

Table S1. Clinical studies on the use of adiponectin in the management of DM.

First author / Year	Pathology	Patient group (Total / Male/ Female)	Patient age (years) mean $\pm$ SD	Adiponectin	Marker values ($\mu\text{g/mL}$)	Timing of analysis	Medication	Other pathologies
Abdella / 2018 [133]	T2DM	575 FDR (undiagnosed risk) 376 known T2DM patients	FDR: Normal: 28.2 $\pm$ 8.6 Undiagnosed DM: 32 $\pm$ 9.7 T2DM: <53 mmol/mol: 55.4 $\pm$ 13.5 >53 mmol/mol: 57.8 $\pm$ 9.4	Plasma	FDR: Normal: 8.57 $\pm$ 4.42 Undiagnosed DM: 6.92 $\pm$ 2.86 T2DM: <53 mmol/mol: 8.58 $\pm$ 4.5 >53 mmol/mol: 7.37 $\pm$ 4.35	Baseline	None at time of study	-
Alnaggar / 2019 [134]	T2DM $\pm$ Diabetic nephropathy	44 patients (26 M, 18 F)	35-55	Serum	Normoalbuminuric: 61.22 $\pm$ 44.18 (9.5–170); Microalbuminuric: 140.74 $\pm$ 93.37 (34–358)	Baseline	Not detailed (all had T2DM treatment)	Hypertension Dyslipidaemia
Hartman / 2020 [135]	T2DM MASLD	316 patients Placebo: 51 (29 M, 22 F) TIR 1mg: 52 (29 M, 23 F) TIR 5mg: 55 (34 M, 21 F) TIR 10mg: 51 (30 M, 21 F) TIR 15 mg: 53 (22 M, 31 F) DUL 1.5 mg: 54 (24 M, 30 F)	Placebo: 56.6 $\pm$ 8.9 TIR 1mg: 57.4 $\pm$ 8.9 TIR 5mg: 57.9 $\pm$ 8.2 TIR 10mg: 56.5 $\pm$ 9.9 TIR 15 mg: 56.0 $\pm$ 7.6 DUL 1.5 mg: 58.7 $\pm$ 7.8	Serum	Baseline: Placebo: 4.0 $\pm$ 0.4 TIR 1mg: 5.4 $\pm$ 0.4 TIR 5mg: 4.2 $\pm$ 0.4 TIR 10mg: 4.3 $\pm$ 0.4 TIR 15 mg: 5.1 $\pm$ 0.5 DUL 1.5 mg: 4.5 $\pm$ 0.41 Change from Baseline at 26 Weeks: Placebo: -0.1 $\pm$ 0.2 TIR 1mg: -0.1 $\pm$ 0.2 TIR 5mg: 0.4 $\pm$ 0.2 TIR 10mg: 0.9 $\pm$ 0.2 TIR 15 mg: 0.9 $\pm$ 0.3 DUL 1.5 mg: 0.3 $\pm$ 0.2	Baseline and after 26 months	TIR (1, 5, 10, 15 mg), DUL (1.5 mg), or placebo; metformin allowed if stable dose;	
Bidulescu / 2020 [136]	T2DM	3363 patients (1230 M, 2133 F) T2DM: 584 (216 M, 368 F) Control: 2779 (1014 M, 1765 F)	T2DM: 54.7 $\pm$ 0.5 Control: 52.5 $\pm$ 0.2	Plasma	T2DM: 4.092 $\pm$ 0.115 (3.203 $\pm$ 0.149 M, 4.625 $\pm$ 0.155 F) Control: 5.566 $\pm$ 0.077 (4.061 $\pm$ 0.095 M, 6.439 $\pm$ 0.103 F)	Baseline	1404 Antihypertensive, 6 Antihyperlipidemic 275 Antihypertriglyceridemic	Hypertension and Dyslipidemia
Werida / 2021 [137]	T2DM Dyslipidemia	160 patients ATOR 80 (38 M, 42 F) ROSU 80 (36 M, 44 F)	ATOR 54.38 $\pm$ 5.84 ROSU 55.45 $\pm$ 5.94	Serum	Baseline ATOR: 1.36 $\pm$ 0.46 ROSU: 1.49 $\pm$ 0.53 At 6 month: ATOR: 2.40 $\pm$ 0.74	Baseline and after 6 months	Baseline medications used ATOR: 38 Glimepiride 28 Glibenclamide 14 Vildagliptin	Hypertension OB

