Factors influencing pharmaceutical industry-affiliated clinical trial publication timelines

Poster number 31

Steve J Banner,[1] Tomas Rees,[1] Andrew Liew,[2] Nick Brown,[3a] Vini Dhanky,[4a] Luke Humphreys,[1] Hicham Naimy,[4] David H Peters,[4] Fran Young[4]

[1]Oxford PharmaGenesis, Oxford, UK; [2]Oxford PharmaGenesis, Melbourne, Australia; [3]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [4]Takeda Development Center Americas, Inc., Cambridge, MA, USA

[a]At the time the study was performed

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Background

- Multiple factors, such as author and study participant numbers, as well as external influences, such as journal impact factors, can affect the time taken between study completion and publication of scientific studies.[1–4]
- However, the impact of these factors on time to publication (TtP) are often conflicting; for example, higher author numbers have been associated with both increased and decreased TtP.[1,2]
- An understanding of the factors that influence TtP and the magnitude of their effect may help to inform optimal publication strategies and enhance the timeliness of scientific communication to the community.

Objective

- To identify and quantify the association of pre- and post-submission variables with the time taken for the primary publication of data following completion of a clinical trial sponsored by a pharmaceutical company.

Methods

- Metadata for clinical trials completed between December 1, 2016, and December 1, 2021, were extracted from Trialtrove (Citeline). Clinical trial registration identifiers were used to locate clinical trial publications via PubMed.
  - Trial completion dates (the date that the final patient was treated or evaluated for the primary endpoint) were extracted from Trialtrove; primary publication dates were extracted from PubMed.
- Phase 2–4 clinical trial publications with at least one author affiliated with a top 20 pharmaceutical company (by drug sales) were identified using OpenAlex and included in the analyses. Publication exclusion criteria are detailed in the **supplementary material**.

Factors of interest (FoIs)

- TtP was the primary outcome measure, defined as the time from the clinical trial completion date to the primary publication date.
- Pre- and post-submission FoIs (**Supplementary Table 1**) were obtained from Trialtrove, PubMed, Scopus or PlumX and used for correlation analyses with TtP.

Statistics

- Multiple statistical analyses were performed and are detailed in the **supplementary material** and the footnotes of each figure. Results were considered significant if $p \leq 0.05$.

Results

Study characteristics

- Overall, 1022 primary clinical trial publications had a complete set of data and were included in the analysis, of which 58% (n = 588) were phase 3 trials.
- The mean TtP was 630.3 days (median, 595 days) and mean author count was 15 authors (median, 13 authors) (**Table 1**).
- Therapy areas covered in the studies identified included autoimmune/inflammation, cardiovascular, central nervous system, infectious disease, metabolic/endocrinology and oncology.
- The characteristics of selected FoIs are included in **Table 1**.

Correlations of phase 2–4 pre- and post-submission factors with TtP

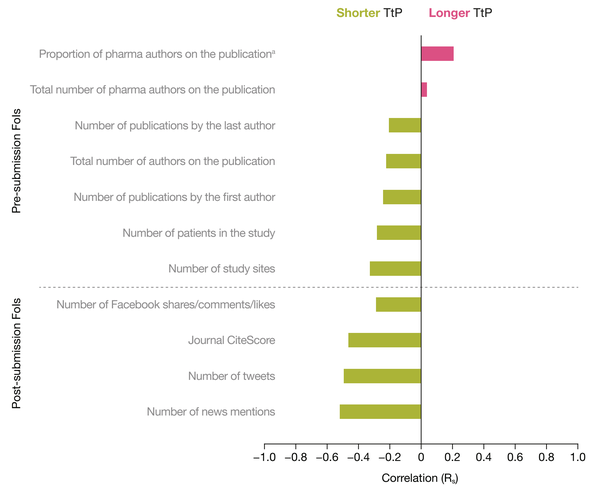
- Most FoIs (n = 9/11) were negatively correlated with TtP (**Figure 1**).
  - Of pre-submission factors, the number of study sites had the strongest association with TtP (Spearman's rank [R_s] –0.328).
  - Of post-submission factors, news mentions and number of tweets (considered proxy measures of study importance) were the most strongly correlated with TtP (R_s –0.516 and –0.493, respectively).
  - Interestingly, author number was negatively correlated with TtP (R_s –0.226), which suggests that an increased number of authors was associated with a reduced TtP.
  - In contrast, the total number of pharmaceutical company-affiliated authors ('pharma authors') had minimal correlation with TtP, whereas an increasing proportion of pharma authors was associated with a longer TtP.

