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THE UNIVERSITY of EDINBURGH
The Royal (Dick) School of Veterinary Studies

A method for estimating mutation frequencies based on DNA test results in pedigree dogs

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UKRI Biotechnology and Biological Sciences Research Council

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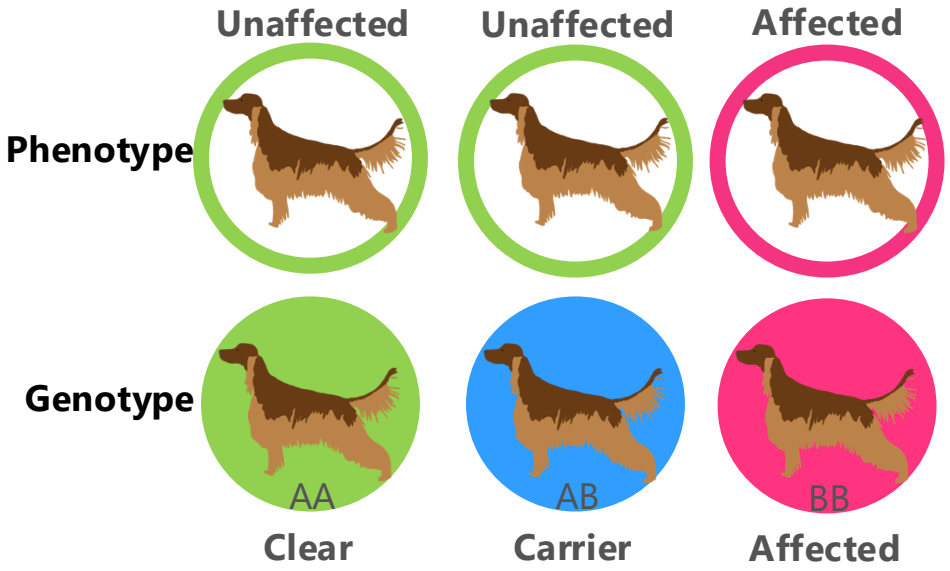
DNA testing



- DNA testing identifies disease-causing alleles
- Results are recorded by RKC for population monitoring

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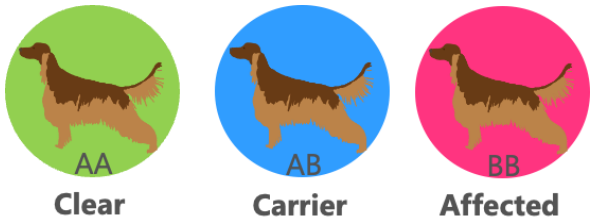
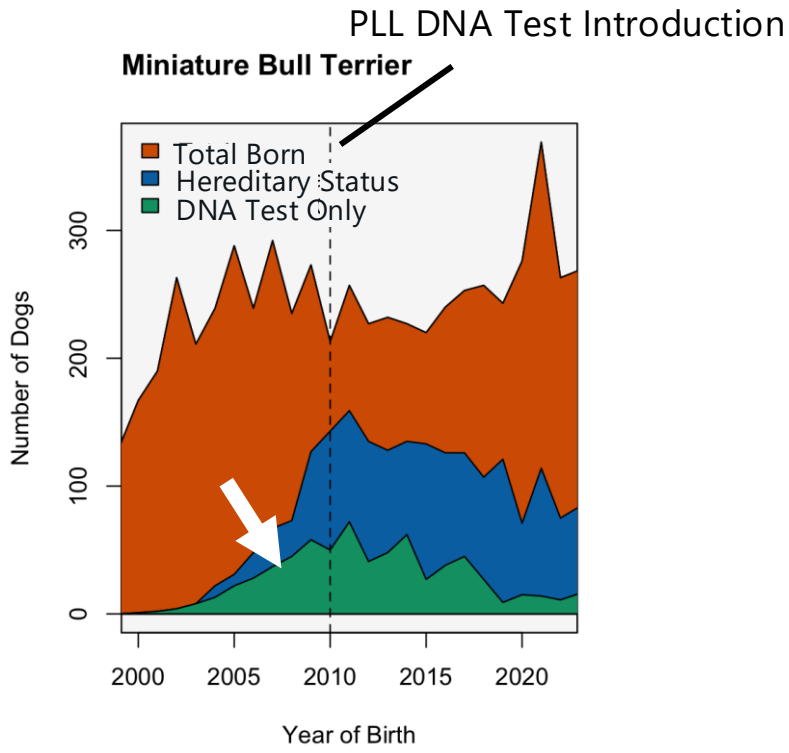
However, DNA testing is not always widespread





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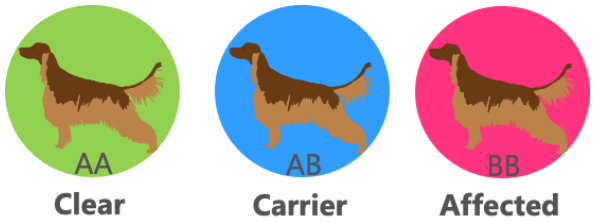

