National Pharmaceutical Council®

Policy & Evidence Brief

Do Early Signals Persist? Updated Evidence on the IRA's Potential Impact on Clinical Development in Approved Drugs

June 2026

Executive Summary

The Inflation Reduction Act (IRA)'s Drug Price Negotiation Program (DPNP) of 2022 shortened the timeline towards price erosion for approved drugs, generating concerns around reduced incentives for industry investments in ongoing clinical development. NPC's prior research reported early signals that the IRA's passage was associated with reductions in industry-funded clinical trials, but not government-funded trials, for approved drugs across therapeutic areas and molecule types. Decreases in industry-funded trial initiation were disproportionately greater in small molecule drugs than biologics, overall and in an oncology-specific analysis. As more mature evidence becomes available, this analysis revisits NPC's two published works. We extend the post-IRA period to include 10 additional months of post-IRA follow-up and discuss the methods and updated findings in the context of evolving research in this area.

Our analysis included all Phase I-III trials that started from July 2014 to June 2025 for which the primary tested drug was an approved drug by/before March 2026. We excluded vaccine-related trials and those for the prevention and treatment of COVID-19. Unless otherwise noted, summarized findings were statistically significant at the p-value < 0.05 level.

- Following the IRA's passage, the average monthly number of industry-sponsored trials on previously approved drugs decreased by 36.6%.
- The IRA's passage was associated with an immediate drop of 11.9 industry-funded trials, followed by an additional downward trend of 1.4 trials per month post-IRA.
- The IRA's passage was not associated with a statistically significant drop or downward trend post-IRA for government-funded trials.
- The average monthly number of industry-sponsored trials for previously approved oncology drugs decreased by 40.7% and 36.3% post-IRA, for small molecule and biologic drugs, respectively.

- Compared with biologics, small molecule oncology drugs were associated with an additional decrease of 3.4 trials/month after the IRA's passage.

Why It Matters: The updated evidence shows a sustained decline in industry-funded Phase I–III trials of approved drugs associated with the IRA, with a disproportionately greater decline in small molecule oncology drugs compared to biologics. Our findings inform discussions on potential unintended consequences of the IRA as well as considerations for health policy.

Background

The Inflation Reduction Act (IRA)'s Drug Price Negotiation Program (DPNP) of 2022 shortened the timeline towards price erosion for approved drugs, generating concerns around incentives for industry investment in ongoing clinical development.[1-3] Because small molecule drugs face a shorter timeline from initial FDA approval to eligibility for DPNP selection (i.e., 7 years) than biologic drugs (i.e., 11 years), the law may disproportionately impact development incentives for small molecules.

NPC's prior research reported early signals that the IRA's passage was associated with reductions in industry-funded clinical trials, but not government-funded trials, for approved products across therapeutic areas and molecule types.[4,5] Decreases in industry-funded trial initiation were disproportionately greater in small molecule drugs than biologics, overall[4] and in an oncology-specific analysis.[5]

As more mature evidence becomes available, this analysis revisits NPC's two published analyses. This Policy & Evidence Brief extends the post-IRA period by including 10 additional months of post-IRA follow-up and discusses the methods and updated findings in the context of the rapidly evolving evidence in this area. Specifically, we assess whether the initially observed decline in industry-funded clinical development for approved drugs persists across therapeutic areas and molecule types. In comparative analyses, we compare post-IRA trends in industry-funded versus government-funded trials and small molecule versus biologic oncology drugs.

Approach

Trial Identification and Extended Follow-Up Period

We used Citeline's Trialtrove database to obtain the aggregated monthly number of clinical trials initiated in previously approved drugs between July 2014 and June 2025. This approach extended the analytic window in our original analyses (July 2014 – August 2024) by 10 months, capturing additional post-IRA observations to assess persistence of previously reported results. This time horizon also mitigated confounding from separate policy developments throughout 2025, including the Most Favored Nation (MFN) Executive Order (May 2025), international reference pricing models (December 2025), and potential operational disruptions to government-funded trials amid federal workforce reductions.

