

SUPPLEMENTARY FILES

TABLES

Supplementary Table S1. Risk of Bias Assessment

A. RCTs (Risk of Bias 2 Tool)

Study	Randomisation	Deviations	Missing Data	Measurement	Selection	Overall
Kondoh 2020	Low	Low	Low	Low	Low	Low
Naccache 2022	Low	Low	Some concerns	Low	Low	Low

B. Observational Studies (Newcastle-Ottawa Scale)

Study	Selection (0-4)	Comparability (0-2)	Outcome (0-3)	Total (0-9)	Judgment
Sakamoto 2018	4	2	3	9	Low risk
Arai 2019	4	2	3	9	Low risk
Anan 2022	4	2	3	9	Low risk
Hyung 2024	4	2	3	9	Low risk
Oishi 2016	4	1	3	8	Low-moderate
Abe 2015	4	1	3	8	Low-moderate
Hozumi 2019	4	1	3	8	Low-moderate
Kawamura 2017	4	1	3	8	Low-moderate
Shuto 2025	4	1	3	8	Low-moderate
Sugino 2021	4	1	3	8	Moderate
Kataoka 2015	4	0	3	7	Moderate
Enomoto 2015	4	0	3	7	Moderate
Higo 2022	4	0	3	7	Moderate
Sakamoto 2010	4	0	3	7	Moderate
Simmons 2017	3	0	3	6	Moderate

Supplementary Table S2. Sensitivity Analysis Results

Analysis	Treatments	Studies	rhTM OR (95% CrI)	PMX-DHP OR (95% CrI)	CYC OR (95% CrI)
Primary	11	17	0.40 (0.11–1.27)	0.15 (0.02–1.03)	1.18 (0.17–7.06)

Analysis	Treatments	Studies	rhTM OR (95% CrI)	PMX-DHP OR (95% CrI)	CYC OR (95% CrI)
Exclude abstracts	10	16	0.40 (0.10–1.38)	0.15 (0.02–1.16)	1.16 (0.14–8.29)
Strict 90-day only	8	14	0.40 (0.10–1.35)	0.15 (0.02–1.09)	1.17 (0.15–8.23)
Exclude 6-month	10	16	0.40 (0.11–1.24)	0.15 (0.02–1.03)	1.18 (0.17–6.93)
High quality only	7	10	0.26 (0.04–0.95)	0.19 (0.01–2.62)	0.58 (0.04–8.25)

Bold indicates statistical significance (95% CrI excludes 1.0).

Supplementary Table S3. League Table (All Pairwise Comparisons)

	Antifibrotic	AZM	Control	CsA	CYC	Early_taper	IVIG	PMX_DHP	Pulse_CS	rhTM	TPE_RTX_IVIG
Antifibrotic	Antifibrotic	-1.452157336	0.4742136673	-1.623228672	0.6494783341	-1.055931609	-1.316817917	-1.433968832	-0.02563491588	-0.4340174573	-2.260671907
AZM	1.452157336	AZM	1.936428109	-0.2050507065	2.106429961	0.3964919273	0.1338731366	0.02302546887	1.439708627	1.031140142	-0.8145661854
Control	-0.4742136673	-1.936428109	Control	-2.118411379	0.1676667663	-1.535660901	-1.797889426	-1.912650186	-0.5001490257	-0.9173260353	-2.739768399
CsA	1.623228672	0.2050507065	2.118411379	CsA	2.284807005	0.5808861135	0.3498583673	0.2101329105	1.638698829	1.202141464	-0.6081743655
CYC	-0.6494783341	-2.106429961	-0.1676667663	-2.284807005	CYC	-1.712789387	-1.966693032	-2.081542134	-0.6722395492	-1.085614371	-2.909262634
Early_taper	1.055931609	-0.3964919273	1.535660901	-0.5808861135	1.712789387	Early_taper	-0.2694632349	-0.3756099437	1.03528776	0.6284394337	-1.211545474
IVIG	1.316817917	-0.1338731366	1.797889426	-0.3498583673	1.966693032	0.2694632349	IVIG	-0.1182620636	1.30939995	0.8829197771	-0.9420075096
PMX_DHP	1.433968832	-0.02302546887	1.912650186	-0.2101329105	2.081542134	0.3756099437	0.1182620636	PMX_DHP	1.414556824	0.9942588768	-0.8310139864
Pulse_CS	0.02563491588	-1.439708627	0.5001490257	-1.638698829	0.6722395492	-1.03528776	-1.30939995	-1.414556824	Pulse_CS	-0.4075238944	-2.247485993
rhTM	0.4340174573	-1.031140142	0.9173260353	-1.202141464	1.085614371	-0.6284394337	-0.8829197771	-0.9942588768	0.4075238944	rhTM	-1.828419147
TPE_RTX_IVIG	2.260671907	0.8145661854	2.739768399	0.6081743655	2.909262634	1.211545474	0.9420075096	0.8310139864	2.247485993	1.828419147	TPE_RTX_IVIG

