Additional file 3. Check of the included set against the original outcome standard, and diagnostic basis of the included entries

This file compares outcome contributions under the original and amended standards and records diagnostic and adult-eligibility evidence. Entry retention and use of a particular result are judged separately.

Part A checks the 54 outcome-eligible candidates against the original outcome standard. Part B provides the actual primary adult restricted synthesis. Three reports have unresolved adult eligibility and their results are retained only in a separate candidate table. The synthesis is structured without meta-analysis; restrictions change which entries and results contribute, rather than a pooled estimate.

Part C records the diagnostic evidence available for the listed reports, including whether biopsy confirmation applies to the full population or only a subset. Part D separately records unresolved age eligibility.

The 92-entry disposition is 51 included, three with adult eligibility unresolved, 36 excluded, one associated report and one duplicate entry. The 54-candidate inventory comprises the 51 included entries and the three unresolved-eligibility entries. Entries, reports, result rows and independent trials are counted separately.

What the amendment changed

The original standard admitted kidney failure (dialysis, transplantation or sustained eGFR below 15 mL/min/1.73 m²), creatinine doubling, pre-specified percentage eGFR decline or an explicitly defined composite of these, and longitudinal eGFR assessed over at least 12 months. Percentage-decline thresholds are kept separate. The 12-month minimum applies to longitudinal eGFR, not progression events.

The 29 September 2026 expansion admitted a trial-reported pre-specified ≥50% serum-creatinine rise as a separate outcome. This result is removed under the original standard even when another outcome keeps the study eligible. Source checks also corrected outcome and population decisions independently of this amendment; their source and verification status are recorded in Additional file 13.

Part A. Every included entry checked against the standard of before 29 September 2026

For each candidate, the table records the original-standard outcome decision, the eligible alternative if needed and adult-eligibility status. A passed outcome condition does not establish adult eligibility. Sources newly checked in this revision are distinguished from retained prior eligibility records; this table does not claim a new independent review of every source.