Table 1. Characteristics of FoIs from included studies (N = 1022).[a]

FoI	Pre- or post-submission metric	Mean	SD	Min	Median	Max
Number of study sites	Pre	117.1	172.4	1	66.0	2234
Number of patients in the study	Pre	876.9	2078.3	7	346.5	37 235
Number of publications by the last author	Pre	331.3	432.9	1	147.5	3957
Total number of authors on the publication	Pre	14.8	7.3	3	13.0	61
Total number of pharma authors on the publication	Pre	4.6	2.4	1	4.0	15
Proportion of pharma authors on the publication[b]	Pre	0.4	0.2	0.02	0.3	1
Journal CiteScore	Post	33.8	36.6	0.2	16.5	115.3
Number of tweets	Post	65.8	210.0	0	7.0	3259
Number of Facebook shares/comments/likes	Post	35.2	118.2	0	0.0	1692
Number of news mentions	Post	8.8	28.3	0	1.0	489

[a]For the purposes of this analysis, studies with missing data for any of the FoIs were excluded listwise. [b]The proportion of pharma authors was calculated as the number of pharma authors divided by the total number of authors.
FoI, factor of interest; max, maximum; min, minimum; SD, standard deviation.

Figure 1. Correlation (R_s) of pre- and post-submission FoIs with TtP.

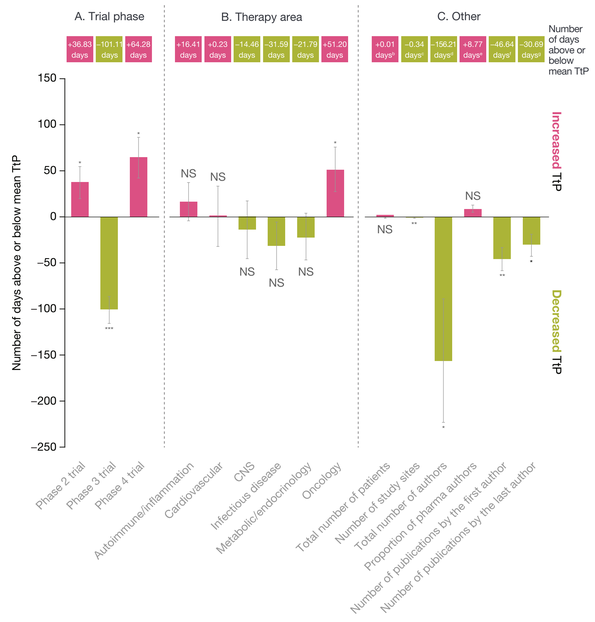


Negative correlations indicate that an increase in the FoI was associated with a reduced TtP. Positive correlations indicate that an increase in the FoI was associated with an increase in TtP.
[a]The proportion of pharma authors for each publication was calculated as the number of pharma authors divided by the total number of authors.
FoI, factor of interest; R_s, Spearman's rank; TtP, time to publication.

Quantifying the association of pre-submission factors with TtP: analysis of covariance (ANCOVA)

- Phase 2 and phase 3 trials were associated with significant, albeit diametrically opposed, directional differences in TtP (**Figure 2A**).
  - Phase 2 trials were associated with a longer TtP (36.8 days above the mean; $p < 0.05$).
  - Phase 3 trials were associated with a shorter TtP (101.1 days below the mean $p < 0.0001$).
- Oncology was the only therapy area significantly associated with TtP (**Figure 2B**).
- Number of study sites, total number of authors and publication count of the first and last authors were significantly associated with a TtP that was shorter than the mean (**Figure 2C**).
- No significant association was observed between mean TtP and the proportion of pharma authors (**Figure 2C**).

Figure 2. Association of pre-submission FoIs with TtP that is longer or shorter than the mean: ANCOVA (n = 950).[a]



*$p < 0.05$, **$p < 0.01$, ***$p < 0.0001$ vs mean TtP.
[a]For the purposes of this analysis, studies with missing data for any of the FoIs were excluded listwise. [b]Per additional patient. [c]Per additional study site. [d]Per 10-fold increase in author number. [e]Per 10 percentile increase in the proportion of pharma authors. [f]Per 10-fold increase in number of publications by the first author. [g]Per 10-fold increase in the number of publications by the last author.
ANCOVA, analysis of covariance; CNS, central nervous system; FoI, factor of interest; NS, nonsignificant; TtP, time to publication.