Supplementary Table S4. Secondary Analysis — In-Hospital Mortality in Mechanically Ventilated Patients

Study	Treatment	Events/n (Int)	Events/n (Ctrl)	OR (95% CI)
Aso 2019	CYC	67/104	830/1743	1.11 (0.75–1.65)
Awano 2022	rhTM	163/212	1976/2602	1.15 (0.81–1.63)
Awano 2023	PMX-DHP	164/199	4151/5417	1.56 (1.03–2.37)
Farrand 2020	CS vs none	14/37	3/45	8.50 (2.19–32.9)

Note: These studies were excluded from primary analysis due to different patient population (mechanically ventilated, administrative database). Results suggest no benefit and possible harm in this severe subgroup.

Supplementary Table S5. Title/Abstract Screening Exclusions (n = 2,132)

Exclusion Reason	n	%
Not AE-IPF related (stable IPF, prevention, other ILD)	780	36.6
Reviews, editorials, commentaries, letters	450	21.1
Case reports, case series with <10 patients	340	15.9
Biomarker, prognostic, or diagnostic studies only	280	13.1
Animal or in vitro studies	130	6.1
Single-arm studies without comparator	100	4.7
Conference abstracts without extractable data	52	2.4
Total excluded at screening	2,132	100

Supplementary Table S6. Full-Text Exclusions with Reasons (n = 22)

A. Protocols Without Results (n = 6)

Record	Description
Glucocorticoids vs Placebo RCT	Registered protocol, no results published
Steroid Pulse Therapy RCT	Registered protocol, no results published
TPE/Rituximab/IVIG RCT	Protocol registered, trial ongoing
Phase III ART-123 protocol	Results published as Kondoh 2020 (included)
EXAFIP protocol	Results published as Naccache 2022 (included)
PEX/Rituximab Phase II protocol	Registered protocol, no results published

B. Duplicate Publications (n = 7)

Record	Duplicate of
Naccache ERS 2021 (EXAFIP abstract)	Naccache 2022 full publication
Aso (Embase) cyclophosphamide	Aso 2018 (batch 1)
Hozumi (Embase) cyclophosphamide	Hozumi 2019 (batch 1)
Oishi ERS 2016 abstract	Oishi 2016 full publication

Record	Duplicate of
Enomoto ATS abstract	Enomoto 2015 full publication
Aso (Scopus)	Aso 2018 (batch 1)
Additional Embase duplicate	Identified via DOI matching

