

Regulatory Designation and Knowledge Dynamics in Pharmaceutical Innovation: Evidence From Breakthrough Therapy Designation

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Abstract: Innovation in the pharmaceutical sector is shaped not only by scientific discovery but also by regulatory mechanisms that influence the direction, speed, and priorities of technological development. In science-based industries such as pharmaceuticals, where innovation depends heavily on the accumulation of scientific knowledge, regulatory frameworks play a central role in shaping innovation trajectories. Among these, the U.S. Food and Drug Administration's Breakthrough Therapy Designation (BTD), introduced under the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012, represents a mechanism designed to accelerate development of promising drugs. While prior research has focused on BTD effects on development timelines, approval outcomes, and firm-level investment, less attention has been given to its relationship with scientific knowledge production. This study examines how BTD is associated with patterns of scientific publication activity across disease areas, focusing on leukemia, lymphoma, and multiple myeloma. Using FDA approval and Web of Science bibliometric data, we construct a group of BTD and comparable non-BTD drugs and analyze publication trends before and after designation using a difference-in-differences approach. The results show that the BTD group shows higher trend of increase in publication activity following designation compared to the non-BTD. Log-transformed trends indicate stronger relative growth for BTD-designated drugs, with a positive DiD. However, the DiD estimate is not statistically significant. These findings suggest that regulatory designation may be associated with increased production of scientific knowledges. Further research is needed to extend the analysis of regulation-induced innovation into knowledge dynamics.

Keywords: Pharmaceutical Innovation, Porter Hypothesis, Regulatory Incentive, Scientometrics, Knowledge Dynamics

1. Introduction

Innovation in the pharmaceutical sector is shaped not only by scientific discovery but also by regulatory mechanisms that influence the speed, direction, and priorities of technological development (Dosi, 1982; Nelson and Winter, 1985; Freeman, 1994). In science-based industries such as pharmaceuticals, innovation depends heavily on the production, accumulation, and integration of scientific knowledge across multiple stages of research and development (R&D) (Pavitt, 1984; Freeman and Soete, 1997). Because pharmaceutical R&D is characterized by high uncertainty, long development timelines, and significant financial risk, regulatory arrangements constitute a key institutional factor shaping R&D costs, incentives, and the direction of innovation in drug development (Grabowski and Vernon, 2000; Nightingale and Mahdi, 2006; Pisano, 2006; Sampat and Lichtenberg, 2011; DiMasi et al., 2016). Regulation should therefore be understood not merely as a constraining factor, but also as an accelerating and directional mechanism.

A distinctive example is the U.S. Food and Drug Administration's breakthrough therapy designation (BTD), introduced under the Food and Drug Administration Safety and Innovation Act in 2012. BTD accelerates the development and review of therapies that may offer substantial improvement over existing treatments (Sherman et al., 2013; Kesselheim et al., 2015). Unlike earlier FDA pathways such as fast track, breakthrough therapy designation emphasizes early recognition of promising innovations and prioritizes development through enhanced regulatory engagement (Baird et al., 2014). It combines procedural acceleration with early prioritization.

BTD can influence innovation by shaping firms' R&D behavior and directing effort toward more promising therapies (Thomas, 1990; Eisenberg, 2006). In sectors where scientific publication is a key form of knowledge production, regulatory designation may influence outcomes beyond approval timelines. BTD may therefore be associated with changes in scientific publication patterns.

Existing research has examined regulatory incentives in terms of approval speed, development timelines, and firm-level investment. However, the relationship between regulatory designation and scientific knowledge production remains less understood. Few studies have focused on the association between regulatory mechanisms and patterns of scientific publication activity.

This study examines how BTB relates to scientific knowledge production across disease areas. Specifically, it investigates whether BTB is associated with changes in scientific publication activity relative to comparable non-designated drugs.

2. Literature Review

2.1 Regulation and Innovation

Innovation emerges from interactions among firms, institutions, knowledge infrastructures, and policy environments (Freeman, 1994; Breschi et al., 2000; Lundvall, 2007). In science-based sectors such as pharmaceuticals, innovation depends heavily on scientific knowledge (Pavitt, 1984). Regulation is a critical institutional mechanism shaping innovation by governing clinical trial standards and the validation of safety and efficacy (Cockburn and Henderson, 1998; 2001; Orsenigo et al., 2001; Pisano, 2006).

The Porter Hypothesis suggests that regulation can incentivize firms to develop new technologies (Porter, 1990; Porter and Vanderlinde, 1995). Empirical findings indicate that these effects vary across contexts (Wagner, 2003). Most research has focused on economic outcomes such as patents and firm performance (Lanoie et al., 2011; Ambec et al., 2013), with limited attention to scientific knowledge dynamics.

This gap is important in pharmaceuticals, where innovation depends on the accumulation and use of scientific evidence (Eisenberg, 2006). Understanding how regulation influences knowledge production extends existing research.

2.2 Breakthrough Therapy Designation as a Regulatory Incentive

Regulatory frameworks have incorporated expedited mechanisms to accelerate drug development under uncertainty. FDA programs such as Fast Track, Priority Review, and Accelerated Approval improve access to therapies (Kesselheim et al., 2015; Haffner, 2016).

