Public Disclosure of Clinical Research Is an Important Factor for Evidence-Based Decision-Making: Is the Current Evidence Being Disclosed in a Timely Manner?

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INTRODUCTION

- Public registration of clinical trials, along with the timely and full reporting, are internationally accepted measures to promote transparency, identify existing trials, deter selective reporting, and increase the value of clinical research
- The importance of public disclosure and dissemination of both positive and negative results of clinical trials cannot be overemphasized from the viewpoint of a patient, the final beneficiary of any research activity
- Importantly, dissemination of results in public domain, either as a journal publication or online provision of data via websites, is necessary for all clinical trials, irrespective of meeting the endpoints. ClinicalTrials. gov provides a public platform wherein the main results of trials should be disseminated
- Traditionally, in scientific literature, clinical trials with positive results tend to be overrepresented because of the preference for publishing positive results, both by investigators and journals leading to publication bias. However, negative results are also equally (if not more) important for widening the knowledge base, and journals are increasingly encouraging the publication of negative results of well-conducted clinical trials.
- Another somewhat similar problem is the delayed publication of results of clinical trials
- Timely disclosure of results would provide real-time clinical trial data to physicians/patients helping them to take evidence-based, informed decisions together. This, in turn, will translate the efficacy and safety data from clinical trials to realistic effectiveness and tolerability outcomes, improving the quality of healthcare in a real-world setting
- Thus, regulatory agencies and health organizations have formulated guidance documents on the conduct and public disclosure of results of clinical trials
- According to the World Health Organization statement on public disclosure of clinical trial results,¹ the main findings of clinical trials should be submitted for publication, preferably to be published as open access, in a peer-reviewed journal within 12 months of study completion. Additionally, the key outcomes should be made publicly available within 12 months of study completion by posting to the results section of the primary clinical trial registry. The results should otherwise be made available publicly at most within 24 months of study completion. These time frames are the longest possible acceptable time frames for reporting, though shorter time frames are preferred
- The Food and Drug Administration Amendments Act mandates reporting summary results in the database of ClinicalTrials.gov within 12 months of study completion²
- As we decided to assess whether clinical trial results were being publicly disclosed in a timely manner (within 12/24 months), we needed to focus on a particular disease facet. Thus, we decided to evaluate this issue using clinical trials on psoriasis
- Psoriasis is a chronic, inflammatory, immune-mediated disease with variable clinical presentations, affecting up to 3% of the general population, and substantially lowering the quality of life.³ With its chronic and relapsing nature, management of psoriasis is always challenging. Prior to the development of targeted biologic therapies, therapeutic options for psoriasis were limited
- With the advent of newer biologic therapies, better therapeutic options with higher efficacy are available, specifically for patients with moderate to severe psoriasis. It is important that the clinical trials on newer therapies for psoriasis are published within the stipulated time frame for the utmost benefit of patients

OBJECTIVES

- To assess the proportion of completed clinical trials on psoriasis, that have publicly disclosed the primary results within 1 or 2 years of the primary completion date
- To evaluate the trends pertaining to time, phases of clinical trial, and funding, if any

METHODS

- We included Phase 1/2/3 completed clinical trials on psoriasis on the ClinicalTrials.gov, trials completed between 2000–2020 were included
- Search strategy in ClinicalTrials.gov:
- Disease Psoriasis
- Time frame 2000–2020 (trial completion)
- Study type Clinical trials, Phase 1/2/3
- Restrictions Humans
- Exclusion criteria:
- Primary completion date before January 2000
- Primary completion date after December 2020
- No completion date
- Publication date before primary completion date
- Primary endpoint not available

