Supplementary tables

Supplementary Table 1. Results of PubMed and EMBASE search. Last search: 6 October 2025.

Number	PubMed and EMBASE query	PubMed	EMBASE
#1	**PubMed** “TNF inhibitor*”[tiab] OR TNFi[tiab] OR “tumor necrosis factor inhibitor*”[tiab] OR “TNF Alpha Inhibitor*”[tiab] OR “TNF-a inhibitor”[tiab] OR adalimumab[tiab] OR certolizumab[tiab] OR etanercept[tiab] OR golimumab[tiab] OR infliximab[tiab] OR tocilizumab[tiab] OR anakinra[tiab] OR vedolizumab[tiab] OR sarilumab[tiab] OR ustekinumab[tiab] OR mirikizumab[tiab] OR ixekizumab[tiab] OR Secukinumab[tiab] OR brodalumab[tiab] OR guselkumab[tiab] OR risankizumab[tiab] OR tildrakizumab[tiab] OR filgotinib[tiab] OR Bimekizumab[tiab] OR brodalumab[tiab] OR “biologic drug*”[tiab] OR “biologic treatment”[tiab] OR “biologic therapy”[tiab] **EMBASE** 'tnf inhibitor*':ti,ab,kw OR tnfi:ti,ab,kw OR 'tumor necrosis factor inhibitor*':ti,ab,kw OR 'tnf alpha inhibitor*':ti,ab,kw OR 'tnf-a inhibitor':ti,ab,kw OR adalimumab:ti,ab,kw OR certolizumab:ti,ab,kw OR etanercept:ti,ab,kw OR golimumab:ti,ab,kw OR infliximab:ti,ab,kw OR tocilizumab:ti,ab,kw OR anakinra:ti,ab,kw OR vedolizumab:ti,ab,kw OR sarilumab:ti,ab,kw OR ustekinumab:ti,ab,kw OR mirikizumab:ti,ab,kw OR ixekizumab:ti,ab,kw OR secukinumab:ti,ab,kw OR guselkumab:ti,ab,kw OR risankizumab:ti,ab,kw OR tildrakizumab:ti,ab,kw OR filgotinib:ti,ab,kw OR bimekizumab:ti,ab,kw OR brodalumab:ti,ab,kw OR 'biologic drug*':ti,ab,kw OR 'biologic treatment':ti,ab,kw OR 'biologic therapy':ti,ab,kw	54 179	116 623
#2	**PubMed** “drug monitoring” [Mesh] OR “drug monitoring”[tiab] OR “therapeutic monitoring”[tiab] OR “drug level*”[tiab] OR “medication monitoring”[tiab] OR “medication level*”[tiab] OR “drug concentration” [tiab] OR TDM[tiab] OR therapeutic drug monitor*[tiab] OR guide*[tiab] OR “antibody level*”[tiab] OR “monitoring, drug” [tiab] OR “through concentration” [tiab] **EMBASE** 'drug monitoring':ti,ab,kw OR 'therapeutic monitoring':ti,ab,kw OR 'drug level*':ti,ab,kw OR 'medication monitoring':ti,ab,kw OR 'medication level*':ti,ab,kw OR 'drug concentration':ti,ab,kw OR tdm:ti,ab,kw OR 'therapeutic drug monitor*':ti,ab,kw OR guide*:ti,ab,kw OR 'antibody level*':ti,ab,kw OR 'monitoring, drug':ti,ab,kw OR 'through concentration':ti,ab,kw	1 205 101	1 779 747
#3	**PubMed** Rheumatoid arthritis[tiab] OR “Inflammatory Bowel Diseases”[Mesh] OR “Inflammatory Bowel Disease*”[tiab] OR IBD[tiab] OR ulcerative colitis[tiab] OR Colitis Gravis[tiab] OR Idiopathic Proctocolitis[tiab] OR Crohn* disease[tiab]	412 228	684 191

