Nature Reviews Cardiology | Published online 29 Jun 2017

IN BRIEF

DIABETES

Lower risk of cardiovascular death with canagliflozin

Patients with type 2 diabetes mellitus have an increased risk of cardiovascular and renal disease. The CANVAS Program Collaborative Group sought to determine the cardiovascular safety and efficacy of canagliflozin, a sodium–glucose cotransporter 2 inhibitor, by combining data from two trials (CANVAS and CANVAS-R) involving 667 centres across 30 countries. In both trials, patients were randomly assigned to receive canagliflozin or placebo. In total, 9,734 participants completed the trial in which they were enrolled. The primary composite outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke occurred less frequently in the canagliflozin group than in the placebo group. Furthermore, patients who received canagliflozin had a lower risk of hospitalization for heart failure and progression of albuminuria than those who received placebo. Notably, patients receiving canagliflozin had a greater risk of amputation, an observation that requires further investigation in future studies.

ORIGINAL ARTICLE Neal, B. *et al.* Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1611925 (2017)

VALVULAR DISEASE

Cadherin 11 in calcific aortic valve disease

Idiopathic calcific aortic valve disease (CAVD) has been associated with silencing of the *NOTCH1* gene. Valve interstitial cells from *Notch1*$^{+/-}$ mice have been shown to overexpress cadherin 11, a cell junction protein. To determine whether targeting cadherin 11 can prevent CAVD in *Notch1*$^{+/-}$ mice, Clark and colleagues administered either 10 mg/kg of SYN0012 (a cadherin 11-blocking antibody) or an IgG2a isotype control to *Notch1*$^{+/+}$ and *Notch1*$^{+/-}$ mice. *Notch1*$^{+/-}$ mice that received IgG2a had decreased ejection fraction velocity ratio compared with SYN0012-treated mice. On histology, SYN0012-treated *Notch1*$^{+/-}$ mice had thin leaflets (indicating healthy valve morphology), whereas mice that received IgG2a had hyperplastic leaflets with calcified regions. In addition, expression of IL-6, an inflammatory cytokine, was upregulated in leaflets from mice that received IgG2a compared with leaflets from SYN0012-treated mice. Together, these observations show that blocking cadherin 11 expression can prevent the pathological phenotype seen in *Notch1*$^{+/-}$ mice.

ORIGINAL ARTICLE Clark, C. R. *et al.* Targeting cadherin-11 prevents Notch1-mediated calcific aortic valve disease. *Circulation* http://dx.doi.org/10.1161/CIRCULATIONAHA.117.027771 (2017)

RISK FACTORS

Low educational attainment linked to high CVD risk

Socioeconomic factors such as education and income are thought to contribute to the risk of cardiovascular disease (CVD). Researchers in the Atherosclerosis Risk in Communities Study assessed the lifetime risks of CVD according to educational attainment in 13,948 individuals followed up from 1987 to 2013. An inverse dose–response relationship was identified between educational attainment and cumulative CVD risk. In men, lifetime CVD risks were 59.0% for grade school graduates, 50.9% for high school graduates, and 42.2% for college/professional school graduates. The lifetime CVD risks for women with these levels of education were 50.8%, 36.3%, and 28.0%, respectively. These results emphasize the need for strategies to minimize CVD inequalities related to differences in educational attainment.

ORIGINAL ARTICLE Kubota, Y. *et al.* Association of educational attainment with lifetime risk of cardiovascular disease: the Atherosclerosis Risk in Communities Study. *JAMA Intern. Med.* http://dx.doi.org/10.1001/jamainternmed.2017.1877 (2017)