

A Multi-Database, Retrospective, Long-term, Observational Safety Study of Pediatric Patients with Inflammatory Bowel Disease

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Clinical:
Pediatric Safety

Methodology:
Prespecified diagnostic-driven reproducible analytics

Why this study was needed

Background

Infliximab is widely used for pediatric Crohn's disease and ulcerative colitis

- CD pediatric approval: May 19, 2006
- UC pediatric approval: Sept 23, 2011

Long-term pediatric safety data remain limited, analysis complements post-marketing registry commitment

Safety outcomes of interest included hospitalization, serious infection, tuberculosis, malignancy, and autoimmune disease

Clinical Question

What is the comparative safety of infliximab among pediatric patients with IBD?

Comparators

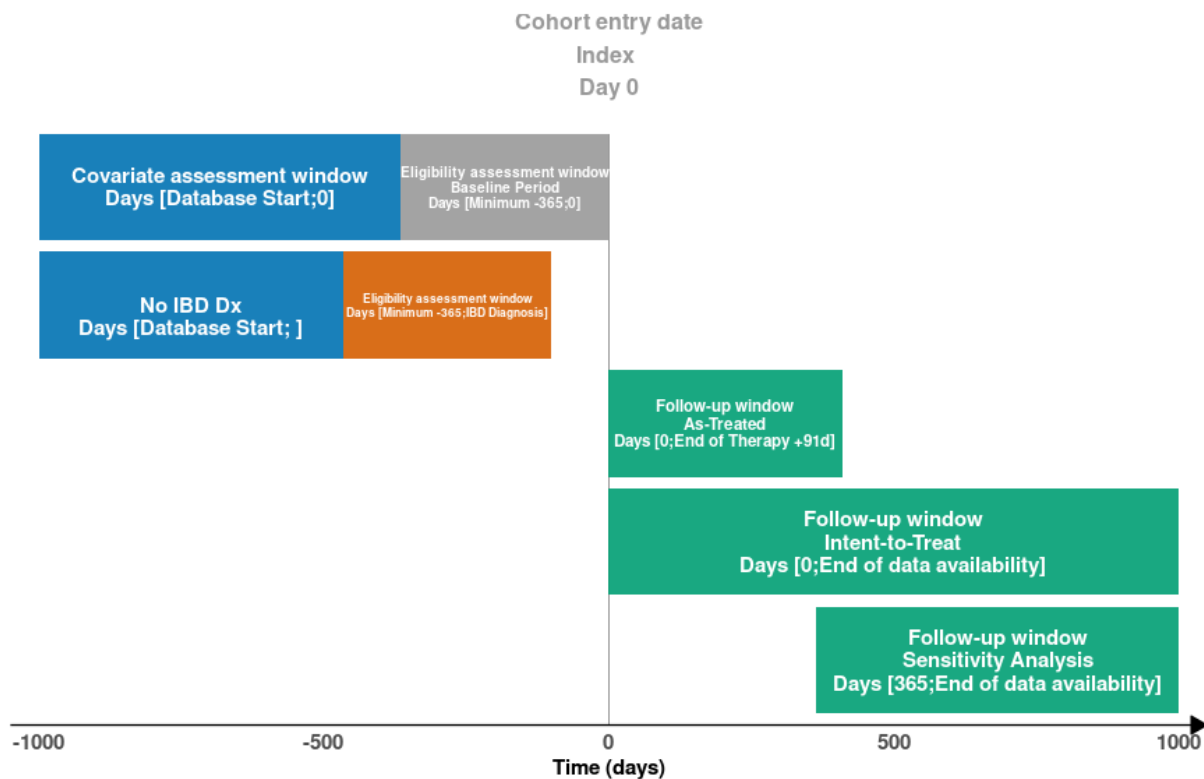
Non-TNF therapies

Adalimumab

What did a standardized, multi-database RWE framework reveal about pediatric infliximab safety?