Number	PubMed and EMBASE query	PubMed	EMBASE
	OR Regional Enteritis[tiab] OR Ileocolitis[tiab] OR Granulomatous Enteritis[tiab] OR JIA[tiab] OR Juvenile idiopathic arthritis[tiab] OR Juvenile arthritis[tiab] OR Childhood Arthritis[tiab] OR ankylosing spondylitis[tiab] OR axial spondyloarthritis[tiab] OR psoriatic arthritis[tiab] OR PSA[tiab] OR Spondyloarthropath*[tiab] OR psoriasis[tiab] **EMBASE** rheumatoid AND arthritis:ti,ab,kw OR 'inflammatory bowel diseases':ti,ab,kw OR 'inflammatory bowel disease*':ti,ab,kw OR ibd:ti,ab,kw OR (ulcerative:ti,ab,kw AND colitis:ti,ab,kw) OR 'colitis gravis':ti,ab,kw OR 'idiopathic proctocolitis':ti,ab,kw OR (crohn*:ti,ab,kw AND disease:ti,ab,kw) OR 'regional enteritis':ti,ab,kw OR ileocolitis:ti,ab,kw OR 'granulomatous enteritis':ti,ab,kw OR jia:ti,ab,kw OR (juvenile:ti,ab,kw AND idiopathic:ti,ab,kw AND arthritis:ti,ab,kw) OR (juvenile:ti,ab,kw AND arthritis:ti,ab,kw) OR 'childhood arthritis':ti,ab,kw OR (ankylosing:ti,ab,kw AND spondylitis:ti,ab,kw) OR 'axial spondyloarthritis':ti,ab,kw OR (psoriatic:ti,ab,kw AND arthritis:ti,ab,kw) OR psa:ti,ab,kw OR spondyloarthropath*:ti,ab,kw OR psoriasis:ti,ab,kw		
#4	**PubMed** ((((((((((((((budget*[tiab]) OR value for money[tiab]) OR ((expenditure*[tiab] NOT energy[tiab]))) OR (((economic*[tiab] OR cost[tiab] OR costs[tiab] OR costly[tiab] OR costing[tiab] OR price[tiab] OR prices[tiab] OR pricing[tiab] OR pharmacoeconomic*[tiab])))) OR "Economics, Pharmaceutical"[Mesh]) OR "Economics, Nursing"[Mesh]) OR "Economics, Medical"[Mesh:noexp]) OR "Economics, Hospital"[Mesh]) OR "Economics, Dental"[Mesh:noexp]) OR (("Costs and Cost Analysis"[Mesh]))) OR "Economics"[Mesh:noexp])) NOT (((((energy cost[tiab] OR oxygen cost[tiab]))) OR metabolic cost[tiab]) OR ((energy expenditure[tiab] OR oxygen expenditure[tiab])))))) NOT (((historical article[pt]) OR editorial[pt]) OR letter[pt]))) NOT ((animals[mesh:noexp]) NOT ((humans[mesh]) AND animals[mesh:noexp])) **EMBASE** 'health economics'/de OR 'cost'/de OR 'cost'/exp/mj OR 'pharmacoeconomics'/exp OR 'economic evaluation':de OR 'economic evaluation'/exp/mj OR economic$:ab,ti OR cost:ab,ti OR costs:ab,ti OR costly:ab,ti OR costing:ab,ti OR price:ab,ti OR prices:ab,ti OR pricing:ab,ti OR pharmacoeconomic$:ab,ti OR (expenditure$:ab,ti NOT energy:ab,ti) OR 'value for money':ab,ti OR budget$:ab,ti NOT ((energy OR oxygen) NEAR/1 cost):ab,ti NOT (metabolic NEAR/1 cost):ab,ti NOT ((energy OR oxygen) NEAR/1 expenditure):ab,ti NOT letter:it NOT editorial:it NOT (‘historical article’:it) NOT ('animal'/de NOT ('animal'/de AND 'human'))	1 295 594	1 798 942
#5	#1 AND #2 AND #3 AND #4	342	1 120

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Supplementary Table 2. Results of Google Scholar search. Last search: 6 October 2025.

Number	Keywords	Records
#1	("therapeutic drug monitoring" OR "therapeutic monitoring" OR "drug monitoring") AND ("cost effectiveness" OR "cost utility") AND (arthritis OR psoriasis OR "Inflammatory Bowel" OR "ulcerative colitis" OR "Crohn disease" OR "ankylosing spondylitis" OR spondyloarthropathy) AND “TNF inhibitor” OR TNFi OR “tumor necrosis factor inhibitor” OR “TNF Alpha Inhibitor” OR “TNF-a inhibitor” OR adalimumab OR certolizumab OR etanercept OR golimumab OR infliximab OR tocilizumab OR anakinra OR vedolizumab OR sarilumab OR ustekinumab OR mirikizumab OR ixekizumab OR Secukinumab OR brodalumab OR guselkumab OR risankizumab OR tildrakizumab OR filgotinib OR Bimekizumab OR brodalumab OR "biologic therapy" OR "biologic drug")	331

Supplementary Table 3. Methodology and results of studies included in the systematic review.

	Methods overview	Summary of the results and conclusions	Reporting quality
Economic evaluations (N=14)			
Alizadeh et al. (2024) [22]	**Design:** model-based EE, CUA **Population**: maintenance CD **Interventions**: model-informed proactive TDM with personalized dosing, proactive TDM alone, symptoms-only reactive intensification **TDM drug(s)**: IFX **Time horizon**: 5 years **Model**: decision tree (induction) + Markow model (maintenance) **Economic perspective, settings**: third-party payer, USA 2022	**Conclusion**: TDM approaches dominant over usual care. **Incremental cost vs usual care (2025EUR):** -€22,914 (personalized dosing) or –€30,267 (TDM alone) **Incremental QALY vs usual care**: 0.23 (personalized dosing) or 0.15 (TDM alone)	CHEERS: 24 / 28 (85.7%) Not reported or limited: health economic analysis plan, characterizing distributional effects, engagement with patients, effect of engagement with patients
Yao et al. (2021) [23, 24]	**Design:** model-based EE, CUA **Population**: maintenance CD **Interventions**: TDM-guided strategy vs empiric dose escalation of infliximab **TDM drug(s)**: Adalimumab; Other biologics as IFX, UST appear as subsequent treatment options in the model. **Time horizon**: 3 years **Model**: Markov model with 6 health states **Economic perspective, settings**: Payer perspective, United States healthcare setting	**Conclusion**: Proactive TDM of ADA is cost-saving (dominant) versus reactive TDM by year 3**Incremental cost vs usual care (2025EUR):** –€1,820 (proactive less costly) **Incremental QALY vs usual care**: +0.196 QALYs	CHEERS: 24 / 28 (85.7%) The study lacks a health economic analysis plan, does not address distributional effects, and does not report any engagement with patients or stakeholders, nor its impact on the study design or findings.
Negoescu et al. (2020) [25]	**Design:** model-based, CUA **Population**: maintenance CD, 1-time TDM **Interventions**: Proactive vs reactive TDM strategies for IFX **TDM drug(s)**: Infliximab (IFX) **Time horizon**: 5 years **Model**: Stochastic microsimulation model transitioning to a Markov cohort model for patients discontinuing IFX **Economic perspective, settings**: Health sector perspective, U.S. healthcare system	**Conclusion**: Proactive TDM may become cost-effective only at lower IFX prices; reactive TDM is the most efficient at current prices. **Incremental cost vs usual care (2025EUR):** +€3,290 **Incremental QALY vs usual care**: +0.03 QALYs	CHEERS: 23 / 28 (82,1%) The study lacks a health economic analysis plan, consideration of subgroup or equity effects, and does not report any engagement with patients or stakeholders or its impact on the study.