Data were extracted in March 2026. We used the Trialtrove filter for previously approved drugs, which categorizes drugs as "previously approved" based on the date the filter is applied. Therefore, the sample includes trials initiated during the study period (July 2014 – June 2025) for drugs that gained approval by or before the data extraction (March 2026). This trial sample was consistent with previously published NPC research and enables capture of both pre- and post-approval subsequent indication development, a theorized and early unintended consequence of the IRA.[2,6,7]

Analysis 1: Post-IRA Trends in Industry-Funded vs. Government-Funded Trials

We estimated the IRA's impact on initiation of industry-funded Phase I-III trials for approved drugs, using government-funded trials for comparison, which were hypothesized to be unaffected by the IRA.

Following the approach in our previous publication, this analysis:

- Identified Phase I-III trials for approved drugs initiated in the study period, stratified by funding (industry-funded and government-funded). We excluded vaccine-related trials and those for the prevention and treatment of COVID-19.
- Compared the monthly trial initiations before and after the IRA's passage using Wilcoxon rank sum tests, stratified by funding (industry-funded and government-funded). Two time windows were used:
    - Full period comparison (July 2014 – July 2022 vs. August 2022 – June 2025)
    - Post-COVID era comparison (August 2021 – July 2022 vs. July 2024 – June 2025)
- Applied interrupted time series analysis (ITSA) to estimate the IRA's impact on trial initiations, accounting for the existing pre-IRA trends.

Analysis 2: Post-IRA Trends in Industry-Funded Oncology Trials: Small Molecules vs. Biologics

We estimated the impact of the IRA and its differential DPNP eligibility timelines on industry-funded Phase I-III oncology trials for approved small molecule drugs, using biologic trials as the comparison group.

Following the approach in our previous publication, this analysis:

- Identified industry-sponsored Phase I-III trials for approved oncology drugs. The study sample included trials with primary tested drug(s) that were exclusively either small molecule or biologic drugs, excluding trials for cancer vaccines. Trials for small molecules versus biologics were determined by Citeline classification and an algorithm-based approach reviewed by two PharmD researchers.

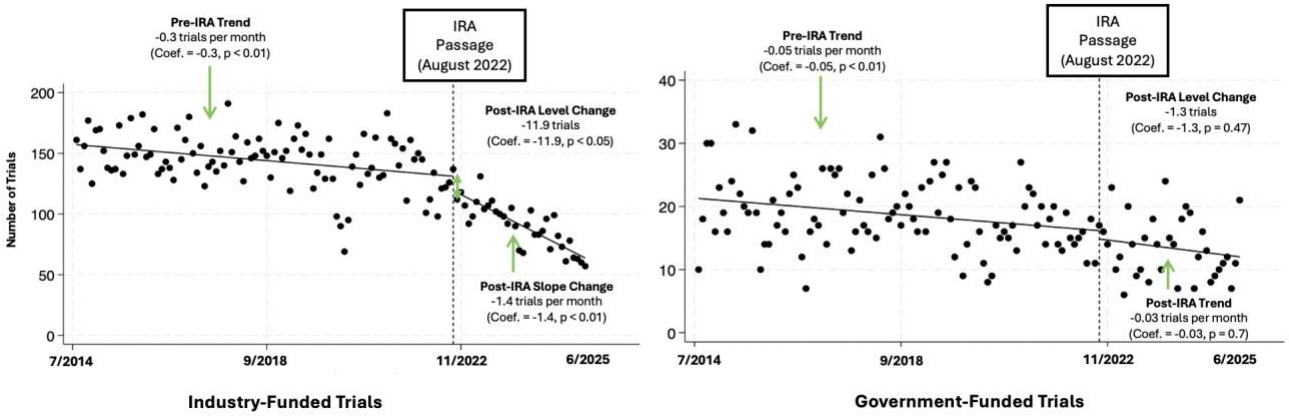
- Compared monthly average trial initiations before and after the IRA's passage across all oncology trials and stratified by drug molecule size (small molecules versus biologics) using Wilcoxon rank sum tests. Two time windows were used:
    - Full period comparison (July 2014 – July 2022 vs. August 2022 – June 2025)
    - Post-COVID era comparison (August 2021 – July 2022 vs. July 2024 – June 2025)
- Applied a difference-in-differences (DiD) design to estimate the impact of the shorter DPNP eligibility timeline on trial initiation for small molecule oncology drugs, using biologic trials as the counterfactual with an underlying assumption that clinical development would have followed a similar trajectory in both small molecules and biologics in the absence of the IRA's differential DPNP eligibility timeline. We did not find statistically significant evidence of differential pre-IRA trends between small molecules and biologics.

