

Supplemental Table 1 – Association of year-1 Substrates With CV Outcomes*

	HF	CV death	HF or CV death	All deaths	Non-fatal MI
Tx alone	0.85 [0.68–1.05]	0.90 [0.70–1.16]	0.85 [0.68–1.05]	0.88 [0.72–1.08]	0.88 [0.66–1.17]
Glucose	2.07 [1.02–4.18]	0.90 [0.52–1.54]	1.18 [0.75–1.85]	1.01 [0.65–0.58]	1.76 [1.01–3.06]
FFA	0.40 [0.22–0.73]	0.42 [0.27–0.67]	0.44 [0.30–0.64]	0.42 [0.29–0.61]	1.04 [0.63–1.74]
Glycerol	2.24 [1.36–3.68]	2.20 [1.51–3.20]	2.12 [1.54–2.90]	1.88 [1.38–2.56]	0.93 [0.64–1.37]
βOH	1.01 [0.67–1.56]	1.08 [0.79–1.49]	1.06 [0.81–1.39]	1.37 [1.06–1.78]	0.95 [0.69–1.31]
AcAc	1.55 [0.92–2.64]	1.49 [1.08–2.23]	1.51 [1.08–2.12]	1.12 [0.82–1.54]	1.17 [0.79–1.75]
Lactate	1.05 [0.54–2.06]	1.20 [0.73–1.98]	1.13 [0.74–1.73]	0.97 [0.66–1.44]	0.70 [0.43–1.16]
Pyruvate	1.09 [0.50–2.48]	0.94 [0.53–1.73]	1.11 [0.67–1.86]	0.82 [0.53–1.32]	2.23 [1.18–4.23]
Glucose-adj	1.46 [0.70–3.01]	0.64 [0.37–1.12]	0.84 [0.53–1.33]	0.76 [0.48–1.21]	1.66 [0.91–3.03]
FFA-adj	0.60 [0.30–1.21]	0.60 [0.37–0.99]	0.63 [0.41–0.97]	0.55 [0.37–0.82]	1.22 [0.71–2.12]
Glycerol-adj	1.78 [0.98– 3.26][†]	2.00 [1.30–3.10]	1.83 [1.30–2.65]	1.73 [1.21–2.47]	0.99 [0.64–1.54]
βOH-adj	1.08 [0.69–1.72]	1.00 [0.72–1.41]	1.03 [0.78–1.38]	1.28 [0.97–1.68]	0.99 [0.72–1.37]
AcAc-adj	1.11 [0.65–1.93]	1.36 [0.90–2.07]	1.30 [0.91–1.84]	1.09 [0.79–1.52]	1.03 [0.69–1.55]
Lactate-adj	0.86 [0.42–1.75]	1.02 [0.61–1.72]	0.95 [0.61–1.49]	0.87 [0.58–1.32]	0.61 [0.36–1.04]
Pyruvate-adj	1.64 [0.73–3.90]	1.28 [0.71–2.40]	1.52 [0.91–2.60]	1.09 [0.68–1.78]	2.81 [1.46–5.46]
Tx-adj	0.84 [0.55–1.30]	0.97 [0.70–1.36]	0.89 [0.68–1.18]	0.86 [0.66–1.13]	1.01 [0.72–1.44]

*Entries are risk ratios and 95% confidence intervals (per 1 log unit of the predictor). Statistically significant HR's are highlighted in bold. [†]*p*=0.06. CV, cardiovascular; HF, heart failure; MI, myocardial infarction; Tx, canagliflozin treatment, combined doses; FFA, free fatty acids; β OH, β -hydroxybutyrate; AcAc, acetoacetate; adj, adjusted for sex; age; body mass index; estimated glomerular filtration rate; HbA_{1c}; systolic blood pressure; prior CV disease; prior HF; smoking; urinary albumin-to-creatinine ratio; high-density lipoprotein; low-density lipoprotein; and use of statins, renin-angiotensin-aldosterone-system inhibitors, antithrombotics, and loop diuretics in addition to all 7 log-transformed metabolites.