

Supplemental material

**Supplemental Table 1. Multivariate association of Year 1  
Substrates with Outcomes. §**

	<b>Primary Comp.</b>	<b>Comp. Renal</b>	<b>HF/CV death</b>	<b>All deaths</b>
<b>Glucose</b>	0.77 [0.53–1.12]	<b>0.62 [0.61–0.97]</b>	1.12 [0.72–1.76]	1.27 [0.76–2.13]
<b>FFA</b>	<b>0.62 [0.44–0.89]</b>	0.71 [0.47–1.08]	<b>0.43 [0.29–0.66]</b>	<b>0.53 [0.33–0.87]</b>
<b>Glycerol</b>	0.95 [0.74–1.21]	0.93 [0.70–1.23]	1.27 [0.94–1.70]	0.99 [0.71–1.38]
<b>β-OH</b>	<b>1.22 [1.02–1.46]</b>	1.13 [0.92–1.39]	<b>1.37 [1.10–1.71]</b>	<b>1.38 [1.07–1.78]</b>
<b>AcAc</b>	<b>0.72 [0.58–0.88]</b>	<b>0.72 [0.56–0.92]</b>	<b>0.74 [0.58–0.95]</b>	0.80 [0.59–1.07]
<b>Lactate</b>	<b>0.40 [0.30–0.55]</b>	<b>0.35 [0.24–0.50]</b>	0.71 [0.49–1.04]	<b>0.60 [0.39–0.93]</b>
<b>Treatment</b>	<b>0.58 [0.44–0.77]</b>	<b>0.45 [0.32–0.62]</b>	0.82 [0.59–1.13]	1.04 [0.71–1.52]
<b>Glucose-adj.</b>	<b>0.70 [0.49–1.00]</b>	<b>0.60 [0.40–0.91]</b>	0.97 [0.62–1.52]	1.16 [0.68–1.99]
<b>FFA-adj.</b>	0.78 [0.54–1.14]	0.91 [0.58–1.41]	<b>0.58 [0.37–0.92]</b>	0.75 [0.44–1.28]
<b>Glycerol-adj.</b>	0.87 [0.65–1.17]	0.82 [0.58–1.15]	1.00 [0.70–1.43]	0.86 [0.58–1.29]
<b>β-OH-adj.</b>	<b>1.23 [1.04–1.46]</b>	<b>1.22 [1.00–1.48]</b>	<b>1.28 [1.02–1.62]</b>	1.22 [0.95–1.58]
<b>AcAc-adj.</b>	<b>0.75 [0.61–0.92]</b>	<b>0.74 [0.58–0.94]</b>	<b>0.75 [0.58–0.98]</b>	0.86 [0.63–1.18]
<b>Lactate-adj.</b>	<b>0.45 [0.32–0.64]</b>	<b>0.39 [0.26–0.59]</b>	<b>0.66 [0.44–0.99]</b>	<b>0.60 [0.38–0.97]</b>

§ Entries are hazard ratios (HR) and [95% confidence intervals] (per 1 log unit of the predictor); significant HRs are in bold. CV, cardiovascular; HF, heart failure; FFA, plasma free fatty acids; β-OH, plasma β-hydroxybutyrate; AcAc, plasma acetoacetate.

-adj = adjusted for sex; age; body mass index; smoking; estimated glomerular filtration rate; HbA<sub>1c</sub>; systolic blood pressure; prior CV disease, HF at baseline; urinary albumin-to-creatinine ratio; high-density lipoprotein cholesterol; low-density lipoprotein cholesterol; triglycerides; and use of statins, anti-thrombotics, loop and/or non-loop diuretics, β-blockers, metformin, sulphonylureas, insulin, and GLP-1 Ra's in addition to all 6 (log-transformed) substrates.

Supplemental Figure 1