	Methods overview	Summary of the results and conclusions	Reporting quality
Attar et al. (2019) [26]	**Design:** model-based, CUA **Population**: maintenance CD, 1-time TDM **Interventions**: Therapeutic drug monitoring (TDM)–guided de-escalation of infliximab dosing using a single trough test **TDM drug(s)**: Infliximab (IFX), Testing with Lisa-Tracker® ELISA; switching to adalimumab modeled after loss of response. **Time horizon**: 2 years **Model**: Discrete Event Simulation (DES) based on Harel statecharts **Economic perspective, settings**: France – third-party payer	**Conclusion**: IFX trough testing with guided de-escalation is cost-saving compared with fixed-dose maintenance (no TDM) **Incremental cost vs usual care (2025EUR):** –€3,054 **Incremental QALY vs usual care**: Not reported	CHEERS: 18 / 28 (64.13%) The study does not report the development of a health economic analysis plan, the perspective of the analysis, the discount rate, or how outcomes were selected, measured, and valued. Additionally, it lacks discussion on heterogeneity, distributional effects, and stakeholder engagement, as well as how such engagement might have influenced the study
Laine et al. (2016) [27]	**Design:** model-based, Cost/Resource Utilization Analysis **Population**: RA **Interventions**: Combined drug trough level (DL) and anti-drug antibody (ADAb) monitoring (IFX ≥2 µg/mL, ADA ≥5 µg/mL; Ab positivity ≥12 U/mL). Algorithm-based treatment adjustment (Vincent et al.); no dose escalation modeled. Comparator: No testing (standard clinical practice). **TDM drug(s)**: Infliximab and adalimumab **Time horizon**: 3-6 months (short-term) for cost analysis; 3 years for Markov modeling **Model**: Markov model with transitions between first TNFα blocker, second biologic, and quitting biologics **Economic perspective, settings**: Health care perspective; Finnish setting	**Conclusion**: Routine DL + ADAb testing can be cost-saving if even a small proportion (≈2.5–5%) of patients would otherwise be managed suboptimally for one cycle (e.g., continued on ineffective biologic for 3-6 months)**Incremental cost vs usual care (2025EUR):** Not numerically reported. **Incremental QALY vs usual care**: Not reported	CHEERS: 18 / 28 (64.13%) The study does not report the development of a health economic analysis plan, the economic perspective, the discount rate, or how outcomes were selected, measured, or valued. Additionally, it lacks consideration of heterogeneity, distributional effects, and any engagement with patients or stakeholders, including how such engagement may have influenced the study.
Krieckaert et al. (2015) [28, 29]	**Design:** cohort study + model-based CUA **Population**: RA **Interventions**: Personalised (TDM-guided) care: At 6 months, algorithm combines EULAR response + adalimumab trough drug level (DL)	**Conclusion**: Personalised (TDM + EULAR–guided) strategy was dominant vs usual care **Incremental cost vs usual care (2025EUR):** Adjusted to 2025 EUR (approx. ×1.45 for	CHEERS: 23 / 28 (82.1%) The study does not report a health economic analysis plan, fails to characterize heterogeneity and distributional effects, and omits both

