

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Table 1: Search Strategy for the Systematic Review

Disease	Gene Names and Variants	Treatments
Lipodystrophy	<i>LMNA</i>	Medication
Severe Insulin resistance	Lamin A/C	Therapy
Type A insulin resistance	<i>BSCL2</i>	Medical management
Donohue syndrome	Seipin	Treatment
Rabson Mendenhall syndrome	<i>AGPAT2</i>	SGLT2 inhibitor
Leprechaun	<i>PTRF</i>	SGLT2i
Leprechaunism	<i>CAVIN1</i>	SGLT-2 inhibitor
FPLD	<i>CAV1</i>	SGLT-2i
FPLD2	<i>ZMPSTE24</i>	Sodium Glucose Transporter 2 inhibitor
FPLD3	<i>PPARG</i>	Dapagliflozin
FPLD4	<i>PLIN1</i>	Empagliflozin
FPLD5	<i>MFN2</i>	Ertagliflozin
FPLD6	<i>CIDEA</i>	Canagliflozin
FPLD7	<i>LIPE</i>	Flozin
SHORT syndrome	<i>PCYT1A</i>	Thiazolidinedione
SOFT syndrome	<i>INSR</i>	PPAR γ Agonist
vSOFT	<i>AKT2</i>	PPAR gamma agonist
Werner syndrome	<i>PIK3R1</i>	TZD
Bloom syndrome	<i>AKT2</i>	Rosiglitazone
MOPDII	<i>WRN</i>	Pioglitazone
Osteodysplastic primordial dwarfism of Majewski type 2	<i>BLM</i>	Troglitazone
Alstrom syndrome	<i>NSMCE2</i>	GLP1RA
MANDIBULAR HYPOPLASIA, DEAFNESS, PROGEROID FEATURES, AND LIPODYSTROPHY SYNDROME	<i>POLD1</i>	GLP1 Receptor Agonists
MDPL	<i>PCNT</i>	GLP-1 Receptor Agonists
Mandibuloacral dysplasia	<i>POC1A</i>	GLP-1RA
MARFANOID-PROGEROID-LIPODYSTROPHY SYNDROME	<i>ALMS1</i>	Exenatide
MFLS	<i>PSMB8</i>	Liraglutide
PROTEASOME-ASSOCIATED AUTOINFLAMMATORY SYNDROME 1	<i>FBN1</i>	Lixisenatide
PRAAS1		Semaglutide

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

	Dulaglutide
	Albiglutide
	Bariatric surgery
	Obesity Surgery
	Weight reduction surgery
	gastric band
	Roux-en-Y
	Gastric sleeve
	Gastric bypass
	metabolic surgery
	IGF-1
	rhIGF-1
	somatokine
	recombinant human insulin like growth factor 1
	Insulin like growth factor 1
	Increlex
	Mecasermin
	IGF-1/IGFBP3
	IGF1
	rhIGF1
	IGF1/IGFBP3
	leptin
	rhleptin
	metreleptin
	Myalept
	Myalepta

Legend: Search terms used to search PubMed, MEDLINE, and Embase included variations of the disease, gene, and treatment.

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Table 2: Number of individuals by intervention and genotype in included studies

		Treatment						
		rhIGF-1 or rhIGF-1/IGFBP3 composite	SGLT2i	TZD	Bariatric surgery	Metformin	Metreleptin	Total
Gene	<i>AGPAT2</i>	0	0	0	0	1	20	21
	<i>BSCL2</i>	0	1	1	0	0	19	21
	<i>PTRF</i>	0	0	0	0	0	1	1
	<i>LMNA</i> (<i>progeroid</i>)	0	0	0	0	0	2	2
	<i>LMNA</i> (<i>FPL</i>)	0	0	9	2	2	59	72
	<i>PPARG</i>	0	0	5	0	0	12	15
	<i>PLIN1</i>	0	0	0	2	0	0	2
	<i>PIK3R1</i>	0	1	0	0	0	0	1
	<i>INSR</i>	17	0	0	0	2	0	19
<i>All partial LD</i>		--	1	14	4	2	71	90
<i>All generalised LD</i>		--	1	1	0	1	40	43
<i>All LD</i>		--	2	15	4	3	111	135