RWE design

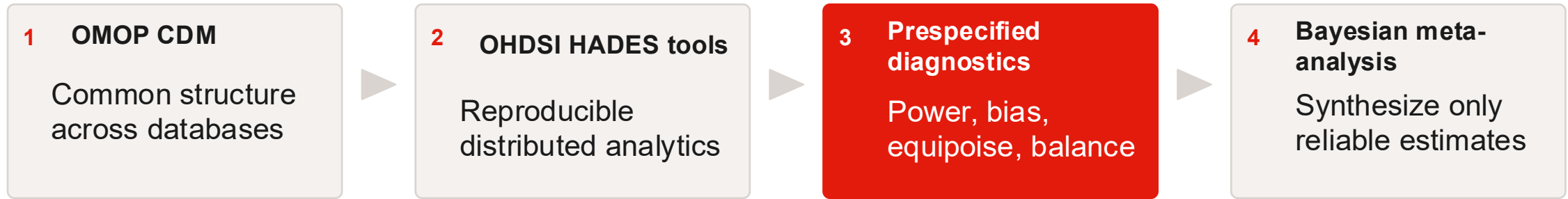
Study design: new-user, active-comparator safety evaluation



- Retrospective, observational cohort study across five U.S. electronic healthcare databases
- Databases mapped to OMOP CDM v5.4
- Patients aged <17 years with IBD and ≥ 1 IBD complication
- Two primary comparisons: infliximab vs non-TNF therapies and infliximab vs adalimumab
- As-treated risk windows for hospitalization, serious infection, TB, and autoimmune disease; intent-to-treat for malignancy

Design principle:
Emulate a credible safety comparison before looking at results

What makes this study different: validity diagnostics before interpretation



Diagnostic thresholds

MDRR <10 | EASE <0.25 | Preference-score equipoise | Max SMD <0.1

Only analyses passing diagnostics were unblinded and synthesized.