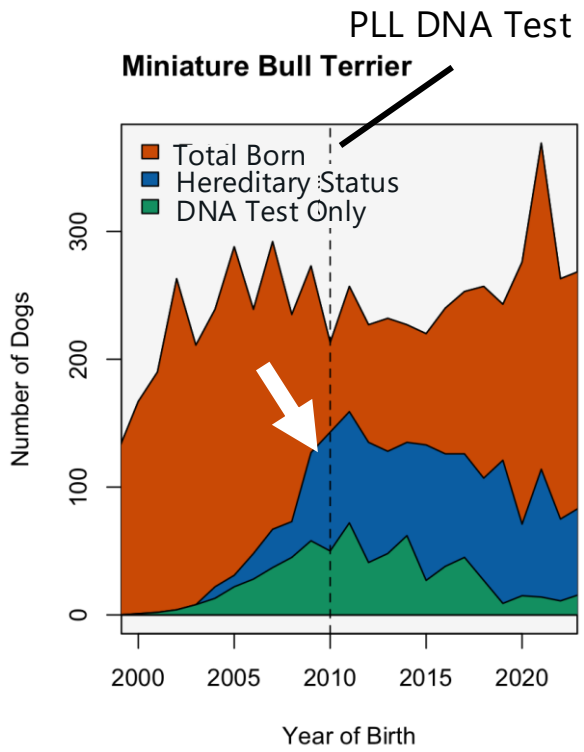

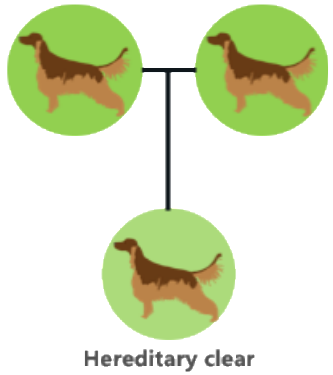

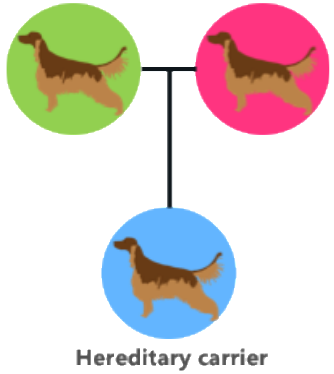

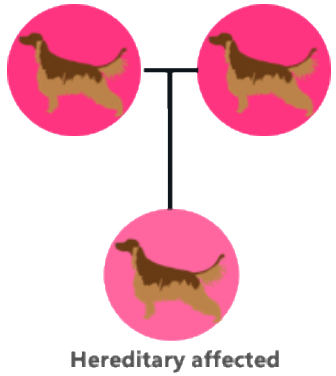

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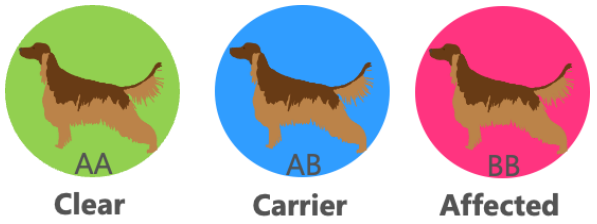