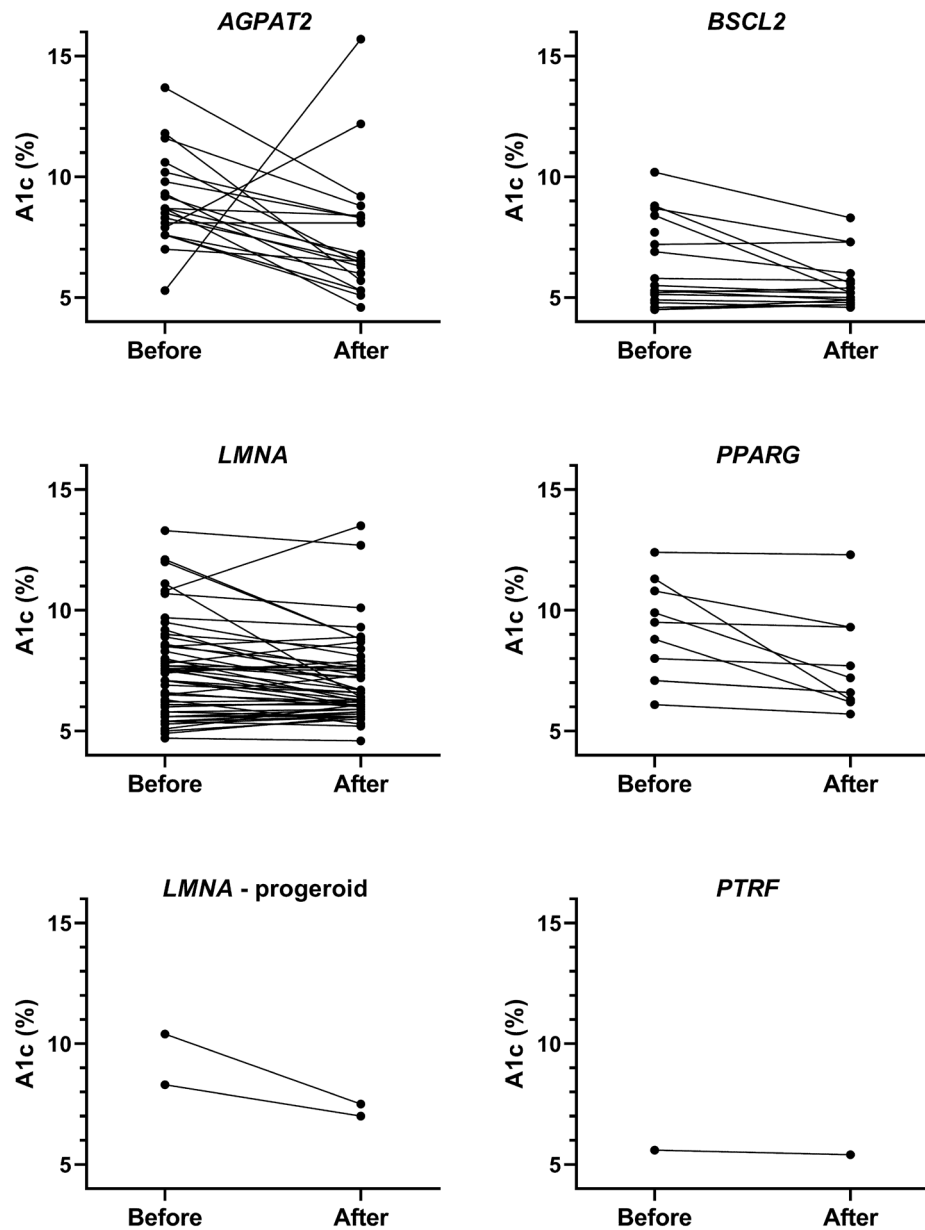
Abbreviations: rhIGF-1, recombinant human insulin-like growth factor 1; IGFBP3, insulin-like growth factor binding protein 3; SGLT2i, sodium-glucose co-transporter-2 inhibitor; TZD, thiazolidinedione; FPL = Familial Partial Lipodystrophy