Population: Pediatric IBD cohorts across five databases

>9,000

new infliximab pediatric patients

3.1 yrs

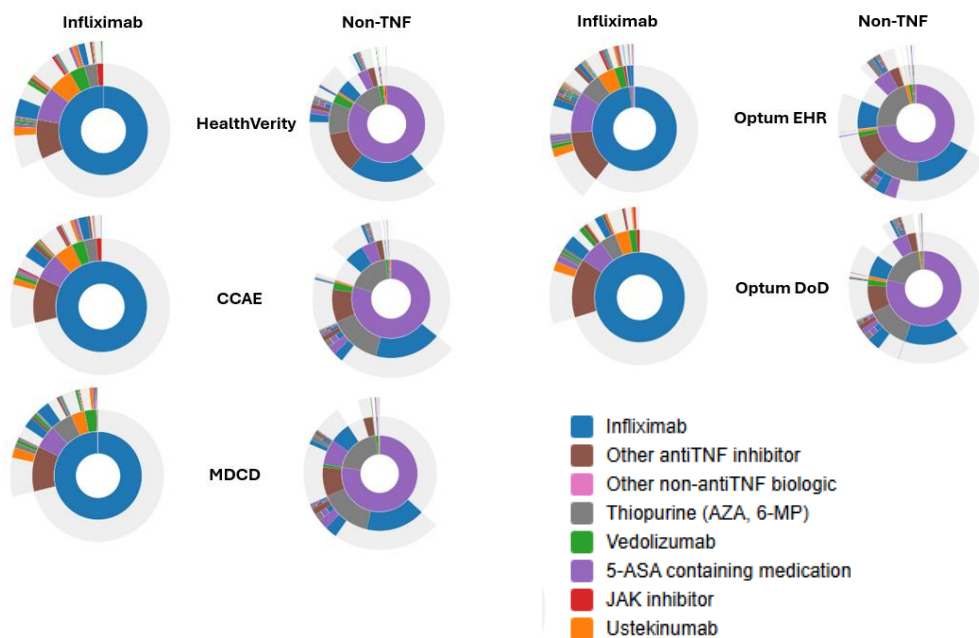
mean follow-up

~12.5

mean age at cohort entry

5

U.S. OMOP databases



Real-world treatment dynamics

Patients largely adhered to initial treatments

Therapeutic switching was observed in routine practice

Non-TNF initiators most commonly switched to infliximab or other anti-TNF agents

Switching is informative context

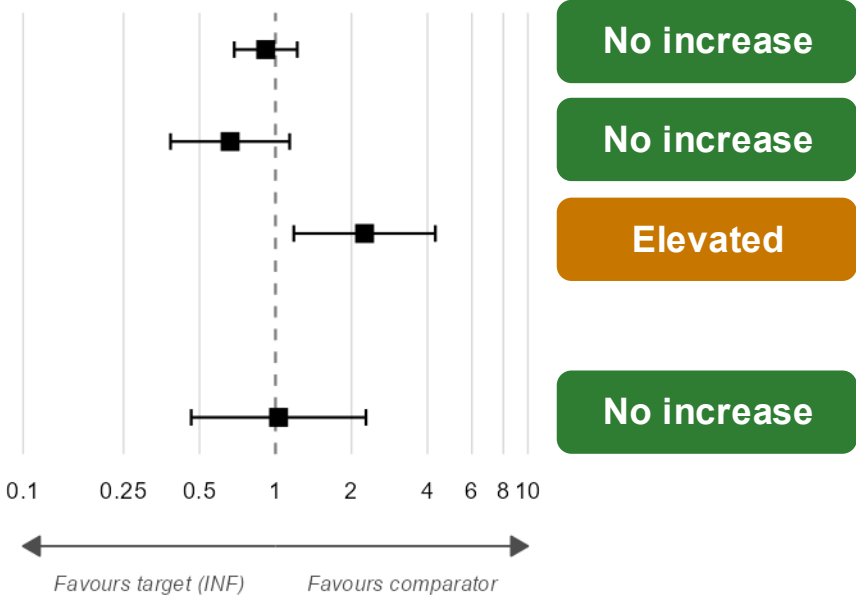
Infliximab vs non-TNF initiators

Primary results: no increased risk for hospitalization, serious infection, or malignancy

Meta-analysis Summary — nonTNF

Outcome	Number of databases	INF	nonTNF	INF Events	nonTNF Events	INF IR per 1,000 PY	nonTNF IR per 1,000 PY	HR (95% CI)
On-Treatment Meta-analysis								
Hospitalization	4	2,990	6,183	496	857	98.3	130.7	0.91 (0.69, 1.22)
Serious Infection	4	7,317	10,540	198	171	14.0	14.4	0.66 (0.38, 1.14)
Autoimmune	4	7,838	10,869	446	106	30.1	8.7	2.25 (1.18, 4.30)
Intent-to-Treat Meta-analysis								
Malignancy	4	7,879	10,932	<52	<40	--	--	1.03 (0.46, 2.28)

TB was too rare for inferential analysis.



Focused interpretation

Interpreting the autoimmune signal: primarily psoriasis and consistent with class effect

Infliximab vs non-TNF

HR 2.26

95% CI 1.18 - 4.31

Autoimmune disease increase was driven predominantly by new-onset psoriasis

Psoriasis accounted for >70% of autoimmune events among infliximab users

Other autoimmune outcomes were uncommon

Infliximab vs adalimumab

HR 0.96

95% CI 0.53 - 1.72

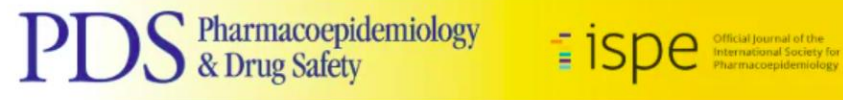
Interpretation

No differential risk between anti-TNF agents

Take-home message

**Large standardized multi-database RWE study of pediatric IBD:
Infliximab was not associated with increased risk of hospitalization,
serious infection, or malignancy**

**Scalable path to generate transparent, reproducible,
regulatory-relevant pediatric safety evidence**



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**Active Safety Surveillance Using Real-World Evidence (ASSURE)
Implementation: Transparent and Reproducible Real-World
Evidence Standardized Framework to Support Safety Signal
Evaluation**

Infliximab versus adalimumab results

Outcome	HR (95% CI)	Interpretation
Any hospitalization	0.95 (0.54, 1.66)	No differential risk
Serious infection	0.77 (0.37, 1.62)	No differential risk
New malignancy	1.18 (0.45, 3.08)	No differential risk
New autoimmune disease	0.96 (0.53, 1.72)	No differential risk

Objective study validity diagnostics