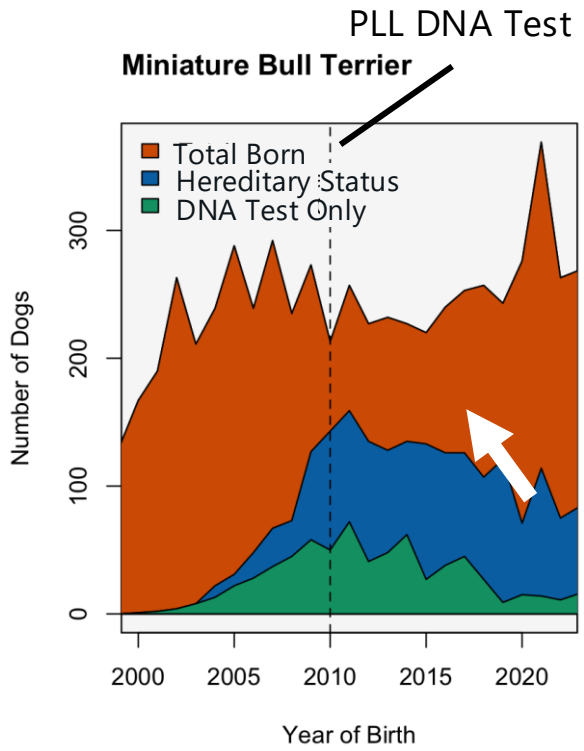

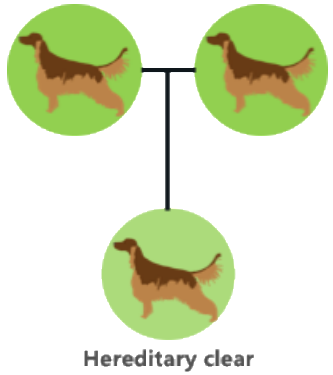

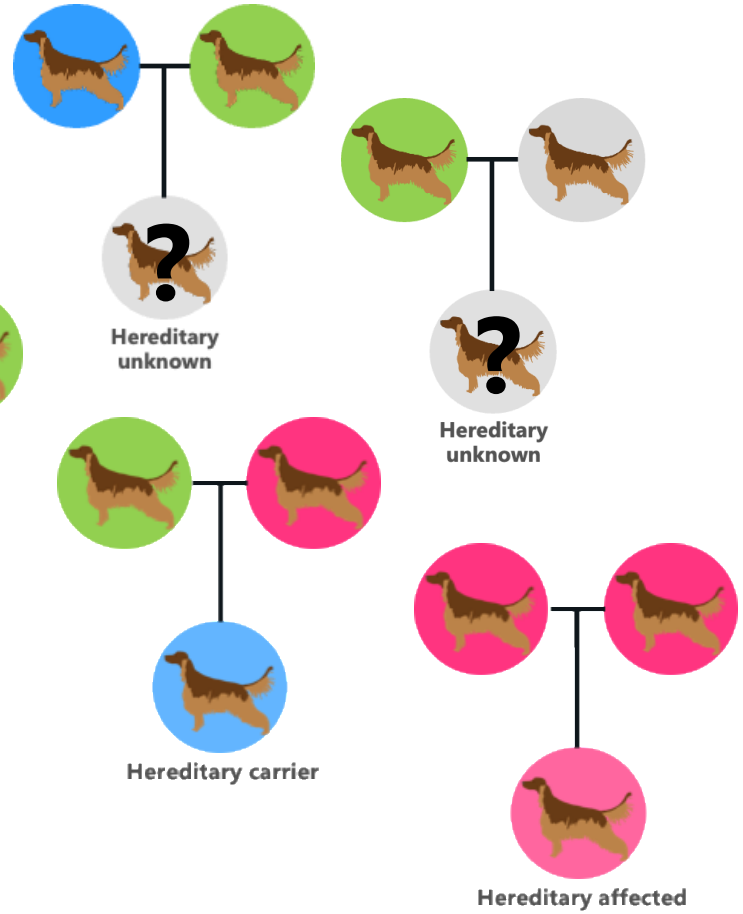

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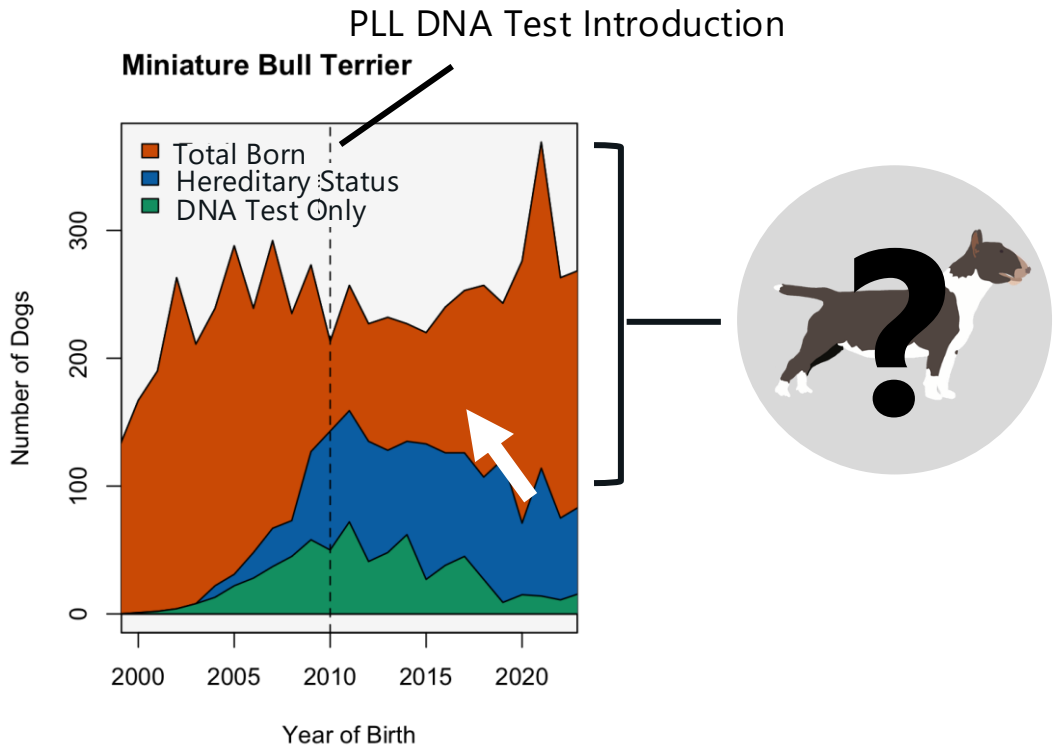