					ROSU: 2.95 ±0.94		8 ACEIs 7 ARBs ROSU: 37 Glimepiride 24 Glibenclamide 19 Vildagliptin 11 ACEIs 10 ARBs	
Pena / 2023 [138]	T2D risk in adolescents + OB	64 patients (38 M, 26 F) INT: 40 (24 M, 16 F) UC: 24 (15 M, 9 F)	13.3±1.4 INT: 13.4±1.4 UC 13.2±1.4	Serum	Baseline: 1.5 ±1.7 INT: 1.67±0.12 UC 1.28±0.11 At 6 months: INT: 1.42±0.11 UC 1.21±0.11	Baseline and after 6 months	No DM medications; only lifestyle or usual care interventions	-
Reddy / 2023 [139]	T2DM + MASLD	42 patients (17 M, 25 F) LFD: 22 baseline 19 at the end MedDiet: 19 baseline 18 at the end	52.3 ± 12.6	Serum	Baseline: 11.3 ± 13.9 LFD: 17.3 ± 14.4 MedDiet: 13.7 ± 9.2 At 12 weeks: LFD: 19.5 ± 21.0 MedDiet: 17.0 ± 12.6	Baseline and after 12 weeks	35 patients on prescription medication; 24 patients took supplements; stable during intervention	-
Hayashishita / 2024 [140]	T2DM	24 patients T2DM 17 (14 M, 3 F); Controls 7 (4 M, 3F)	T2DM: 62.2±23.0 Controls: 39.3±13.3	Serum	T2DM: 5.9 ± 4.0 Controls: 10.9 ± 10.1;	Blood sample collected prior to insulin administration	T2DM: 8 Antihypertensives, 8 Hyperlipidemic agent Antidiabetic Medication Use: 6 Metformin 5 Insulin 2 SGLT2i 5 DPP-4i 2 Sulfonylureas	Hypertension and Dyslipidemia
Yaikwawong / 2024 [141]	T2DM + OB	229 patients Curcumin: 114 (62 M, 73 F) Placebo: 115 (54 M, 80 F)	≥35 years	Serum	Curcumin group: 0: 8.75 (7.04–10.56) 3: 8.91 (7.04–10.56) 6: 13.73 (5.32–52.05) 9: 13.74 (5.46–53.02) 12: 14.51 (5.78–54.67) Placebo group: 0: 8.85 (7.04–10.56) 3: 8.89 (7.04–10.56) 6: 10.13 (3.81–29.28) 9: 10.38 (3.43–27.45)	Baseline, 3, 6, 9, 12 months	Metformin (monotherapy); no change allowed antihypertensive and antidyslipidemic medications Curcumin	Hypertension and Dyslipidemia

					12: 10.36 (3.21–26.21)			
Lee / 2025 [142]	T2DM + MASLD	44 patients PIO: 14 (8 M, 6 F) EMPA: 16 (9 M, 7 F) PIO+EMPA: 14 (7 M, 7 F)	53.8 ± 12.5 PIO: 49.6±10.2 EMPA: 56.3±10.1 PIO+EMPA: 55.1±16.4	Serum	Baseline: 2.6 [2.1, 3.9] PIO: 2.5 [2.2, 3.6] EMPA: 2.6 [2.1, 3.5] PIO+EMPA: 3.6 [1.8, 4.1] At 24 weeks: PIO: 10.1 [17, 13.7] EMPA: 7.0 [5.8, 11.4] PIO+EMPA: 14.8 [9.8, 18.6]	Baseline and after 24 weeks	PIO 15 mg/day, EMPA 10 mg/day, or both in combination Antidiabetic Medication Use: Metformin Sulfonylurea DPP-4I Insulin	-
Barb / 2025 [143]	T2DM + MASLD	38 patients (21 M, 17 F)	Placebo: 58 ± 11; LAN: 61 ± 7	Serum	Baseline: Placebo: 5.0 ± 3.7 LAN: 4.5 ± 2.8 Fold change from baseline in Adiponectin: Placebo: 1.0 [0.6; 1.4] LAN: 2.4 [2.0; 2.7]	Baseline and after 24 weeks	LAN 800 mg/day or placebo; Antidiabetic Medication Use: Metformin, GLP-1Ras, SGLT2i, DPP-4i, Sulfonylureas	

ACS – Acute Coronary Syndrome, ATOR – Atorvastatine, DM – Diabetes Mellitus, DPP-4i – dipeptidyl peptidase-4 inhibitors, DUL – Dulaglutide, EMPA – empagliflozin, F – Female, FDR – First-degree relatives with a T2DM diagnosed patient, GLP-1Ras – glucagon-like peptide-1 receptor agonists, HbA1c – glycated hemoglobin, INT – Intervention Group, LAN – Lanifibranor, LVESD – Left Ventricular End-Systolic Diameter, M – Male, MASLD – Metabolic Dysfunction-Associated Steatotic Liver Disease, OB – Obese, PIO – pioglitazone, ROSU – Rosuvastatine, SGLT2i – sodium–glucose cotransporter-2 inhibitors, T2DM – Type 2 Diabetes Mellitus, TIR – Tirzepatide, UC – Usual Care Group.