	Methods overview	Summary of the results and conclusions	Reporting quality
	measured by ELISA; Comparator: Usual care (standard clinical management without TDM). **TDM drug(s)**: Adalimumab; Subsequent biologics: rituximab, etanercept **Time horizon**: 3 years **Model**: Patient-level Markov microsimulation **Economic perspective, settings**: Societal perspective in the Netherlands	cumulative inflation): ≈ –€13,200 to –€19,700 per patient **Incremental QALY vs usual care**: +0.0141 QALYs	the engagement of patients or stakeholders and the impact of such engagement on the study's findings.
Gavan (2017) [30]	**Design:** model-based, using a Discrete Event Simulation (DES) model developed in R **Population**: RA, PHD **Interventions**: Compared 13 TDM-based and no-testing strategies including adalimumab **TDM drug(s)**: adalimumab **Time horizon**: Lifetime **Model**: Discrete Event Simulation **Economic perspective, settings**: United Kingdom, NHS and Personal Social Services perspective (health-sector)	**Conclusion**: Strategy 3 (drug and antibody level testing every 3 months plus drug-level testing in remission after 2 years) was dominant compared to current practice-lower cost and better outcomes. Strategy 1 was also cost-effective. **Incremental cost vs usual care (2025EUR):** St –£3,305 (2016 GBP) → ≈ –€4,000 (2025 EUR) Strategy 1: +£835 (2016 GBP) → ≈ +€1,010 (2025 EUR) **Incremental QALY vs usual care**: Strategy 3: +0.0211; Strategy 1: +0.099	CHEERS: 23 / 28 (82.1%) The study lacks a reported health economic analysis plan, does not address heterogeneity or distributional effects, and omits any engagement with patients or stakeholders and its impact on the study.
Tikhonova et al. (2021) [31]	**Design:** model-based, CUA **Population**: RA, NICE **Interventions**: ELISA-based TDM during maintenance to guide dose tapering vs standard care (no TDM) **TDM drug(s)**: Adalimumab (ADA), monitored via Promonitor® ELISA testing (once per year) **Time horizon**: 1.5 years **Model**: Decision tree **Economic perspective, settings**: UK NHS and Personal Social Services (public payer perspective)	**Conclusion**: Cost-effectiveness of TDM highly depends on clinical data source. In Scenario 1 (Ucar), TDM shows a small QALY gain (+0.007) at a cost of ~£5,575, yielding an acceptable ICER (~£5,600/QALY). In Scenario 2 (Arango), standard care dominates (lower cost and better outcomes), reflecting evidence uncertainty. **Incremental cost vs usual care (2025EUR):** Scenario 1: +£38 (2018 GBP) ≈ +€50 (2025 EUR) Scenario 2: +£51 (2018 GBP) ≈ +€65 (2025 EUR) **Incremental QALY vs usual care**: Scenario 1: +0.007	CHEERS: 25 / 28 (89,3%) The study did not report on characterizing distributional effects, it lacked information on engagement with patients and other stakeholders in both the design phase and in evaluating the impact of such engagement on the study findings.

	Methods overview	Summary of the results and conclusions	Reporting quality
		Scenario 2: −0.007	
Bastida et al. (2020) [32]	**Design:** PKPD simulation, Cost/resource utilization analysis **Population**: RA **Interventions**: Strategy 1: Continue label dosing of tocilizumab (8 mg/kg q28d) Strategy 2: Mild empirical taper (6 mg/kg) if in remission/LDA at 6 months Strategy 3: Intense empirical taper (4 mg/kg) Strategy 4: TDM-guided tapering using drug levels to target trough ≈5 µg/mL **TDM drug(s)**: Tocilizumab **Time horizon**: 1 year (post-tapering period) **Model**: Microsimulation based on PK/PD (pharmacokinetic/pharmacodynamic) models **Economic perspective, settings**: none	**Conclusion**: TDM-guided tapering resulted in similar disease control (remission/LDA) compared to mild empirical tapering but achieved a ~9–10 percentage point reduction in relative dose intensity, indicating better drug-sparing. TDM also reduced inter-patient variability. Intense tapering had the lowest drug use but increased flares. **Incremental cost vs usual care (2025EUR):** Not reported (costs not monetized) **Incremental QALY vs usual care**: Not reported (no utility or ICER calculations provided)	CHEERS: 15 / 28 (53,6%) The study lacks a clear title and abstract as an economic evaluation, economic analysis plan, stated perspective, outcome valuation, cost valuation, currency/year info, uncertainty analysis, subgroup/distributional effects, and any stakeholder engagement.
Freeman et al. (2016) [33]	**Design:** model-based, CUA **Population**: CD, NICE **Interventions**: Infliximab (and subsequent Adalimumab) with TDM strategies: (a) concurrent drug + anti-drug antibody (ADA) testing every 3 months; (b) reflex ADA testing if drug sub-therapeutic; versus standard care (no testing) **TDM drug(s)**: Infliximab (and Adalimumab as next line) **Time horizon**: 10 years **Model**: Markov model with 4-week cycle length **Economic perspective, settings**: Public payer (UK NHS & Personal Social Services)	**Conclusion**: Standard care (no TDM) was found to dominate (lower cost and more QALYs) over TDM strategies at 10-year horizon under base-case; TDM strategies may approach cost-effectiveness under less frequent testing or shorter horizons. **Incremental cost vs usual care (2025EUR):** Not explicitly stated per patient; cohort differences: e.g., concurrent testing vs no testing: -£11,800 to -£16,595 (approx. -€13,900 to -€19,600) in certain scenarios. **Incremental QALY vs usual care**: Again, not explicitly provided per patient; example given: -0.2447 to -0.3154 QALYs in certain models.	CHEERS: 25 / 28 (89,3%) The study lacks reporting on distributional effects, stakeholder engagement in the study design, and the impact of such engagement on outcomes.
Roblin et al. (2015) [34]	**Design:** model-based, Cost/resource utilization analysis (no QALYs or ICERs reported) **Population**: CD **Interventions**: Standard care: Empirical dose escalation; TDM strategy: One-time testing at loss of response (LOR) for trough levels and	**Conclusion**: TDM-guided treatment resulted in significant cost savings (up to €13,100 per patient over 5 years), primarily from avoiding unnecessary treatment escalation and improving treatment selection.	CHEERS: 18 / 28 (64,3%) The study lacks details on the economic analysis plan, discounting, outcome selection and valuation, price year and currency info, heterogeneity, distributional effects,

