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Intensive Glucose Lowering for Diabetes: Long-term Impact on Absolute Risk of Mortality

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It has been reported that intensive control of blood sugar in diabetic patients is associated with suboptimal survival.[1] This possibility was also supported by findings of the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial, which described outcomes in 10,104 patients randomized to intensive or standard therapy (target glycated haemoglobin levels <6.0% versus 7 to 7.9%) for a mean treatment duration of 3.7 years.[2] Whatever the reason, the clinical significance of such results should be appreciated in absolute terms and not merely as relative risks (RRs). We therefore calculated relevant unadjusted number-needed-to-treat (NNT)/year and RR values from data detailed in ACCORD (see table), as previously described.[3]

Fatal Event	**RR (95% CI)**	**NNT/year (95% CI)**
Death (from any cause)	1.22 (1.02 to 1.46)	-367 (-196 to -2750)
Cardiovascular		
Unexpected presumed cardiovascular	1.14 (0.84 to 1.56)	-1699 (-510 to 1278)
Myocardial infarction	1.67 (0.80 to 3.46)	-2337 (-969 to 5674)
Congestive heart failure	1.30 (0.72 to 2.36)	-3115 (-957 to 2481)
Procedure related	2.20 (0.75 to 6.47)	-3115 (-1336 to 9380)
Arrhythmia	0.33 (0.10 to 1.06)	2337 (1169 to 2359681)
Stroke	0.75 (0.31 to 0.69)	6231 (-3037 to 1538)

The only statistically significant harmful effect of intensive therapy was on all-cause mortality, and in absolute terms it was small (the NNT/year being -367). By comparison, the mortality benefit (NNT/year) conferred by simvastatin in the high risk 4S (Scandinavian Simvastatin Survival Study) patients was 163.[3] After a mean follow up of 3.7 years, all ACCORD patients were switched to standard therapy, in which case the 5 year mortalities were similar.

Though the 'number-needed-to-harm'/year from such intensive glucose lowering appears negligible, the public and regulatory authorities have come to expect zero or close to zero harm for pharmacological treatments. Patients must therefore be fully informed of potential harms as well as benefits of aiming to attain such low glycated haemoglobin levels.

References: 1) Currie CJ et al 2010. Lancet 375:481-9; 2) ACCORD study group 2011. NEJM 364:818-28; 3) Kumana CR et al 1999. JAMA 282:1899-1901