

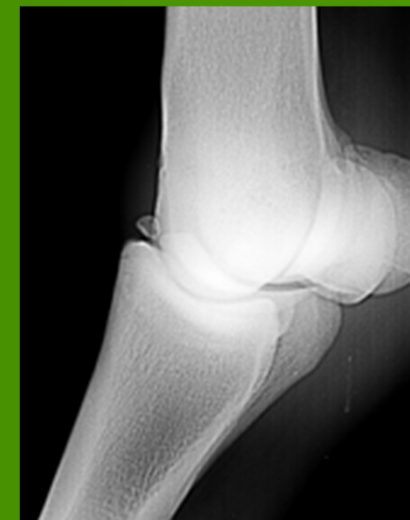


## A genome-wide association scan for loci affecting osteochondrosis in German Warmblood horses

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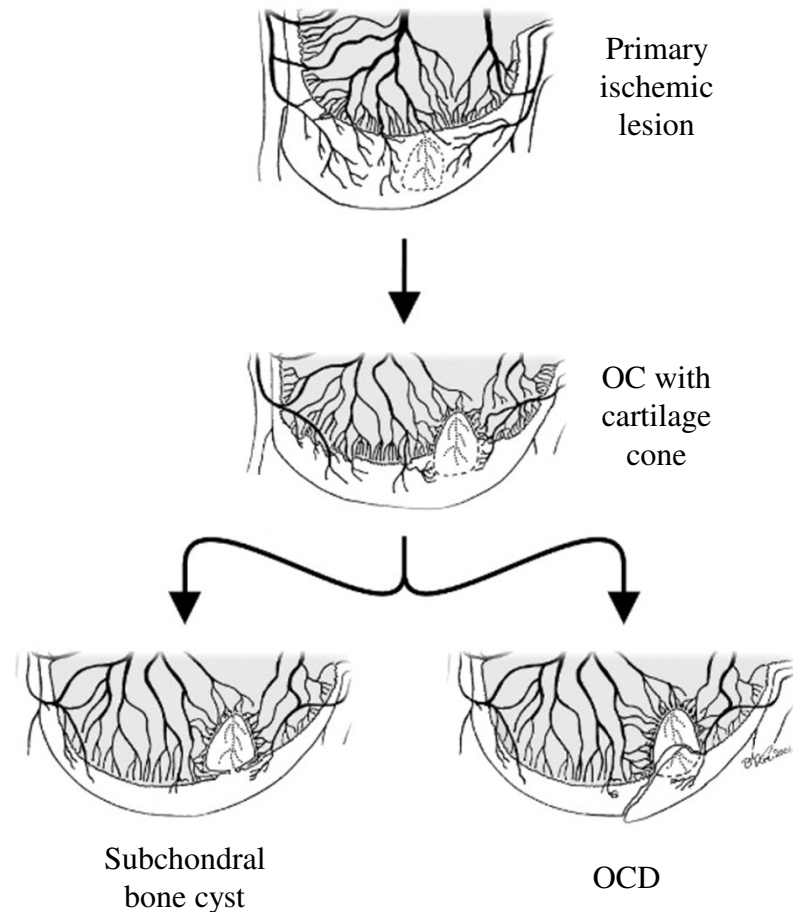




# Introduction

## Osteochondrosis - Definition

- **Common** joint disorder in young domestic animals and humans
- Focal disturbance of enchondral ossification
- Osteochondrosis dissecans (OCD): Presence of an osteochondral fragment (chip)
- Predilection sites\*
  - Caud. aspect of the prox. articular surface of the humerus
  - Medial aspect of the condyle of the humerus
  - Lateral trochlear ridge of the femur
  - Medial condyle of the femur
  - Intermediate ridge of the distal tibia
  - Lateral trochlear ridge of talus
  - Dorsal aspect of the distal metacarpus and metatarsus
- Multifactorial: **Hereditiy**, rapid growth, anatomic conformation, trauma, dietary imbalances...