	Methods overview	Summary of the results and conclusions	Reporting quality
	anti-drug antibodies to guide treatment modification **TDM drug(s)**: Infliximab (IFX), Adalimumab (ADA) **Time horizon**: 5 years **Model**: Discrete Event Simulation (DES) using Harel statecharts (AnyLogic + R) **Economic perspective, settings**: Health-sector (public payer), France	**Incremental cost vs usual care (2025EUR):** −€13,100 over 5 years per patient (approximate, based on €13.1k saving) **Incremental QALY vs usual care**: Not reported	and patient or stakeholder engagement.
Velayos et al. (2013) [35]	**Design:** model-based, CUA **Population**: CD **Interventions**: Intervention: Testing-based strategy (IFX + anti-IFX TDM to guide dose escalation, imaging, switch to ADA) Comparator: Empiric dose escalation strategy **TDM drug(s)**: Infliximab (IFX), with ADA as a follow-up therapy **Time horizon**: 1 year **Model**: State-transition/decision tree; 4-week cycles; software not reported **Economic perspective, settings**: Third-party payer; U.S./Canada setting	**Conclusion**: DM-based strategy is dominant—less costly and similarly effective compared to empiric escalation. Cost savings (~$5,396) with marginal QALY gain (+0.001). **Incremental cost vs usual care (2025EUR):** Approx. −€5,084 **Incremental QALY vs usual care**: +0.001	CHEERS: 22 / 28 (78,6%) The study is missing reporting on the economic analysis plan, price year, model analytics, distributional effects, and stakeholder engagement, limiting transparency and equity assessment.
Dupenloup et al. (2025) [36]	**Design:** model-based, CUA **Population**: UC **Interventions**: No TDM vs Reactive TDM vs Proactive TDM vs Hybrid strategies (e.g., Proactive for 1 year then Reactive) **TDM drug(s)**: Infliximab (and switch to Adalimumab/Ustekinumab) **Time horizon**: Lifetime **Model**: Markov model (cycle length: 8 weeks) **Economic perspective, settings**: Health-sector (public payer) in the US; costs in 2021 USD (converted to EUR for reporting)	**Conclusion**: Reactive TDM vs No TDM: cost-effective (~$3,200/QALY) Hybrid 1-year vs Reactive: ~$63,800/QALY Proactive long-term strategies were generally dominated or not cost-effective **Incremental cost vs usual care (2025EUR):** Not explicitly provided for a specific strategy → approximate values for illustrative arms (e.g., Proactive vs No TDM: Incremental cost +$11,100 ≈ +€10,300) **Incremental QALY vs usual care**: For Proactive vs No TDM: +0.17 QALYs	CHEERS: 23 / 28 (82,1%) The study does not mention whether a health economic analysis plan was developed, limiting transparency in planning methodology. It also omits any analysis of heterogeneity and distributional effects, which are important for understanding how results apply across different patient subgroups or populations. Additionally, there is no evidence of engagement with patients, the public, or other stakeholders during the design or conduct of the study.

	Methods overview	Summary of the results and conclusions	Reporting quality
Gómez-Arango et al. (2021) [37]	**Design:** EE alongside clinical study, pragmatic nonrandomized trial, **Population**: RA, PA, AS **Interventions**: Intervention group: Proactive TDM-guided adalimumab tapering strategy; Control group: Standard care **TDM drug(s)**: Adalimumab **Time horizon**: 18 months **Model**: Not model-based; economic evaluation conducted alongside INGEBIO clinical trial **Economic perspective, settings**: Public payer perspective (health-sector) in Spain	**Conclusion**: Proactive TDM-guided tapering reduced adalimumab use and total costs while slightly increasing QALYs. The strategy was dominant (more effective and less costly) in 97.5% of bootstrapped simulations and remained cost-effective across various sensitivity analyses. **Incremental cost vs usual care (2025EUR):** –€2,067 **Incremental QALY vs usual care**: +0.085	CHEERS: 23 / 28 (82,1%) The study lacks reporting on economic analysis plan, heterogeneity, distributional effects, or patient/stakeholder involvement.
Other studies (N=12)			
Nguyen et al. (2024) [38]	**Design & comparison:** simulation of dose tapering/intensification vs registered dosing based on the retrospective cross-sectional, single centre study **Population**: IBD, maintenance **TDM**: proactive, model-based personalized dosing with TDM **TDM drug(s)**: IFX **Time horizon**: mean 2.4 doses per patient **Cost categories**: drug acquisition **Economic perspective, settings**: health-care provider, Australia 2020	**Conclusion**: TDM approach increases the drug cost vs registered dosing **Incremental cost (2025EUR):** €3,394 (per patient)	STROBE 19 / 22 (86.4%) Not reported or limited: study size calculation; description of statistical methods; description of participant flow
Steenholdt et al. (2014) [39]	**Design & comparison:** RCT, single-blind, multicenter, prospective study; algorithm-guided (TDM)—interventions based on serum IFX and anti-IFX antibody (ATI) results vs empirical dose intensification to IFX 5 mg/kg every 4 weeks **Population**: CD **TDM**: reactive, radioimmunoassay at failure to classify IFX level as therapeutic (≥0.5 mg/mL) vs subtherapeutic **TDM drug(s)**: IFX; natalizumab	**Conclusion**: Algorithm cut total costs with no efficacy loss .Value driven by avoiding unnecessary IFX escalation in patients with therapeutic IFX/negative ATI or non-IBD causes of symptoms. **Incremental cost (2025EUR):** €3,394 (per patient)	Modified Jadad: 6 / 8 (75%) No double blinded design