Table S2. Clinical studies on the use of adropin in the management of DM.

First author / Year	Pathology	Patient group (Total / Female / Male)	Patient age (years) mean ± SD	Adropin	Marker values (ng/mL)	Timing of analysis	Medication	Other pathologies
Hu / 2016 [144]	T2DM	81 Control (46 M, 35 F) 110 NOA (58 M, 52 F) 95 MIA (49 M, 46 F) 40 MAA (21 M, 19 F)	Control 58.35±7.80 NOA 57.52±11.33 MIA 58.45±13.16 MAA 59.92±10.78	Serum	Control 3.71 (2.82–4.56) NOA 3.17 (2.63–3.68) MIA 2.85 (2.32–3.27) MAA 2.56 (2.07–2.85)	Baseline	Antidiabetic drugs	-
Es-haghi / 2021 [145]	T2DM DKD	44 T2DM with DKD (21 M, 23 F) 45 T2DM (23 M, 22 F) 45 Control (22 M, 23 F)	T2DM with DKD 51.43±6.04 T2DM 47.60±4.87 Control 48.67±5.08	Serum	T2DM with DKD 2.77±0.36 T2DM 3.35±0.36 Control 4.21±0.52	Baseline	-	-
Li / 2021 [146]	MASLD and its progression to T2DM	62 patients 30 MASLD (10 M, 20 F) MASLD-NGT (5 M, 8 F) MASLD-T2DM (5 M, 12 F)	MASLD: 35.1±9.5 MASLD-NGT: 32.2±9.5 MASLD-T2DM: 37.3±9.1 Control: 35.1±4.8	Serum	MASLD: 2.02±2.92 Control: 5.52±0.65 MASLD-NGT: 4.00±3.52 MASLD-T2DM: 0.51±0.73	Baseline	No drug intervention was given in patients with T2DM.	-

		32 control (11 M, 11 F)						
Smith / 2022 [147]	Vascular insulin resistance due to short-term obesogenic lifestyle	36 patients (18 M, 18 F)	M: 25±1 F: 22±1	Plasma	M: ↓ from baseline (exact ng/mL not specified) F: unchanged	Before and after 10-day intervention	None reported; healthy volunteers	-
Wang / 2022 [148]	T2DM	35 T2DM: (21 M, 14 F) 28 Control (16 M, 12 F)	T2DM: 50.31±13.43 Control: 50.25±13.49	Serum	Baseline: T2DM: 3.12±0.73 Control: 5.90±1.22 At 17 weeks: T2DM: 4.97±1.01	Baseline and after 17 weeks	Sitagliptin 100 mg/day	-
Wei / 2022 [149]	Carotid atherosclerosis in T2DM	503 patients (297 M, 206 F) 223 WCP (133 M, 90 F) 280 CP (164 M, 116 F)	WCP: 51.6±9.8 CP: 61.5±10.1	Serum	WCP: 20.5±4.0 CP: 20.6±3.7	Baseline	Insulin 36 WCP, 58 CP OADs 123 WCP, 173 CP Statins WCP 6, CP 17	Hypertension WCP 75, CP 131 MASLD 116 WCP, 117 CP
Aydın / 2022 [150]	COVID-19 T2DM	100 patients (40 M, 60 F)	T2DM: 23–70 COVID: 23–87 COVID+DM: 38–92 Control: 31–75	Serum	Control: 0.6426±0.387 T2DM: 0.2561±0.07085 COVID: 0.3673±0.1797 COVID+T2DM: 0.1624±0.1151	Baseline	OADs or insulin	Hyperlipidemia Depression Parkinson's disease Dry eye syndrome
Berezin / 2023 [151]	T2DM CHF	417 patients (231 M, 186 F)	53 (41–64) M: 52 (40–63) F: 54 (42–66)	Serum	T2DM: 2.37 (1.91–2.75) M: 2.11 (1.82–2.68) F: 2.69 (2.32–3.04) At 6 months: T2DM: 3.00 (2.68–3.36) M (male): 2.60 (2.07–3.21) F (female): 3.65 (3.40–3.89)	Baseline and at 6 months	Dapagliflozin 10 mg/day Other medication: 198 ACEi, 106 M, 92 F 67 ARBs, 34 M, 33 F 165 ARNi, 92 M, 73 F 372 beta-blockers, 201 M, 171 F 59 ivabradine, 32 M, 27 F 75 calcium channel blocker, 38 M, 37 F 283 MRA, 150 M, 133 F 358 loop diuretic, 196 M, 162 F 367 antiplatelet, 201 M, 166 F 51 anticoagulant, 34 M, 17 F	346 dyslipidemia, 198 M, 150 F 352 hypertension, 192 M, 160 F 141 stable CAD, 75 M, 66 F 135 MIA, 79 M, 56 F 334 LV hypertrophy, 191 M, 143 F 112 DKD 1–3 grades, 62 M, 50 F 57 atrial fibrillation, 34 M, 23 F