C. Ineligible Study Design or Population (n = 5)

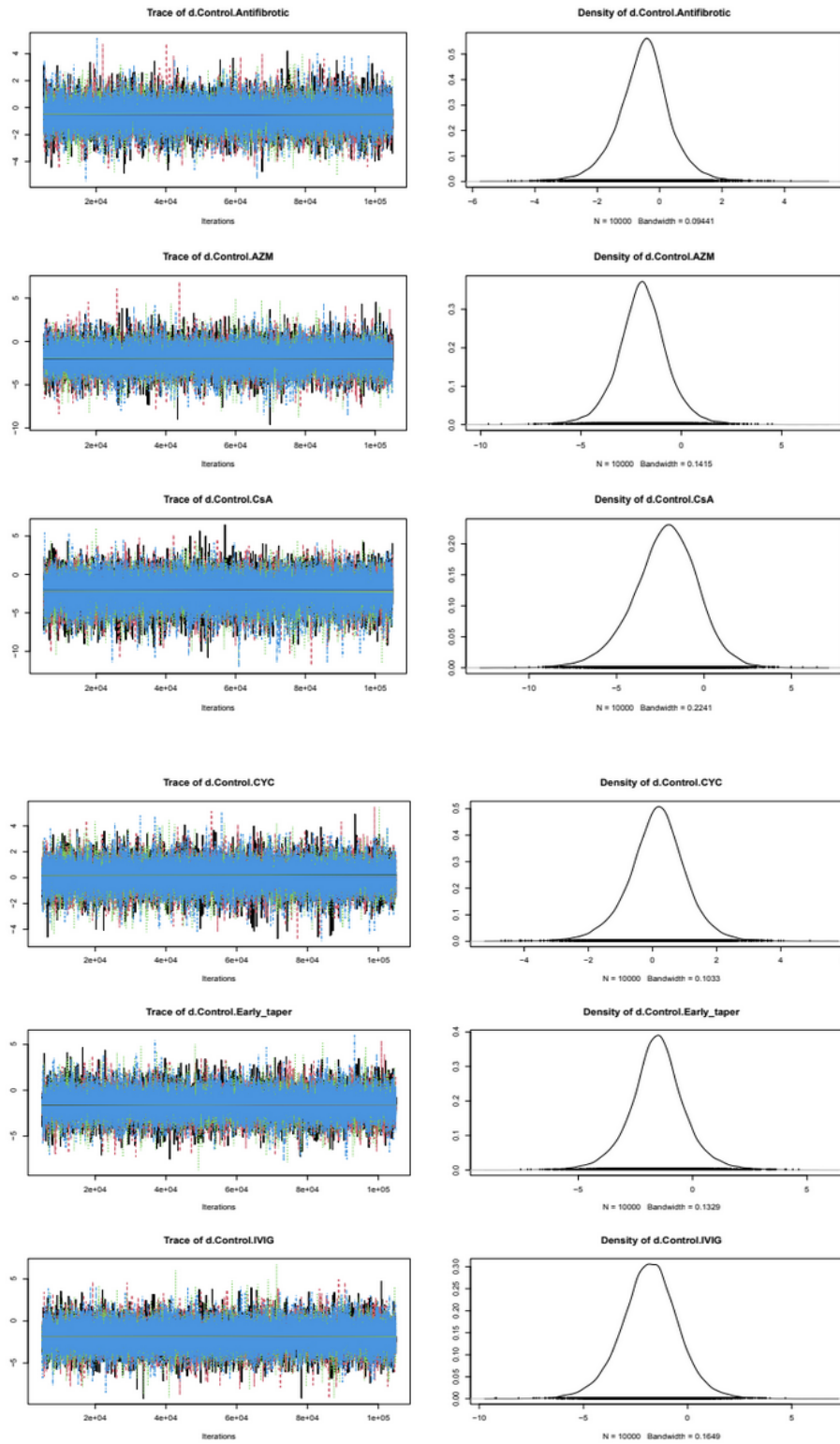
Study	Year	Intervention	Reason for Exclusion
Vianello	2019	Pirfenidone	Control group n = 9, below minimum 10 per group
Ding	2013	Procalcitonin-guided antibiotics	Antibiotic stewardship strategy, not AE-IPF treatment
Richeldi	2016	Nintedanib	AE-IPF prevention study, not treatment of established AE
Aso	2018	Cyclophosphamide	DPC database overlap with other included studies
Shankar	2025	Mixed interventions	No extractable event counts for mortality outcome