Phase 3 trials

- Several pre- and post-submission FoIs analyzed were significantly associated with shorter TtP in a multiple linear regression model (**Table 2**).
- An assessment of associations between journal CiteScore,[5] the number of pharma authors and TtP of phase 3 trials (**Figure 3**) revealed that:
  - journals with high CiteScores were associated with a shorter TtP than journals with low CiteScores ($p = 0.0139$)
  - in journals with:
    - high CiteScores, the number of pharma authors did not affect TtP
    - low CiteScores, a low number of pharma authors was associated with longer TtP than those with a high number of pharma authors (706.5 days vs 634.1 days, respectively; $p = 0.05$).

Table 2. Association of number of patients, first author publication count, CiteScore, tweets and news mentions with TtP in phase 3 trials (n = 588): MLR.

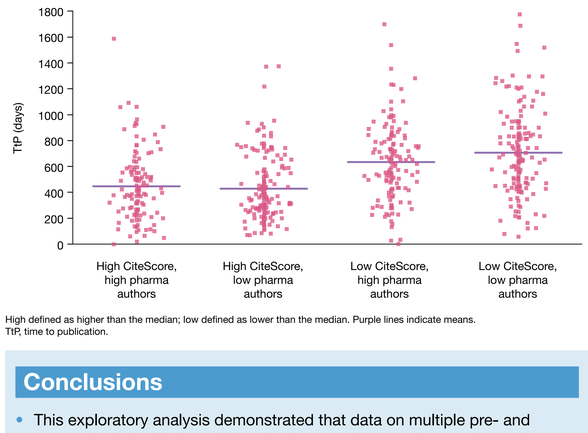
FoI	Estimate (days)	95% CI	*p* value
TtP (constant)	**893.4**	**809.7 to 977.2**	**< 0.0001**
Number of patients[a]	–0.02	0.03 to 0.004	0.0141
First author publication count[b]	–32.3	–57.1 to –7.5	0.0107
Journal CiteScore[b]	–94.6	–169.9 to –19.3	0.0139
Number of tweets[b]	–56.7	–100.6 to –12.9	0.0113
Number of news mentions[b]	–102.8	–155.2 to –50.4	0.0001

All pre- and post-submission FoIs (**Supplementary Table 1**) were entered into an MLR model with stepwise removal of those that did not show a significant interaction ($p \leq 0.05$). Those remaining are shown here.
[a]Estimates are per additional patient. [b]Estimates are per 10-fold change in the FoI.
CI, confidence interval; FoI, factor of interest; MLR, multiple linear regression; TtP, time to publication.

Limitations

- These data were based on TtP, which includes peer review. This process can be variable and may be a confounder of our results. However, we observed similar results when time to submission data were used, albeit using a smaller number of studies (n = 702, **supplementary material**).
- The FoIs analyzed in this study are not continuous, normally distributed or homoscedastic. However, these analyses represent a useful exploratory tool to identify which factors might be important with respect to TtP.
- This was an exploratory analysis; therefore, results need careful interpretation and/or further analysis.

Figure 3. Association between journal CiteScore, number of pharma authors and TtP in phase 3 trials (n = 588).



High defined as higher than the median; low defined as lower than the median. Purple lines indicate means.
TtP, time to publication.

Conclusions

- This exploratory analysis demonstrated that data on multiple pre- and post-submission FoIs could be obtained, and correlations performed to quantify their potential association with TtP.
- Overall, study importance seemed to be the primary influence on TtP as news mentions and number of tweets were significantly associated with shorter TtP.
  - Consistent observations were noted for time to submission in a subset of studies.
- Certain correlations were seemingly counterintuitive, highlighting the need to interpret findings carefully with due consideration to competing factors.
- Further analyses are needed to understand these observations and identify FoIs that could be used to enhance timely publication of clinical trial data.

References

1. Taçkın Z *et al. Scientometrics* 2022;127:7499–515.
2. Dhoot AS *et al. Ophthalmic Epidemiol* 2022;29:465–72.
3. Ross JS *et al. JAMA Intern Med* 2013;173:825–28.
4. Suñé P *et al. PLoS One* 2013;8:e54583.
5. James C *et al. Learn Publ* 2019;32:367–74.

Disclosures

SJB, TR, AL and LH are employees of Oxford PharmaGenesis. NB was an employee of Takeda at the time of the study. VD was a postdoctoral fellow at the time of the study and employed full-time by Northeastern University, Boston, MA, USA, with Takeda supporting funding for the fellowship. HN and FY are employees of Takeda. DHP is a contractor to Takeda.

