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Repurposing metformin for cardiovascular disease

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Trial (NCT number)	Patient group	Enrolled patients; duration & dose of metformin	Publication date	Selected outcome measures
Jadhav and co-workers	Cardiac syndrome X	33; up to 500mg BID for 8 weeks	2006	Improved endothelium-dependent microvascular responses; Stress Test: maximal ST-segment depression, Duke score and chest pain incidence
TAYSIDE (NCT00473876)	Chronic HF with insulin resistance	62; 1000mg BID for 4 months	2012	No effect on primary endpoint of peak VO_2. Improved pre-determined secondary endpoints of $VE/VCO_{2,}$, fasting insulin resistance index and decreased body weight
CAMERA (NCT00723307)	Coronary artery disease with central obesity	173; 850mg BID for 18 months	2014	No effect on primary endpoint of mean distal cIMT

	already taking statins			
GIPS III (NCT01217307)	STEMI without diabetes	380; 500mg BID for 4 months	2014	No effect on the primary endpoint of LVEF
REMOVAL (NCT01483560)	Type 1 diabetes	428; 1000mg BID for 3 years	2017	No effect on the primary endpoint of mean far-wall cIMT. Improvement in the secondary/tertiary endpoints of HbA_{1c}; LDL cholesterol; eGFR and maximal cIMT.
MET-REMODEL (NCT01483560)	Normotensive with insulin resistance and coronary artery disease	64; 2g daily for one year	2018 (expected end of study)	Primary: LV mass index Secondary: Fasting insulin resistance index; obesity; LV size, function and improvement in endothelial function
VA IMPACT (NCT02915198)	Pre-diabetes and established atherosclerotic	7868; up to 2g daily for 4.5 years	2024 (expected end of study)	Primary: Time to non-fatal myocardial infarction;

	cardiovascular disease			stroke; hospitalization for unstable angina; or symptom-driven coronary revascularization. Secondary: Cumulative/recurrent incidence of primary endpoints

Table 1 Summary of CVD outcomes in selected repurposing trials for metformin.
Abbreviations: BID is twice daily. HF is heart failure. VO2 is oxygen consumption.
VE/VCO2 is minute ventilation − carbon dioxide production ratio. cIMT is carotid intimal
media thickness. STEMI is ST-segment elevation myocardial infarction. LVEF is Left
ventricular ejection fraction. HbA1c is glycated hemoglobin. LDL is low-density
lipoprotein. eGFR is estimated glomerular filtration rate. LV is left ventricle