Signe Westring Worm, PhD dissertation 29.01.2009
The thesis is based on the three original papers published in peer-reviewed journals and in addition a review, available on the internet, is included.

The introduction of combination antiretroviral therapy (cART) in 1996 has dramatically improved the survival of HIV-infected individuals and significantly reduced HIV-related morbidity and mortality. However, this efficient treatment is associated with metabolic side effects; and a high prevalence of potential CVD risk factors have been reported. The clustering of many of the metabolic side effect associated with the use of cART, has striking similarities to the metabolic syndrome (MS), a term used to describe a clustering of risk factors for cardiovascular disease (CVD). Recent studies has shown an association between exposure to cART and a risk of myocardial infarction (MI), but also HIV per se has a yet not completely understood role for the risk of CVD.
Concepts for the management of CVD in the general population needs validation amongst HIV-infected individuals, before the concepts or entities can be adapted in to daily clinical care. The analysis of the MS, recognised as a CVD risk enhancer by the NCEP guidelines, is such an entity. This PhD thesis discussed the importance of identifying all CVD risk factors, and not only the risk factors in the MS definition, as we found a strong association between an increasing number of the risk factors in HIV-infected patients and an increased CVD risk. The presence of the MS in HIV-infected individuals did not appear to increase the CVD risk over and above that conferred by the components of the syndrome separately. The identification of one CVD risk factor should immediately lead the physician to search for other CVD risk factors as an increasing number of risk components is strongly associated with a risk of CVD.
Another concept discussed was the 'DM as a CHD risk equivalent'. We compared the impact of development of DM to the impact of pre-existing CHD for the future risk for CHD. We found DM to be an important and independent risk factor for CHD in HIV-infected populations, but it does not appear to confer the same risk as pre-existing CHD. We have evidence to suggest that DM is becoming an increasing problem among those infected with HIV, and we have recently reported an increase of DM among patients under follow-up from 3.8% in 1999/2000 to 5.2% in 2005/6. Regardless of whether diabetic patients have a risk of CHD identical to that of patients with prior CHD, the absolute risk of CHD in this subgroup of patients remains high. Thus, we suggest that targets for interventions among HIV-infected individuals should be based on the entire risk factor profile rather than just the presence or absence of DM. *And*, it is still of great importance to screen for this modifiable risk factor and to intervene against the development of DM.
The thesis has further discussed that not all of the risk associated with cART can be directly explained through classical metabolic mechanisms. Although thymidine analogues from the NRTI drug class have been associated with the development of IR, DM and dyslipedemia, these were not associated with an excess risk of MI. Unexpectedly, we found abacavir, a drug with no reported metabolic side effect, significantly associated with an increased risk of MI. Guidelines on treatment of the HIV-infection have already notified the signal between abacavir and MI, but requires additional confirmation of our findings. Further investigations are initiated to explore the biological explanation for the association between abacavir and MI, especially focusing upon the importance of inflammation amongst HIV-infected individuals.