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Figure 1: Effects of Metreleptin therapy on glycated haemoglobin (A1c) by genotype

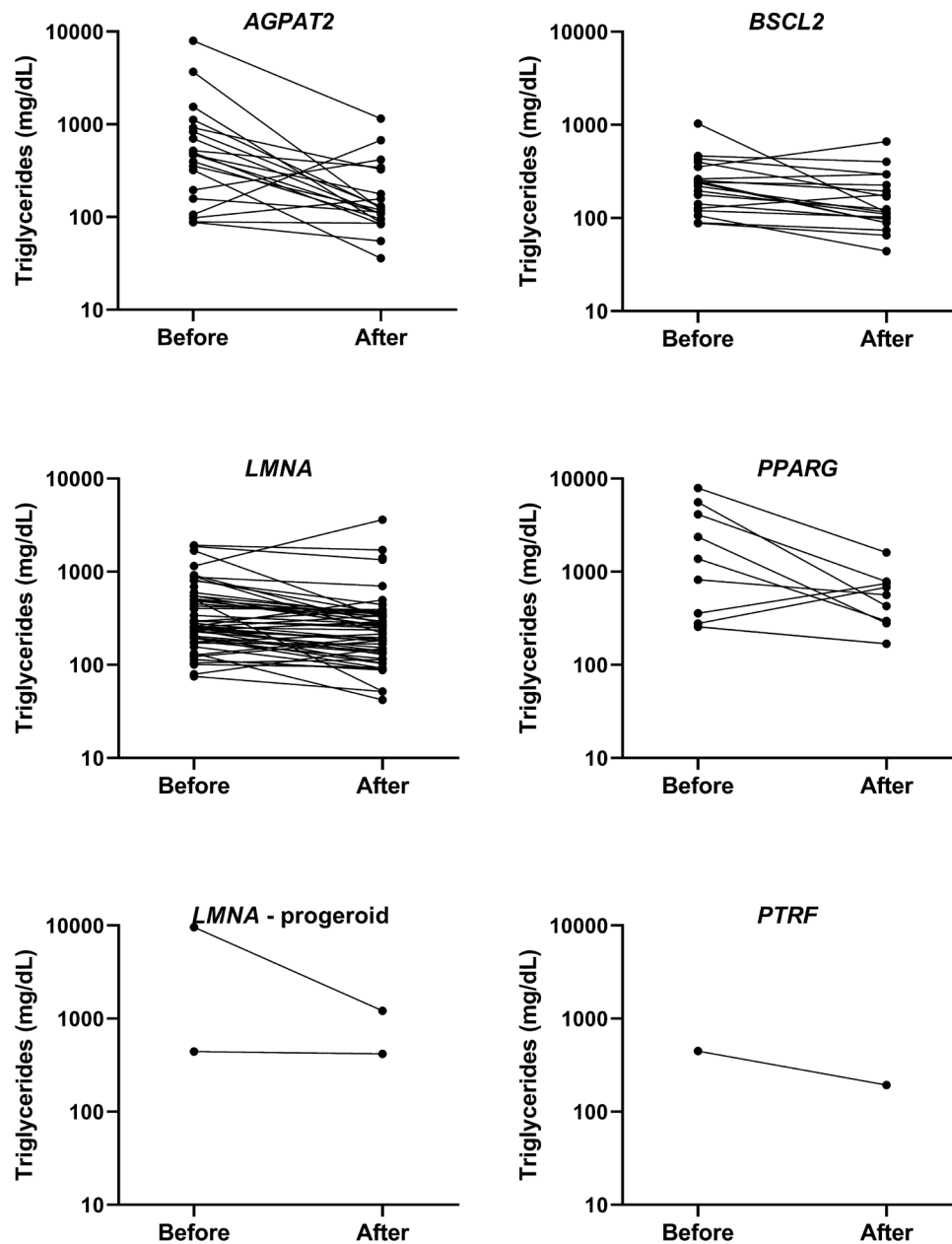


Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Figure 2: Effects of Metreleptin therapy on serum triglyceride concentration by genotype