\*according to McIlwraith (2002) and Pool (1993)



# Introduction

## Osteochondrosis – Prevalence and Heritability

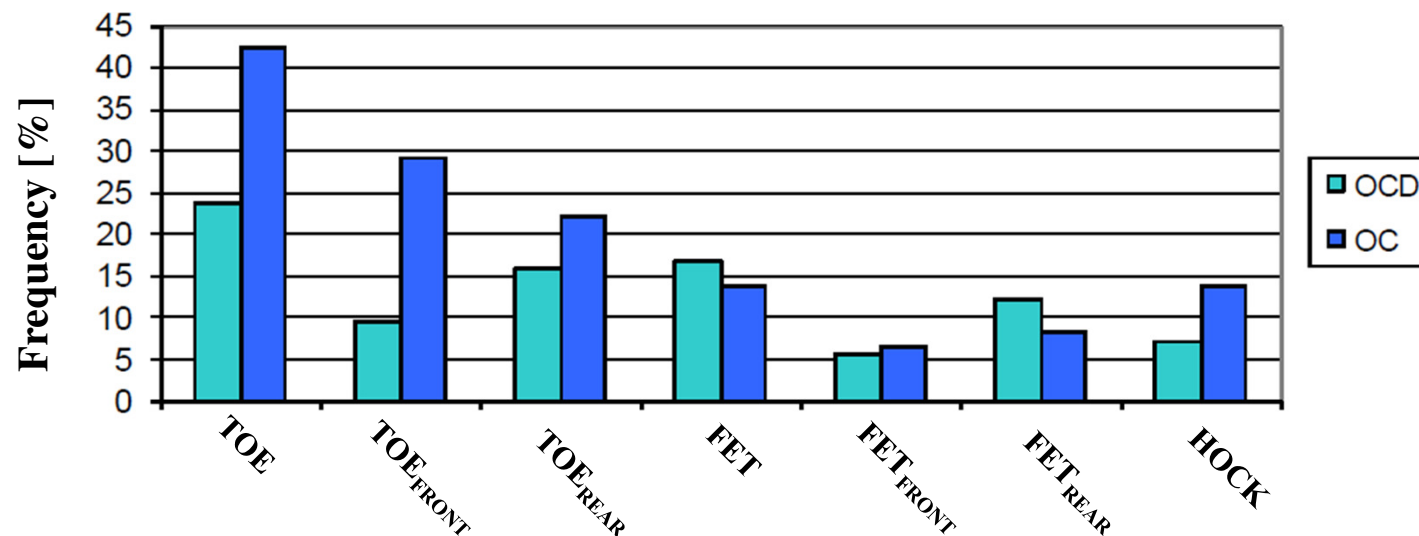
Author	Breed	Joint	Prevalence	Heritability
Winter <i>et al.</i> (1996)	German Riding Horse		11 %	0.06-0.07
Willms <i>et al.</i> (1999)	German Riding Horse	Toe, hock	5 %	0.45-0.64
Pieramati <i>et al.</i> (2003)	Maremmanos	Stifle, hock, fetlock	16.6 %	0.19-0.58
Stock <i>et al.</i> (2005)	Hanoverian Warmblood	Fetlock Hock	20.8 % 9.6 %	0.08-0.14 0.19



# Material and Methods

## Animals and phenotypes

- X-ray protocols of 1,162 stallions presented for licensing in the years 2005 to 2008 in four German breeding organizations: Hanoverian Society, Holsteiner Verband, Oldenburger Horse Breeders Society, Trakehner Verband
- Osteochondrotic findings (OC and OCD) were recorded for stifle, hock, fetlock and toe and coded as a binary trait (1 = at least one finding in the respective localization vs. 0 = no finding )
  - Assignment to predilection sites?
  - The localization „toe“ includes the fetlock joint and is not a common definition!