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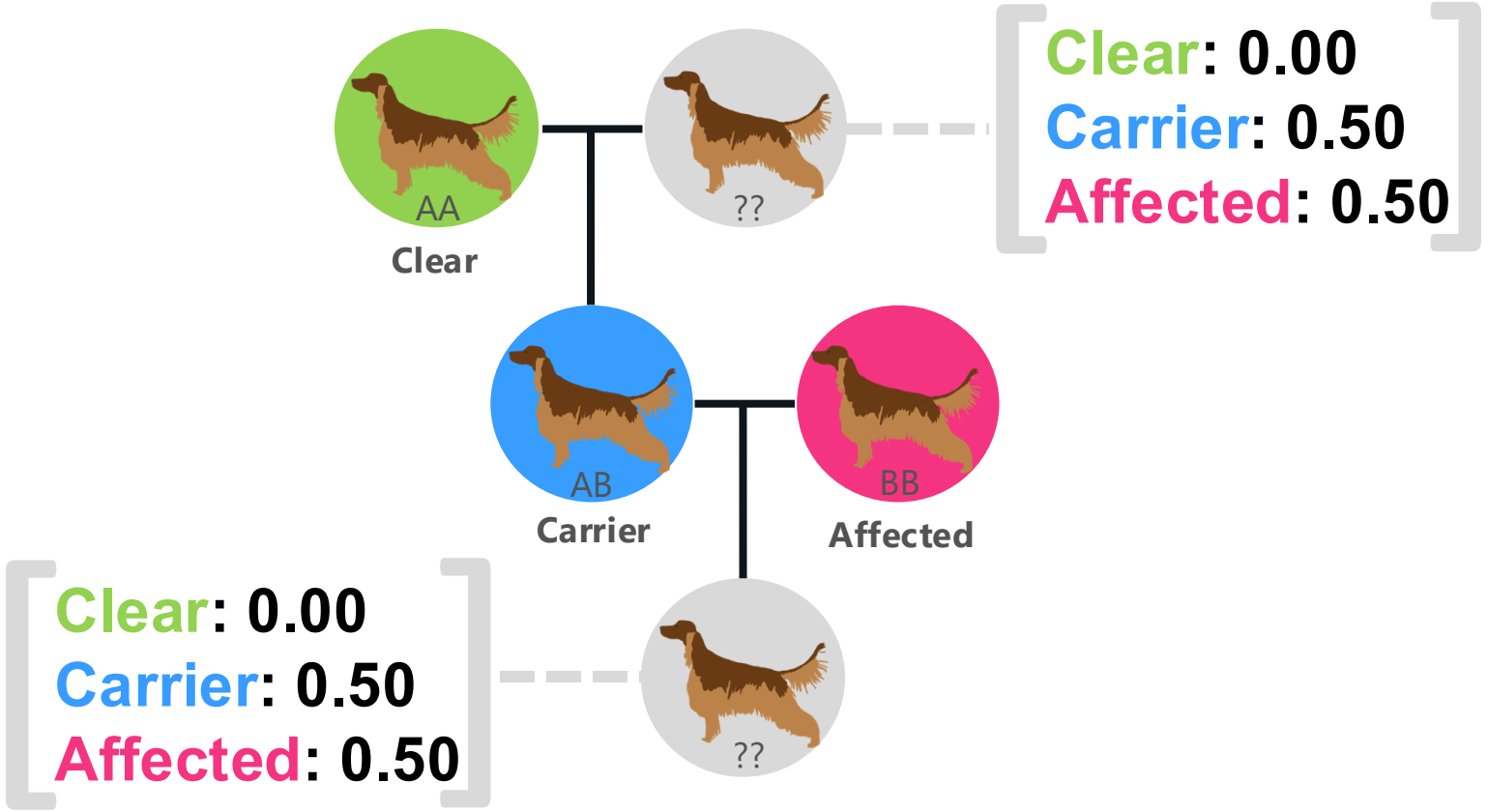
AA
Clear
??
Clear: 0.00
Carrier: 0.50
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AB
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BB
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Clear: 0.00
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Affected: 0.50
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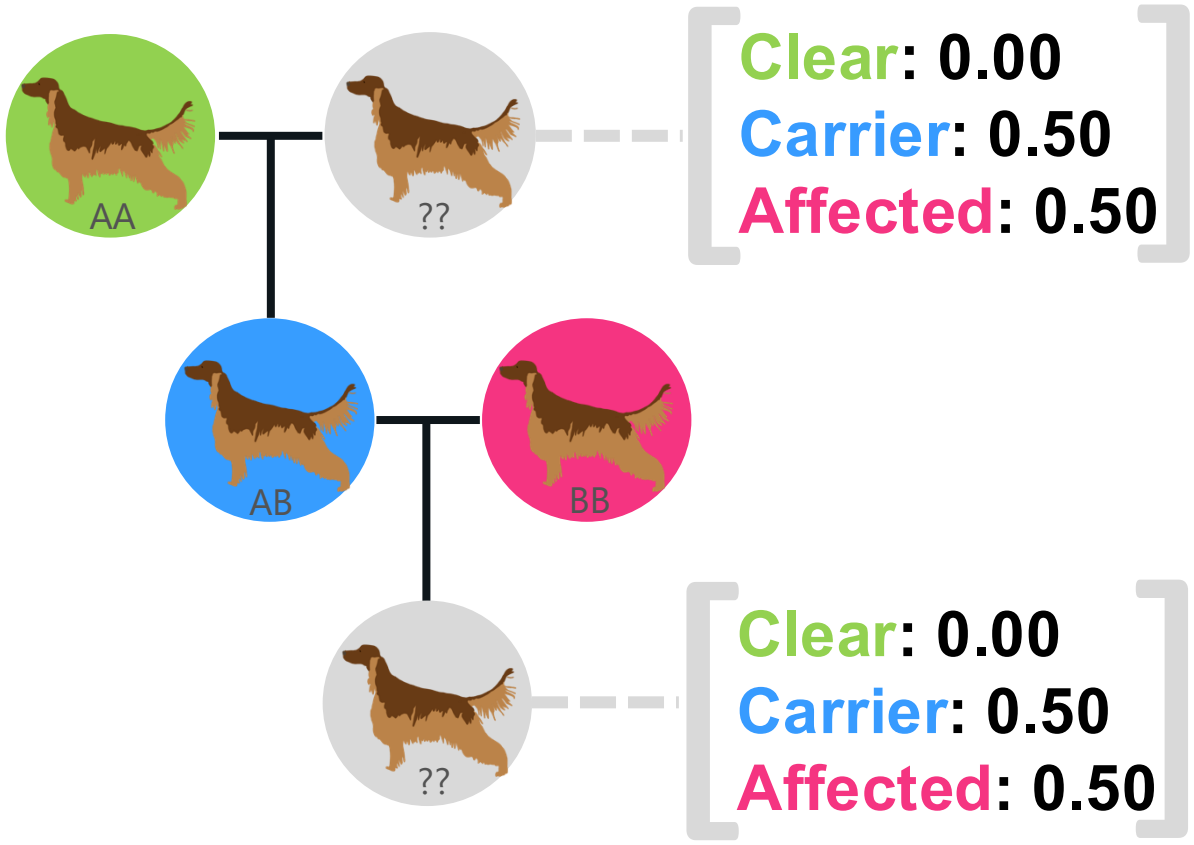

