evaluation of candidate genes/SNPs. The availability of GWAS should, theoretically, solve the second problem. We have very few GEWIS (genome-wide interaction study) on occupational exposures and they suffer even more than candidate-gene studies from sample size and also from lack of available studies for replication.

Results Apart from exposures, GEWIS may help identify new diseases genes since many may only have an effect in combination with exposure. In addition GEWIS should provide a much more complete evaluation of specific pathways, e.g. oxidative stress. The use of a specific pathway-based approach is still valuable if based on biological knowledge. Contrary to major advances brought by molecular epidemiology, studies on gene-environment interactions have proven to be complex and with few well-established findings.

Conclusions I will discuss reasons for this, discuss recent changes from the use of genome-wide analyses and compare with earlier approaches based on evaluations of interactions of occupational exposures with few candidate genes. I will provide examples from a recent GEWIS on occupational asthma.

Objective: Derivation of the exposure-response curve at low (occupational) exposures is often troubled by the fact that within epidemiological investigations power to discern the exposure-response curve (ERC) at low exposure levels is often limited. Conversely, we often observe non-linear exposure-response curves at the higher end of the exposure range which amongst others may be due to metabolic saturation.

Method: Derivation of the exposure-response curve at low (occupational) exposures is often troubled by the fact that within epidemiological investigations power to discern the exposure-response curve (ERC) at low exposure levels is often limited. Conversely, we often observe non-linear exposure-response curves at the higher end of the exposure range which amongst others may be due to metabolic saturation.

Results: Studies on benzene exposed occupational populations have indicated 1) non-linear production of reactive metabolites at low levels of exposure; 2) non-linear production of benzene-oxide adducts; and 3) non-linear associations between benzene and hematotoxicity. This is of particular interest as there have been indications of a possible non-linear association between benzene and leukaemia in epidemiological studies.

Conclusions: The evidence on a molecular and clinical level may provide evidence for a possible non-linear association between benzene and leukaemia and provides promise that molecular data can directly be integrated in epidemiological risk analyses to inform ERCS.