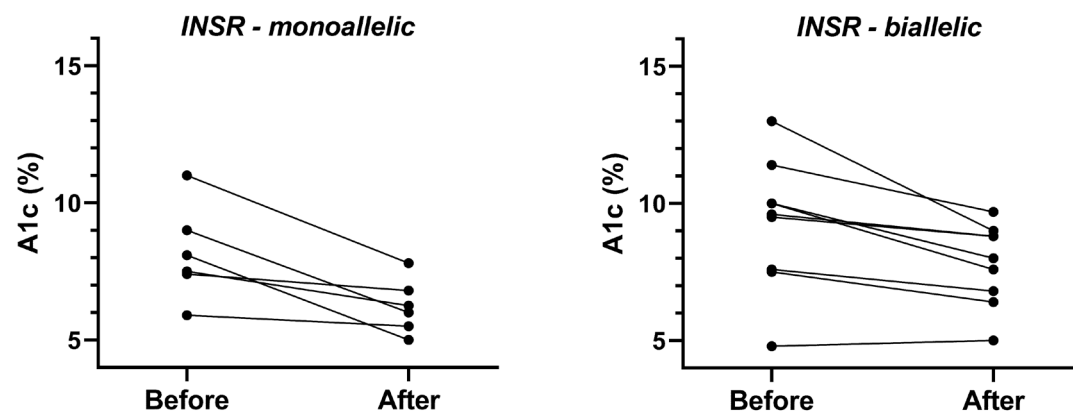


Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Figure 3: Effects of Metreleptin therapy on body mass index (BMI) by genotype