Acknowledgments

This study was jointly funded by Takeda Development Center Americas, Inc., MA, USA and Oxford PharmaGenesis, Oxford, UK. The authors would like to acknowledge Paul Farrow of Oxford PharmaGenesis, Oxford, UK for his contribution to the study design and data analysis.

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[1]Oxford PharmaGenesis, Oxford, UK; [2]Oxford PharmaGenesis, Melbourne, Australia;
[3]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [4]Takeda Development Center Americas, Inc., Cambridge, MA, USA
[a]At the time the study was performed

Supplementary methods

Publication exclusion criteria

Publications with:

- PubMed tags: 'Case Reports', 'Clinical Trial Protocol', 'Comment', 'Letter', 'Meta-Analysis', 'Practice Guideline', 'Review' and 'Systematic Review'
- duplicate digital object identifiers (publications associated with more than one trial)
- 'study protocol' or 'rationale + design' in the publication title
- a negative publication lag (i.e. earliest publication date [received, accepted or entrez date] before the trial completion date)
- no pharmaceutical company-affiliated authors ('pharma authors').

Statistics

- Data pre-processing, extraction and wrangling were performed in R, BioPython was used for PubMed searches and exploratory analyses were conducted in Microsoft Excel.
- Spearman's rank (R_s) and analysis of covariance (ANCOVA) were used to identify associations between factors of interest (FoIs) and time to publication (TtP).
- Studies with FoI data missing were excluded listwise from analyses.
- The following analyses were conducted using phase 3 trial data only: multiple linear regression (MLR) to estimate the relationship between pre- and post-submission variables and TtP associations between high (> median) and low (< median) journal CiteScores[1] and number of pharma authors with TtP.
- Results were considered significant if $p \leq 0.05$.

Poster presented at the 19th Annual Meeting of the International Society for Medical Publication Professionals (ISMPP)
Washington, DC, USA | April 24–26, 2023

Supplementary results

Supplementary Table 1. Pre- and post-submission variables.

FoIs were determined by author consensus and included:

Pre-submission variables	Post-submission variables
Trial phase	Journal CiteScore
Number of study sites	Number of tweets[a]
Number of patients in the study	Number of Facebook shares/comments/likes[a]
Number of authors	Number of news mentions[a]
Number and proportion[b] of pharma authors	
Number of publications by the first and last author	
Therapy area	

[a]Variables were considered to be a proxy measure of study importance. [b]The proportion of pharma authors was calculated as the number of pharma authors divided by the total number of authors.
FoI, factor of interest.

Supplementary Table 2. Characteristics of FoIs from included studies for TtS analysis (n = 702).

FoI	Pre- or post-submission metric	Mean	SD	Min	Median	Max
Number of study sites	Pre	101.5	144.9	1	64.0	2234
Number of patients in the study	Pre	789.5	2104.6	7	323.0	37 235
Number of publications by the first author	Pre	369.4	427.6	1	237.0	3388
Number of publications by the last author	Pre	328.2	444.4	1	133.5	3957
Total number of authors on the publication	Pre	14.1	6.7	3	13.0	52
Total number of pharma authors on the publication	Pre	4.7	2.4	1	4.0	15
Proportion of pharma authors on the publication[a]	Pre	0.4	0.2	0.03	0.4	1.0
Journal CiteScore	Post	28.6	31.5	1.8	15.2	115.3
Number of tweets	Post	29.3	118.7	0	5.0	2893
Number of Facebook shares/comments/likes	Post	25.8	65.4	0	0.0	714
Number of news mentions	Post	5.5	26.6	0	0.0	489

[a]The proportion of pharma authors was calculated as the number of pharma authors divided by the total number of authors.
FoI, factor of interest; max, maximum; min, minimum; SD, standard deviation; TtS, time to submission.

Supplementary Table 3. Association of number of patients, first author publication count, CiteScore, tweets and news mentions with TtS in phase 3 trials (n = 374): MLR.

FoI	Estimate (days)	95% CI	*p* value
TtS (constant)	**681.3**	**582.3 to 780.3**	**< 0.0001**
Number of patients[a]	–0.01	–0.03 to 0.01	0.1662
First author publication count[b]	–8.8	–35.3 to 17.7	0.5126
Journal CiteScore[b]	–98.7	–185.3 to 12.1	0.0256
Number of tweets[b]	–62.2	–109.6 to –14.7	0.0104
Number of news mentions[b]	–53.4	–114.2 to 7.3	0.0847

[a]Estimates are per additional patient. [b]Estimates are per 10-fold change in the FoI.
CI, confidence interval; FoI, factor of interest; MLR, multiple linear regression; TtS, time to submission.