							387 metformin, 210 M, 177 F 408 statins, 226 M, 182 F	
Zhang / 2023 [152]	T2DM with MASLD	22 T2DM (17 M, 5 F) 22 Controls (17 M, 5 F)	38.55±9.33 40.18±10.64	Serum	Baseline T2DM: 2.79±0.47 Control: 3.27±0.79 At 12 weeks: T2DM: 3.65 (3.20, 3.85)	Baseline and after 12 weeks	Liraglutide (0.6 to 1.8 mg/day SC over 12 weeks)	-
Berezina / 2023 [153]	T2DM, CHF	480 patients (272 M, 208 F) 88 PCE (51 M, 37 F) 392 PWCE (221M, 171F)	53 (40–67) PCE 56 (46–68) PWCE 51 (40–64)	Serum	2.37 (1.90–2.75) PCE 2.07 (1.80–2.35) PWCE 2.69 (2.10–3.17) At 52 weeks: PCE 1.98 (1.61–2.27) PWCE 2.85 (2.34–3.11)	Baseline and 52 weeks	296 ACEi, 52 PCE, 244 PWCE 72 ARBs, 16 PCE, 56 PWCE 112 ARNi, 22 PCE, 90 PWCE 427 beta-blockers, 77 PCE, 350 PWCE 93 ivabradine, 12 PCE, 81 PWCE 131 calcium channel blockers, 27 PCE, 104 PWCE 147 MRA, 24 PCE, 123 PWCE 383 loop diuretics, 75 PCE, 308 PWCE 166 antiplatelet, 33 PCE, 133 PWCE 105 anticoagulants, 41 PCE, 64 PWCE 480 metformin, 88 PCE, 392 PWCE 429 SGLT2i, 76 PCE, 353 PWCE 453 statins, 78 PCE, 375 PWCE	385 dyslipidemia, 70 PCE, 315 PWCE 307 hypertension, 55 PCE, 252 PWCE 166 stable coronary artery disease, 38 PCE, 128 PWCE 19 dilated cardiomyopathy, 5 PCE, 14 PWCE 105 atrial fibrillation, 37 PCE, 68 PWCE 56 paroxysmal/persistent atrial fibrillation, 18 PCE, 38 PWCE 49 permanent atrial fibrillation, 19 PCE, 30 PWCE 215 abdominal obesity, 40 PCE, 175 PWCE 382 left ventricular hypertrophy, 72 PCE, 310 PWCE 118 DKD grades 1–3, 31 PCE, 87 PWCE
Berezina / 2024 [154]	Newly diagnosed prediabetes Post STEMI	498 patients (263 M, 235 F) 126 COG (77 M, 49 F) 372 COFR (186 M, 186 F)	63 (51–75) COG 65 (52–77) COFR 62 (50–75)	Serum	Baseline: 2.96 (1.92–4.30) COG: 2.14 (1.80–2.83) COFG: 3.64 (2.70–5.58)	At baseline	316 ACEi, 80 COG, 236 COFR 78 ARBs, 21 COG, 57 COFR 456 beta-blockers, 115 COG, 341 COFR	425 dyslipidemia, 113 COG, 312 COFR 353 hypertension, 88 COG, 265 COFR 216 chronic HF, 55 COG, 161 COFR

							82 ivabradine, 21 COG, 61 COFR 61 calcium channel blockers, 16 COG, 45 COFR 43 thiazide-like diuretics, 11 COG, 32 COFR 216 loop diuretics, 55 COG, 161 COFR 173 MRA, 39 COG, 134 COFR 429 antiplatelet agents, 112 COG, 317 COFR 90 anticoagulants, 24 COG, 66 COFR 116 metformin, 28 COG, 88 COFR 95 GLP-1RAs, 18 COG, 77 COFR 297 SGLT2i, 59 COG, 238 COFR 498 statins, 126 COG, 372 COFR	43 HFpEF, 11 COG, 32 COFR 173 HFmrEF, 44 COG, 129 COFR 90 atrial fibrillation, 24 COG, 66 COFR 211 smoking, 57 COG, 154 COFR 194 abdominal obesity, 53 COG, 141 COFR 467 left ventricular hypertrophy, 118 COG, 349 COFR 131 DKD grades 1–3, 37 COG, 94 COFR
Chen / 2025 [155]	T2DM DKD	58 T2DM: 40 ADKD (27 M, 13 F) 18 EDKD (11 M, 7 F) 9 Control (4 M, 5 F)	T2DM: ADKD 67.10±10.13 EDKD 52.89±12.95 Control 56.44±11.18	Serum	T2DM: ADKD 6.848±1.287 EDKD 5.380±1.826 Control 3.470±1.284 DKD progression: 7.52±0.84 Non- DKD Progression: 6.15±1.66	Baseline	T2DM: metformin, 17 ADKD, 17 EDKD sulfonylurea, 27 ADKD, 9 EDKD TZD, 9 ADKD, 5 EDKD DPP4i, 20 ADKD, 5 EDKD GLP-1RAs, 8 ADKD, 4 EDKD SGLT2i, 7 ADKD, 8 EDKD insulin injection, 21 ADKD, 6 EDKD use of anti-hypertensive agent, 36 ADKD, 10 EDKD statin, 27 ADKD, 9 EDKD Control:	