Breakthrough Therapy Designation is granted when preliminary evidence indicates substantial improvement over existing therapies (Sherman et al., 2013; Baird et al., 2014). It involves early interaction between regulators and firms, reducing uncertainty and supporting efficient development.

Existing research has examined its effects on development timelines and investment (Shea et al., 2016; Chandra et al., 2026). Less attention has been paid to its relationship with scientific knowledge dynamics. This study addresses this gap by examining publication activity.

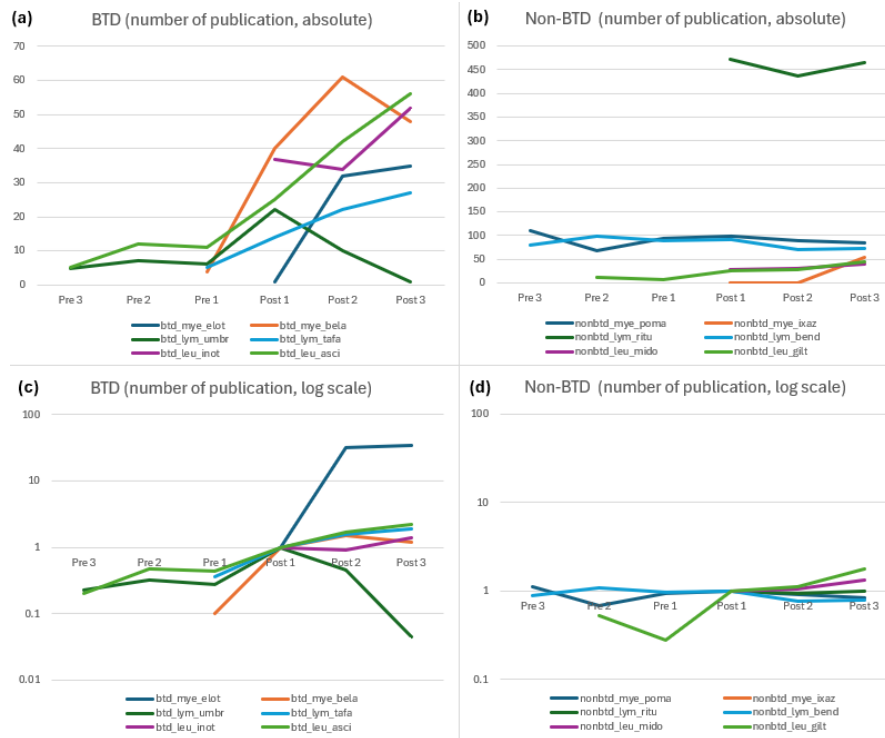
3. Methods

To examine the association between regulatory designation and scientific knowledge dynamic, BTB data were obtained from the FDA database, which provides information on approved drugs and indications. A total of 303 approvals were granted between 2013 and 2024.

The dataset was refined using a 10-year window (2013–2023), including only original treatment approvals, yielding 73 cases. The analysis focuses on leukemia, lymphoma, and multiple myeloma. For each, matched non-BTB drugs were selected based on similar indications and approval timing using the FDA Orange Book.

Scientific knowledge production is measured using publication activity. Annual publication counts were collected from the Web of Science Core Collection using *Title [drug name] AND All field [disease name]*.

A three-year pre and post designation window was applied. Publication counts were log-transformed. An event-time difference-in-differences (DiD) model was used with drug and relative-period fixed effects:



where Y_{it} is the publication count for drug i in period t ; BTD_i indicates treated drugs; and $Post_t$ denotes post-designation periods. The model includes drug fixed effects (α_i) and relative-period fixed effects (δ_t).

4. Results

BTD-designated drugs show remarkable increase in publication activity following designation compared to non-BTD drugs (Figure 1). After log transformation to account for absolute differences, the DiD is positive (+0.85), indicating higher relative growth in BTD (Table 1). This suggests that regulatory designation is associated with increased scientific knowledge production. However, the DiD estimate is not statistically significant ($\beta = 0.116$, $SE = 0.569$), indicating no robust causal evidence.



Figure 1: Publication Trends of BTD and Non-BTD (Absolute and Log Scales)

Table 1: Group Means of Log-Transformed Publication Counts (Pre- and Post-Designation)

Group	Pre (Log Mean)	Post (Log Mean)	Change
BTD	1.39	3.33	+1.94
Non-BTD	3.24	4.33	+1.09
DiD	-	-	+0.85

5. Discussion and Conclusion

The findings suggest that BTD is associated with trend of increased scientific publication activity. Although not statistically significant, the positive trend indicates that regulatory signals may influence knowledge production.

This aligns with research showing that regulation can promote innovation (Wagner, 2003). The results extend this perspective by focusing on knowledge dynamics.

This study contributes by examining regulation-induced innovation beyond traditional outcomes such as patents and development speed. It highlights the role of regulation in shaping scientific activity.

The small sample size is limitation of this research; therefore, further research should expand the larger dataset and examine knowledge networks and structures.

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Ethics Declaration

This research does not require ethic declaration.

AI Declaration

This article used ChatGPT (OpenAI, 2026) for language editing and translation. All content was reviewed and finalized by the authors, and the ideas and conclusions are their own.

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