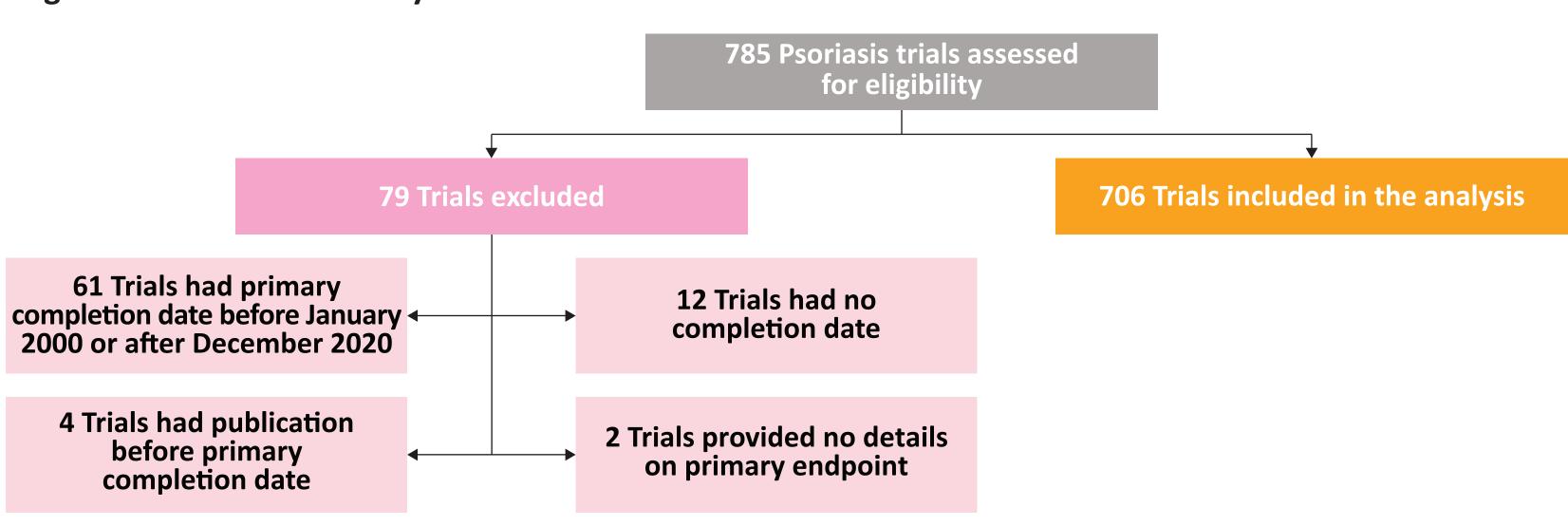
- We checked for result dissemination for these trials on ClinicalTrials.gov and also identified relevant publications from PubMed using trial details and NCT number
- We recorded the "Primary completion date" and the "First posted results date" from ClinicalTrials.gov and the "First primary online publication date" from PubMed; the earlier of these dates was identified as the "Results revealed date"
- We calculated the difference between the "Primary completion date" and the "Results revealed date"

RESULTS

Trial Selection

• We excluded 79 of the 785 clinical trials identified through ClinicalTrials.gov; we excluded 61/79 (77%) trials because the "Primary completion date" was either before January 2000 or after December 2020. Overall, we included 706 clinical trials in the analysis (**Figure 1**)