	Methods overview	Summary of the results and conclusions	Reporting quality
	Time horizon: 0.23 (12-week) **Cost categories**: direct medical; drug acquisition **Economic perspective, settings**: health-sector (public payer), Denmark 2014		
Rentsch et al. (2023) [40]	**Design & comparison:** prospective TDM cohort vs standard maintenance **Population**: IBD **TDM**: pharmacist led proactive rapid TDM **TDM drug(s)**: IFX **Time horizon**: 0.91 (48 weeks) **Cost categories**: Direct medical: IFX drug acquisition; rapid assay costs **Economic perspective, settings**: health-care provider, Australia	**Conclusion:** the cost of dose escalation in patients with sub-therapeutic levels can be largely offset by reducing the dosage in those with supratherapeutic levels, which may lessen the barrier to funding a TDM program **Incremental Cost (2025EUR)**: € 16,771	STROBE: 20 / 22 (91%) Not reports or limited: non-randomised; excludes admin/hospitalisation costs
González-Fernández et al. (2018) [41]	**Design & comparison:** population study, single centre (mean cost depending on utilized treatment approaches each year), **Population**: spondylarthritis **TDM**: optimisation by dose reduction and/or interval extension with clinical oversight. **TDM drug(s)**: IFX, ENT, ADA, GOL **Time horizon**: 1 (52 weeks) **Cost categories**: biologic drug acquisition (units/mg) with applied rebates/bonuses **Economic perspective, settings**: public payer, Spain	**Conclusion**: optimisation was the largest savings driver (24% vs 11% rebates), with nearly half of patients optimised and lower disease activity in that group I**ncremental Cost (2025EUR**): € 6,302	STROBE: 18 / 22 (82%)
Wu et al. (2021) [42, 43]	**Design & comparison:** prospective observational audit vs hypothetical savings from avoiding unnecessary IFX use, **Population**: IBD **TDM**: proactive TDM (maintenance); reactive TDM (loss of response) **TDM drug(s)**: IFX; TNF-alfa; VED **Time horizon**: 13 months **Cost categories**: Direct medical	**Conclusion**: Identification of unnecessary IFX use I**ncremental Cost (2025EUR**): € 219,796	STROBE: 20 / 22(91%) **Not reported or limited:** No clinical outcomes; scenario-based, single-lab dataset; no formal SAs

	Methods overview	Summary of the results and conclusions	Reporting quality
	Economic perspective, settings: public payer, Australia		
Sagar et al. (2021) [44]	**Design & comparison:** retrospective observational, TDM caused change vs no change, **Population**: IBD **TDM**: Proactive TDM; Subsequent TDM proactive after 2 infusions if dosing changed, otherwise reactive if LOR **TDM drug(s)**: IFX; ADA, VED, UST **Time horizon**: 1 (52 weeks) **Cost categories**: Direct medical **Economic perspective, settings**: health-care provider; UK	**Conclusion**: Proactive TDM safely guides management without worsening outcomes; budget impact depends heavily on contemporaneous biologic prices and use of biosimilars. I**ncremental Cost (2025EUR)**: € 2,611 per patient	STROBE: 18 / 22 (82%)
Guidi et al. (2018) [45]	**Design & comparison:** prospective TDM cohort vs historical control, **Population**: IBD **TDM**: TDM-guided algorithm vs empirical intensification **TDM drug(s)**: IFX; ADA **Time horizon**: 0.22 (12 weeks) **Cost categories**: Direct medical **Economic perspective, settings**: public payer, Italy	**Conclusion**: Savings robust in biosimilar scenarios; magnitude sensitive to IFX price mix. Main driver: escalation rate I**ncremental Cost (2025EUR)**: € 1,226 per patient	STROBE: 18 / 22
González Fernández et al. (2021) [46]	**Design & comparison:** population study, single centre (mean cost depending on utilized treatment approaches each year), **Population**: RA **TDM**: pharmacy computerized prescribing/dispensing system (FarmaTools 2.5) for biologic drug acquisitions, and the La Paz Biological Registry of Rheumatology for clinical measures **TDM drug(s)**: ETN, ADA, IFX, CER, GOL, TOC **Time horizon**: 1 (52 weeks) **Cost categories**: Direct medical	**Conclusion**: Implementing drug-level–guided optimization substantially reduces biologic spend without evident loss of disease control; prices, rebates and biosimilar competition modulate magnitude. I**ncremental Cost (2025EUR)**: € 5,616 per patient	STROBE: 18 / 22 (82%)