Results

Analysis 1: Post-IRA Trends in Industry-Funded vs. Government-Funded Trials

- Sample identification: The sample included 17,194 industry-funded and 2,288 government-funded Phase I-III trials on approved drugs initiated during the study period.
- Monthly average trial initiations: Across the full study period, the average monthly number of industry-funded trials declined by 36.6% after the IRA's passage ($p < 0.01$), decreasing from 144.2 (SD = 21.7) to 91.5 (SD = 20.1) trials per month. The average monthly number of government-funded trials declined by 28.3% after the IRA's passage ($p < 0.01$), decreasing from 18.7 (SD = 5.5) to 13.4 (SD = 4.8) trials per month. Findings from the post-COVID era comparison were consistent (Appendix, Figure A1).
- ITSA (Figure 1): The IRA's passage was associated with an immediate drop (level change) of 11.9 industry-funded trials ($p < 0.05$), followed by an additional downward trend (slope change) of 1.4 trials per month post IRA ($p < 0.01$). The IRA's passage was not associated with a statistically significant change in government-funded trials, although a modest downward pre-trend was present (-0.05 trials per month, $p < 0.01$).

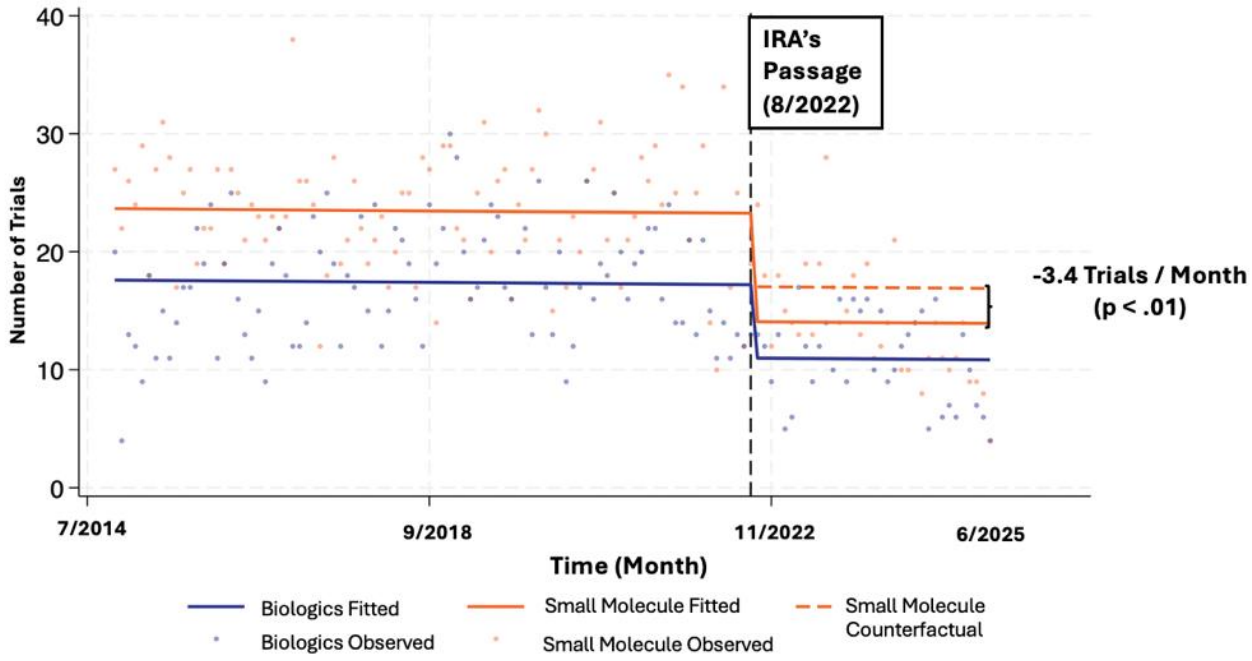
Figure 1. ITSA of Trial Initiations on Approved Drugs Following Passage of the Inflation Reduction Act, by Funding Source (Industry-Funded and Government-Funded)



Analysis 2: Post-IRA Trends in Industry-Funded Oncology Trials: Small Molecules vs. Biologics

