APPLICATION OF SELF-CONTROLLED PRE-POST OBSERVATIONAL DESIGNS IN REAL-WORLD EFFECTIVENESS RESEARCH: A SYSTEMATIC LITERATURE REVIEW

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BACKGROUND & OBJECTIVE

- Self-controlled pre-post observational designs assess outcomes within the same individuals across defined pre- and post-treatment periods.
- Each participant serves as their own control, accounting for time-invariant characteristics such as baseline disease severity, comorbidities, and demographics.
- Objective is to identify real-world studies using these designs and describe study structure, observation windows, therapeutic areas, and outcomes.

METHODS & STUDY IDENTIFICATION

- Search concepts: self-controlled, within-patient, pre-post, observational, and real-world evidence terminology.
- Human studies; past-five-year publication restriction.
- Title/abstract screening followed by full-text assessment.
- Eligible: within-patient pre-post or explicitly self-controlled observational approach.

SEARCH FLOW

1,906	1,559	1,145	738	8
Total results	After exclusions	Last 5 years	Human studies	Included

WHY SELF-CONTROLLED DESIGNS?

Time-Invariant Confounding
Within-patient comparisons inherently adjust for stable characteristics.

Real-World Feasibility
Applicable to registries, EHR, claims, and pragmatic protocols.

Longitudinal Evidence
Supports long-term effectiveness, persistence, and treatment burden.

Evidence Beyond RCTs
Captures routine-care populations and outcomes beyond typical trial horizons.

Efficient Evidence Generation
Supports multiple endpoints without a separate comparator cohort.

HOW THE DESIGN WORKS

DESIGN TIMELINE

PRE-TREATMENT PERIOD	INDEX DATE	POST-TREATMENT FOLLOW-UP
Commonly 6 or 12 months	Treatment initiation	12 to 48 months

SAME PATIENT • TWO TIME WINDOWS • ONE INDEX DATE

EVIDENCE LANDSCAPE

8	7	1	8/8
Included studies	Asthma studies	Cystic fibrosis	Observational

All studies used a single-arm cohort with a self-controlled or pre-post framework. Treatment initiation consistently defined the index date. Pre-treatment periods were commonly 6 or 12 months; post-treatment follow-up ranged from 12 to 48 months.

SELECTED STUDY EVIDENCE

Individual-study evidence

REALITI-A | n=822
24-month international prospective observational cohort; 1-year pre-post interim analysis
- mOCS median dose: 10.0 → 2.5 mg/day
- 64% achieved ≥50% reduction; 43% discontinued mOCS
- Exacerbation rate ratio: 0.29 (95% CI 0.26–0.32)

NEST | n=525
12-month pre/post design
- Exacerbations reduced 76%
- OCS use: 52.8% → 16.6%; 36.1% became OCS-free
- Hospitalizations: 22.5% → 6.9%

REDES | n=318
12-month pre/post analysis
- Exacerbations reduced 77.5%; 50.6% exacerbation-free
- FEV_1: +0.21 L; ACT: +6.7 points

AUSTRALIAN MEPOLIZUMAB REGISTRY | n=309
12-month observational registry analysis
- Median maintenance OCS dose: 10 → 2 mg/day at 12 months
- OCS burst use: 96% → 50%
- 55% remained on maintenance OCS at 12 months

COMMONLY ASSESSED OUTCOMES

1. Exacerbations
2. Oral corticosteroids
3. Healthcare resource use
4. Symptom control
5. Lung function
6. Patient-reported outcomes

The same cohort can support several clinically relevant endpoints without a separate control group.

METHODOLOGICAL VISIBILITY GAP

ONLY 2 OF 8
Studies explicitly used “self-controlled” terminology

SELF-CONTROLLED ✓ | **PRE-POST** | **BEFORE-AFTER**
PROSPECTIVE OBSERVATIONAL
LONGITUDINAL COHORT
REAL-WORLD EFFECTIVENESS

Inconsistent labelling may reduce retrieval when searches rely on “self-controlled” terminology alone.

STAKEHOLDER RELEVANCE

H — HTA & Payers
Long-term effectiveness, OCS sparing, persistence, adherence, and healthcare utilization.

G — Guideline Committees
Longitudinal routine-care evidence on treatment effectiveness and patient trajectories.

R — Regulatory Relevance
A pragmatic framework for early real-world evidence where long-term RCT evidence is limited.

C — Clinical Practice
Evidence on effectiveness, treatment burden, monitoring, persistence, and biologic optimization.

IMPLICATIONS & FUTURE RESEARCH

Standardize
Use explicit terms such as “self-controlled pre-post cohort” in titles, abstracts, and protocols.

Broaden
Extend structured pre-post logic beyond asthma to other chronic therapy areas.

Replicate
Promote harmonized protocols across sponsors, geographies, and data sources.

Position
Frame as a complementary RWE pillar alongside active-comparator cohorts and pragmatic trials.

LIMITATIONS

- Limited number of eligible studies.
- Evidence concentrated in severe asthma.
- Heterogeneity prevented pooling.
- Inconsistent terminology may have reduced retrieval.
- No quantitative meta-analysis conducted.

CONCLUSIONS

Consistent Application
Self-controlled pre-post designs are consistently applied in real-world effectiveness studies, particularly severe asthma.

Aligned Structure
Observation windows and clinically relevant endpoints were aligned across the evidence base.

Visibility Challenge
Inconsistent terminology may limit methodological visibility in the literature.

Standardized terminology and transparent reporting can improve identification, replication, and interpretation of these designs.

“Self-controlled pre-post designs provide a structured and feasible approach to longitudinal real-world effectiveness assessment, but inconsistent naming can make this evidence difficult to find.”

ABBREVIATIONS

ACT, Asthma Control Test; CF, cystic fibrosis; EHR, electronic health record; FEV_1, forced expiratory volume in 1 second; HCRU, healthcare resource utilization; HTA, health technology assessment; mOCS, maintenance oral corticosteroid; OCS, oral corticosteroid; PRO, patient-reported outcome; RCT, randomized controlled trial; RWE, real-world evidence; SLR, systematic literature review.

Conflicts of interest: Sandeep J, Manpreet K, Manasa V and Mahendra Kumar R are employees of Trinity Life Sciences

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