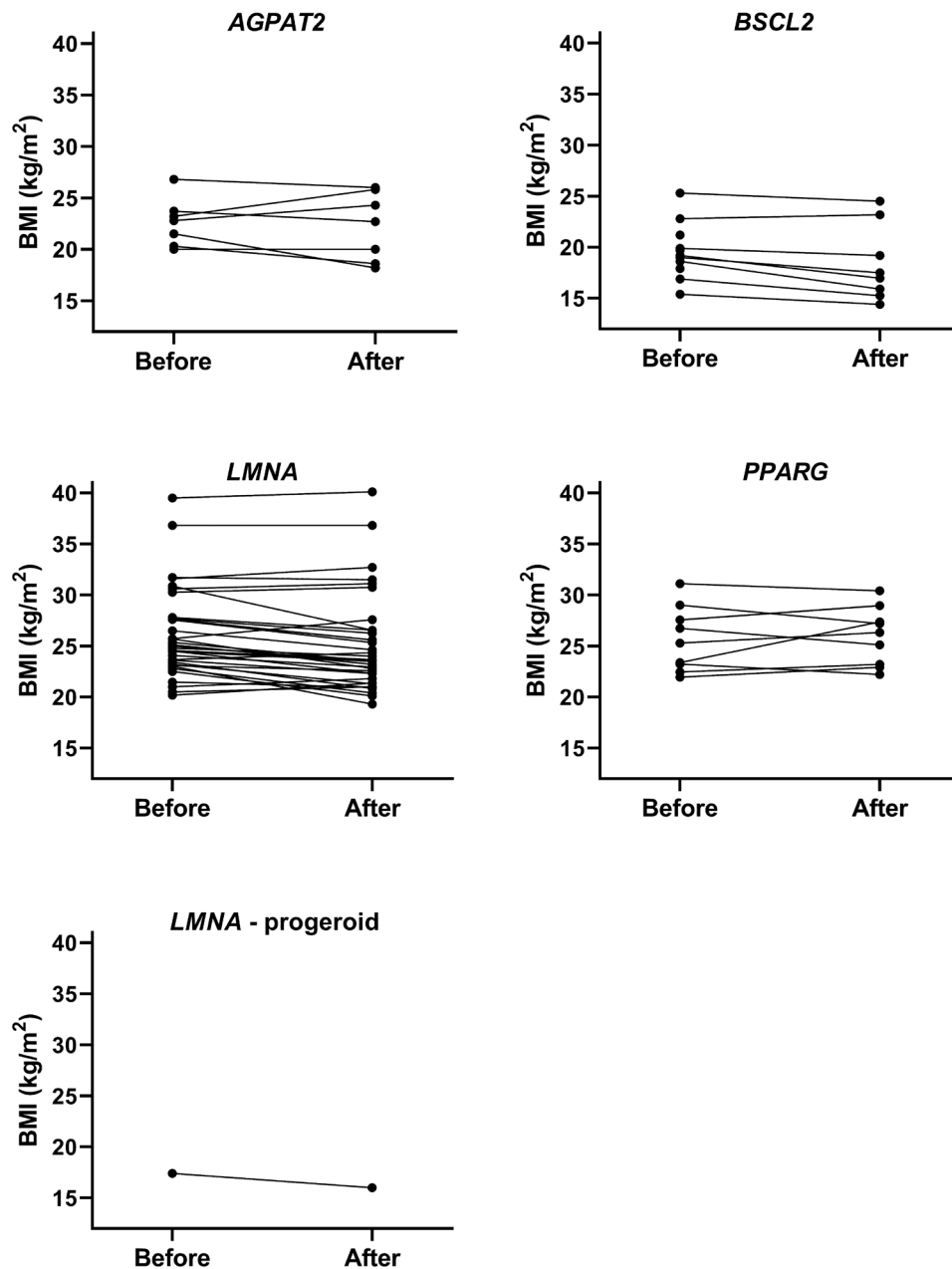


Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

Supplementary Figure 4: Effects of recombinant IGF-1 or IGF-1 plus IGFBP3 therapy on glycated haemoglobin (A1c) in monallelic and biallelic insulin receptoropathy