The ≥50% serum-creatinine outcome is inadmissible under the original standard in every study. Kidney-failure, doubling and qualifying eGFR outcomes remain usable only on their independent definitions and with population eligibility established. No serum-creatinine hazard ratio is transferred to another outcome.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T07	TESTING	Composite of 40% eGFR decline, kidney failure or kidney death; kidney failure alone	Pass	eGFR-threshold composite and kidney failure were both in the earlier standard Adult status: Included. Source: Existing eligibility ledger T07. Verification: Legacy verified; not completely re-reviewed this round.
T47	MAIN	Composite of creatinine doubling, kidney failure or death from a kidney or cardiovascular cause	Pass	Creatinine doubling and kidney failure were both in the earlier standard Adult status: Included. Source: Existing eligibility ledger T47. Verification: Legacy verified; not completely re-reviewed this round.
T03	STOP-IgAN	Composite of death, end-stage kidney disease or >40% eGFR decline	Pass	End-stage kidney disease and the eGFR-threshold component were both in the earlier standard Adult status: Included. Source: Existing eligibility ledger T03. Verification: Legacy verified; not completely re-reviewed this round.
T30	NefIgArd	2-year time-weighted average eGFR; confirmed 30% eGFR decline or kidney failure	Pass	Both quantities are within the earlier standard Adult status: Included. Source: Existing eligibility ledger T30. Verification: Legacy verified; not completely re-reviewed this round.
T51	PROTECT	Confirmed 40% eGFR reduction, end-stage kidney disease or death; chronic and total slope	Pass	Both families were within the earlier standard Adult status: Included. Source: Existing eligibility ledger T51. Verification: Legacy verified; not completely re-reviewed this round.
T08	DAPA-CKD(IgA 亚组)	Composite of sustained ≥50% eGFR decline, end-stage kidney disease or death from a kidney or cardiovascular cause	Pass	Sustained ≥50% eGFR decline, end-stage kidney disease, renal or cardiovascular death Adult status: Included. Source: Existing eligibility ledger T08. Verification: Legacy verified; not completely re-reviewed this round.
T39	EMPA-KIDNEY(IgA 亚组)	Kidney disease progression; chronic slope	Pass	Both families were within the earlier standard Adult status: Included. Source: Existing eligibility ledger T39. Verification: Legacy verified; not completely re-reviewed this round.
T01	FIND-CKD 非奈利酮	Kidney failure or ≥40% eGFR decline; total and chronic slope	Pass	Both families were within the earlier standard Adult status: Included. Source: Existing eligibility ledger T01. Verification: Legacy verified; not completely re-reviewed this round.
T12	APPLAUSE-IgAN	24-month total slope; composite kidney-failure endpoint	Pass	Slope over 24 months, and a composite including a sustained eGFR threshold Adult status: Included. Source: Existing eligibility ledger T12. Verification: Legacy verified; not completely re-reviewed this round.
T09	ALIGN	Total slope; week-136 eGFR change; composite kidney outcome	Pass	Both families were within the earlier standard Adult status: Included. Source: Existing eligibility ledger T09. Verification: Legacy verified; not completely re-reviewed this round.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T10	Pozzi-Aza-2013	Renal survival defined by a 50% rise in plasma creatinine	Pass	Dialysis9vs10intheexistingAF14extraction;correspondsrelatedPozzitrialreports,donotcountT10/T11independentwithoutidentitycheck. Adult status: Included. Source: Existing eligibility ledger T10. Verification: AF14priorverifiedextraction_not_independently_reread.
T11	Pozzi-Aza-2010	Renal survival defined by a 50% rise in creatinine	Pass	Dialysis6vs4intheexistingAF14extraction;notHRsubstitute. Adult status: Included. Source: Existing eligibility ledger T11. Verification: AF14priorverifiedextraction_not_independently_reread.
T17	Pozzi 1999	50% rise in plasma creatinine; 100% rise in plasma creatinine	Pass	100%SCrrise1/43vs9/43 (doubling);useoriginalsourceeventlabelandnoborrowedHR. Adult status: unresolved. Source: Existing eligibility ledger T17. Verification: AF14priorverifiedextraction_not_independently_reread.
T20	Lv-Pred+ACEI-2009	SCr≥50%rise plus independently reported CKDstage5 0vs2	Pass	RemoveSCr≥50%1vs7. RetainCKDstage5 0vs2. Keep25%eGFRdecline3vs13 separate and do not borrowSCrHR. Adult status: Included. Source: 33.pdf physicalpp.3,4. Verification: Legacy verified by hand; not completely re-reviewed this round.
T28	Wang-2013	Kidney failure events	Pass	End-stage kidney disease was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T28. Verification: Legacy verified by hand; not completely re-reviewed this round.
T37	Stangou 2011	Kidney function over the treatment period	Pass	The recorded basis is not the amended endpoint Adult status: Included. Source: Existing eligibility ledger T37. Verification: Legacy verified by hand; not completely re-reviewed this round.
T38	Katafuchi-2003	Kidney failure events with counts	Pass	The recorded basis is not the amended endpoint Adult status: Included. Source: Existing eligibility ledger T38. Verification: Legacy verified by hand; not completely re-reviewed this round.
T46	Tacrolimus-2018	eGFR over the 5-year follow-up after a 16-week randomized course	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T46. Verification: Legacy verified by hand; not completely re-reviewed this round.
T48	Min 2017 leflunomide	End-stage renal disease; ≥50% creatinine rise	Pass	ESRD5/45CSvs3/40LEF(meanfollowup88m),11.1%vs7.5%;reportinterventionfirst3/40vs5/45. Adult status: Included. Source: 下载.pdf physicalpp.1. Verification: Legacy verified by hand; not completely re-reviewed this round.
T59	C06-甲泼尼龙脉冲	eGFR measured repeatedly to month 18	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T59. Verification: Legacy verified by hand; not completely re-reviewed this round.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T60	Liang 2022	>25%eGFRdecline1/34vs1/34 at6months; outcome qualifies under original rule, age unresolved	Pass	Remove SCr≥50%0vs0. Keep >25%eGFRdecline candidate with adult eligibility unresolved. Progression events have no12monthminimum. Adult status: unresolved. Source: https://link.springer.com/content/pdf/10.1186/s12882-022-02661-6.pdf physicalpp.2,3,5,6,8. Verification: Legacy verified by hand; not completely re-reviewed this round.
T19	Hou 2017	Adult parallel RCT, MMF plus reduced-dose prednisone versus full-dose prednisone. ESRD 0 versus 2 by 12 months; one control event at 6 and one at 12 months. The event need not be primary. Counts are descriptively usable; do not confuse the 6-month safety table with the 12-month narrative.	Pass	Adult parallel RCT, MMF plus reduced-dose prednisone versus full-dose prednisone. ESRD 0 versus 2 by 12 months; one control event at 6 and one at 12 months. The event need not be primary. Counts are descriptively usable; do not confuse the 6-month safety table with the 12-month narrative. Adult status: Included. Source: 29.pdf physicalpp.2,3,5,6. Verification: Targeted source-text verification available.
T29	Tang-MMF-longterm	≥50% rise in serum creatinine; composite of creatinine doubling or end-stage renal disease	Pass	SecondarydoublingSCr/ESRDdefinedassessed. Numericaleventcountnotextractablefrom2005report:retainonlydescriptiveoutcome, not a substituted laterfollow-upcount. Adult status: Included. Source: 1-s2.0-S0085253815509022-main.pdf physicalpp.3,5. Verification: Legacy verified; not completely re-reviewed this round.
T31	Maes-MMF-2004	Kidney function over the follow-up	Pass	The recorded basis is the longitudinal outcome, not the amended endpoint Adult status: Included. Source: Existing eligibility ledger T31. Verification: Legacy verified by hand; not completely re-reviewed this round.
T33	Frisch-MMF-2005	≥50% rise in serum creatinine (primary); end-stage renal disease	Pass	SeparateESRD5/17vs2/15;countscoincidebutendpointmustberelabelednotassumedequivalent. Adult status: Included. Source: Existing eligibility ledger T33. Verification: AF14priorverifiedextraction_not_independently_reread.
T62	C09-来氟米特	Serum creatinine and eGFR	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T62. Verification: Legacy verified by hand; not completely re-reviewed this round.
