging belief that targeted exercise training may combat age-related decreases in cognitive function. Furthermore, there was a significant reduction in health care resource utilization costs of falls 12 months after trial completion for the 1×RT and 2×RT groups compared with the BAT (control) group. Thus, both cognitive and economic benefits of participating in a 12-month resistance training intervention were sustained for the 1×RT group, whereas these benefits were not sustained for the 2×RT group. The 1×RT group demonstrated a 5% increase (P > .05) in current physical activity level from baseline compared with a 6.6% reduction (P > .05) in the 2×RT group. Hence, maintaining physical activity level may be essential in sustaining the benefits of resistance training. Such findings should remain guarded as future studies investigate factors that

### Table. Outcome Measures and Results of Base Case Analysis for Economic Evaluation

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>BAT</th>
<th>1×RT</th>
<th>2×RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroop CW – Stroop C, s</td>
<td>43.98 (15.1)</td>
<td>47.37 (26.2)</td>
<td>45.02 (15.8)</td>
</tr>
<tr>
<td>Trail B – Trail A, s</td>
<td>47.12 (41.3)</td>
<td>41.35 (26.5)</td>
<td>49.53 (36.6)</td>
</tr>
<tr>
<td>Digit Forward – Digit Backward</td>
<td>3.2 (2)</td>
<td>3.5 (2)</td>
<td>3.4 (2)</td>
</tr>
<tr>
<td>Physical Activity Scale for the Elderly, 12-mo follow-up (n=109), mean (SD)</td>
<td>126 (51)</td>
<td>116 (61)</td>
<td>121 (60)</td>
</tr>
<tr>
<td>No. of falls per year over 9 mo</td>
<td>38</td>
<td>30</td>
<td>38</td>
</tr>
<tr>
<td>No. of falls per year over 12-mo follow-up study</td>
<td>20</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>Total No. of falls over 21 mo</td>
<td>58</td>
<td>47</td>
<td>65</td>
</tr>
<tr>
<td>Incremental No. of falls prevented over 21 mo</td>
<td>[Reference]</td>
<td>11</td>
<td>–7</td>
</tr>
<tr>
<td>Incremental cost (total health resource utilization), $</td>
<td>[Reference]</td>
<td>$-1857^a</td>
<td>$-1077^a</td>
</tr>
</tbody>
</table>

Abbreviations: BAT, balance and tone program; RT, resistance training; Stroop C, Stroop colored-X’s condition; Stroop CW, Stroop color-words condition.

^aSignificantly different from the BAT group at P < .05.

^bTotal number of falls for 9 months of the 12-month randomized controlled trial.
explain this observed variation in exercise-induced cognitive benefits in terms of costs and consequences.

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Author Contributions: All authors had full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Marra, Beattie, Graf, and Liu-Ambrose. Acquisition of data: Nagamatsu and Liu-Ambrose. Analysis and interpretation of data: Marra, Beattie, Robertson, Najafzadeh, Nagamatsu, and Liu-Ambrose. Drafting of the manuscript: Liu-Ambrose. Critical revision of the manuscript for important intellectual content: Marra, Beattie, Robertson, Najafzadeh, Nagamatsu, and Liu-Ambrose. Statistical analysis: Marra, Najafzadeh, and Liu-Ambrose. Obtained funding: Beattie, Graf, and Liu-Ambrose. Administrative, technical, and material support: Nagamatsu and Liu-Ambrose. Study supervision: Marra, Robertson, and Liu-Ambrose.

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