

## Editorial

# Getting to the Heart of Diabetes: Translational Science to Interventional Cardiology

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For the first time since 1993, data from the Centers for Disease Control and Prevention (CDC) show a decrease in life expectancy and an increase in deaths particularly among people younger than 65. Life expectancy decreased by 0.1 year from 78.9 to 78.8 and the age-adjusted death rate increased 1.2% from 724.6/100,000 standard population to 733.1 for the total U.S. population from 2014 to 2015. (figure 1)[1]. This raises significant concerns over the increasing obesity and diabetes pandemic.

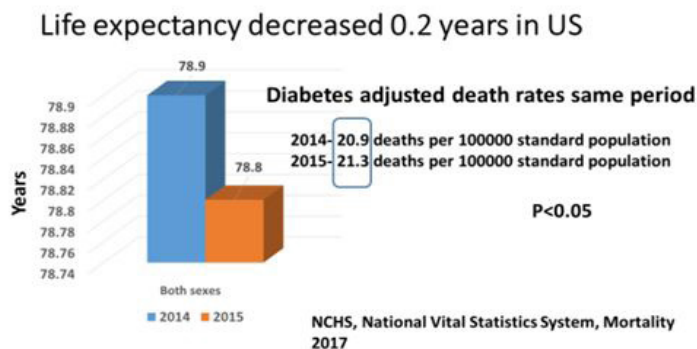


Figure 1: Diabetes continues to have increasing deaths, etiologies and exact causes are complex but obesity and diabetes with CV disease are major risk factors. The drop in overall life expectancy was seen for the first time since 1993, particularly among people younger than 65.

Using animal models in translational research, we were able to understand some of the mechanisms by which diabetes increases Cardiovascular (CV) risks in patients.

Starting as early as the postnatal period, overfeeding in small animals was found to be associated with an increase in metabolic CV risk. In an elegant small animal study, Li et al found overweight animals have an increased production of reactive oxygen species in the heart as well as an increase in left ventricular dimension associated with a reduction in left ventricular ejection fraction [2]. With caloric reduction, there was improvement in left ventricular dimension and ejection fraction. Additionally, overfeeding causes early changes in cardiovascular gene expression resulting in an abnormal increase in the production of endothelin [1], Matrix Metalloproteinase (MMP) [2], and collagen density along with a decrease in the production and function of the antioxidant enzyme SOD superoxide dismutase [3]. These studies from animal research support previous human long term cardiovascular health outcomes [4,5].

The delivery of micronutrients to cardiac and skeletal muscle depends on adequate perfusion. We have known for years that insulin increases nitric oxide production and dilates arterioles in normal subjects [6]. However, in the insulin resistant state, nitric oxide production is decreased due to endothelial cell dysfunction [7]. Recent studies evaluating the effects of overfeeding found that overfeeding reduces nitric oxide production and stimulates endothelin 1 function (vasoconstriction) in skeletal muscle [8]. (Figure 2) Additionally, prior studies found that insulin increases the sympathetic drive leading to an increased release of noradrenalin from postganglionic fibers [9]. Patients with type 2 diabetes were

frequently noted to have hypertension as noted in the SAVOR, EXAMINE, TECOS and EMPA-REG trials[10].

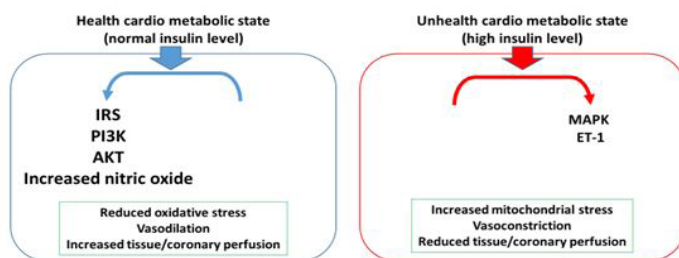
### Take home messages

- Healthy lifestyle early in life is important to long term survival
- Recent evidence from CDC finds reduced life expectancy in US population, first time since 1993 with increasing deaths in diabetes patients.
- Obesity & diabetes both improved by healthy lifestyle
- Revascularization options for ischemic heart disease treatment
  - FREEDOM trial (revascularization in diabetes patients)
    - 3% per year death, stroke or MI (CABG)

Figure 2: The importance of the FREEDOM trial has many important facts, but one that is frequently overlooked is the continued high CV event rate in the best know revascularization procedure for ischemic heart disease in diabetes.

In summary, translational changes seen in diabetes makes one consider the close inter-relationship of metabolic disease to cardiovascular disease. The increased incidence of obesity and diabetes and the decreased life expectancy require more than drug treatment to lower glucose level, blood pressure, and biomarkers. Lifestyle modifications remain the best option but at present, seem to be difficult to achieve by many people. The absolute risk reduction with medications remains suboptimal (figure 3).

### Translational view



**Figure 3:** This shows the important inter-relationship of diabetes and CV disease at a basic level.

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