Aims

- To improve population monitoring of disease-causing alleles.
- To provide insights into the genetic processes that have driven the changes in allele frequencies over time.

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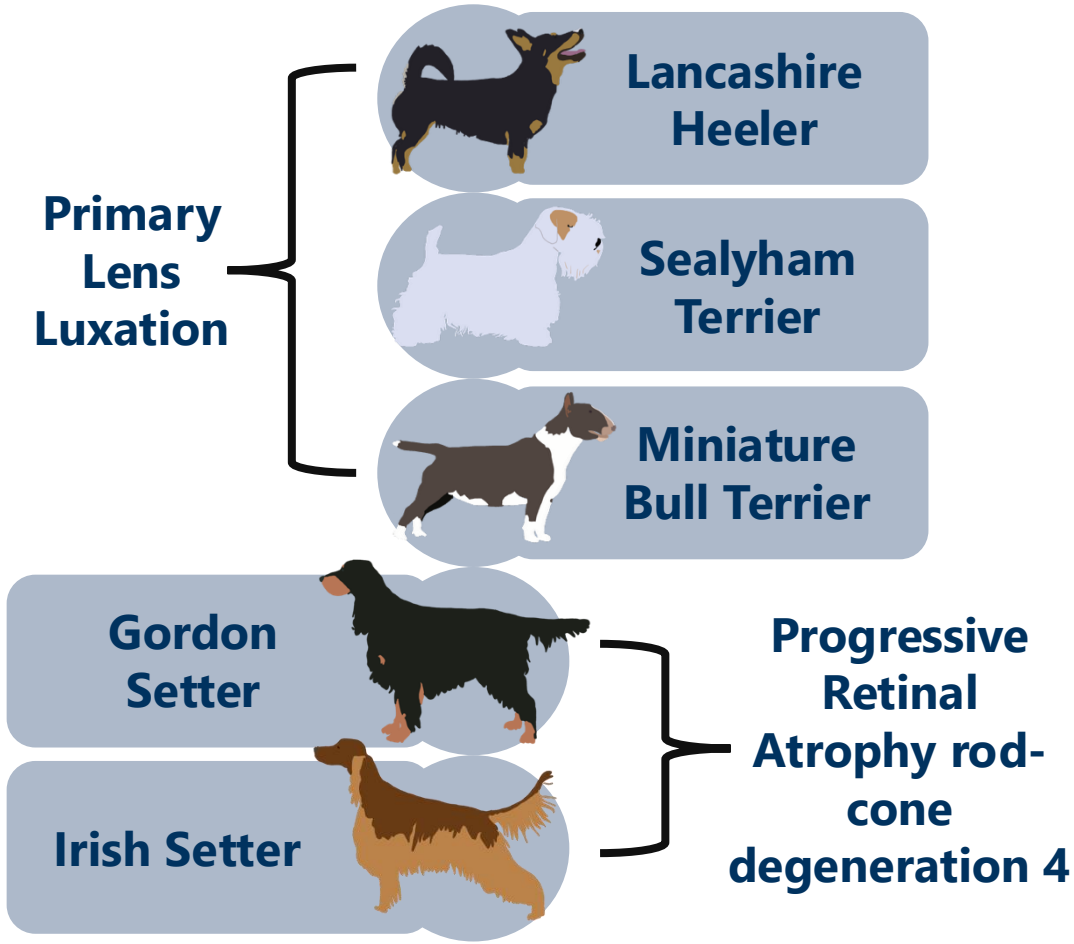
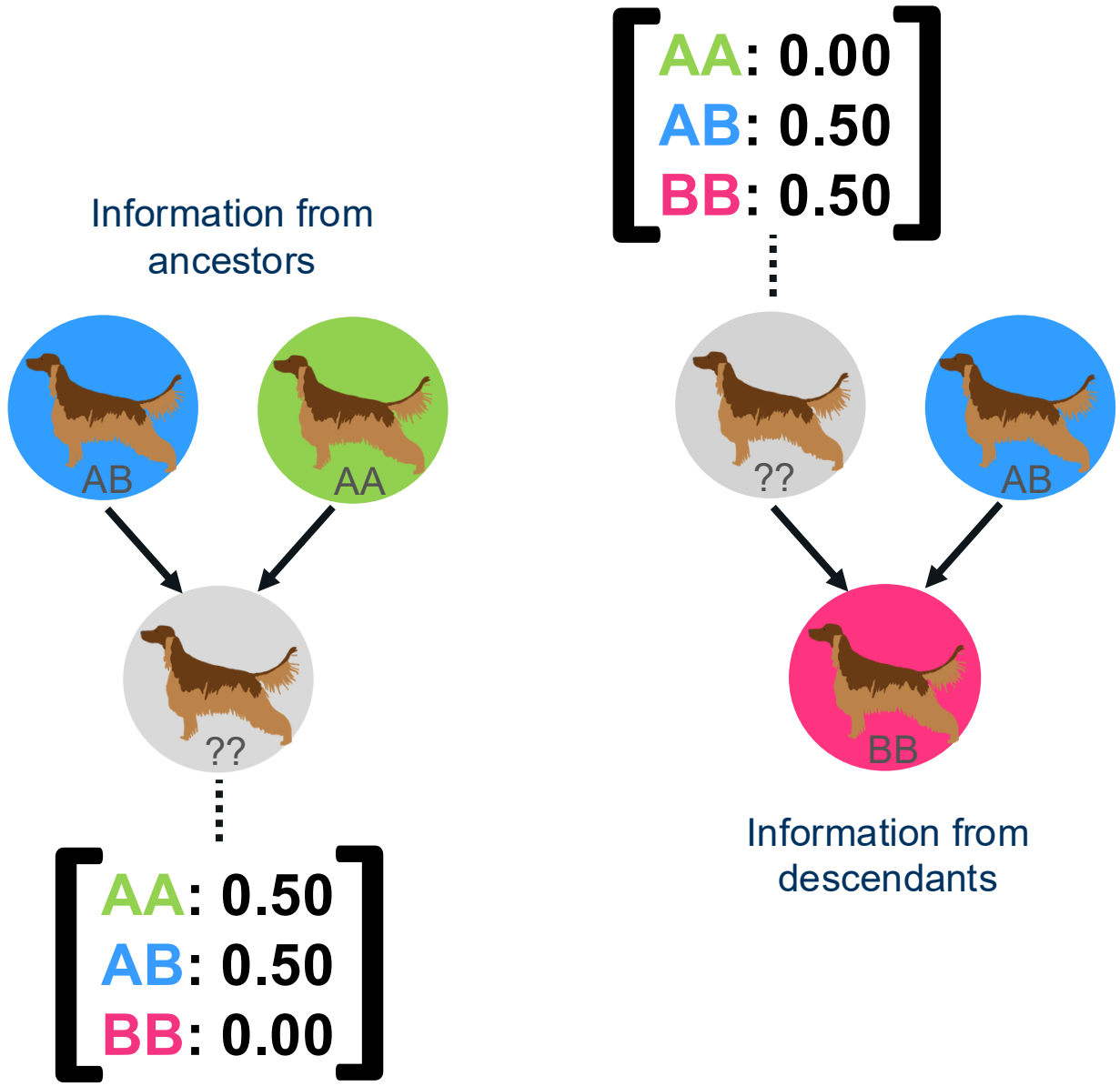
Materials