T05	Woo-Losartan-2009	End-stage renal failure events at 6 years	Pass	Kidney failure was in the earlier standard; this result is withdrawn from numerical use for other reasons Adult status: Included. Source: Existing eligibility ledger T05. Verification: Legacy verified by hand; not completely re-reviewed this round.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T16	HKVIN	Composite progression event	Pass	Creatinine doubling and end-stage renal disease were both in the earlier standard Adult status: Included. Source: Existing eligibility ledger T16. Verification: Legacy verified by hand; not completely re-reviewed this round.
T23	Cheng-1998	Kidney failure events during follow-up	Pass	Creatinine doubling was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T23. Verification: Legacy verified by hand; not completely re-reviewed this round.
T32	Praga-ACEI-2003	Renal survival defined by a 50% rise in serum creatinine	Fail	No other eligible outcome found; its 3/23 vs 12/21 event result is carried in the amended-standard event table only. Adult status: Included. Source: 53.pdf physical pp.1,2,3,4. Verification: source re-read for this revision.
T41	Li-Early-ACEI-2013	Between-group eGFR and slope over 60 months	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T41. Verification: Legacy verified by hand; not completely re-reviewed this round.
T45	Alexopoulos 2004	Participants reaching end-stage renal disease requiring dialysis or transplantation	Pass	IndependentESRD1/14vs6/14at4yr,Table2physicalp5;GFR≥50%decline1vs7isaseparaterowandnotthesameendpoint. Fish-oilpanelcanretainESRDORifrecomputedandrelabeled;do notsaypanelhasnothingtodisplay. Adult status: Included. Source: Treatment of Severe IgA Nephropathy With Omega 3 Fatty Acids The Effect of a Very Low Dose Regimen.pdf physicalpp.2,3,4,5,6. Verification: Legacy verified by hand; not completely re-reviewed this round.
T25	Mayo-FishOil	SCr≥50%; separately reportedESRD	Pass	RemoveSCr≥50%17/55vs29/51. RetainESRD8/55vs19/51, repeateddialysis/transplantation, from1999extension; not ESRD-or-death. Adult status: Included. Source: Existing eligibility ledger T25. Verification: primary_source_Table1_verified; supersedes previous AF14 composite wording.
T49	Donadio 2001	Slope and end-stage renal disease	Pass	Both were within the earlier standard Adult status: Included. Source: A-Randomized-Trial-of-High-Dose-Compared-with-Low-Dose-Omega-3-Fatty-Acids-in-Severe-IgA-Nephropathy.pdf physicalpp.1,2,3,6,7,8. Verification: Targeted source-text verification available.
T04	Liu-CsA-2014	Secondary endpoint of a 50% creatinine rise or a 25% eGFR fall at 12 months	Pass	Separate25%eGFRdecline1vs0andlongitudinaleGFR;prespecifiedpercentdeclineisprogressionregardless12m. Adult status: Included. Source: Existing eligibility ledger T04. Verification: latestledger_and_AF14_not_independently_reread.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T13	Probucol-2013	Doubling of serum creatinine	Pass	Creatinine doubling was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T13. Verification: Legacy verified by hand; not completely re-reviewed this round.
T21	Cruzado 2011	Adult age18–70 biopsy IgAN RCT:14 sirolimus plus enalapril/atorvastatin versus9 enalapril/atorvastatin. Dialysis/transplant prospectively assessed as therapeutic failure; all alive and dialysis-free at1year gives0/14 versus0/9. Zero events remain eligible; no relative effect can be estimated.	Pass	Adult age18–70 biopsy IgAN RCT:14 sirolimus plus enalapril/atorvastatin versus9 enalapril/atorvastatin. Dialysis/transplant prospectively assessed as therapeutic failure; all alive and dialysis-free at1year gives0/14 versus0/9. Zero events remain eligible; no relative effect can be estimated. Adult status: Included. Source: 34.pdf physicalpp.1,2,4. Verification: Targeted source-text verification available.
T22	Abelmoschus-2020	Doubling of serum creatinine	Pass	Creatinine doubling was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T22. Verification: Legacy verified by hand; not completely re-reviewed this round.
T24	Cheng 2015	Adult18–55 randomized double-blind four-arm trial,42perarm,24months. Haemodialysis4,1,0,0 and SCr>50%5,2,1,1 in valsartan alone,plusclopidogrel,plusleflunomide,plusboth. Original standard retains haemodialysis; amended also SCr. Safety-table location is not a reason to exclude hard kidney outcomes.	Pass	Adult18–55 randomized double-blind four-arm trial,42perarm,24months. Haemodialysis4,1,0,0 and SCr>50%5,2,1,1 in valsartan alone,plusclopidogrel,plusleflunomide,plusboth. Original standard retains haemodialysis; amended also SCr. Safety-table location is not a reason to exclude hard kidney outcomes. Adult status: Included. Source: 4.pdf physicalpp.2,6. Verification: Targeted source-text verification available.
T26	Chan-Antiplatelet-1987	A progression or longitudinal outcome within the recorded basis	Pass	The recorded basis is not the amended endpoint, and no other row below rests on it either Adult status: Included. Source: Existing eligibility ledger T26. Verification: Legacy verified by hand; not completely re-reviewed this round.
T15	Woo-ACEI/ ATRA-2007	Progression events	Pass	Kidney failure was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T15. Verification: Legacy verified by hand; not completely re-reviewed this round.
T34	Calcitriol-2026	Annual eGFR decline over 12 months	Pass	Longitudinal eGFR with 12 months of follow-up Adult status: Included. Source: Existing eligibility ledger T34. Verification: Legacy verified by hand; not completely re-reviewed this round.
T40	ENVISION	Change in eGFR at month 12	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T40. Verification: Legacy verified by hand; not completely re-reviewed this round.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T42	Felzartamab-2025	Change in eGFR at month 24	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T42. Verification: Legacy verified by hand; not completely re-reviewed this round.
T43	JANUS-2022	Renal function over 72 weeks	Pass	Longitudinal kidney function beyond 12 months; values graphic only Adult status: Included. Source: Existing eligibility ledger T43. Verification: Legacy verified by hand; not completely re-reviewed this round.
T57	NEFIGAN-2b	eGFR change at 9 and 12 months	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T57. Verification: Legacy verified; not completely re-reviewed this round.
T58	Ballardie 2002	ExplicitESRF; withdrawal-sensitive renal-survival curve	Pass	ESRF defines eligibility. 72%vs6%curve includes selectedwithdrawals; not a clean kidney-failure risk. Twoarms19each. Adult status: Included. Source: N15__10.1681_asn.v131142.pdf physicalpp.2,3,4. Verification: Legacy verified; not completely re-reviewed this round.
T52	HR19042(恒瑞)	Between-group difference in eGFR change at month 12	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T52. Verification: Legacy verified; not completely re-reviewed this round.
T66	Manno 2009	Creatinine doubling or end-stage kidney disease; end-stage kidney disease alone	Pass	Creatinine doubling and end-stage kidney disease were both in the earlier standard Adult status: unresolved. Source: Existing eligibility ledger T66. Verification: Legacy verified by hand; not completely re-reviewed this round.
T67	Rituximab trial	Change in eGFR over 1 year	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T67. Verification: Legacy verified by hand; not completely re-reviewed this round.
T81	Dipyridamole plus low-dose warfarin (Lee 1997)	End-stage kidney disease during a 3-year trial	Pass	End-stage kidney disease was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T81. Verification: Legacy verified by hand; not completely re-reviewed this round.
T86	Mizoribine (Hirai 2017)	eGFR over 36 months	Pass	Longitudinal eGFR beyond 12 months Adult status: Included. Source: Existing eligibility ledger T86. Verification: Legacy verified by hand; not completely re-reviewed this round.
T89	Steroid pulse with or without mizoribine (Masutani 2016)	Creatinine doubling or ≥50% eGFR decline	Pass	Creatinine doubling and the eGFR-threshold component were both in the earlier standard Adult status: Included. Source: Existing eligibility ledger T89. Verification: Legacy verified by hand; not completely re-reviewed this round.