							use of anti-hypertensive agent 3	
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ACEi – Angiotensin-Converting Enzyme Inhibitor, ADKD – Advanced Diabetic Kidney Disease, ARBs – Angiotensin II Receptor Blocker, ARNi – Angiotensin Receptor–Neprilysin Inhibitor, CAD – Coronary Artery Disease, CHF – Chronic Heart Failure, DPP-4i – dipeptidyl peptidase-4 inhibitors, DKD – Diabetic Kidney Disease, COFG – Clinical Outcomes Free Group, COG – Clinical Outcomes Group, CP – With Carotid Plaque, EDKD – Early Diabetic Kidney Disease, F – Female, GLP-1RAs – glucagon-like peptide-1 receptor agonists, HF – Heart Failure, IGT – Impaired Glucose Tolerance, LV – Left Ventricle, MAA – Macroalbuminuria, MASLD – Metabolic Dysfunction-Associated Steatotic Liver Disease, M – Male, MIA – Microalbuminuria, MRA – Mineralocorticoid Receptor Antagonist, NGT – Normal Glucose Tolerance, NOA – Normoalbuminuria, OADs – Oral Antidiabetic Drugs, PCE – Patients with Composite Endpoint, PWCE – Patients without Composite Endpoint, SC – subcutaneous, SGLT2i – sodium–glucose cotransporter-2 inhibitors, STEMI – ST Elevation of Myocardial Infarction, TZD – thiazolidinediones, T2DM – Type 1 Diabetes Mellitus, WCP – Without Carotid Plaque.

Table S3. Clinical studies on the use of Fetuin-A in the management of DM.

First author / Year	Pathology	Patient group (Total / Male/ Female)	Patient age (years) mean $\pm$ SD	Fetuin-A	Marker values ($\mu\text{g/mL}$)	Timing of analysis	Medication	Other pathologies
Wedick / 2011 [156]	T2DM	45 patients (16 M, 29 F)	CafC 38.7 (7.3) DCafC 41.9 (14.6) NCaf 41.2 (17.4)	Serum	Baseline: CafC 246.1 (45.3) DCafC 270.7 (37.4) NCaf 280.2 (56.9) At 8 weeks: CafC 261.52 (228.83, 298.84) DCafC 233.71 (201.54, 270.99) NCaf 291.07 (212.94, 333.94)	Baseline and Week 8	None allowed	Overweight only
Özenç / 2013 [157]	T2DM	137 patients: (M: 107 / F: 30) Control (23 M, 8 F) T2DM (37 M, 12 F) T2DMWDF (47 M, 10 F)	Control: 51 (36–78) T2DM: 59 (39–87) T2DMWDF: 64 (42–82)	Serum	Control: 0.036 T2DM: 0.085 T2DMWDF: 0.123	Baseline	T2DM: Oral antidiabetic and insulin treatment T2DMWDF Insulin	Atherosclerosis in peripheral arteries (graded by ultrasound);
Jüllig / 2014 [158]	T2DM	15 patients 8 GBP (0 M, 8 F) 7 SG (1 M, 6 F)	GBP: 41.0 ± 3.1 ; SG: 46.8 ± 2.9	Serum	Decreased to 75% of baseline after GBP	3 days before and 3 days after surgery	metformin monotherapy pre-surgery, stopped post-surgery	OB
Otten / 2018 [159]	T2DM	26 patients 13 PD (9 M, 4 F) 13 PD-EX (8 M, 5 F)	PD 60 (54–64) PD-EX 61 (58–67)	Plasma	Decreased by 11% in PD group; unchanged in PD-EX group.	Before and after 12-week intervention	Diet $\pm$ metformin (patients were treated with diet and/or metformin only)	OB
Krajnc / 2019 [160]	Coronary calcification in T2DM	45 patients (23 M, 22 F)	59 ± 8 (M: 60 ± 7 , F: 58 ± 8)	Serum	Baseline: 0.0262 ± 0.0055 At 18 months: 0.0280 ± 0.0070	Baseline and after 18 months	35 Metformin 20 Insulin 11 Insulin + metformin 37 Statin 34 ACEI/sartan	OB
Khalili / 2019 [161]	T2DM	40 patients (20 M, 20 F) Placebo (7 M, 13 F) Probiotic (7 M, 13 F)	Placebo 45.00 (5.37) Probiotic 43.95 (8.14)	Serum	Baseline: Placebo: 139.95 (45.36)	Baseline and at 8 weeks	15 Glibenclamide (7 placebo, 8 probiotic)	-