# Material and Methods

## Influencing factors

- Logistic regression (procedure glm in R), logit-link function
- Significant covariates and fixed effects were included in the respective GWAS

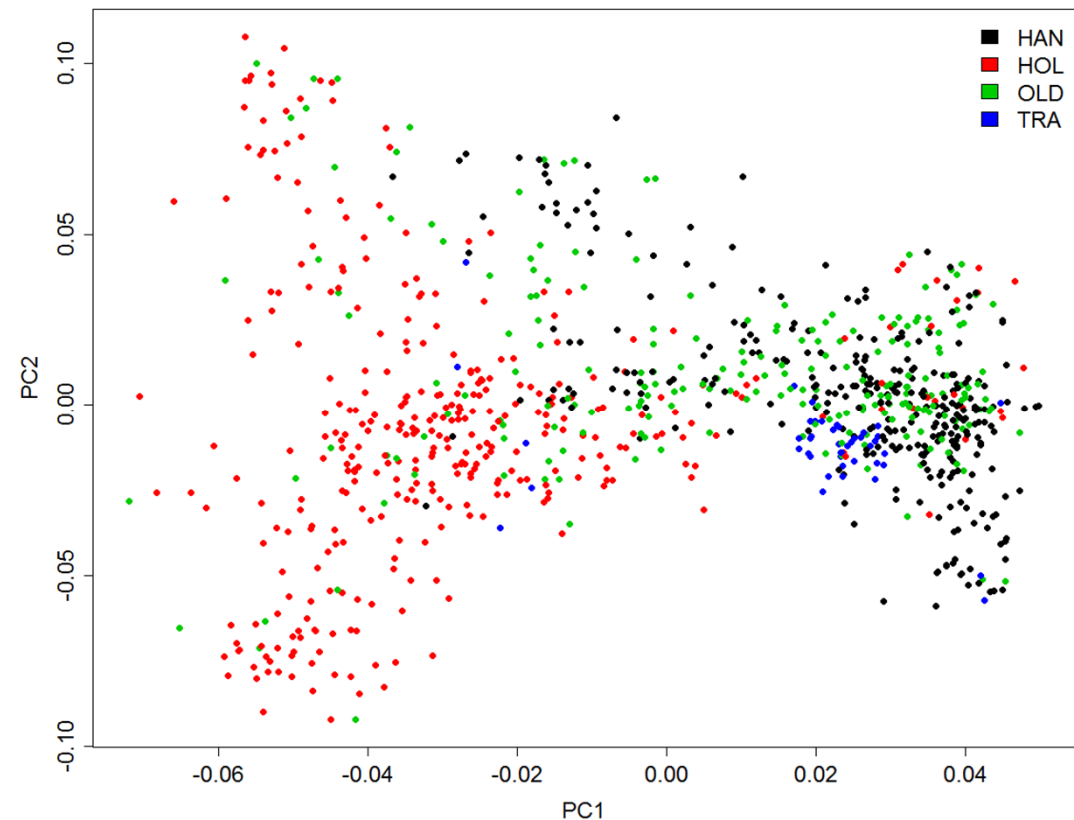
	Age	Height	Year	Principal consultant	Breeding Organisation
OCD <sub>TOE</sub>					
OCD <sub>TOE-FRONT</sub>					
OCD <sub>TOE-REAR</sub>					
OCD <sub>FET</sub>					
OCD <sub>FET-FRONT</sub>					
OCD <sub>FET-REAR</sub>					
OCD <sub>HOCK</sub>					



# Material and Methods

## GWAS

- Genotyping: 943 stallions typed with Illumina EquineSNP50 Bead Chip featuring 54,602 SNPs
- Preprocessing: Individual callrate  $\geq 0.95$ , SNP callrate  $\geq 0.9$ , MAF  $\geq 0.05$ ,  $p_{\text{HWE}} \leq 10^{-9}$ , filtering for individuals with a pairwise IBS  $> 0.95$ 
  - 916 individuals
  - 44,410 SNPs
- Principal components to correct for population structure\*
- Correction of p-values using genomic control