Supplementary Figure 1. Correlation (R_s) of pre- and post-submission FoIs with TtS (n = 702).

Negative correlations indicate that an increase in the FoI was associated with a reduced TtP. Positive correlations indicate that an increase in the FoI was associated with an increase in TtP.

[a]Proportion of pharma authors for each publication was calculated as the number of pharma authors divided by the total number of authors.

FoI, factor of interest; R_s, Spearman's rank; TtS, time to submission.

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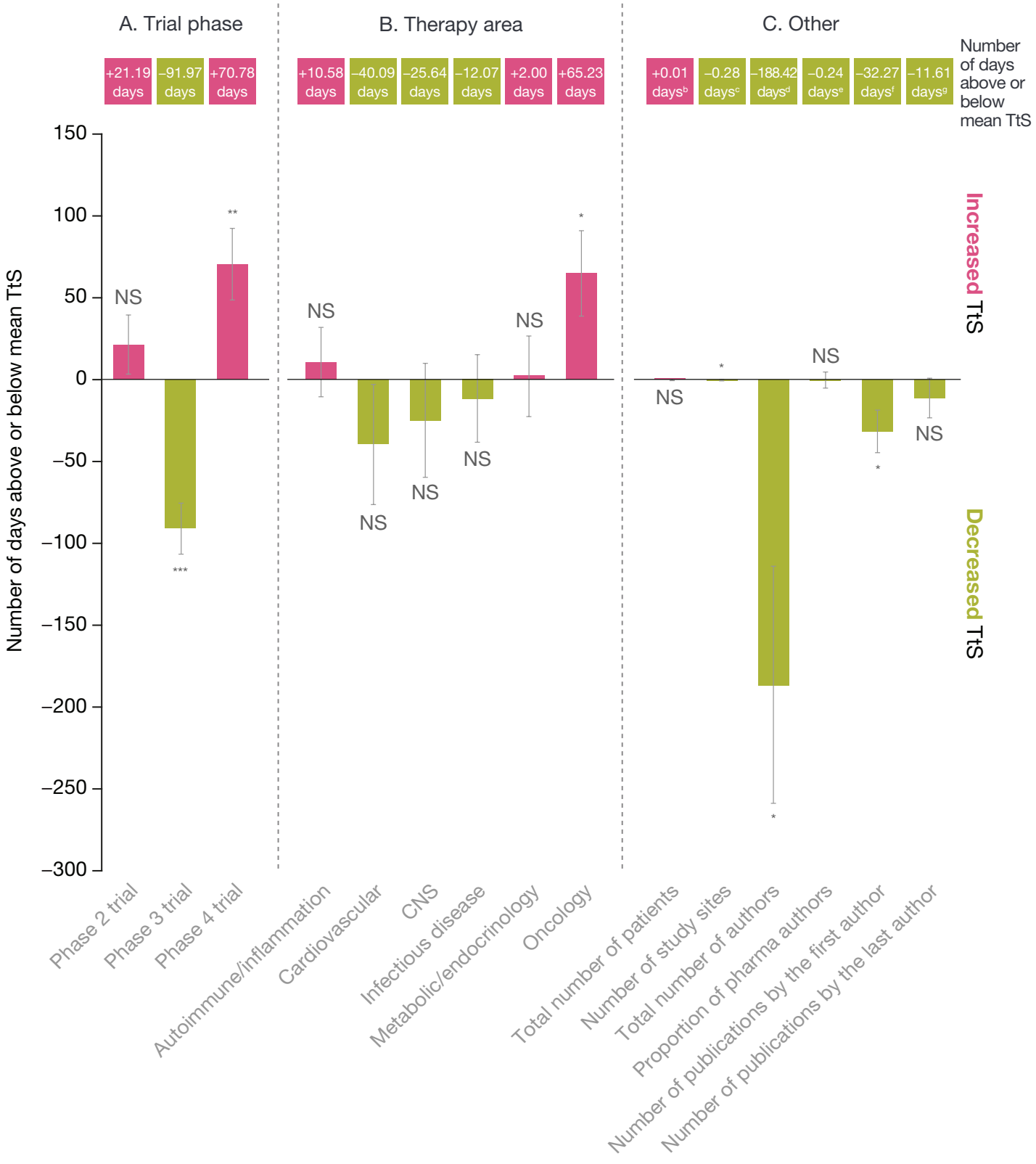
Supplementary Figure 2. Association of pre-submission FoIs with TtS that is longer or shorter than the mean: ANCOVA (n = 648).[a]