D. Studies Used in Secondary Analysis Only (n = 4)

Study	Year	Intervention	Reason
Aso	2019	Cyclophosphamide	In-hospital mortality only, MV population (DPC database)
Awano	2022	Thrombomodulin	In-hospital mortality only, MV population (DPC database)
Awano	2023	PMX-DHP	In-hospital mortality only, MV population (DPC database)
Farrand	2020	Corticosteroids	In-hospital mortality only, MV population (US database)

Note: These 4 studies were included in a separate secondary analysis examining in-hospital mortality in mechanically ventilated patients (Supplementary Table S4).

FIGURES



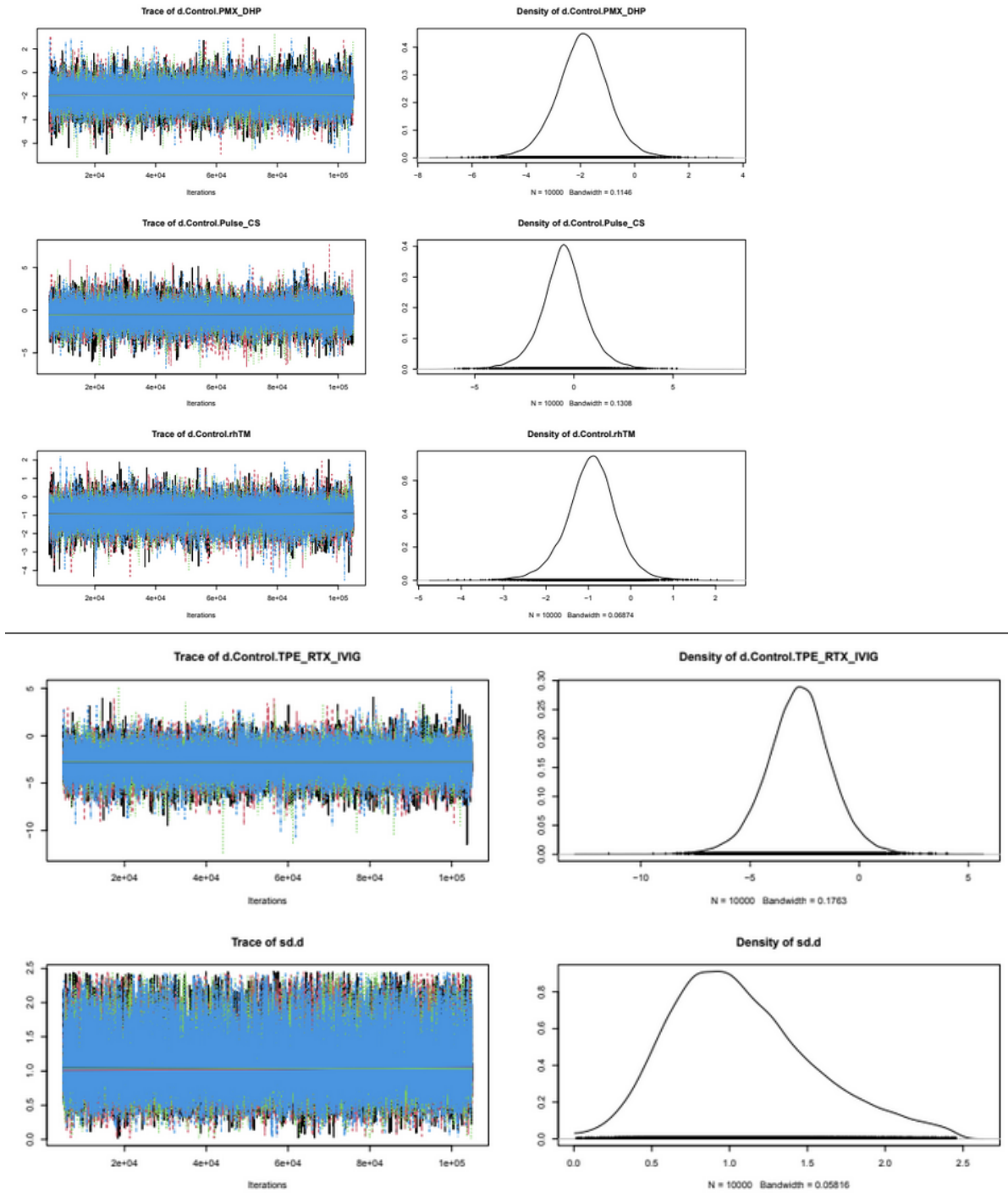
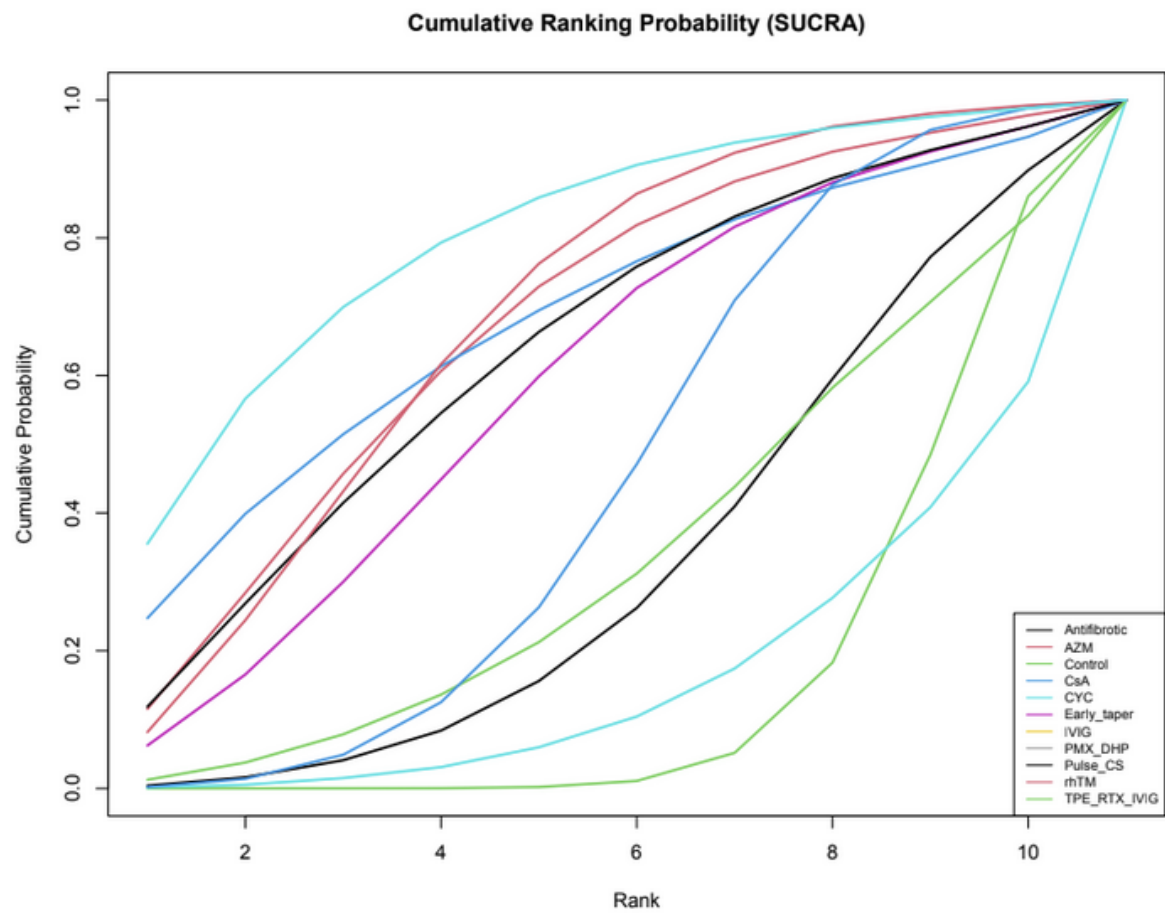