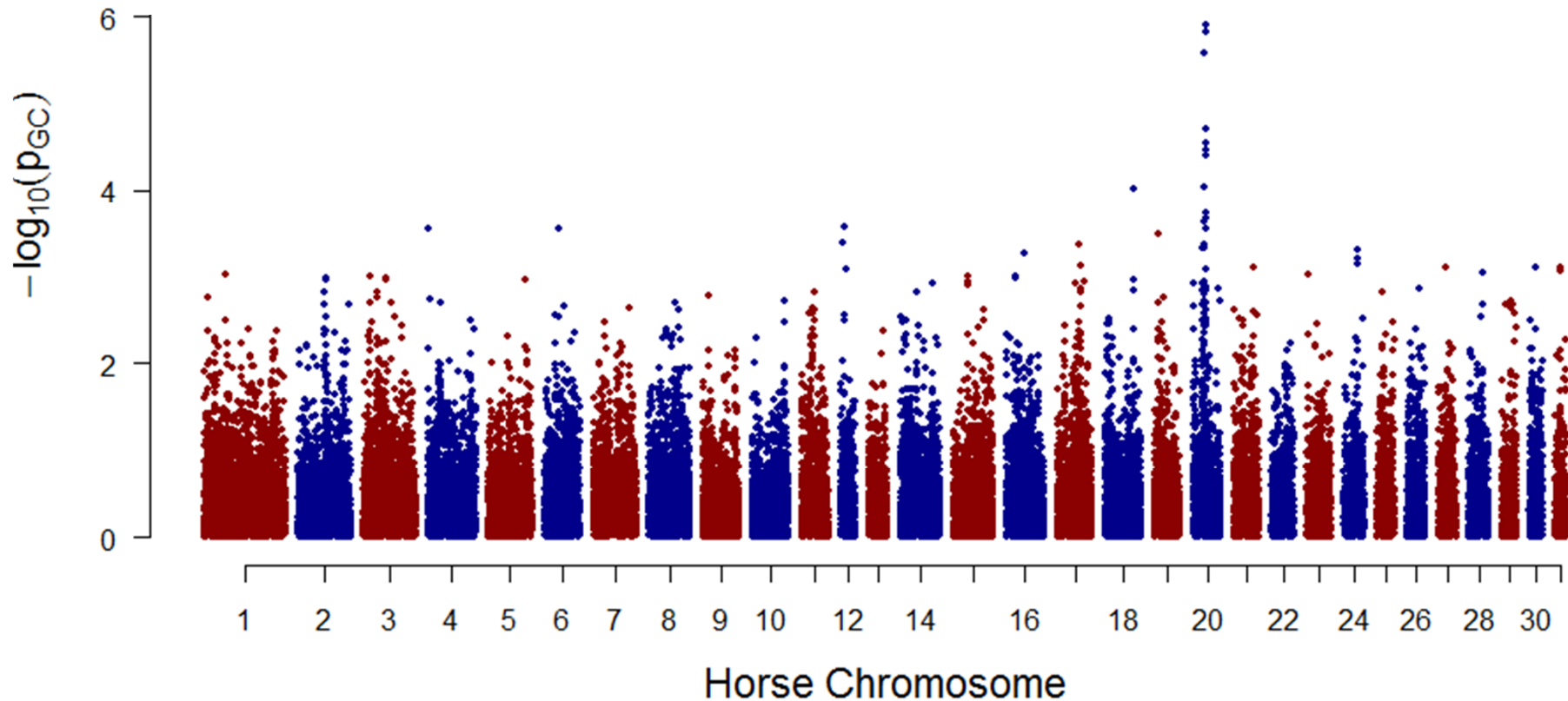
\*according to Price *et al.*, 2006 as implemented in GenABEL by Aulchenko *et al.*, 2007



# Results and Discussion

## GWAs results for $OCD_{TOE}$

- Phenotype: at least one OCD-finding in one of the toes including fetlock
- Fixed effects: Year of licensing
- Estimated inflation factor  $\lambda$ : 1.04