	Methods overview	Summary of the results and conclusions	Reporting quality
	Economic perspective, settings: public payer, Spain		
Mc Gettigan et al. (2019) [47]	**Design & comparison:** retrospective, proactive vs reactive from different years, **Population**: IBD **TDM**: Proactive-TDM era vs earlier reactive-TDM **TDM drug(s)**: IFX **Time horizon**: 15 months **Cost categories**: Direct medical **Economic perspective, settings**: hospital/provider, Ireland	**Conclusion**: Proactive-TDM within a VBC improves markers of control and reduces acute utilisation, with tangible drug-cost savings; fuller cost categories not assessed. **Incremental Cost (2025EUR)**: € 35,709 annual savings	STROBE: 18 / 22 (82%)
Taks et al. (2017) [48]	**Design & comparison:** prospective post-TDM cohort vs pre-TDM (baseline extrapolated), **Population**: IBD **TDM**: Algorithm-guided dose-interval decrease, dose increase, switch to ADA/GOL, or discontinue vs baseline regimen (pre-algorithm). **TDM drug(s)**: IFX; ADA; GOL; other **Time horizon**: 1 (52 weeks) **Cost categories**: Direct medical **Economic perspective, settings**: public payer, Netherlands	**Conclusion**: Algorithm modestly improved disease control and reduced drug costs; no formal SAs; scope excludes non-drug costs. **Incremental Cost (2025EUR)**: € 1,671 per patient	STROBE: 18 / 22 (82%) **Not reported or limited:** No sensitivity analysis conducted
Pedersen et al. (2020) [49]	**Design & comparison:** retrospective with or without TDM cohort comparison, **Population**: RA PA AS **TDM**: TDM-guided management, empirical management **TDM drug(s)**: IFX, GOL, ETA or ADA **Time horizon**: 1 (52 weeks) **Cost categories**: Direct medical **Economic perspective, settings**: health care provider , Denmark	**Conclusion**: TDM supports dose tapering and reduces drug expenditure without compromising outcomes; results limited by retrospective, heterogeneous design and lack of full cost capture. **Incremental Cost (2025EUR)**: IFX: € 2,486; ADA: €1,989; ETA: € 994; GOL: € 497	STROBE: 18 / 22 (82%) **Not reported or limited:** heterogeneity, non-randomisation, potential selection and interpretation bias
Arai et al. (2025) [50]	**Design & comparison:** retrospective post vs pre TDM for a patient, **Population**: IBD	**Conclusion**: PGD supports individualized dosing with better control and lower overall	STROBE: 18 / 22 (82%) **Not reported or limited:** No formal sensitivity analysis; authors

	Methods overview	Summary of the results and conclusions	Reporting quality
	TDM: post-PGD management vs pre-PGD usual care **TDM drug(s)**: IFX; ADA, UST, VED, OZA, UPA **Time horizon**: 24 months **Cost categories**: Direct medical: **Economic perspective, settings**: third-party payer, US	costs; results limited by retrospective design and modelled unit costs. I**ncremental Cost (2025EUR)**: € 3,258 per patient	emphasize association of clearance with actions and outcomes; acknowledge retrospective design and cost-model limits.