		10 M / 10 F per group)			Probiotic :119.53 (46.95) At 8 weeks: Placebo: 145.00 (45.86) Probiotic: 107.63 (41.79)		40 Metformin	
Nada / 2025 [162]	T2DM	60 patients Placebo (8 M, 12 F) Curcumin (9 M, 11 F) Fenofibrate (6 M, 14 F)	Placebo (56.15 ± 5.02) Curcumin 57.40 ± 6.48 Fenofibrate 56.30 ± 8.16	Serum	Baseline: Placebo 132.78 ± 38.61 Curcumin 140.56 ± 43.15 Fenofibrate 157.03 ± 66.49 At 3 weeks: Placebo 141.15 (116.08-207.49) Curcumin 121.2 (111.35-147.5) Fenofibrate 94.40 (74.55-128.60)	Baseline and at 3 months	Glimepirid	Hypertension

TCaFC – Caffeinated Coffee, DCaFC – Decaffeinated Coffee, GBP – Gastric Bypass, NCaF – No Coffee, OB – Obesity, PD – Paleolithic Diet Group, PD-EX – Paleolithic Diet and Exercise Group, SG – Sleeve Gastrectomy, T2DM – Type 2 Diabetes Mellitus, T2DMWDF – Type 2 Diabetes Mellitus with Diabetic Foot.

Table S4. Clinical studies on the use of lipoprotein(a) in the management of DM.

First author / Year	Pathology	Patient group (Total / Male/ Female)	Patient age (years) mean ± SD	Lipoprotein A (Lp (a))	Marker Values (mg/dL)	Timing of analysis	Medication	Other pathologies
Atamer / 2013 [163]	T2DM	50 patients (30 M, 20 F)	58.7 ± 9.2	Serum	Baseline: 28.20±6.47 At 3 months: 19.32±3.74	Before and at 3 months	Metformin, sulfonylurea, insulin + rosiglitazone	-
Bays / 2015 [164]	T2DM	796 patients ERN/LRPT (≤6.8%): (134 M, 83 F) Placebo (≤6.8%): (115 M, 60 F) ERN/LRPT (>6.8%): (122 M, 93 F) Placebo (>6.8%): (99 M, 62 F)	ERN/LRPT (≤6.8%): 62.59±9.15 Placebo (≤6.8%): 61.61±9.41 ERN/LRPT (>6.8%): 61.47±9.29 Placebo (>6.8%): 62.32 ± 9.37	-	Baseline: ERN/LRPT (≤6.8%): 10.00 Placebo (≤6.8%): 11.00 ERN/LRPT (>6.8%): 8.50 Placebo (>6.8%): 10.00 At 12 weeks, treatment with ERN/LRPT significantly reduced Lp (a) by approximately 22–26%, regardless of baseline HbA1c or FPG levels. At 36 weeks, no quantitative data on Lp (a) are provided, so the	Baseline and at 12, 36 weeks	Fish oils Statins Fibrates (gemfibrozil, fenofibrate) Ezetimibe Ezetimibe / simvastatin combination tablet Bile acid sequestrants Antidiabetic medication	Dyslipidemia