Entry	Report	Recorded outcome	Original-standard outcome	Usable contribution and adult status
T90	Blisibimod (BRIGHT-SC), abstract-level	End-stage kidney disease, one participant per arm	Pass	End-stage kidney disease was in the earlier standard Adult status: Included. Source: Existing eligibility ledger T90. Verification: Legacy verified by hand 2026-10-07; not completely re-reviewed this round.

Part B. What restricting the review to the earlier standard does to the evidence synthesis

Of 54 candidates, 53 meet the original outcome standard; Praga 2003 (T32) does not. After separating the three reports of unresolved adult eligibility, 50 of 51 primary adult entries retain an eligible outcome. Those three reports also meet the original outcome condition through their other results, but were not included in the primary adult synthesis. All 23 results from the ten focused comparisons remain eligible, so their treatment-specific conclusions and GRADE rows are unchanged.

The candidate event inventory contains 37 rows. Five results from the three reports of unresolved adult eligibility are set aside, leaving 32 primary adult event rows. Seven candidate rows use the ≥50% serum-creatinine endpoint: one belongs to Pozzi 1999 and six to the primary adult set. The actual original-standard primary adult event table contains 26 rows after those six results are removed.

Report	Removed result	Candidate status	Eligible alternative	Adult restriction action
Lv 2009 (open-label, 63) [44]	Kidney survival (≥50% rise in SCr); 1 versus 7 events; post-treatment-adjusted model is not used as the randomized effect	Primary adult set	CKD stage 5 0 vs 2; independently reported	SCr50 result removed; alternative remains only if population eligible
Frisch 2005 (double-blind, 32 analysed) [45]	≥50% rise in SCr, required to be sustained for ≥2 consecutive months (the trial's primary outcome); 5/17 vs 2/15	Primary adult set	ESRD 5/17 vs 2/15	SCr50 result removed; alternative remains only if population eligible
Tang 2005 (40) [46]	≥50% rise in SCr, no persistence requirement stated; 1/20 vs 3/20	Primary adult set	2010 extension doubling/ESRD 3/20 vs 10/20; linked cohort	SCr50 result removed; alternative remains only if population eligible
Mayo/Dobos 1994 (double-blind, 106) [47, 48]	≥50% rise in SCr; 17/55 vs 29/51	Primary adult set	ESRD 8/55 vs 19/51 during extension	SCr50 result removed; alternative remains only if population eligible
Alexopoulos 2004 (34 assigned; 28 analysed) [49]	≥50% rise in SCr at 4 years; reported separately from ≥50% GFR decline; 1/14 vs 6/14	Primary adult set	Author-reported ESRD 1/14 vs 6/14; completers	SCr50 result removed; alternative remains only if population eligible
Pozzi 1999 (open-label, 86) [21]	50% rise in plasma creatinine by 5 y; 9/43 vs 14/43	Eligibility unresolved	Creatinine doubling 1/43 vs 9/43; adult eligibility unresolved	SCr50 result removed; alternative remains only if population eligible

Report	Removed result	Candidate status	Eligible alternative	Adult restriction action
Praga 2003 (44 randomised) [50]	Renal survival (50% rise in baseline SCr); 3/23 vs 12/21	Primary adult set	None. The trial reports no other kidney-progression outcome.	SCr50 result removed; no alternative outcome exists, so the entry contributes to no original-standard table

The preceding table lists all seven removed candidate serum-creatinine results. The following restricted table contains the 26 retained primary adult event rows; the separate five-row table of unresolved-eligibility results does not enter that synthesis. Figure 2_restricted contains these 26 results and omits the creatinine-based fish-oil odds-ratio panel. Eligible alternative dialysis, ESRD and doubling results remain separately defined.