Figure 1. Flowchart of study selection



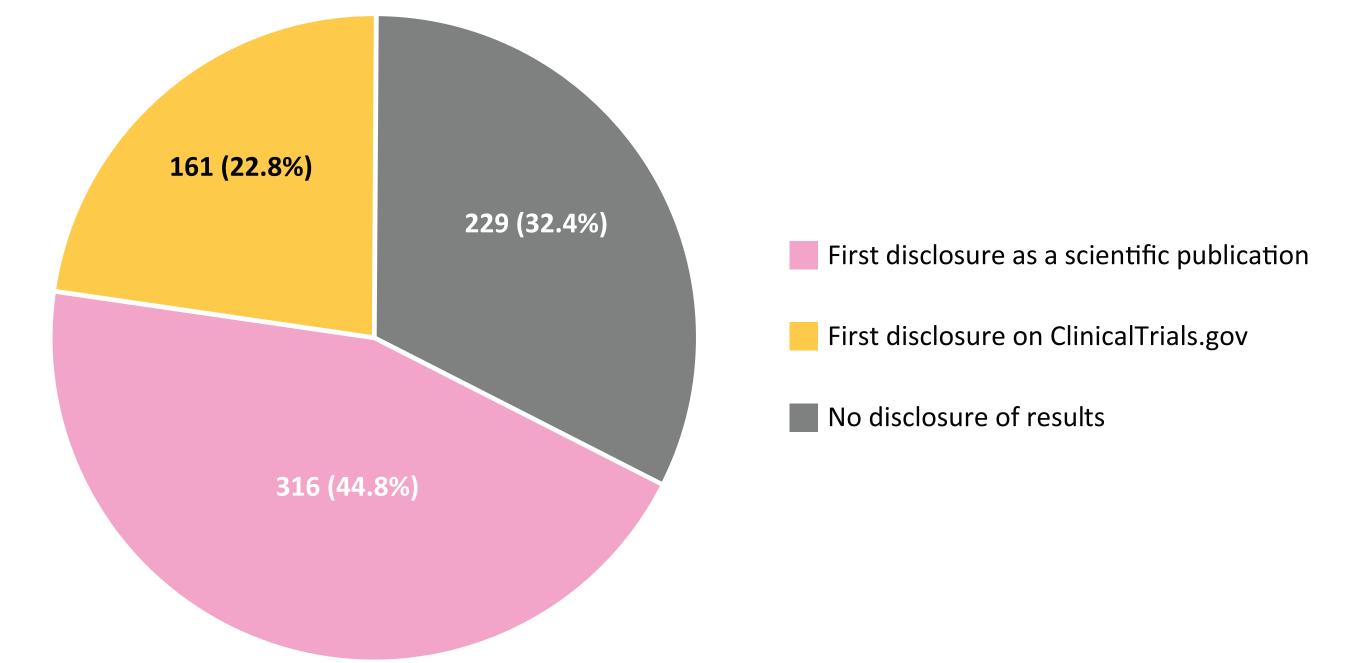
Trial Characteristics

- Of the 706 included trials, 50 (7.1%) trials were completed between 2000–2005, 149 (21.1%) between 2006–2010, 221 (31.3%) between 2011–2015, and 286 (40.5%) between 2016–2020
- A total of 130 trials were Phase 1 (18.4%), 23 (3.3%) trials were Phase 1/2, 262 (37.1%) were Phase 2, 10 (1.4%) were Phase 2/3, and 281 (39.8%) were Phase 3
 Most (n=659, 93.3%) trials were funded by industry (34 of these were also funded by "Other" and one
- Most (n=659, 93.3%) trials were funded by industry (34 of these were also funded by "Other" and one was also funded by the National Institutes of Health [NIH]). Additionally, 9 (1.3%) trials were funded by the NIH (3 of these were also funded by "Other"), and further 37 (5.2%) trials were funded by "Other" (that included universities, hospitals, associations, societies, institutes), and only one (0.1%) trial was funded by the US Federal Reserve System

Overall Public Disclosure of Primary Results

• Of the 706 trials, 477 (67.6%) had revealed the results, while 229 (32.4%) had not disclosed the results publicly (Figure 2)

Figure 2. Number of trials with public disclosures of primary results



- Among the 477 trials that revealed the results, mean (standard deviation [SD]) time to first public disclosure of primary results was 31.5 (25.1) months
- For the 316 (44.8%) trials that first presented the results as scientific journal publications, the mean (SD) time to first public disclosure of primary results was 26.2 (16.6) months. For the 161 (22.8%) trials that first reported the results on ClinicalTrials.gov, the mean (SD) time to first public disclosure of primary results was 41.8 (31.3) months
- The results of 6.5% trials were revealed within 1 year and of 29.9% trials were revealed within 1 to ≤2 years; thus, 36.4% trials publicly revealed results within the 2-year window (**Table 1**)

Table 1. Time to public disclosure of primary results

	No Disclosure of Results	Results First Disclosed in ≤1 Year	Results First Disclosed in 1 to ≤2 Years	Results First Disclosed After 2 Years
Number of trials, n (%)	229 (32.4%)	46 (6.5%)	211 (29.9%)	220 (31.2%)
Time, mean (SD), months	Not applicable	9.6 (3.1)	18.2 (3.7)	48.8 (28.1)

SD, standard deviation

Time trends in public disclosure of primary results

- Results of recently completed trials were disclosed more often (~70%) vs the trials completed before 2006 (38%). Specifically, results of 38.0%, 67.8%, 69.7%, and 71.0% trials completed from 2000–2005, 2006–2010, 2011–2015, and 2016–2020 were disclosed, respectively (Figure 3)
- Also, a trend of earlier disclosures of results in recent years was evident (Table 2)