					progression beyond week 12 cannot be evaluated.			
Derosa / 2016 [165]	T2DM	221 patients Olmesartan: 74 (36 M, 38 F) Amlodipine: 72 (35 M, 37 F) Olmesartan / Amlodipine: 75 (35 M, 40 F)	Adults ≥18	Plasma	Baseline: Olmesartan: 45.2±39.5 Amlodipine: 43.4±38.7 Olmesartan / Amlodipine: 45.1±39.7 At 12 months: Olmesartan: 39.4±36.1 Amlodipine: 42.5±38.1 Olmesartan / Amlodipine: 32.5±31.8	Baseline and at 12 months	Olmesartan Amlodipină Olmesartan+Amlodipină	Hypertension
Leiter / 2017 [166]	T2DM T1DM	441 T2DM: ARLI (161 M, 133 F) Placebo (78 M, 69 F) 76 T1DM: ARLI (29 M, 22 F) Placebo (17 M, 8 F)	<65 T2DM: ARLI 143 Placebo 73 T1DM: ARLI 42 Placebo 19 ≥65 to <75 T2DM: ARLI 126 Placebo 55 T1DM: ARLI 8 Placebo 6 ≥75 T2DM: ARLI 25 Placebo 19 T1DM: ARLI 1 Placebo 0	Plasma	Baseline: T2DM: ARLI 16.0 (5.0:55.0) Placebo 14.0 (5.0:38.0) T1DM: ARLI 17.0 (6.0:28.0) Placebo 12.0 (4.0:37.0) Change from Baseline to Week 24 T2DM: ARLI -19.0% ± 1.6% Placebo -0.5% ± 2.2% T1DM: ARLI -23.0% ± 3.8% Placebo -4.3% ± 5.3%	Baseline and at 24 weeks	Insulin (all), Statins (majority), Ezetimibe metformin Other antihyperglycaemic drugs alirocumab	High CV risk
Gulati / 2017 [167]	T2DM	50 patients (27 M, 23 F)	45.8±9.3	Serum	Baseline: 21.8 (9.38–122) At 24 weeks: 19.8 (9.38–111)	Baseline and at 24 weeks	Metformin	Cardiovascular Risk
Lorenzatti / 2018 [168]	T2DM	981 patients 657 EVO (290 M, 367 F) 324 Placebo (199 M, 195 F)	EVO 62 (33-80) Placebo 62 (35-80)	Serum	Baseline: EVO 69.4 (94.3) nmol/L Placebo 69.4 (93.6) nmol/L At 12 weeks: EVO Q2W: -35.9%	Baseline, and at 12 weeks	Alpha-glucosidase inhibitors – Placebo: 36 – EVO: 110 Biguanides – Placebo: 223	Hypertension Cerebrovascular or peripheral arterial disease CAD

					EVO QM: -37.9% Placebo: +26.5%		– EVO: 454 DPP-4i – Placebo: 32 – EVO: 56 GLP-1RAs – Placebo: 5 – EVO: 7 Insulin – Placebo: 91 – EVO: 211 Meglitinides – Placebo: 12 – EVO: 31 SGLT2i – Placebo: 10 – EVO: 19 Sulfonylureas – Placebo: 120 – EVO: 223 TZD – Placebo: 14 – EVO: 19 Other – Placebo: 3 – EVO: 11	
Mahmoodi / 2022 [169]	T2DM	253 patients 125 T2DM (70 M, 55, F) 128 control (67 M, 61 F)	47.79±5.65	Serum	Baseline Total Participants: T2DM: 68.04±3.74 ng/mL Control: 66.98±2.57 ng/mL M: T2DM: 64.45±4.40 ng/mL Control: 68.18±3.79 ng/mL F: T2DM: 72.61±6.37 ng/mL Control: 65.65±3.42 ng/mL	Baseline	Other antihyperglycaemic drugs	Cardiometabolic risk
Qiu / 2024 [170]	T2DM	896 patients T2DM+CAD: 217 (140 M, 77 F) Controls: 679 (431 M, 248 F)	T2DM+CAD: 57.61 ± 10.13 Control: 55.81 ± 9.17	Plasma	T2DM+CAD: 16.53±20.19 Control: 14.00±15.08	Baseline	DM medication	CAD

Ma / 2024 [171]	T2DM	93 patients 31 Control (11 M, 20 F) 30 AE (16 M, 14 F) 32 BFR-RT (16 M, 16 F)	Control 56.29±5.92 AE 57.73±5.85 BFR-RT 57.56±4.85	Serum	Baseline: Control 111.58±45.32 AE 115.60±46.06 BFR-RT 110.03±43.22 At 3 months: Control 112.95±45.23 AE 116.64±44.02 BFR-RT 105.44±40.69 At 6 months: Control 114.09±45.71 AE 108.93±44.77 BFR-RT 101.34±43.61	Baseline and at 3 and 6 months	Glucose-lowering medication Medications used for dyslipidemia Medications used for blood pressure	ASCVD Dyslipidemia Hypertension
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AE – aerobic exercise, ARLI – arlilocumab, ASCVD – atherosclerotic cardiovascular disease,, BFR-RT – blood flow-restrictive resistance training, CAD – coronary artery disease, DM – Diabetes Mellitus, DPP-4i – dipeptidyl peptidase-4 inhibitors, ERN/LRPT – extended-release niacin/laropiprant, EVO – evolocumab, FPG – fasting plasma glucose, GLP-1RAs – glucagon-like peptide-1 receptor, HbA1c – glycated hemoglobin, Lp(a) – lipoprotein A, Q2W – every 2 weeks, QM – every month, SGLT2i – sodium–glucose cotransporter-2 inhibitors, TZD – thiazolidinediones, T1DM – type 1 diabetes mellitus, T2DM – type 2 diabetes mellitus, Lp(a) concentrations are reported in nmol/L, ng/mL or mg/dL, as provided in the original studies; direct conversion between units is not recommended due to apo(a) isoform variability.