Trial (design)	Comparison	Outcome	Result	Effect measure and model
TESTING (double-blind, 503)[3]	Methylprednisolone vs placebo	40% eGFR decline, kidney failure or kidney death	HR 0.53 (0.39–0.72)	Cox, stratified
TESTING[3]	as above	Kidney failure alone	50/257 vs 67/246; HR 0.59 (0.40–0.87)	Cox, stratified
STOP-IgAN (open-label, 162) [27–29]	Immunosuppression vs supportive care	Death, ESKD or >40% eGFR decline (10 y)	35/77 vs 36/72; HR 1.20 (0.75–1.92), reported with supportive care as the reference category	Cox
MAIN (open-label, blinded endpoint, 170) [26]	MMF + supportive care vs supportive care	Creatinine doubling, kidney failure, death from a kidney or cardiovascular cause	6/85 vs 18/85; aHR 0.23 (0.09–0.63)	Cox, adjusted
Dipyridamole + low-dose warfarin (randomized, 21) [41]	Dipyridamole + low-dose warfarin vs no treatment	ESKD during a 3-year trial	1/10 vs 4/11	Event counts reported; no effect estimate presented
Frisch 2005[45]	as above	ESRD	5/17 vs 2/15	Event counts reported; crude HR 2.47 (0.48–12.8), P=0.28
Liu 2014 (open-label, 48 analysed) [51]	Methylprednisolone + cyclosporine A vs methylprednisolone alone	≥25% fall in eGFR within 12 months (the trial secondary kidney endpoint)	2/23 vs 0/25	Event counts reported; no effect estimate presented
DAPA-CKD (IgA subgroup, 270) [30]	Dapagliflozin vs placebo	Composite of sustained ≥50% eGFR decline, end-stage kidney disease or death from a kidney or cardiovascular cause	6/137 vs 20/133; HR 0.29 (0.12–0.73)	Cox, pre-specified subgroup
EMPA-KIDNEY (IgA subgroup, 817) [31]	Empagliflozin vs placebo	Composite of sustained ≥40% eGFR decline, end-stage kidney disease, sustained eGFR <10 mL/min/1.73 m² or death from kidney failure	51/413 vs 67/404; HR 0.67 (0.46–0.97)	Cox, post hoc classification

Trial (design)	Comparison	Outcome	Result	Effect measure and model
PROTECT (202 vs 202) [5]	Sparsentan vs irbesartan	Composite kidney failure endpoint (confirmed 40% eGFR reduction, ESKD or all-cause death)	18 (9%) vs 26; RR 0.7 (0.4–1.2)	Relative risk, as reported
NefIgArd (182 vs 182)[6]	Targeted-release budesonide vs placebo	Confirmed 30% eGFR reduction or kidney failure	21 (12%) vs 39 (21%); HR 0.45 (0.26–0.75)	Cox
APPLAUSE-IgAN (double-blind, 238 vs 239)[8]	Iptacopan vs placebo	Composite kidney-failure endpoint (sustained ≥30% eGFR decline, sustained eGFR <15, dialysis, transplant, kidney-failure death)	21.4% vs 33.5%; HR 0.57 (0.40–0.81)	Cox, secondary endpoint
ALIGN (main stratum, double-blind, 170 vs 170) [9]	Atrasentan vs placebo	Composite kidney outcome (≥30% eGFR decline, kidney failure, death)	26/170 (15%) vs 37/170 (22%); HR 0.64 (0.39–1.05)	Cox, secondary endpoint (not significant)
FIND-CKD (IgA subgroup, double-blind, 226 vs 190)[10]	Finerenone vs placebo	Kidney failure or ≥40% eGFR decline (sustained ≥4 weeks)	52/226 (23.0%) vs 51/190 (26.8%); HR 0.82 (0.56–1.21)	Cox, pre-specified exploratory subgroup
Abelmoschus manihot (1470) [52]	A. manihot vs losartan	Creatinine doubling (the eligible component of the trial's composite)	6 vs 10 (P=0.451); 1 participant in the losartan arm required haemodialysis	No effect estimate reported for the component
Steroid-pulse ± mizoribine (40) [53]	Steroid-pulse therapy plus mizoribine vs steroid-pulse therapy alone	Creatinine doubling or ≥50% eGFR decline	No participant reached the endpoint in either group	Event counts reported; no relative effect estimate presented
Lv 2009 [44]	Prednisone + cilazapril vs cilazapril	CKD stage 5 during follow-up	0 versus 2	33 versus 30 randomized; three lost overall. Distinct from the ≥50% SCr outcome; no borrowed HR.
Alexopoulos 2004 [49]	Very-low-dose omega-3 vs symptomatic care	Author-reported ESRD over 4 years	1/14 vs 6/14	Completer analysis of 18 versus 16 assigned; dialysis/SCr definition and exclusions described in Additional file 10.
Mayo/Donadio 1999 extension [47]	Original fish-oil vs original placebo assignment	ESRD: repeated dialysis or transplantation	8/55 vs 19/51	Mean 6.4 years; 2-year randomized phase followed by open-label care and treatment crossover.
Tang 2010 follow-up [54]	Original MMF vs control assignment	Creatinine doubling or ESRD over ≥6 years	3/20 vs 10/20	Same 40-patient Tang 2005 cohort, not a new trial. ESRD 2 vs 9; all patients alive; Methods composite also included death.

Trial (design)	Comparison	Outcome	Result	Effect measure and model
Pozzi 2010 [33]	Azathioprine + corticosteroids vs corticosteroids	Dialysis during follow-up	6/101 vs 4/106	Reported separately from the ≥50% SCr renal-survival endpoint; no borrowed HR; outcome-specific RoB 2: some concerns; not graded.
Pozzi 2013 [34]	Azathioprine + corticosteroids vs corticosteroids	Dialysis during follow-up	9/20 vs 10/26	Related protocol/reporting programme to Pozzi 2010; not assumed independent; outcome-specific RoB 2: some concerns; not graded.
Hou 2017 [39]	MMF + reduced-dose prednisone vs full-dose prednisone	ESRD by 12 months	0 versus 2	87 vs 89 randomized; 86 vs 88 efficacy set. ESRD analysis denominator not specified; counts only.
Cruzado 2011 [40]	Sirolimus + enalapril/atorvastatin vs enalapril/atorvastatin	Dialysis at 1 year	0/14 vs 0/9	All alive and dialysis-free; no relative effect estimable. Measured GFR is not relabelled as eGFR.
Cheng 2015 [42]	Valsartan alone / plus clopidogrel / plus leflunomide / plus both	Haemodialysis during 24 months	4/42; 1/42; 0/42; 0/42	One four-arm trial; shared control not counted repeatedly. Retain haemodialysis label; maintenance status not specified.
Donadio 2001 [43]	High-dose vs low-dose omega-3 fatty acids	ESRD during follow-up	8/36 vs 10/37	Minimum 2 years of treatment; follow-up up to 5 years. Randomized dose comparison only; historical placebo excluded.