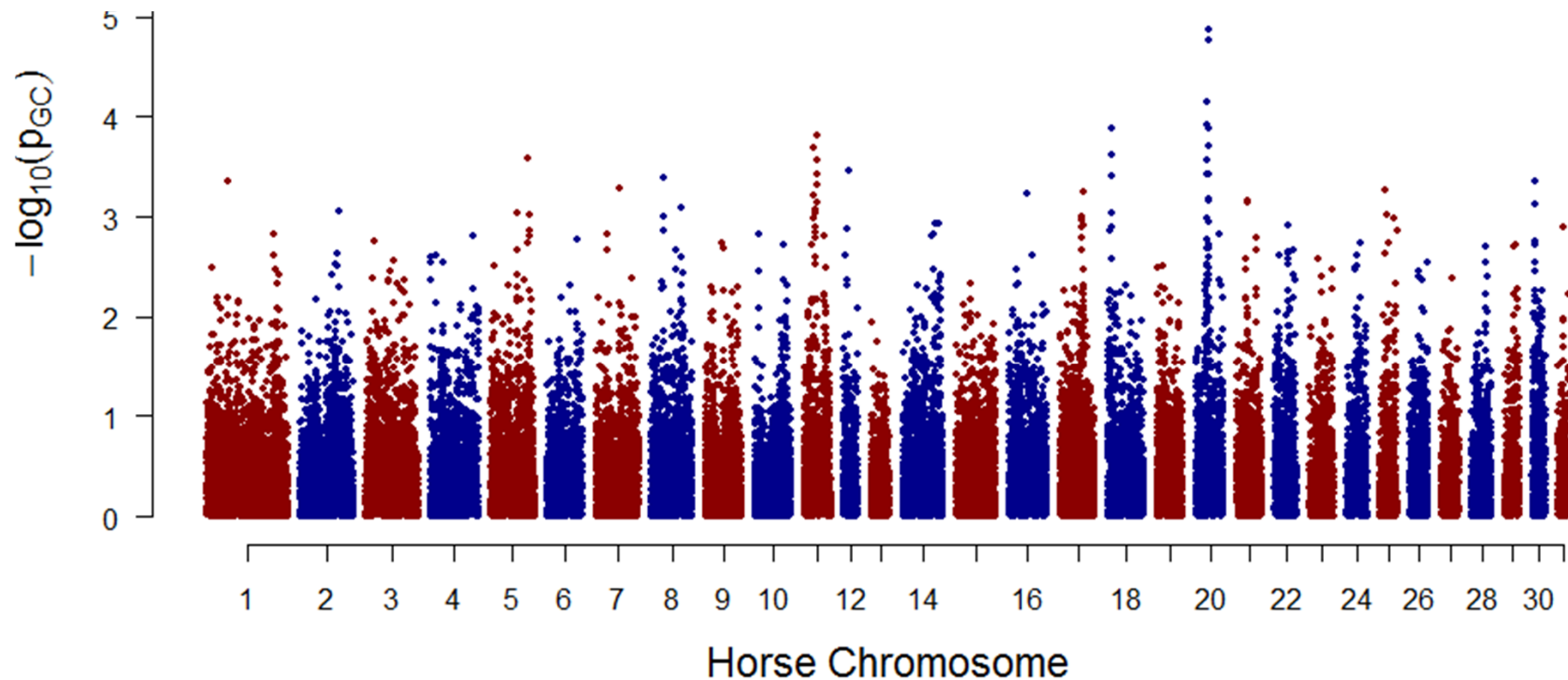




# Results and Discussion

## GWAs results for $OCD_{FET}$

- Phenotype: at least one OCD-finding in one of the fetlock joints
- Fixed effects: Year of licensing and breeding organization
- Estimated inflation factor  $\lambda$ : 1.05