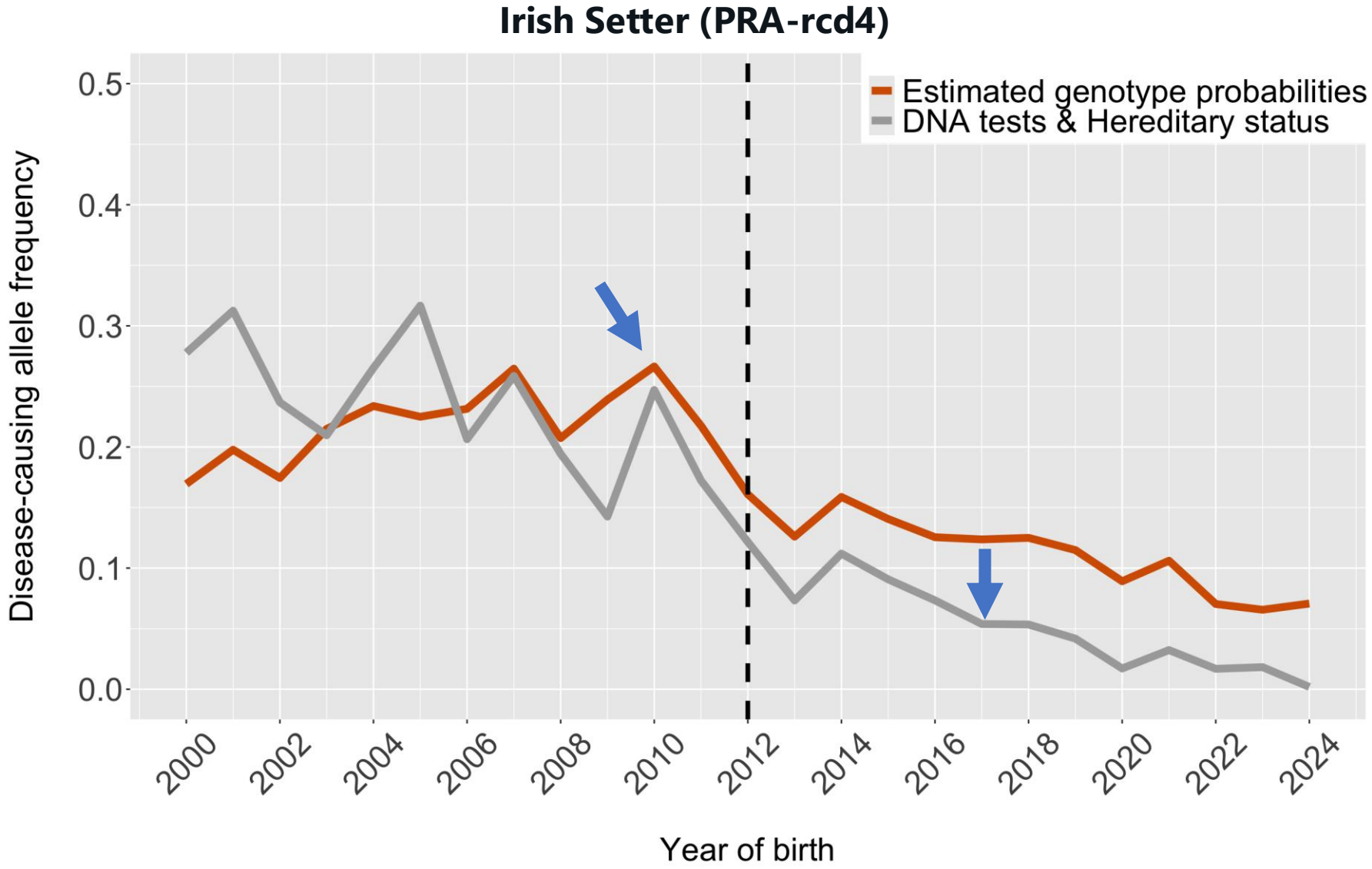
Pedigree records and
DNA test results

Methods

Estimate genotype probabilities for every individual in each pedigree using AlphaPeel (Whalen *et al.*, 2019)



Current methods underestimate the disease-causing allele after DNA test introduction



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How are mutation frequencies used?