Longitudinal eGFR. All 25 displayed primary adult longitudinal rows meet the original outcome standard; the DAPA-CKD display contains two separately assessed slopes. The restricted longitudinal table is supplied as a separate CSV. No result from the three reports of unresolved adult eligibility was added to it. The candidate-only progression table below preserves their five results, which were not used as adult evidence.

Trial (design)	Comparison	Outcome	Result	Effect measure and model
Manno 2009 (open-label, 97) [22]	Prednisone + ramipril vs ramipril	Creatinine doubling or ESKD	2/48 vs 13/49; HR 0.13 (0.03–0.61)	Cox, multivariate
Manno 2009[22]	as above	ESKD alone	1/48 vs 7/49; HR 0.09 (0.01–0.86)	Cox, multivariate
Pozzi 1999 (open-label, 86) [21]	Methylprednisolone + prednisone vs supportive care	50% rise in plasma creatinine by 5 y	9/43 vs 14/43	HR 0.41 (0.17–0.98); Cox, baseline covariates only; reported by the investigators as a relative risk
Pozzi 1999[21]	as above	100% rise in plasma creatinine by 5 y	1/43 vs 9/43	Separate creatinine-doubling counts; the HR for the 50% threshold is not reused.

Trial (design)	Comparison	Outcome	Result	Effect measure and model
Liang 2022 [23]	Methylprednisolone months 1–2–3 vs 1–3–5	>25% eGFR decline at 6 months (Table 4)	1/34 vs 1/34	74 assigned (36/38); 68 analysed (34/34) after 6 exclusions. Completer secondary event; RoB 2: high; not graded. Entry ages 14–65.

The exploratory two-trial mycophenolate calculation uses ≥50% serum-creatinine rise and is not carried into the original-standard synthesis. The two trials can contribute their separately reported eligible progression outcomes without that calculation. MAIN's randomized composite and trial-phase eGFR results, and their respective certainty ratings, remain unchanged.

Four entries were added to this revision after the original reports were re-read, and the table records only what each report prints. Praga 2003 reports its primary endpoint as event counts and a Kaplan-Meier estimate (3/23 versus 12/21; renal survival 100% versus 70% at four years) with no hazard ratio and no confidence interval, so its row carries counts only. Liu 2014 reports one secondary kidney endpoint with counts (2/23 versus 0/25); the group eGFR values it prints are each arm's own change from its own baseline, so no between-group interval is available and none has been constructed. Li 2012 prints arm-level eGFR at 60 months and an arm-level rate of decline, each with a standard deviation and a P value, but no between-group estimate or interval. NEFIGAN 2b prints a mean percentage change from baseline at 12 months with a between-group ratio and interval, but no absolute eGFR levels in the material held; the percentage change is tabulated as reported and no absolute difference has been reconstructed from it. Panels (a) to (c) of Figure 4 plot published between-group differences, and panel (d) plots arm-level values for two trials that report no between-group contrast; the four results added in this revision are tabulated and are not plotted. None of the four enters a pooled estimate, because the synthesis contains none.

Interpretive effect. The restriction removes the specified older creatinine-rise results and the exploratory calculation while retaining all focused comparison–outcome conclusions. It does not create a pooled clinical estimate. The ≥50% creatinine narrative for Min 2017 is also omitted from the original-standard account; the independently reported ESRD outcome remains. Previously excluded records were not all re-screened in this targeted reconciliation; retained verification levels are shown per entry.

Part C. Diagnostic basis of the included trials, as each report states it

The population criterion of this review admits trials in adults with primary IgA nephropathy and admits IgA subgroups of trials in broader glomerular-disease or chronic kidney disease populations. Those two kinds of entry differ in what the review can say about diagnosis, and the difference is recorded here rather than hidden behind one population label. Where a report states that participants required a biopsy diagnosis, that statement is quoted; where the report does not address diagnosis, that is recorded as not stated, and no assumption is made in either direction.

Entry	Report	Diagnostic basis, as stated	Biopsy confirmation across the participants contributing the result
T07	TESTING	Eligibility required a prior kidney biopsy: "kidney biopsy (without time limits)" (source file for this trial, idx07)	Required of all randomized participants
T12	APPLAUSE-IgAN	"Eligible patients were 18 years of age or older and had biopsy-confirmed IgA nephropathy" (idx52)	Required of all randomized participants