Figure S1. Trace plots for MCMC convergence diagnostics



- **Figure S2.** Cumulative ranking probability plot

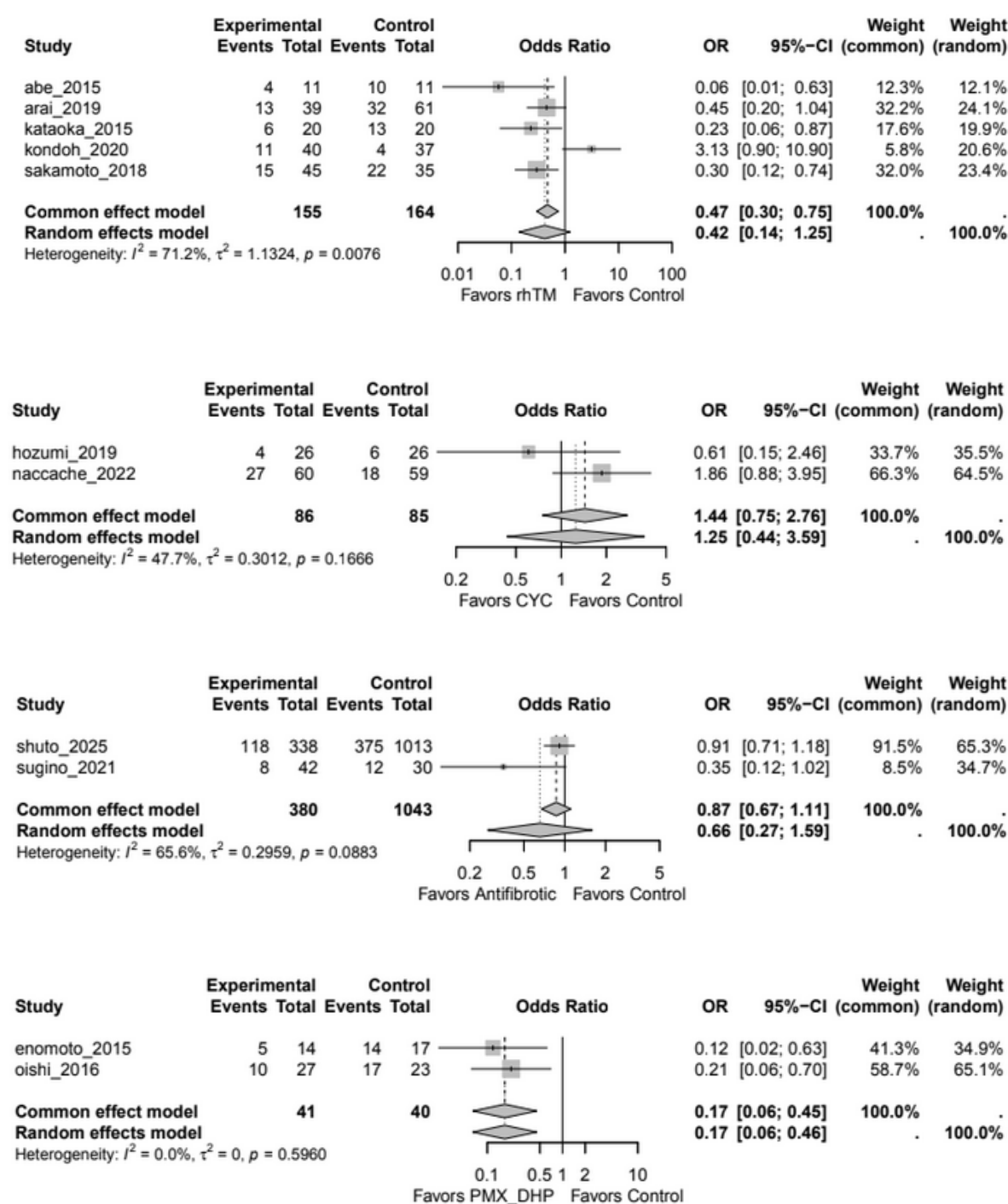
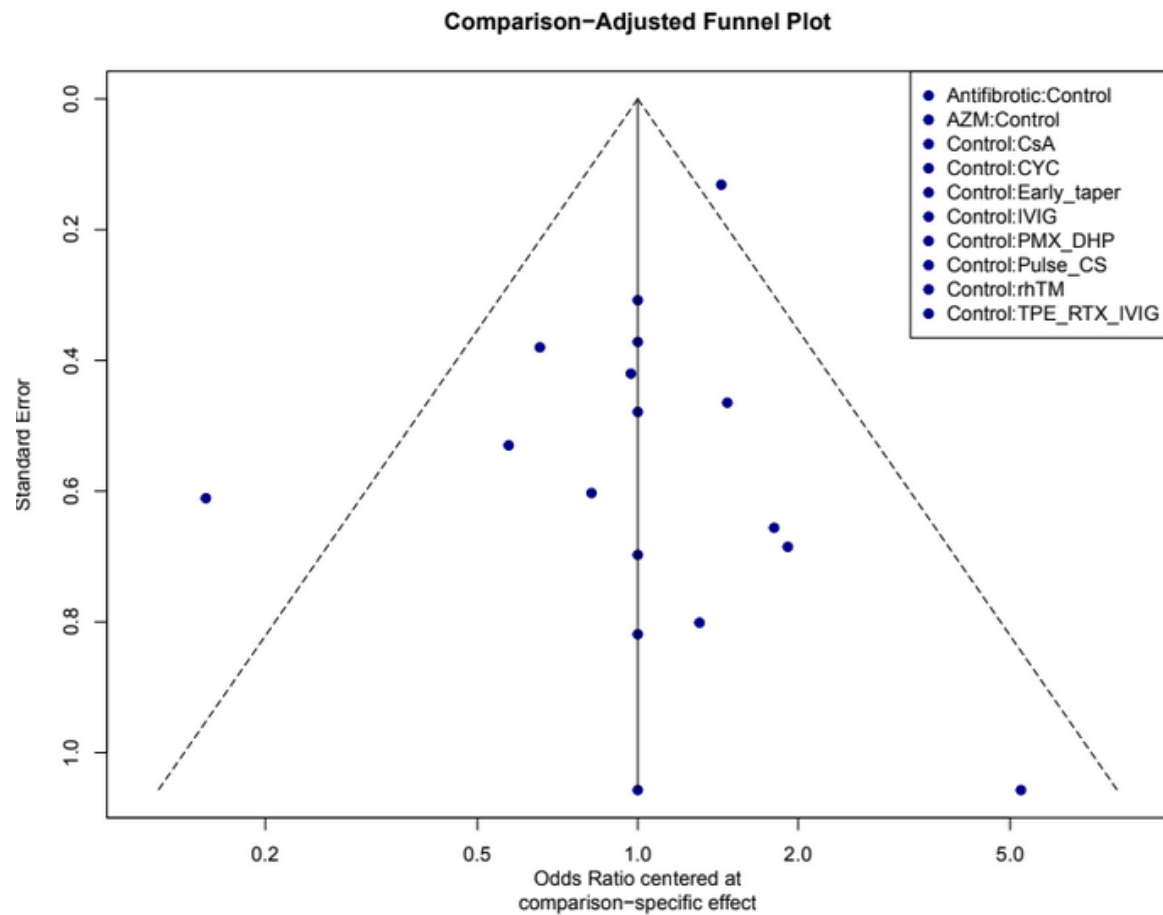