Figure 3. Time trends in public disclosure of primary results

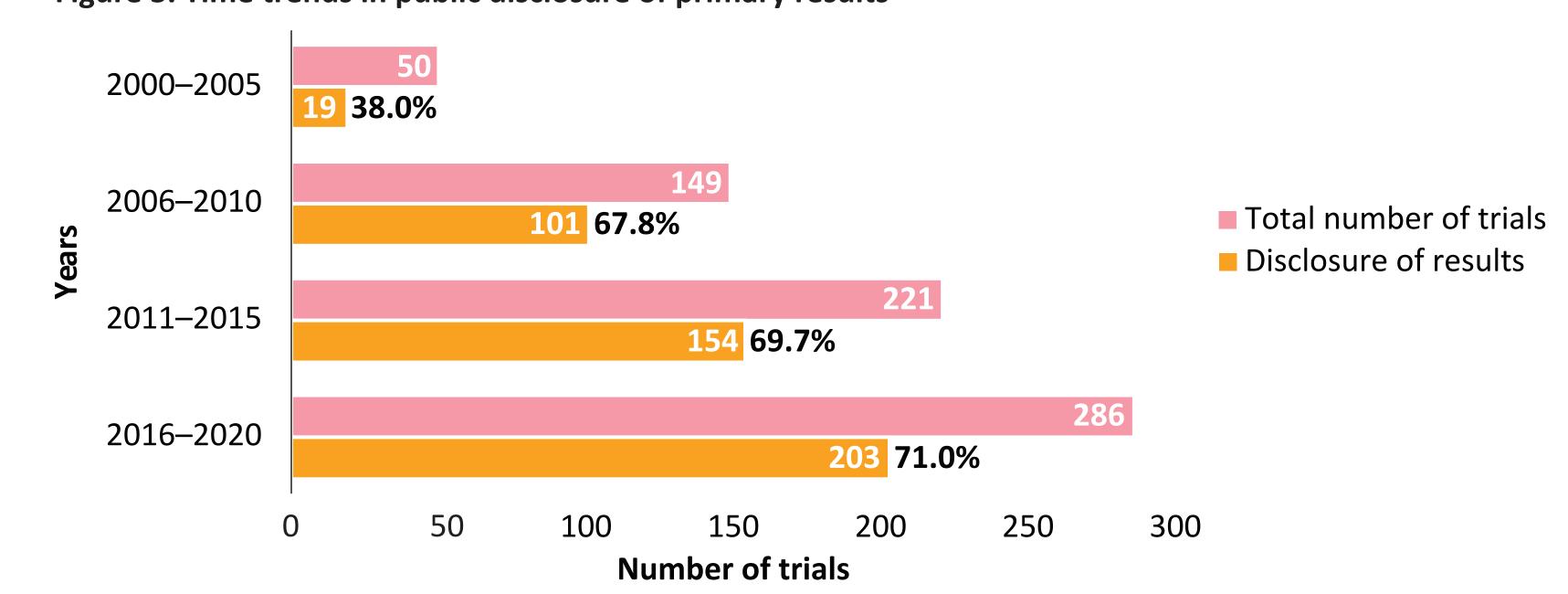
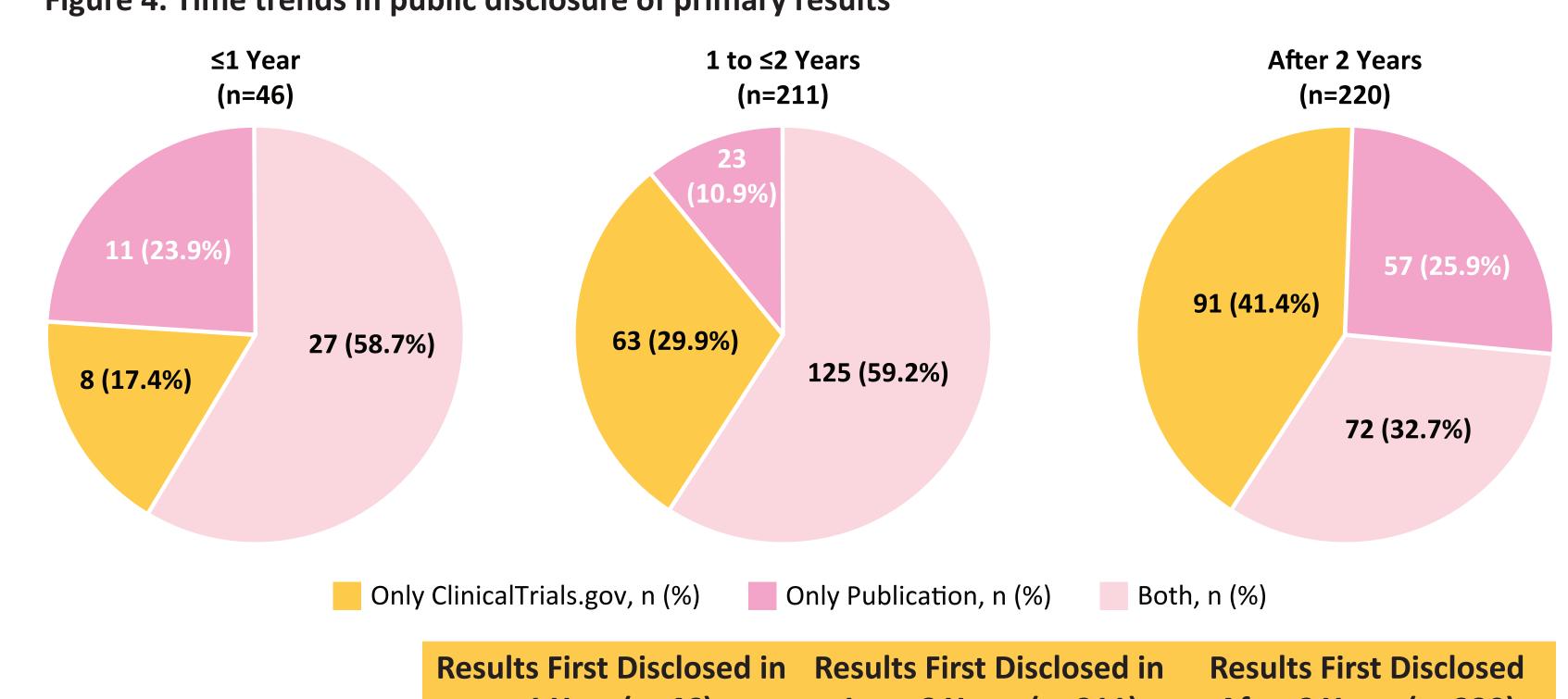