- **Sample identification:** The sample included 4,820 Phase I-III industry-funded oncology trials on approved drugs initiated during the study period, including 2,780 (57.7%) primarily testing small molecules and 2,040 (42.3%) primarily testing biologics.
- **Monthly average trial initiations:** Across the full study period, the average monthly number of **oncology trials** declined by **38.8%** after IRA's passage ($p < 0.01$), with a reduction by **40.7%** in **small molecule trials** ($p < 0.01$) and reduction by **36.3%** in **biologic trials** ($p < 0.01$). Findings from the post-COVID era comparison were consistent (Appendix, Figure A2).
- **DiD analysis (Figure 2):** The IRA's shorter DPNP eligibility timeline was associated with an additional reduction of **3.4** trials per month ($p < 0.01$) for small molecule oncology drugs, compared with the counterfactual modeled by the biologics' trends.

Figure 2. DiD Model Estimating the Impact of the IRA's Differential Drug Price Negotiation Program Eligibility Timeline on Industry-Funded Trials for Approved Oncology Small Molecule Drugs



Discussion

Our updated investigation of early signals of the IRA's impact on clinical development shows a sustained decline in industry-funded Phase I–III trials of approved drugs across therapeutic areas associated with the IRA, with a disproportionately greater decline in small molecule oncology drugs.

This updated analysis adds to a growing body of literature on the law's impact on clinical development. Descriptive and modeling-based studies have illustrated areas in which the DPNP may disproportionately reduce manufacturer incentives to invest in clinical development, including in small molecule drugs, drugs treating Medicare-heavy populations, and development toward subsequent indications.[1,6-9] Accordingly, NPC researchers[4,5] and others[3] have taken a targeted approach to early signals research, evaluating areas that are both likely to be the first impacted by the law and most likely to reflect and isolate the impacts of the IRA in a dynamic environment. Studies taking this targeted approach support concerns around IRA-related changes to clinical development. They provide complementary evidence in similar yet distinct samples of trials: exclusively Phase I-III post-approval trials among U.S.-approved drugs, and Phase I-III trials among globally approved drugs.[3-5] In contrast, other research has taken an untargeted approach of analyzing all global clinical trials.[10] This approach is fraught with other possible dynamics within the environment alongside variable timelines and magnitude of anticipated IRA impact by therapeutic area, stage of development, and molecule type. While past untargeted research has reported stability in overall trial activity, it nevertheless has captured decreases in trials where signals may be more likely in the first years following the law's passage (e.g., reduced trial initiation by manufacturers with drugs subject to the DPNP).[10]

Consistent with our earlier work, this analysis takes a methodologically rigorous approach, leveraging control groups to quasi-experimentally isolate the impact of the IRA. In our ITSA, we used government-funded trials as a control group to account for secular trends unrelated to the IRA. In our DiD, we used biologic trials to model the counterfactual trajectory in which small molecule trials had not been subject to a shorter DPNP timeline. Our approach nevertheless has limitations, including that our findings are not causal, with limitations discussed in more detail in the original publications.[4,5] Our sample included trials of drugs that had received approval at the time of data extraction. It thereby captured trials on drugs that had achieved regulatory success, including trials supporting initial approval and both pre- and post-approval trials towards subsequent indications. This approach captured a broader array of pre- and post-approval research likely associated with subsequent indications, where modeling studies suggest the IRA may have disproportionate impact.[2] It therefore does not constrain the sample of trials based on timing relative to U.S. approval or introduce researcher judgment about trial population alignment with initial or subsequent indication populations.

Conclusion

This evidence supports concerns around IRA-related reductions in incentives for clinical development, including post-approval research and research toward subsequent indications. With an extended follow-up period, our analysis shows a sustained decline in industry-funded Phase I–III trials of approved drugs across therapeutic areas associated with the IRA's passage. Our oncology-specific analysis suggests that the decline in clinical development has been disproportionately larger for small molecules relative to biologics. This finding supports concerns that the pill penalty — the IRA's shorter timeline toward DPNP eligibility for small molecule drugs — has disproportionately disincentivized clinical development in small molecules. Our findings inform ongoing discussions on the potential unintended consequences of the IRA on patient access to future innovation as well as considerations for health policy.