Figure S3. Pairwise forest plots (rhTM, PMX-DHP, CYC, Antifibrotic)



- **Figure S4.** Comparison-adjusted funnel plot for publication bias assessment

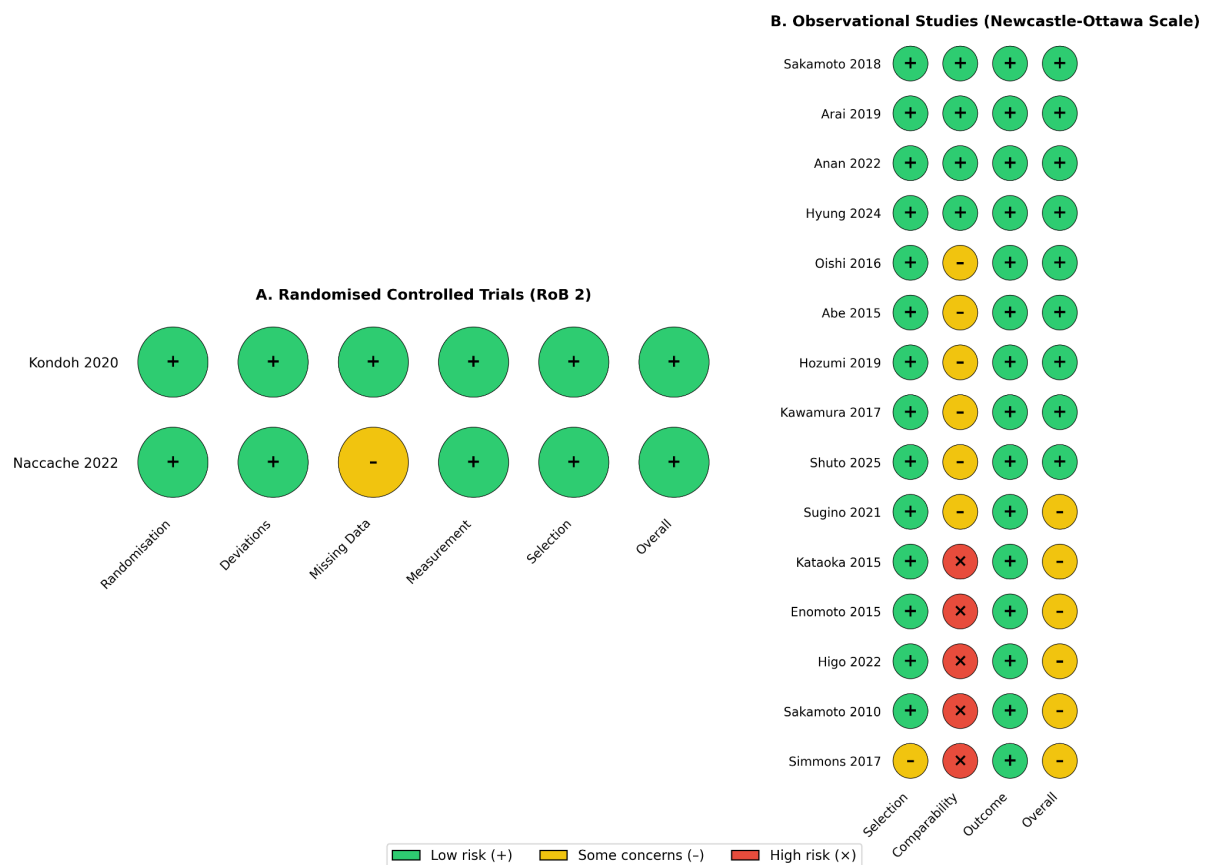


Figure S5. Risk of bias traffic light plot: (A) RCTs assessed with RoB 2 tool; (B) Observational studies assessed with Newcastle-Ottawa Scale