Recent data from the studies of the Japanese atomic bomb survivors have demonstrated a statistically significant association between radiation dose and mortality from non-cancer disease. Some of these non-cancer diseases include cancer precursor lesions, such as myeloplastic syndrome, but the significant association is largely derived from the effect of radiation on cardiovascular disease. It is also in part due to the effect on respiratory and digestive diseases. The small relative risk observed for disparate and seemingly unrelated disease categories naturally raises a question regarding the causality of the statistical association, but detailed analyses of the atomic bomb survivor data have ruled out the possibility of confounding, bias, cohort selection, or disease misclassification. There are features of the non-cancer disease risk that have important implications for radiobiology and radiological protection. The excess non-cancer risk is evident at doses lower than levels traditionally considered inducing deterministic (or non-stochastic) effects that are assumed to result from “direct” changes in the exposed cells. A persistent temporal pattern of the non-cancer risk, apparently dependent on age, resembles the pattern well known for radiation-induced solid cancer risk. These suggest that we need to consider new, yet to be identified mechanisms in the development of radiation-induced diseases. The relative risk of non-cancer disease associated with radiation dose is rather small – about one-third of that of radiation-associated cancer. However, when the small relative risk is applied to cardiovascular disease and other non-cancer diseases that have high background rates, the absolute number of excess cases attributable to radiation will be substantial – hence public health concern.

Some corroborating epidemiological data on the non-cancer effects are available from populations other than the atomic bomb survivors. Excess mortality from cardiovascular disease is known to occur as sequelae to radiotherapy for cancer, such as Hodgkin’s disease and breast cancer that results in high-dose irradiation of the heart. The heart diseases observed after cancer radiotherapy are not limited to pericardial changes that have been specifically associated with high doses but also include myocardial infarction. At moderate doses, higher than expected mortality of cardiovascular disease has been found in some, though not all, of the studies of patients irradiated for benign diseases. More important evidence comes from a recent analysis of data from patients irradiated for peptic ulcer, which showed a significant dose response for coronary heart disease that was not confounded by smoking or other risk factors. In a low to moderate dose range, excess cardiovascular mortality has also been found in early radiologists and radiological technologists in the US, but the lack of dose data in these populations currently precludes risk estimates. When dose reconstructions are completed in some of these populations, more informative data will be forthcoming. At much lower dose, studies of nuclear industry workers and Chernobyl clean-up workers have reported excess cardiovascular diseases mortality, although the possibility that the observed association is attributable to factors other than radiation cannot be discarded. Very little data exist on radiation effects on digestive or respiratory disease.

The non-cancer disease effects are thus evident at a modest dose, especially for cardiovascular disease, but remain uncertain at a low dose. Further data from the ongoing studies of the atomic bomb survivors and other irradiated populations will help clarify the risk at a low dose. There is currently a problem of scientific acceptance of the non-cancer effects in relation to low-dose radiation, as there is no established biological model. However, several plausible mechanisms exist, particularly for atherosclerosis. For example, recent molecular biological studies have suggested that cancer and atherosclerosis may share a common molecular pathway in the disease development and progression. This is supported by the monoclonal origin of atherosclerotic plaques. Also, a recent paradigm states that atherosclerosis is an inflammatory process involving endothelial damage and dysfunction. This may be a route in the development of myocardial infarction in relation to radiation. Atherosclerosis is a multifactorial disease process resulting from a lifelong interaction among genetic, environmental and behavioral factors. As with carcinogenesis, radiation may accelerate the atherosclerotic process by interacting with other factors in the disease pathways. Further research in this area is awaited, as a useful insight into the low-dose risk will likely come from understanding of the fundamental mechanisms.