Table S5. Clinical studies on the use of Netrin-1 in the management of DM.

First author / Year	Pathology	Patient group (Total / Female / Male)	Patient age (years) mean ± SD	Netrin-1	Marker values (pg/mL)	Timing of analysis	Medication	Other pathologies
Okutucu / 2021 [172]	DR (NPDR and PDR) in T2DM	50 patients with T2DM (10 NPDR, 13 PDR) + 27 controls	NPDR 66.70 ± 12.37 PDR 67.85 ± 8.93 Control 65.74 ± 7.17	Serum	Baseline: NPDR: 253 ± 75 PDR: 318 ± 68 Control: 983 ± 664 1 week: NPDR: 416.3 ± 123.0 PDR: 476.6 ± 225.0 4 weeks: NPDR: 747.5 ± 89.6 PDR: 676.6 ± 187.5	At the time of ophthalmic evaluation, 1 and 4 weeks after BCZ injection	BCZ injection	Hypertension
Inderjeet / 2022 [173]	T2DM ± ACS	84 patients: T2DM with ACS: 42 (31 M, 11 F) T2DM 42 (29 M, 13F)	T2DM with ACS: 58.29 ± 10.24 T2DM 56.02 ± 7.22	Serum Netrin-4 (serum)	Netrin-1: T2DM with ACS 510.47 ± 85.72 T2DM 623.25 ± 68.55 Netrin-4: T2DM with ACS 43.96 ± 9.80 T2DM 142.71 ± 24.01	Within 24–30 h of T2DM with ACS (patientst); routine OPD visit (T2DM)	-	-
Garcia Galindo / 2022 [174]	OB and newly diagnosed T2DM	90 patients Healthy: 30 (1 1F / 9 M)	Healthy: 22.8 ± 4.3 OB: 21.9 ± 4.5	Serum	Healthy: 130 ± 60 OB: 150 ± 70 T2DM: 330 ± 220	Single time-point blood sample	None reported	

		OB: 30 (14 F / 6 M) T2DM: 30 (10 F / 10 M)	T2DM: 51.3 ± 5.5					
Mondal / 2024 [175]	T2DM, DN (with and without small fiber loss)	117 patients: 45 controls 42 DN- 30 DN+	Control: 43.1 ± 10.5; DN-: 49.4 ± 10.3; DN+: 53.2 ± 8.0	Serum	Control: 1,034 ± 352 DN-: 810.2 ± 308.6 DN+: 522.3 ± 182	Single time-point blood sample	-	-
Mentxaka / 2024 [176]	T2DM ± OB	91 patients LN: 18 (10 F/8 M) OB-NG: 32 (25 F/7 M) OB-T2DM: 41 (28 F/13 M)	LN: 42 ± 5 OB-NG: 40 ± 3 OB-T2DM: 47 ± 2	Serum	LN: 578 ± 33 OB-NG: 924 ± 64 OB-T2DM: 841 ± 50	Single time-point blood sample	None reported explicitly (patients with T2DM were untreated)	-
Matter / 2025 [177]	T1DM with DKA and transient renal tubulopathy	40 patients (36 F, 4 M)	10.59 ± 2.17	Urine	Day 1: Median 723.08 (range: 210.5–4223) Day 3: Median 764.33 (range 518.73–1159) Day 14: Median 180.3 (range: 153.48–255.43)	Day 1 (on DKA presentation) Day 3 Day 14 (follow-up)	Insulin	-
Chaitra / 2025 [178]	T2DM ± DFS	260 patients: 130 DF 130 T2DM	-	Serum	Median Netrin-1: DF = 180.83 (IQR 118.93–280.45) T2DM = 164.37 (IQR 108.73–210.72)	Single time-point blood sample	-	-

ACS – Acute coronary syndrome, BCZ – bevacizumab, DKA – Diabetic ketoacidosis, DN – Diabetic Neuropathy, DR – Diabetic Retinopathy, DFS – Diabetic Foot Syndrome, F – Female, IQR – interquartile range, LN – lean, M – Male, NPDR – non-proliferative diabetic retinopathy, OB – obese, OB-NG – obese with normoglycaemia, OB-T2DM – obese with Type 2 Diabetes Mellitus, PDR – proliferative diabetic retinopathy, T1DM – Type 1 Diabetes Mellitus, T2DM – Type 2 Diabetes Mellitus.