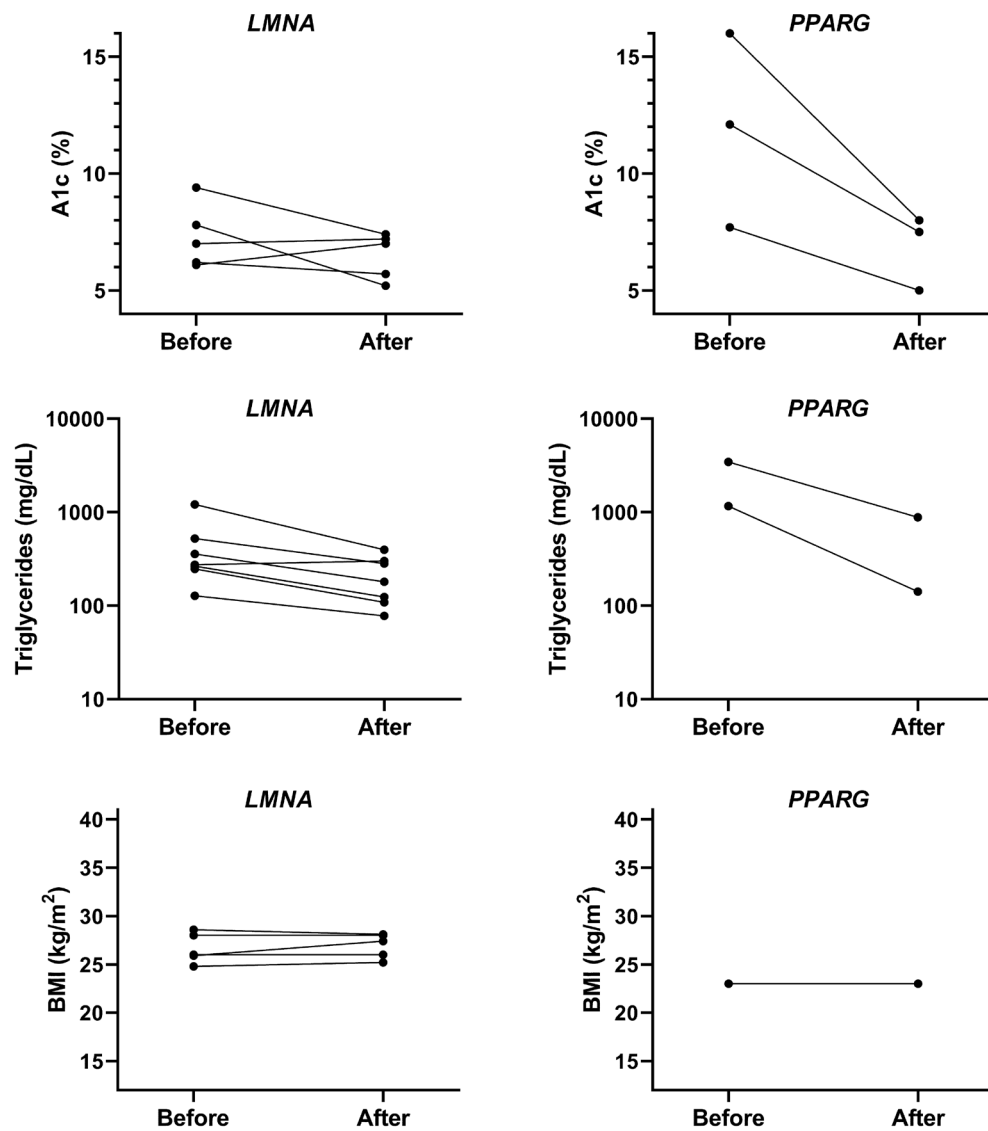


Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