Monitoring of disease prevalence

To inform guidance and priorities

To evaluate previous strategies

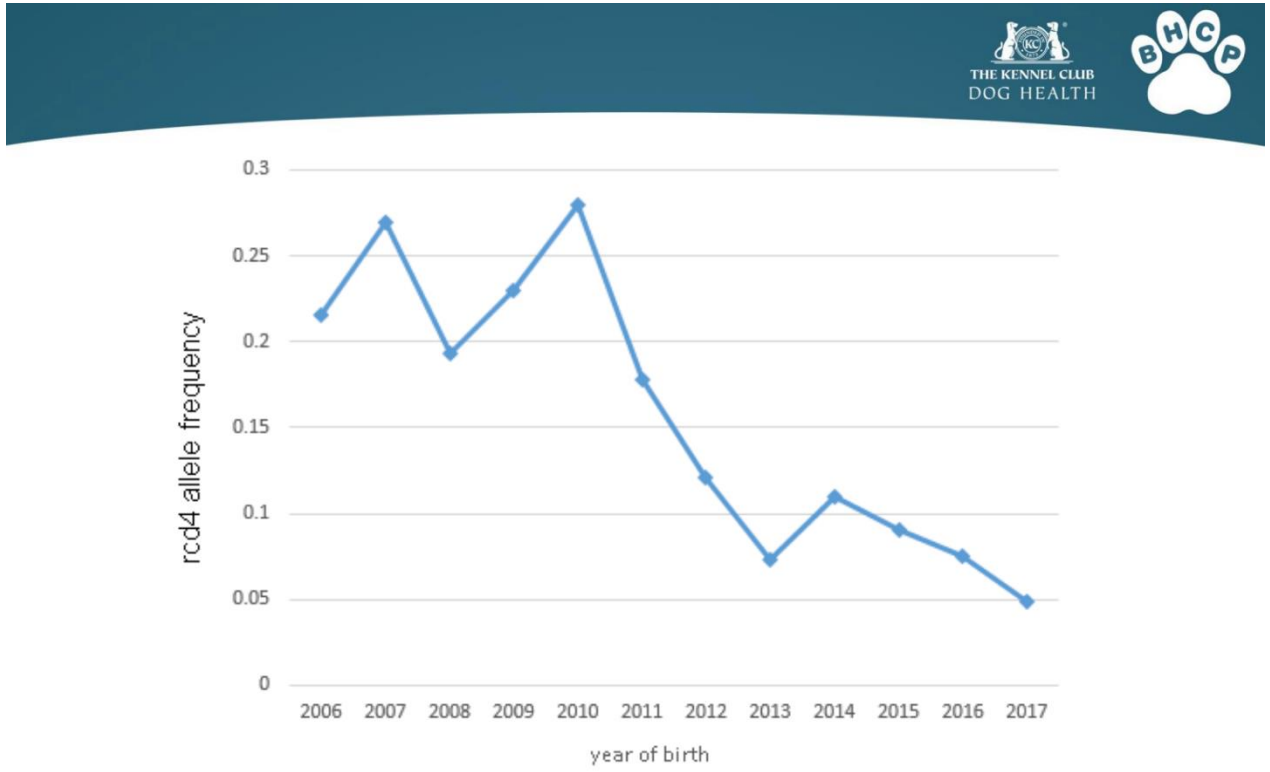

Figure 5: PRA (rcd4) allele frequency, 2006 to 2017, for the Irish Setter

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