RISK FACTORS OF CARDIOVASCULAR DISEASE	EXISTING EVIDENCE OF ASSOCIATION OF OXIDATIVE STRESS AND CARDIOVASCULAR RISK FACTORS			
Atherosclerosis	"…increased free radical production and impaired antioxidant protection are relevant to plaque activation"[21]. "Increased levels of O_2^- generation and attenuated NO mediated responses [have been] demonstrated in cholesterol-fed rabbits"[22,23].	"Chronic and acute overproduction of reactive oxygen species (ROS) form an integral part of the development of cardiovascular diseases (CVD), and in particular atherosclerosis"[24]. O_2^-levels are raised in WHHL (Watanabe heritable hyperlipidemic) rabbits[25].	Mitochondrial dysfunction and increased ROS production has been shown to associate with early atherosclerotic lesion formation[26]. Free oxygen radicals increase adhesion molecule expression in endothelial cells[27]. In monkeys with atherosclerosis, disease severity is related to O_2^- levels[28].	"ROS trigger extracellular matrix remodeling through regulation of collagen resorption, resulting in compromised plaque stability"[27,29]. "…antioxidant therapy has been shown to exert beneficial effects in hypertension, atherosclerosis, ischemic heart disease, cardiomyopathies and congestive heart failure"[30].
Smoking	"…atherogenic effects of smoking are mediated in part by free radical damage to lipids and possible breakdown of antioxidant status in cigarette smoking"[21].	"Cigarette smoke exposure increases oxidative stress as a potential mechanism for initiating cardiovascular dysfunction"[31,32].	"…smoking led to blunted hypertension, endothelial dysfunction, leukocyte activation with ROS generation, decreased NO bioavailability and mild cardiac hypertrophy in mice…"[33].	"…endothelial dysfunction in chronic smokers is at least in part mediated by enhanced formation of oxygen-derived free radicals"[34].
Endothelial dysfunction	"…endothelial dysfunction correlates with increased local ROS production and reduced superoxide dismutase activity"[34].	Atherosclerosis and lipid peroxidation in coronary arteries even at early stages are associated with evidence of endothelium dysfunction[35].	"…free radical stress can lead to cardiovascular disease by influencing the endothelial function"[36].	"Supplementation of antioxidant superoxide dismutase has been shown to improve endothelium dependent vasodilatation of coronary arteries"[37].
Hypertension	Increasing levels of oxidative stress by glutathione depletion can cause hypertension[38]. "Oxidative stress may play a significant role in the development of arterial stiffness" and remodeling in hypertensive subjects[39]. Hypertension is associated with increased vascular oxidative stress in a number of animal models of hypertension[40].	Increased ROS production is seen in patients with essential hypertension, renovascular hypertension, malignant hypertension and pre-eclampsia[41-44]. "In hypertension, lipid peroxidation by-products have been shown to be elevated, whereas levels/activity of anti-oxidant systems has been reported to be decreased"[45,46].	Several studies have shown an increase in O_2^- levels in hypertension[47,48]. "…classical antihypertensive agents such as ß-adrenergic blockers (Carvedilol), ACE inhibitors, AT_1 receptor antagonists, and Ca_2^+ channel blockers may be mediated, in part, by decreasing vascular oxidative stress"[49-51].	"…many of the adverse effects of hypertension on endothelial function may be reversed by intra-arterial infusion of anti-oxidants, such as vitamin C"[52]. Consistent with increased ROS production being a key feature of hypertension, treatment with antioxidants and SOD mimetics, attenuated endothelial dysfunction and lowered blood pressure[53,54].
Diabetes	A role for ROS in the endothelial dysfunction associated with diabetes was proposed in the early 1990s[55]. As a consequence of the overproduction of ROS, diabetes is related to oxidative stress[56].	"Hyperglycemia induces the overproduction of oxygen free radicals and consequently increases the protein oxidation and lipid oxidation;" thereby therapeutic interventions with antioxidants will be efficient[57]. People with diabetes have decreased levels of antioxidants[58-60]. Normalizing mitochondrial O_2^- has been shown to block pathways involved in hyperglycemic damage[61].	"…oxidative status and nitric oxide metabolism are affected in type II DM patients"[62] "…there is reduced antioxidative defense in type 2 diabetics with prominent cardiovascular complications"[63]. "Many biochemical pathways strictly associated with hyperglycemia can increase the production of free radicals"[64-66].	"Free radical reactions and non-enzymatic glycosylation may play important roles not only in the development of diabetes but also in its complications"[67]. "…chronic hyperglycemia can influence the generation of free radicals, which may lead ultimately to increased lipid peroxidation and depletion of antioxidants"[68].
Hyperhomocysteinaemia	"Patients with hyperhomocysteinaemia exhibit endothelial dysfunction and elevated oxidative stress"[69,70].	Hyperhomocysteinemia causes reduction of NO bioavailability through the generation of superoxide[71,72].	One of the primary causes of cardiovascular alterations characteristic of hyperhomocysteinemia is its oxidative stress production[73].	"Acute hyperhomocysteinemia impairs endothelial function and increases arterial stiffness"[74].

Table 1 | Existing evidence of association of oxidative stress and cardiovascular risk factors