Entry	Report	Diagnostic basis, as stated	Biopsy confirmation across the participants contributing the result
T09	ALIGN	"Adults with biopsy-proven IgA nephropathy" (idx10)	Required of all randomized participants
T51	PROTECT	"Adults (aged ≥18 years) with biopsy-proven IgA nephropathy" (idx46 and idx43)	Required of all randomized participants
T03	STOP-IgAN	"379 patients with biopsy-proven IgAN were enrolled into a 6 months run-in phase" (idx03)	Required of all randomized participants
T47	MAIN	Biopsy-based diagnosis stated as an entry criterion in the report	Not individually re-verified against the source for this file
T30	NefIgArd	Biopsy-based diagnosis stated as an entry criterion in the report	Not individually re-verified against the source for this file
T01	FIND-CKD, IgA subgroup	IgA nephropathy diagnosis is that of the parent trial, **which did not require biopsy** : the parent trial report states that "we also conducted additional analyses restricted to biopsy-confirmed cases" (idx01), which is intelligible only if the trial population was not restricted to them	**Not all** : biopsy confirmation was not an entry requirement of the parent trial, and this review does not record how many of the IgA subgroup had it
T08	DAPA-CKD, IgA subgroup	Participants were classified by recorded primary kidney disease in the parent trial; the IgA analysis states that a "sensitivity analysis was restricted to participants with biopsy-proven IgA nephropathy" (idx09)	**Not all** : 270 participants were in the IgA nephropathy stratum and the biopsy-proven sensitivity analysis used 254 of them; this review's row cites the count from the stratum of 270
T39	EMPA-KIDNEY, IgA subgroup	The IgA group is one of three categories into which the pre-specified glomerular disease subgroup was split post hoc	**Not stated in the material held** : the report does not record whether the diagnosis in this split was biopsy-confirmed
T66	Manno 2009	"Ninety-seven biopsy-proven IgAN patients"	Required of all randomized participants
T17	Pozzi 1999	"Eligible patients had biopsy-proven IgA nephropathy"; entry criteria also require "a histological diagnosis of IgA nephropathy with immunofluorescence showing mesangial IgA deposits"	Required of all randomized participants
T10	Pozzi 2013	Same trial population as Pozzi 2010; biopsy-proven disease	Required of all randomized participants
T11	Pozzi 2010	Same trial population as Pozzi 2013; biopsy-proven disease	Required of all randomized participants
T04	Liu 2014	Biopsy-proven IgA nephropathy, an entry criterion of the trial	Required of all randomized participants
T33	Frisch 2005	"All patients had biopsy-proven IgAN with renal biopsy samples examined independently by two pathologists"	Required of all randomized participants, with double reading

Entry	Report	Diagnostic basis, as stated	Biopsy confirmation across the participants contributing the result
T25	Mayo/Dobos fish oil, long-term report	**Not restated** in the long-term report held	**Not stated** in the report held; the diagnosis was an entry requirement of the randomised trial it follows, but that statement is not in the material held for this version
T29	Tang 2005	"The histologic diagnosis of IgAN was based upon the demonstration of mesangioproliferative changes on light microscopy and the concomitant presence of predominant or codominant mesangial deposition of IgA"	Required of all randomized participants
T14	Chen 2004	Biopsy-proven IgA nephropathy, an entry criterion of the trial	Required of all randomized participants
T20	Lv 2009	"Biopsy-proven IgA nephropathy (defined by using standard morphological characteristics, including immunofluorescence criteria)"	Required of all randomized participants
T32	Praga 2003	Biopsy-proven IgA nephropathy, an entry criterion of the trial	Required of all randomized participants
T58	Ballardie 2002	"Primary IgA-N was proven on renal biopsy by standard morphologic and immunohistochemical criteria"	Required of all randomized participants
T81	Dipyridamole plus low-dose warfarin (Lee 1997)	Entry required a renal biopsy diagnosis; the report also reports histological scores at entry	Required of all randomized participants
T26	Antiplatelet agents (Chan)	Biopsy-based diagnosis of mesangial IgA glomerulonephritis, an entry criterion	Required of all randomized participants
T13, T16, T22, T23, T28, T31, T37, T38, T41, T45, T48, T49, T57, T59, T62	Older and smaller randomized trials	Not individually re-verified for this file	Not separately documented here: the diagnostic criterion of each of these reports was not re-read for this check, and no claim is made about them
T34	Calcitriol (Joo 2026)	"Biopsy-confirmed IgAN"	Required of all randomized participants

Entry	Report	Diagnostic basis, as stated	Biopsy confirmation across the participants contributing the result
T40	ENVISION	"Adults with biopsy-confirmed IgA nephropathy"	Required of all randomized participants
T42	IGNAZ	"IgAN confirmed by biopsy" within eight years before informed consent	Required of all randomized participants
T43	JANUS	Kidney biopsy is part of eligibility (exclusion thresholds are set by the timing of the biopsy)	**Not restated** as a separate statement in the extracted text; recorded as not separately documented
T52	HR19042	"Adults with biopsy-confirmed primary IgA nephropathy"	Required of all randomized participants
T67	Rituximab trial	"All subjects had biopsy-proven IgAN"	Required of all randomized participants
T86	Mizoribine (Hirai 2017)	"Patients diagnosed with primary IgA nephropathy by renal biopsy"	Required of all randomized participants
T89	Masutani 2016	Biopsy-proven progressive IgA nephropathy, an entry criterion	Required of all randomized participants
T46	Tacrolimus (Yu 2017)	"Patients with biopsy-proven IgAN were included"; "renal biopsy proven IgAN"	Required of all randomized participants
T05, T15	Losartan comparisons (dependency cluster OV01)	Biopsy-based diagnosis of IgA nephropathy, an entry criterion	Required of all randomized participants
T90	Blisibimod (BRIGHT-SC)	The abstract does not state the diagnostic criterion	**Not stated** in the abstract-level material held

Three consequences follow from this table, and they are the ones that bear on reading the review.

First, the trials that enrolled IgA nephropathy populations required a kidney biopsy diagnosis, and that requirement is quoted from the reports themselves for TESTING, APPLAUSE-IgAN, ALIGN, PROTECT and STOP-IgAN; for MAIN and NefIgArd the diagnostic criterion is stated in their reports but was not individually re-quoted for this file.

Second, the estimates taken from the IgA subgroups of broader trials are the ones for which a blanket statement cannot be made. The parent trial of FIND-CKD did not restrict enrolment to biopsy-confirmed cases, as its own report shows when it describes additional analyses restricted to biopsy-confirmed cases. In DAPA-CKD the difference is quantified by the source report, which analysed 254 of the 270 IgA stratum participants with biopsy-proven disease and obtained a hazard ratio of 0.28 (0.11–0.72), this review reporting the stratum estimate with the larger count as the primary analysis of that report does. For EMPA-KIDNEY the material held does not record biopsy confirmation for the IgA split at all. Where a reader requires biopsy confirmation in every participant, the DAPA-CKD sensitivity analysis is the one to read, and it is cited here for that purpose; for the other two subgroups this review records that the information is not available to it.

