Trends in National Institutes of Health Funding for Clinical Trials Registered in ClinicalTrials.gov

Clinical trials inform evidence-based prevention and treatment recommendations. The National Institutes of Health (NIH) and the pharmaceutical industry have been major funders of trials. In general, the pharmaceutical industry funds trials that test their own products, whereas the NIH’s funding strategies are not commercially motivated.

In 2005, registration of trials became required for publication in major journals. Registration is also required for trials that meet the definition of an “applicable clinical trial” from the US Food and Drug Administration Amendments Act 801 and that were either initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007. There are legal repercussions if sponsors or principal investigators do not register accurately.

We hypothesized that the number of NIH-funded trials has decreased. We investigated trends in funding of trials using the NIH-built database, ClinicalTrials.gov, with a focus on NIH and industry funding.

Methods | We downloaded data from ClinicalTrials.gov, searched for “interventional study” and obtained counts of newly registered trials by funder type: “NIH,” “industry,” “other US federal agency,” or “all others (individuals, universities, organizations).” Funder type “NIH,” for example, retrieves records for which at least 1 NIH institute or center has been listed as the sponsor (generally indicating NIH intramural research) or collaborator (suggesting extramural NIH funding).

We searched for date “first received” and the self-reported “study start.” Counts are by year (“first received” and “study start” dates between 2006 and 2014), as of June 26, 2015.

We calculated differences, 95% confidence intervals, and P values (2-sided χ² test, a level <.05) using Stata version 12.1 (StataCorp).

Results | Examining data according to the first received date, the number of newly registered trials doubled from 9321 in 2006 to 18400 in 2014 (Table 1). The number of industry-funded trials increased by 1965 (43%). Concurrently, the number of NIH-funded trials decreased by 328 (24%).

During this period of relatively few trials being funded by other US federal agencies, funding from the all others category increased by 7357 (227%). In a random sample of 500 trials in this category, a majority (353; 71%) did not have US-based funders.

Using the study start date instead of the first received date led to differences in counts per year but similar patterns (Table 2). From 2006 through 2014, the total number of newly registered trials increased by 5410 (59%) and that of industry-funded trials increased by 758 (17%). The number of NIH-funded trials declined by 316 (27%).

Discussion | From 2006 through 2014, there has been a decrease in newly registered NIH-funded trials, whereas industry-funded trials increased substantially. The decrease in NIH-funded trials

### Table 1. Trials Registered in ClinicalTrials.gov From 2006 Through 2014 by Year First Received

<table>
<thead>
<tr>
<th>Year of trial start</th>
<th>Total No. of Trials</th>
<th>National Institutes of Health</th>
<th>Industry</th>
<th>Other US Federal Agency</th>
<th>All Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>9321</td>
<td>1376 (14.8)</td>
<td>4585 (49.2)</td>
<td>263 (2.8)</td>
<td>3240 (34.8)</td>
</tr>
<tr>
<td>2007</td>
<td>11 122</td>
<td>1247 (11.2)</td>
<td>5462 (49.1)</td>
<td>275 (2.5)</td>
<td>4284 (38.5)</td>
</tr>
<tr>
<td>2008</td>
<td>13 942</td>
<td>1333 (9.6)</td>
<td>7046 (50.5)</td>
<td>327 (2.3)</td>
<td>5385 (38.6)</td>
</tr>
<tr>
<td>2009</td>
<td>13 712</td>
<td>1162 (8.5)</td>
<td>6390 (46.6)</td>
<td>327 (2.4)</td>
<td>5963 (43.5)</td>
</tr>
<tr>
<td>2010</td>
<td>13 816</td>
<td>1113 (8.1)</td>
<td>5923 (42.9)</td>
<td>309 (2.2)</td>
<td>6595 (47.7)</td>
</tr>
<tr>
<td>2011</td>
<td>14 202</td>
<td>1057 (7.4)</td>
<td>5839 (41.1)</td>
<td>320 (2.3)</td>
<td>7127 (50.2)</td>
</tr>
<tr>
<td>2012</td>
<td>15 468</td>
<td>1015 (6.6)</td>
<td>5738 (37.1)</td>
<td>344 (2.2)</td>
<td>8507 (55.0)</td>
</tr>
<tr>
<td>2013</td>
<td>16 217</td>
<td>1074 (6.6)</td>
<td>5355 (33.0)</td>
<td>363 (2.2)</td>
<td>9566 (59.0)</td>
</tr>
<tr>
<td>2014</td>
<td>18 400</td>
<td>1048 (5.7)</td>
<td>6550 (35.6)</td>
<td>339 (1.8)</td>
<td>10 597 (57.6)</td>
</tr>
</tbody>
</table>

% Difference (95% CI)a,b | −9.1 (−9.9 to −8.3) | −13.6 (−14.8 to −12.3) | −1.0 (−1.4 to −0.6) | 22.8 (21.6 to 24.0) |

Absolute difference, No. (%)c | 9079 (97.4) | −328 (−23.8) | 1965 (42.9) | 76 (28.9) | 7357 (227.1) |

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a Data as of June 26, 2015.
b One trial may have more than 1 funding source.
c Unless otherwise indicated.

All comparisons yielded P values of <.001.
Comparisons are between the year 2006 and 2014.
may have resulted from a decline in discretionary spending by the US federal government.

The 2014 NIH budget is 14% less than the 2006 budget (when adjusted for inflation). An expanding portfolio of NIH research with a flat budget may also have contributed to the decline in NIH-funded trials.

Tracking patterns in trial funding using ClinicalTrials.gov has limitations. First, available data by registration date and study start date differ. A registration date is assigned for all trials, whereas the study start date may have missing values.

In addition, investigators may define study start differently. Registration of ongoing or finished trials during the earlier years may account for larger numbers of NIH-funded trials by registration date relative to study start date. However, trends did not differ.

Second, trend data are valid indicators only to the extent that registration behavior by funding sources is not differential over time. Because of federal regulations, registration of NIH-funded trials on ClinicalTrials.gov is likely to be relatively comprehensive.

If registration behavior has improved over time, we may have underestimated the observed reduction in NIH-funded trials. Also, we do not know if there have been changes in how other trials were registered.

Third, the all others funder category is heterogeneous. It comprises non-US governmental agencies, organizations, universities, and other funders, mainly from outside the United States.

COMMENT & RESPONSE

Pioglitazone Use and Risk of Bladder Cancer

To the Editor Dr Lewis and colleagues reported that more than 4 years’ duration of pioglitazone use was not associated with a statistically significant increased risk of bladder cancer (hazard ratio, 1.22; 95% CI, 0.92-1.61) after adjusting for several covariates, including calendar year at cohort entry. This result contrasts with their previous analysis, and an accumulating body of evidence from other trials and observational studies, which all support an increased risk of bladder cancer with pioglitazone.

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Author Contributions: Drs Ehrhardt and Meinert had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Ehrhardt, Meinert.

Additional Contributions: We are indebted to Jill Meinert (Johns Hopkins Bloomberg School of Public Health) for technical assistance for which she was not compensated.