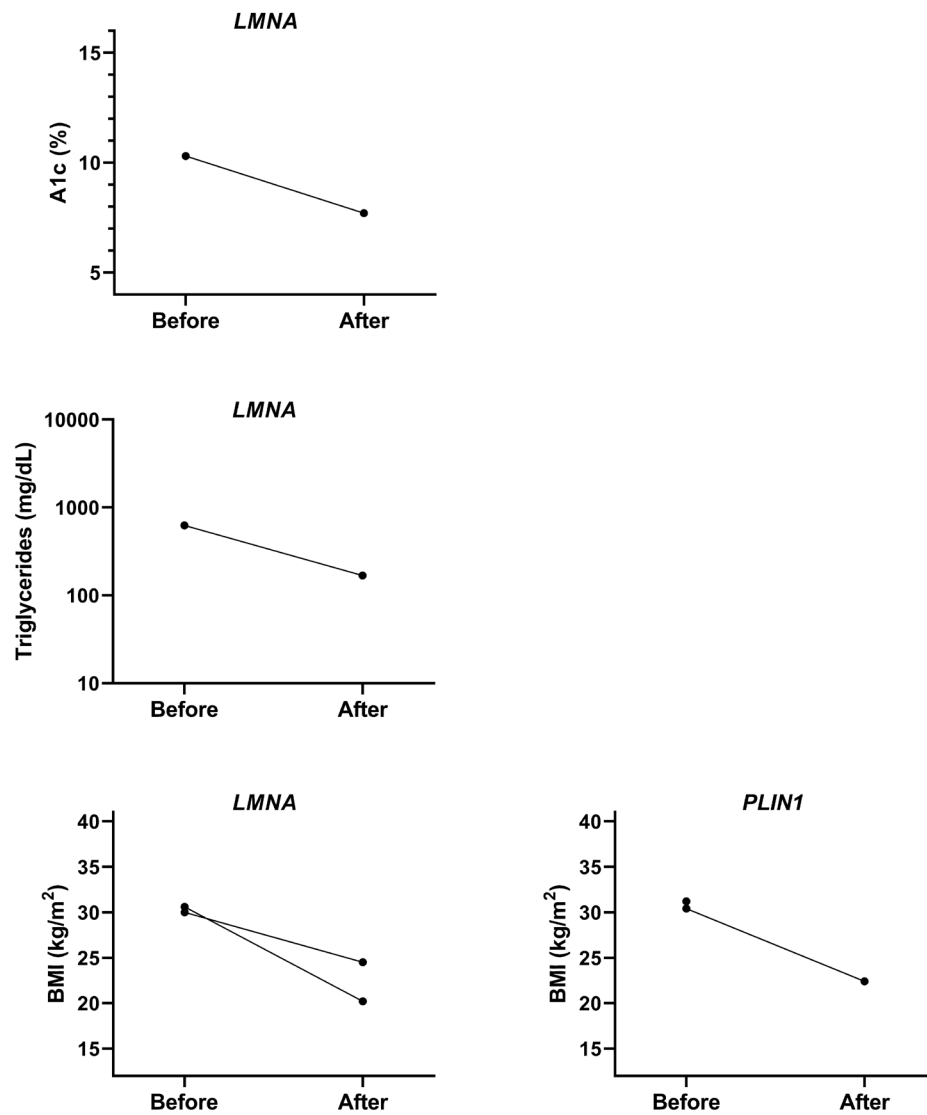
Supplementary Figure 5: Effects of thiazolidinedione therapy by genotype



Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

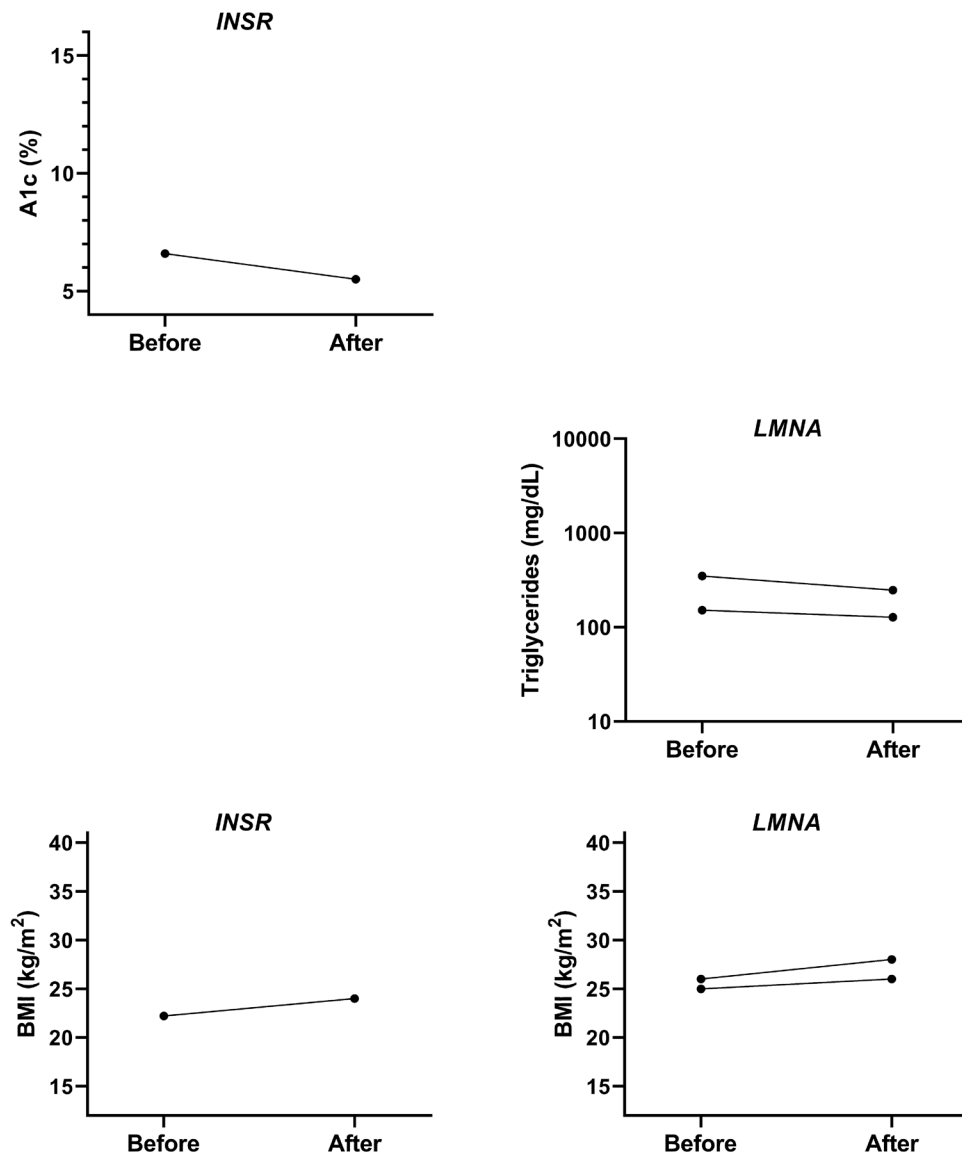


Supplementary Figure 6: Effects of bariatric surgery by genotype

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown

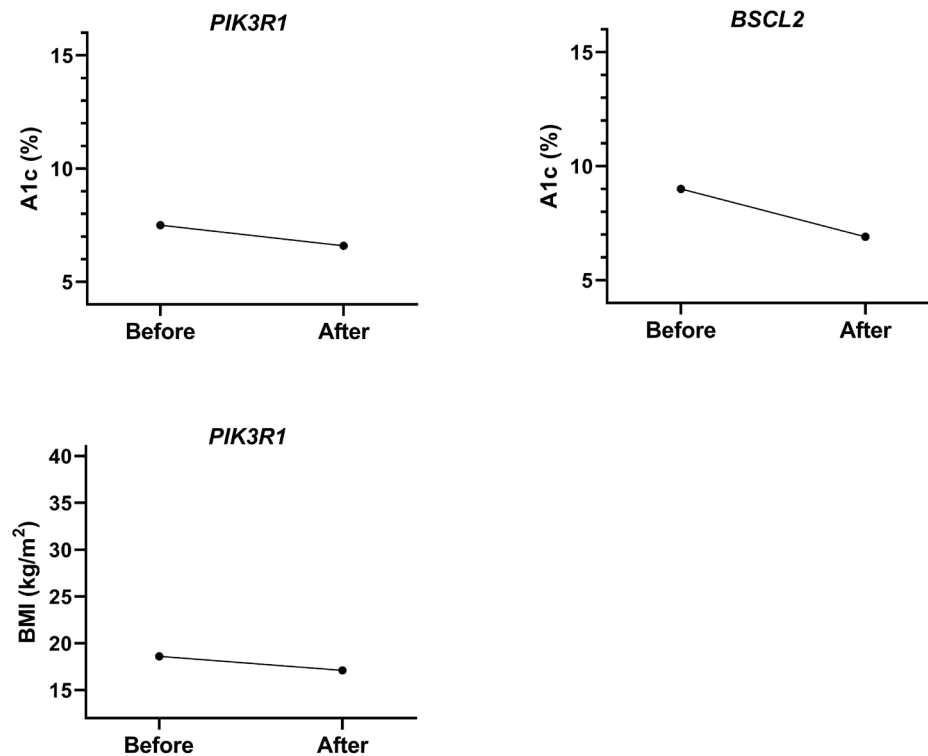


Supplementary Figure 7: Effects of metformin therapy by genotype

Supplementary Information

Genotype-stratified treatment for monogenic insulin resistance: a systematic review

Robert K. Semple, Kashyap A. Patel, Sungyoung Auh, ADA/EASD PMDI, Rebecca J. Brown



Supplementary Figure 8: Effects of SGLT2 inhibitor therapy by genotype