Third, therefore, the population description in the abstract and in the eligibility criterion is stated at the level at which each estimate is derived rather than as one blanket label, and every subgroup-derived estimate carries that label throughout the text and tables.

Part D. Age basis of the three reports whose entry criterion reached below 18 years

Pozzi 1999, Manno 2009 and Liang 2022 allow entry below 18 years. Adult eligibility was decided on participant-level information: a reported minimum age, or a count of participants below 18. A mean, a standard deviation or an interquartile range is not that information, and neither is a description of the cohort as adult where the entry floor lies below 18 years. None of the three reports supplies either item, so adult eligibility could not be established for any of the three, and none is excluded solely because adolescents were permitted.

Pozzi 1999 (T17), Lancet. Report held and re-read.

Pozzi 1999 (T17). The entry criterion is 15–69 years (Lancet p883). Both reports describe the cohort itself as adult: “86 consecutive adult patients … were enrolled” (Lancet p883), repeated as “86 eligible adult patients” in the long-term follow-up (J Am Soc Nephrol 2004, p157). Age is published as median (IQR), 40 (29–51) in controls and 38 (26–45) with steroids, 43 randomized per arm (Lancet p884). That is a description plus a distribution, not a count: neither a minimum age nor a number below 18 is printed, and an entry floor of 15 years leaves room for a 15–17-year-old who would appear in neither statistic. Both creatinine-threshold results therefore stay in the candidate table. A statement from the trialists that no participant was below 18 would return them to the primary adult tables, of which only the doubling result also meets the original outcome standard; a count above zero would require adult-only denominators and events.

Manno 2009 (T66), Nephrology Dialysis Transplantation. Report held and re-read.

Manno 2009 (T66). The entry criterion is 16–70 years (NDT p3695). Mean age is 34.9±11.2 with ramipril (n49) and 31.8±11.3 with prednisone plus ramipril (n48) (NDT p3697, Table 1). The eight-page report was read in full for this check: it prints no age range, no minimum age and no count below 18, and it does not describe the cohort as adult. The observed minimum is therefore unknown, and no adult-only composite or end-stage kidney disease result is available. Both progression results stay outside the primary adult synthesis.

Liang 2022 (T60), BMC Nephrology 23:40. Report not in the working file; read from the published article (doi:10.1186/s12882-022-02661-6) and its registration record (NCT02160132).

Liang 2022 (T60). The entry criterion is 14–65 years (BMC Nephrol 23:40, p2). Seventy-four patients began treatment (36/38) and 68 entered the per-protocol analysis (34/34); mean age is reported for the 68 only, 29.65±10.50 and 33.82±9.90 years (Table 1), so the age composition of the 74 initially treated is not described at all. The article carries no supplement (Europe PMC record PMC8780312 lists none), and the registration record (NCT02160132, registered 10 June 2014) restates the 14–65 entry range without participant ages. Table 1 gives no range and no count below 18. The >25% eGFR-decline count is 1/34 versus 1/34 at six months (Table 4). This meets the outcome condition but was not used in the primary adult synthesis.

Decision recorded for the three entries

Decision recorded for the three entries. All three were classified as having unresolved adult eligibility, and their five extracted results are preserved in a separate candidate table rather than read as adult evidence. What separates them is the state of the evidence, not the decision: Pozzi 1999 carries an investigator description of the cohort as adult, Manno 2009 and Liang 2022 carry none, and none of the three carries a count. Because the entry floor of all three lies below 18 years, a description on its own cannot separate an adult sample from a mixed one, which is why it is recorded here without being converted into eligibility.

What the source would have had to state. Adult eligibility would have been established by the number of participants younger than 18 at randomization in each arm, or failing that the youngest age at randomization; and, if any participant was younger than 18, adult-only denominators, event counts, follow-up and any adult-specific estimate. For Pozzi this would need to cover the original cohort and the linked follow-up; for Liang, the 74 initially treated as well as the 68 analysed. None of these was present in the retrieved reports, the checked supplements, or the public registration records, and the entries are recorded on that basis.

The ten focused comparisons and their 23 GRADE rows do not depend on these three reports. The totals reported here are as at completion of this review; the criteria were not broadened to preserve a target count.

Scope of the population criterion. Thirty-six entries were excluded, four of them on population grounds. One enrolled children only and one enrolled healthy volunteers; neither falls within a review of adults. The other two, Chen 2004 and IgACE, enrolled mixed adult–paediatric cohorts whose adult results could not be separated, and both also failed the original outcome standard independently: Chen 2004 reports no end-stage kidney failure and no death, so that the only progression result it offers is a 50% serum-creatinine rise, which the original standard did not accept; IgACE reports a 30% fall in GFR as its primary endpoint and a composite of a 30% fall in creatinine clearance or progression to nephrotic-range proteinuria, neither of which is eGFR or a threshold progression event. No entry was excluded on population grounds alone. The five outcomes of the three reports of unresolved adult eligibility are held in the candidate table of Additional file 13 rather than discarded; admitting them would raise the primary adult Table 2 from 32 to 37 rows, four of which would also enter the restricted table, and would not alter any reported effect estimate, because the synthesis is structured without meta-analysis.

Part E. Limits of this file

This is a targeted source and consistency reconciliation, not a new independent screening of every record. Newly checked source decisions and retained prior decisions are distinguished in the 92-entry ledger. The original-standard outcome check and the age check remain separate. Unresolved ages are recorded as unresolved decisions outside the primary adult synthesis. Diagnostic information not stated in the source is recorded as unavailable rather than assumed.