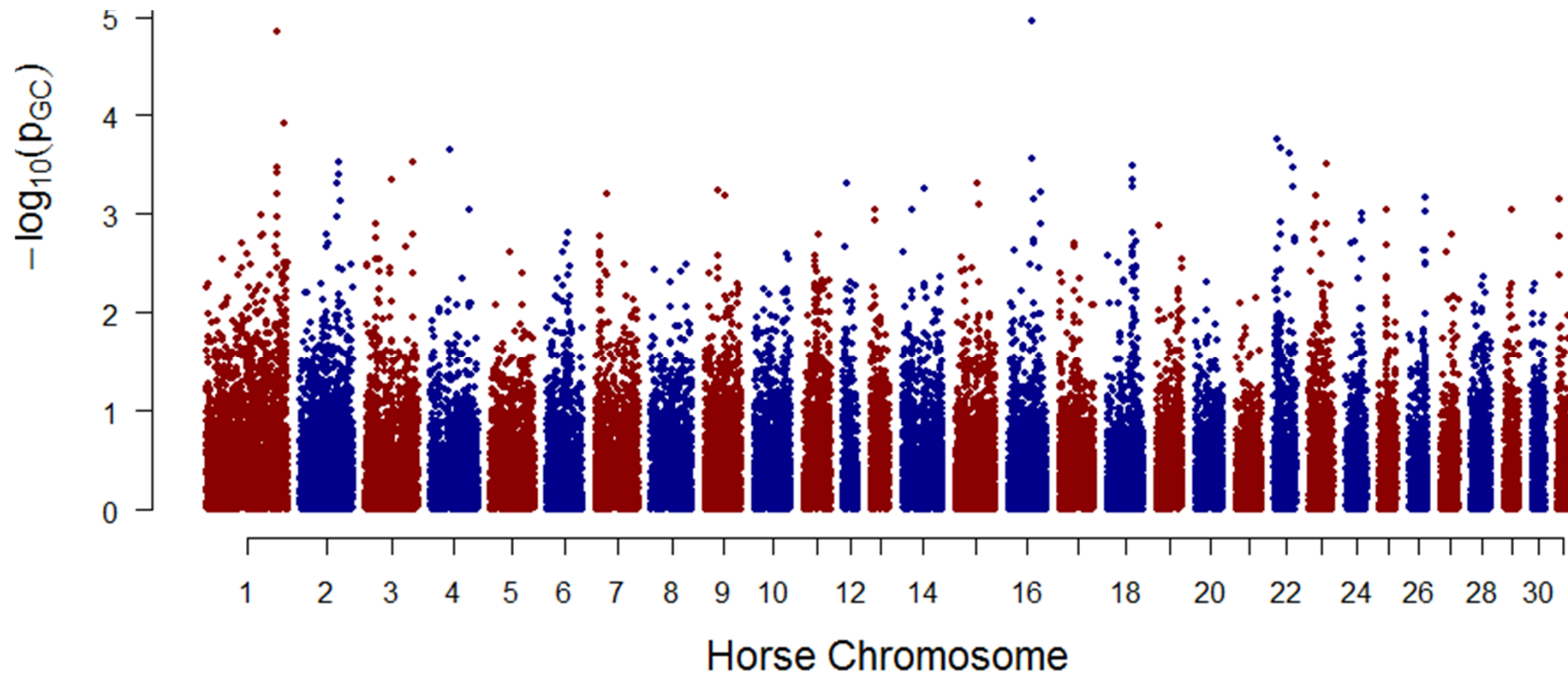




# Results and Discussion

## GWAs results for $OCD_{HOCK}$

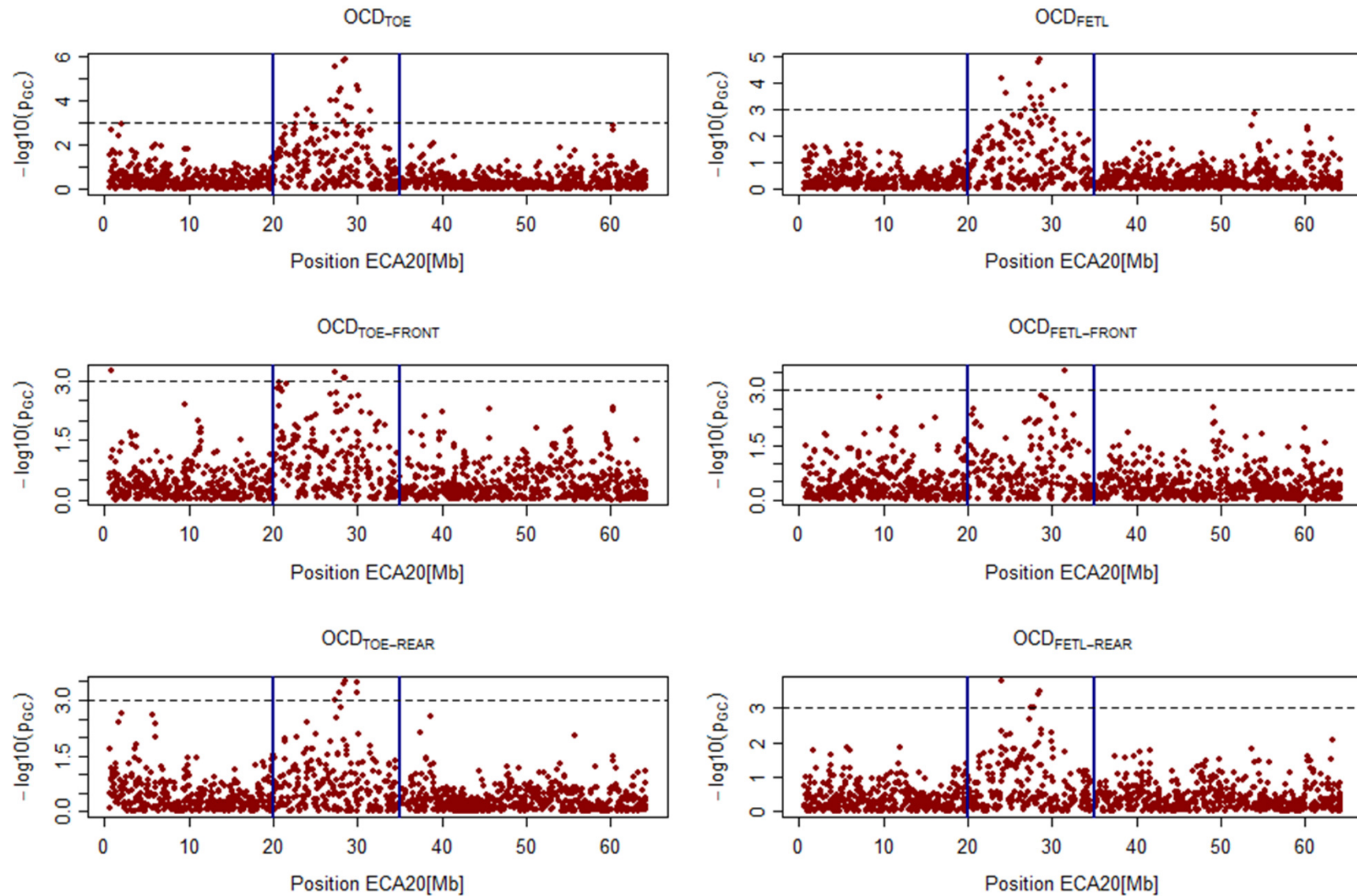
- Phenotype: at least one OCD-finding in one of the hock joints
- Covariate: Age
- Estimated inflation factor  $\lambda$ : 1.05





# Results and Discussion

## A major QTL on ECA20?





## Conclusions and Summary

- The use of X-ray protocols as a source of phenotypic information has some disadvantages making it necessary to define more general phenotypic classes.
- One significant and several suggestive QTL affecting the liability to OCD have been identified within the German Warmblood population.
- We hypothesize that a major QTL resides on ECA20 that generally affects the liability to OCD in the distal limb.



# Acknowledgment

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**...your for your attention !**