Table 2. Time trends in public disclosure of primary results

Year	Total Number of Trials	No Disclosure of Results	Results First Disclosed in ≤1 Year	Results First Disclosed in 1 to ≤2 Years	Results First Disclosed After 2 Years
2000–2005	50	31 (62.0%)	1 (2.0%)	6 (12.0%)	12 (24.0%)
2006-2010	149	48 (32.2%)	3 (2.0%)	28 (18.8%)	70 (47.0%)
2011–2015	221	67 (30.3%)	4 (1.8%)	65 (29.4%)	85 (38.5%)
2016–2020	286	83 (29.0%)	38 (13.3%)	112 (39.1%)	53 (18.5%)

• We also assessed whether scientific publications were the preferred choice for revealing the first results vs ClinicalTrials.gov, when stratified by time. Generally, as the time to disclosure increased, the proportion of trials revealing results only on ClinicalTrials.gov increased, from 17.4% for results first disclosed in ≤1 year vs 41.4% for results first disclosed after 2 years (**Figure 4**)

Figure 4. Time trends in public disclosure of primary results



	Results First Disclosed in ≤1 Year (n=46)	Results First Disclosed in 1 to ≤2 Years (n=211)	Results First Disclose After 2 Years (n=220
First Revealed on ClinicalTrials.gov, n (%)	21 (45.7%)	153 (72.5%)	128 (58.2%)
First Revealed in Publication, n (%)	25 (54.3%)	58 (27.5%)	92 (41.8%)

Trends in Public Disclosure of Primary Results by Phases of Trials

• Results of Phase 2, Phase 2/3 or Phase 3 trials were disclosed publicly more often vs Phase 1 or Phase 1/2 trials (**Table 3**). Also, the mean time to first public disclosure of results was generally shorter in later phases of trials

Table 3. Trends in public disclosure of primary results by Phases of trials

	Phase 1	Phase 1/2	Phase 2	Phase 2/3	Phase 3
With public disclosures of primary results	40	11	174	6	246
%	30.8%	47.8%	66.4%	60.0%	87.5%
Mean (SD)	31.2 (22.1)	46.5 (36.3)	38.8 (32.1)	23.7 (9.9)	25.8 (17.0)
Total trials	130	23	262	10	281

Trends in Public Disclosure of Primary Results by Funding

• We did not assess the trends by funding source as most (93.3%) trials were funded (at least partly) by industry.

CONCLUSIONS

- Compliance to the guidelines for public disclosure of clinical trial results is poor but improving with time
- Low compliance to the CONSORT guidelines between 2000 and 2010 may have impacted our results. The CONSORT statement, most recently updated in March 2010,⁵ is an evidence-based minimum set of recommendations including a checklist and a flow diagram for reporting randomized controlled trials and is intended to facilitate the complete and transparent reporting of trials and aid their critical appraisal and interpretation
- Since trials concerning only one disease (psoriasis) was studied, further investigation with more diseases across therapeutic areas may be required
- We can speculate that the publications in scientific journals were the preferred mode for disclosing the results for the first time
- Results of Phase 2, Phase 2/3 or Phase 3 trials were disclosed publicly more often vs Phase 1 or Phase 1/2 trials
- Prompt public disclosure of clinical trial results can provide real-time clinical trial data to physicians and patients to help them make evidence-based, informed decisions, thus paving the way for real-world outcomes research and eventually improving the quality of healthcare and patient outcomes

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