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**Title**: Accuracy of the post-publication correction for conflict of interest disclosure in the CREATE-X trial in the New England Journal of Medicine

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Ozaki A. Conflict of Interest and the CREATE-X Trial in the New England Journal of Medicine. Sci Eng Ethics. 2017.

**Abstract**

In June 2017, the Capecitabine for Residual Cancer as Adjuvant Therapy (CREATE)-X trial was published in the New England Journal of Medicine. Despite multiple criticisms on its financial aspects and subsequent correction of conflict of interest (COI) disclosure, little is known about the accuracy of this correction on the individual basis. We extracted publicly available payment data in 2016 among 71 pharmaceutical companies in Japan. We assessed the accuracy of the authors’ COI disclosure by comparing it with this payment data. Among the 12 Japanese authors, 9 (75%) received the payment from the Chugai Pharmaceutical Company (CPC), which manufactured the study drug. However, only 3 (33.3%) and 6 (66.7%) correctly disclosed the COI related to the CPC in the original and revised COI statement, respectively. In conclusion, the relevant industry payment was not completely disclosed among the CREATE-X trial authors even after the post-publication correction.

**Text**:

**Introduction**

In June 2017, the Capecitabine for Residual Cancer as Adjuvant Therapy (CREATE)-X trial was published in the New England Journal of Medicine.1 Despite its groundbreaking study findings, we and others pointed out insufficiency in the conflict of interest (COI) disclosure,2 and the original COI disclosure in the article was corrected in August 2017.3 However, it has not been clarified whether the correction of the COI disclosure was appropriately made among these authors in the individual basis. The aim of the present study is to clarify the accuracy of the post-publication correction of conflict of interest in an article in the study.

**Methods**

In Japan, individual physician payment data has been publicly available among 71 pharmaceutical companies, which belong to Japan Pharmaceutical Manufacturers Association (JPMA), since the fiscal year of 2013. We examined the accuracy of COI disclosure among the Japanese authors of the CREATE-X trial, using the 2016 payment data, which is only accessible at present, because of the disclosure policy of the companies. The International Committee of Medical Journal Editors (ICMJE) requires a declaration for all the relevant financial relationships during 36 months prior to the article publication. Thus, all the relevant payment in 2016 should be completely declared in the published article of the CREAT-X trial.

**Result**

As shown in Table 1, among the 12 Japanese authors, 9 (75%) received the payment from the CPC. However, only 3 (33.3%) and 6 (66.7%) correctly disclosed the COI related to the CPC in the original and revised COI statement, respectively. Among the 17 companies with any financial relationships with the authors, 14 (82.4%) manufactured drugs for breast cancer. None of the 10 authors who received the payment outside of the CPC correctly disclosed their relationships either in the original or revised COI statement.

**Discussion**

The present analysis shows that the relevant financial relationships were not completely disclosed among the CREATE-X trial authors even after the post-publication correction. As this analysis only covered the financial relationships among the authors in 2016, the actual gap between the payment and disclosure would be even larger.

The CREATE-X trial article has been cited for 71 times as of July 12, 2018, and its findings have made a large impact on the clinical practice. As shown in the current case, a platform where each stakeholder can easily assess financial relationships of authors plays an important role for readers to obtain an opportunity to assess authors’ COI statement precisely. Given a growing drug market in developing countries, we call for the implementation of such systems, as already achieved in the US, UK, Japan, and Australia. Thereby, an improved transparency will be achieved between physicians and relevant industries.

**References**

1. Masuda N, Lee SJ, Ohtani S, et al. Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy. *N Engl J Med.* 2017;376(22):2147-2159.

2. Ozaki A. Conflict of Interest and the CREATE-X Trial in the New England Journal of Medicine. *Sci Eng Ethics.* 2017.

3. Toi M, Masuda N, Ohashi Y. Adjuvant Capecitabine for Breast Cancer. *N Engl J Med.* 2017;377(8):791-792.

Table 1. Disclosure of conflict of interest among the Japanese author of the Capecitabine for Residual Cancer as Adjuvant Therapy trial

|  |  |
| --- | --- |
|  | N=12 |
| Medical doctor |  |
| Yes | 10 (83.3%) |
| No | 2 (16.7%) |
| Median number of pharmaceutical companies with payment in 2016 (median, IQR) | 7 (5–9) |
| Any payment from the CPC in 2016 |  |
| Yes | 9 (75.0%) |
| No | 3 (25.0%) |
| Value of payment from the CPC in 2016 (JPY, median, IQR) | 263,470 (85,914–1,211,107) |
| COI disclosure for the CPC (among the authors with the payment from the CPC) (in the original version) |  |
| Yes | 3 (33.3%) |
| No | 6 (66.7%) |
| COI disclosure for the CPC (among the authors with the payment from the CPC) (in the revised version) |  |
| Yes | 6 (66.7%) |
| No | 3 (33.3%) |
| Any payment from pharmaceutical companies outside of the CPC in 2016 |  |
| Yes | 11 (91.7%) |
| No | 1 (8.3%) |
| Value of payment from pharmaceutical companies outside of the CPC in 2016 (JPY, median, IQR) | 1,510,394 (491,362–2,983,015) |
| Pharmaceutical companies with any payment outside of the CPC in 2016 (among the authors with the payment from pharmaceutical companies outside of the CPC) |  |
| Kyowa-Kirin | 9 (81.8%) |
| Eisai | 8 (72.7%) |
| Taiho Pharma | 8 (72.7%) |
| AstraZeneca | 7 (63.6%) |
| Novartis | 7 (63.6%) |
| Daiichi-Sankyo | 5 (45.5%) |
| Phizer | 5 (45.5%) |
| Sanofi | 4 (36.4%) |
| Eli-lilly | 4 (36.4%) |
| MSD | 3 (27.3%) |
| Takeda Pharmaceutical Company | 3 (27.3%) |
| Yakult | 2 (18.2%) |
| Torii-Yakuhin | 1 (9.1%) |
| Kowa | 1 (9.1%) |
| Bayer | 1 (9.1%) |
| Nippon Kayaku | 1 (9.1%) |
| Astellas Pharma Inc | 1 (9.1%) |
| Complete COI disclosure for pharmaceutical companies outside of the CPC (among the authors with the payment from pharmaceutical companies outside of the CPC) (in the original version) |  |
| Yes | 0 (0%) |
| No | 11 (100.0%) |
| Complete COI disclosure for pharmaceutical companies outside of the CPC (among the authors with the payment from pharmaceutical companies outside of the CPC) (in the revised version) |  |
| Yes | 0 (0%) |
| No | 11 (100.0%) |

COI=Conflict of interest; CPC=Chugai Pharmaceutical Company