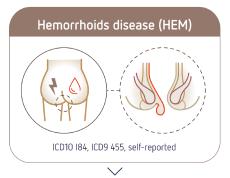
#### Visual Abstract



# GWAS meta-analysis



5 study cohorts: 218,920 cases, 725,213 controls

### Results



102 novel genome-wide significant loci with 819 candidate genes



100 prioritized genes > based on tissue and pathway enrichment, as well as gene expression, analyses



Two missense variants; functional effects observed *in vitro* for F608S (rs2186797) in ANO1 protein



Polygenic risk score analysis



(Genetic) correlation analyses with other diseases/traits

#### Background

Hemorrhoidal disease affects a large and silently suffering fraction of the population but its etiology, including suspected genetic predisposition, is poorly understood. No genome-wide significant association has been described until today.

## Conclusion:

Hemorrhoids disease has a genetic component that compares to that of other complex diseases and that predisposes to smooth muscle, epithelial and connective tissue dysfunction. Patients with a very high polygenic risk score have an increased risk for recurrent invasive procedures and a younger age of onset.