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Appendix

Figure A1. Monthly Average of Trials on Approved Drugs Initiated Before and After the Passage of the IRA, by Funding Source (Industry-Funded and Government-Funded) *(Notes: * p < 0.05; ** p < 0.01)*

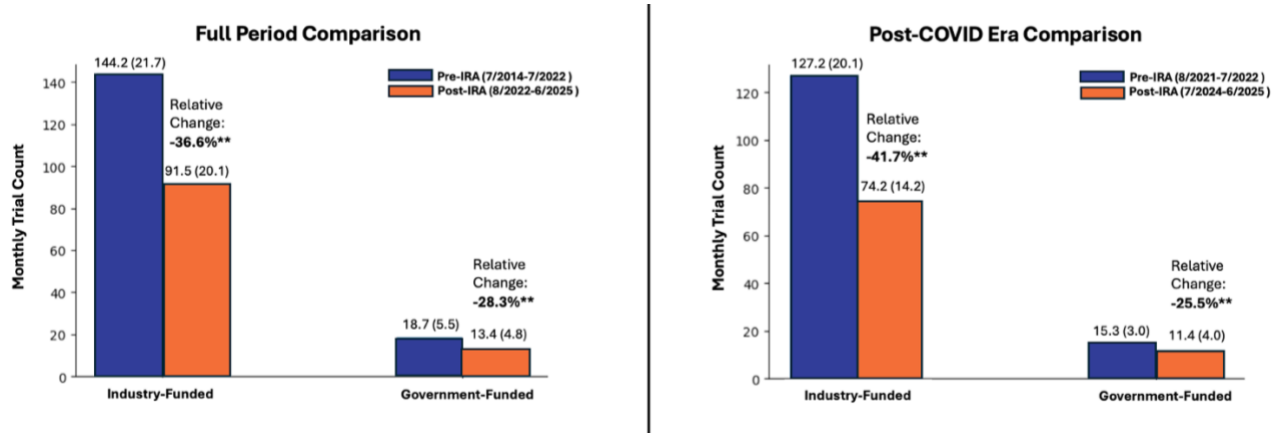
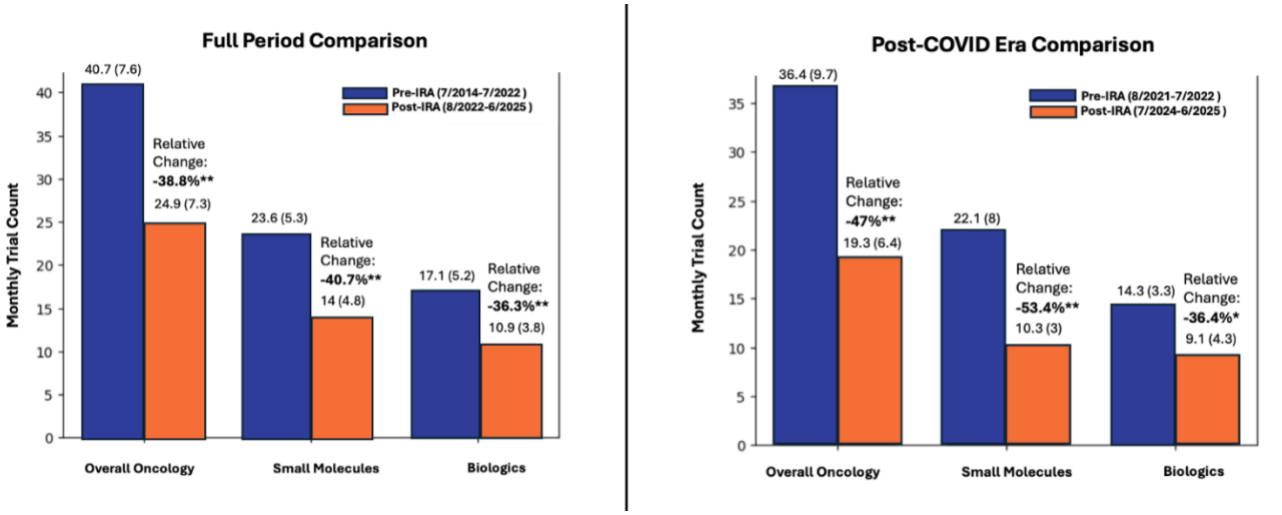


Figure A2. Monthly Average of Industry-Funded Trials on Approved Oncology Drugs Initiated Before and After the Passage of the IRA, Overall and by Molecule Type (Small Molecule and Biologic) *(Notes: * p < 0.05; ** p < 0.01)*



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