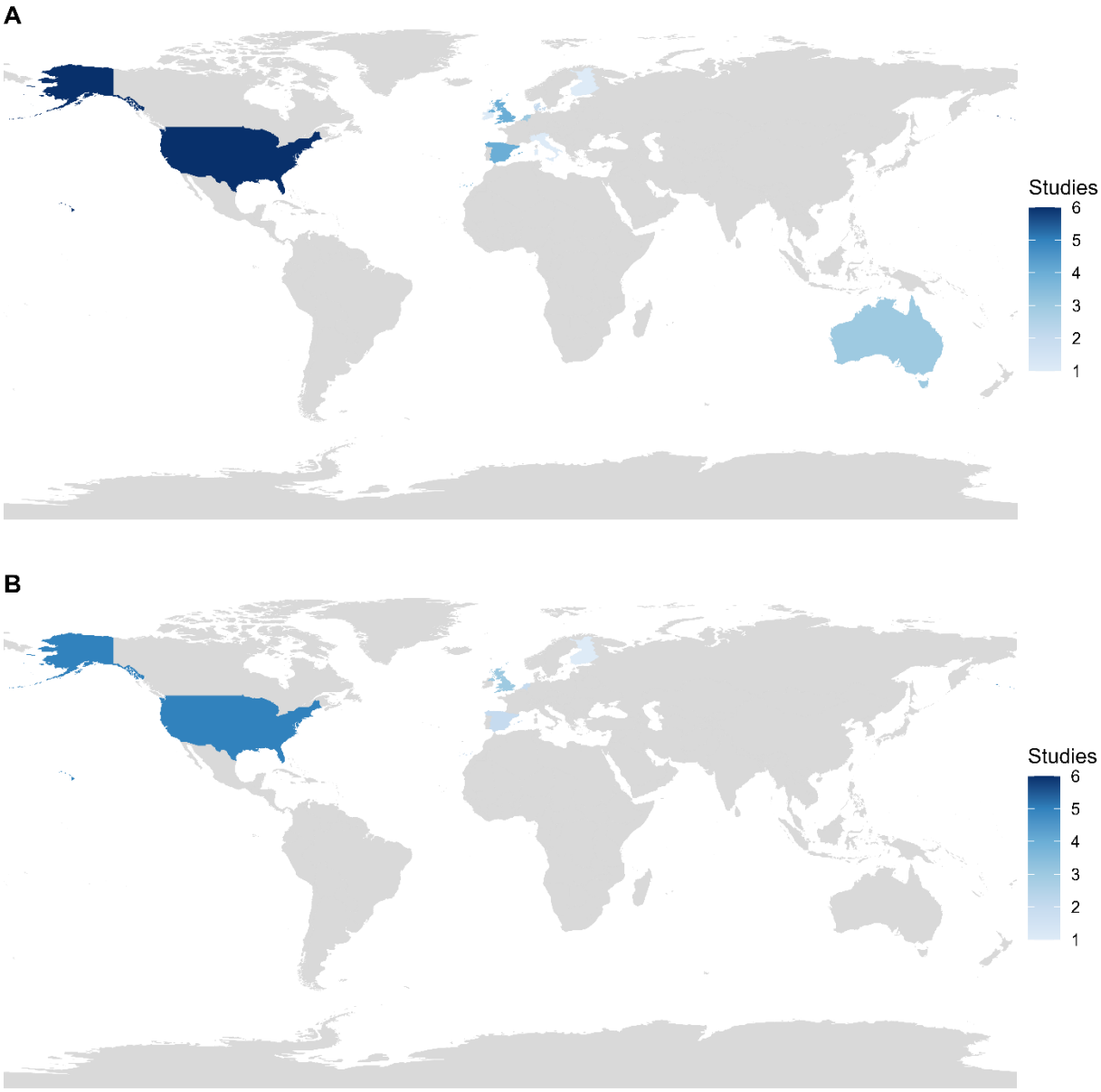
ADA, adalimumab; AS, ankylosing spondylitis; CD, Crohn's disease; CER, certolizumab; CUA, cost-utility analysis; EE, economic evaluation; ETA, etanercept; GOL, golimumab; IBD, inflammatory bowel disease; IFX, infliximab; LOR, lost of response; OZA, ozanimod; PA, psoriatic arthritis; PGD, precision-guided dosing; RA, rheumatoid arthritis; RCT, randomized controlled trial; SA, spondyloarthritis; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; TOC, tocilizumab; UC, ulcerative colitis; UPA, upadacitinib; UST, ustekinumab; VED, vedolizumab.

Methods and results of included studies presented in detail in **Supplementary File**.

Supplementary Table 4. Direct and indirect effects of TDM approaches in the included studies.

	Number of studies [references]
Economic evaluations (N=14): direct effects	
dose tapering (prolongation of the between-dose interval)	10 [22, 23&24, 26, 27, 28&29, 30, 31, 33, 34, 35]
dose tapering (administered-dose reduction)	8 [22, 25, 26, 27, 32, 33, 34, 35]
better maintenance of remission or response	7 [22, 23&24, 25, 30, 31, 33, 36]
earlier discontinuation decisions	6 [28&29, 30, 33, 34, 35, 36]
dose intensification (administered-dose increase)	5 [25, 33, 34, 35, 36]
dose intensification (shortening of the between-dose interval)	4 [23&24, 33, 34, 35]
lower discontinuation rate	3 [22, 23&24, 27]
selection of subsequent biologic treatment	3 [28&29, 33, 36]
modification of concomitant therapy (immunomodulators, steroids)	2 [23&24, 36]
health deterioration due to a false TDM result	1 [30]
lower rate of disease-worsening clinical events	1 [31]
Economic evaluations (N=14): indirect effects (via a linked-evidence approach)	
lower rates of costly events and/or longer time in lower-cost states	11 [22, 23&24, 25, 27, 28&29, 30, 31, 33, 34, 35, 36]
lower rates of events and/or shorter time in higher-activity or lower quality of life states	10 [22, 23&24, 25, 28&29, 30, 31, 32, 33, 35, 36]
lower rates of subsequent biologic treatment	6 [22, 23&24, 25, 26, 27, 28&29]
better maintenance of remission or response	4 [26, 27, 28&29, 32]
avoidance of prolonged ineffective biologic therapy	4 [33, 34, 35, 36]
lower mortality (via fewer surgeries and more time in lower-risk states)	4 [25, 30, 33, 36]
lower surgery rates	3 [22, 23&24, 25]
Other studies (N=12): aspects guided by TDM	
dose tapering (administered-dose reduction)	10 [38, 40, 41, 42&43, 44, 45, 46, 47, 49, 50]
dose tapering (between-dose interval prolongation)	10 [39, 41, 42&43, 44, 45, 46, 47, 48, 49, 50]

	Number of studies [references]
dose intensification (administered-dose increase)	7 [38, 40, 44, 45, 47, 49, 50]
dose intensification (between-dose interval shortening)	7 [39, 44, 45, 47, 48, 49, 50]
quicker discontinuation decisions	7 [39, 42&43, 44, 45, 48, 49, 50]
selection of subsequent biologic treatment	6 [39, 42&43, 44, 45, 49, 50]
modification of concomitant therapy (immunomodulators, steroids)	2 [39, 45]



Supplementary Figure 1. Number of included studies (A) and included economic evaluations (B) by country.

One study without cost assessment was assigned to both Spain and the Netherlands according to authors' affiliations