*$p < 0.05$, **$p < 0.01$, ***$p < 0.0001$ vs mean TtS.
[a]For the purposes of this analysis, studies with missing data for any of the FoIs were excluded listwise. [b]Per additional patient. [c]Per additional study site. [d]Per 10-fold increase in author number. [e]Per 10 percentile increase in the proportion of pharma authors. [f]Per 10-fold increase in number of publications by the first author. [g]Per 10-fold increase in the number of publications by the last author.
ANCOVA, analysis of covariance; CNS, central nervous system; FoI, factor of interest; NS, nonsignificant; TtS, time to submission.

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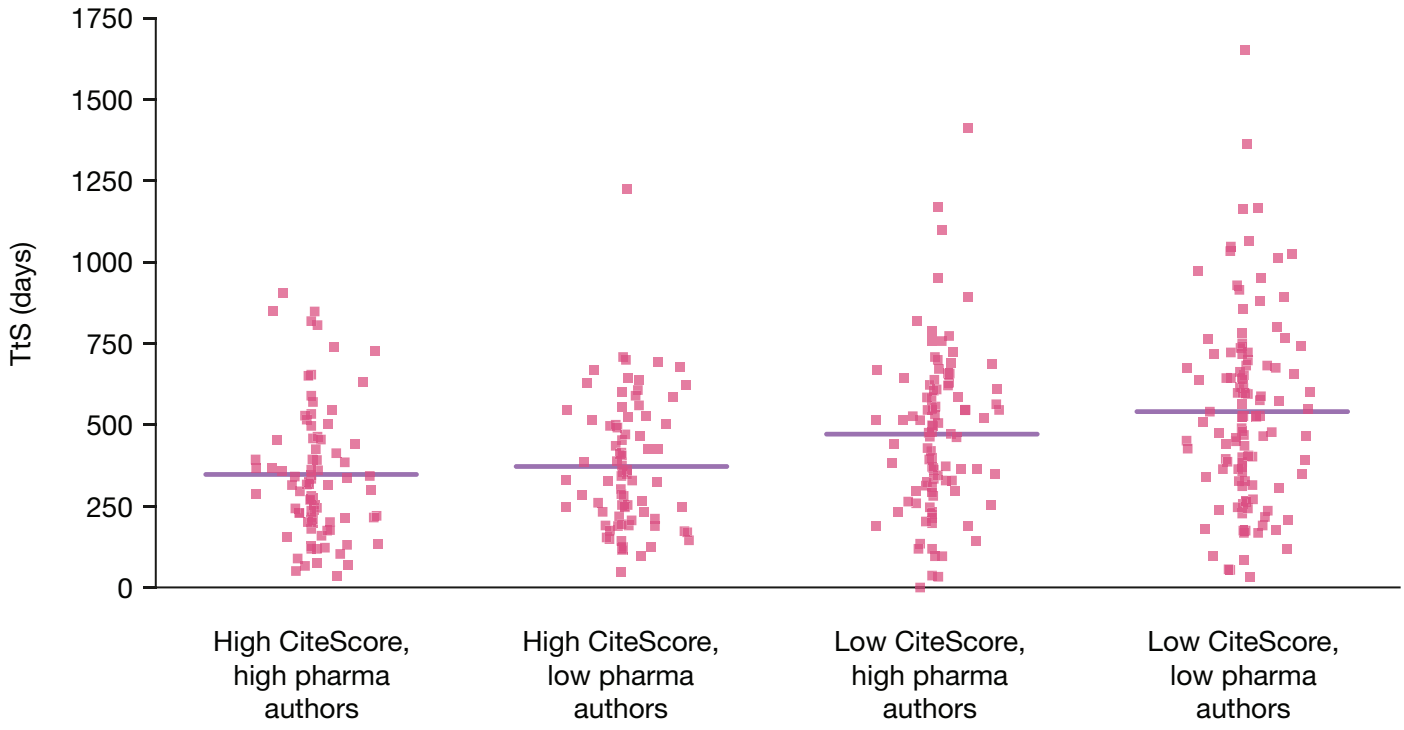
Supplementary Figure 3. Association between journal CiteScore, number of pharma authors and TtS in phase 3 trials (n = 376).



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TtS, time to submission.

Reference

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