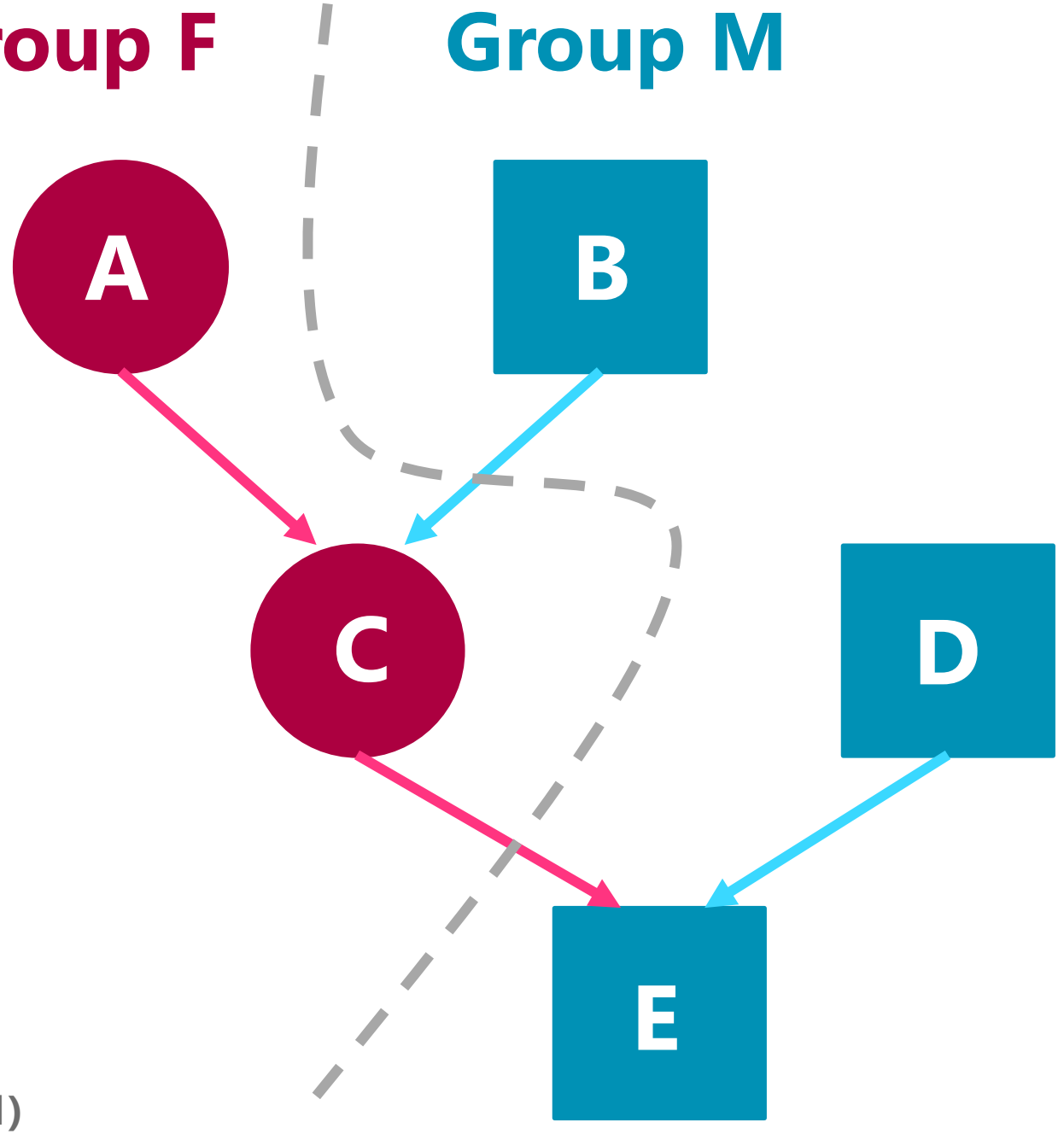
Partitioning of allele frequencies

By tracking the Mendelian sampling terms across user-defined paths.



(García-Cortés *et al.*, 2008; Obšteter *et al.*, 2021)

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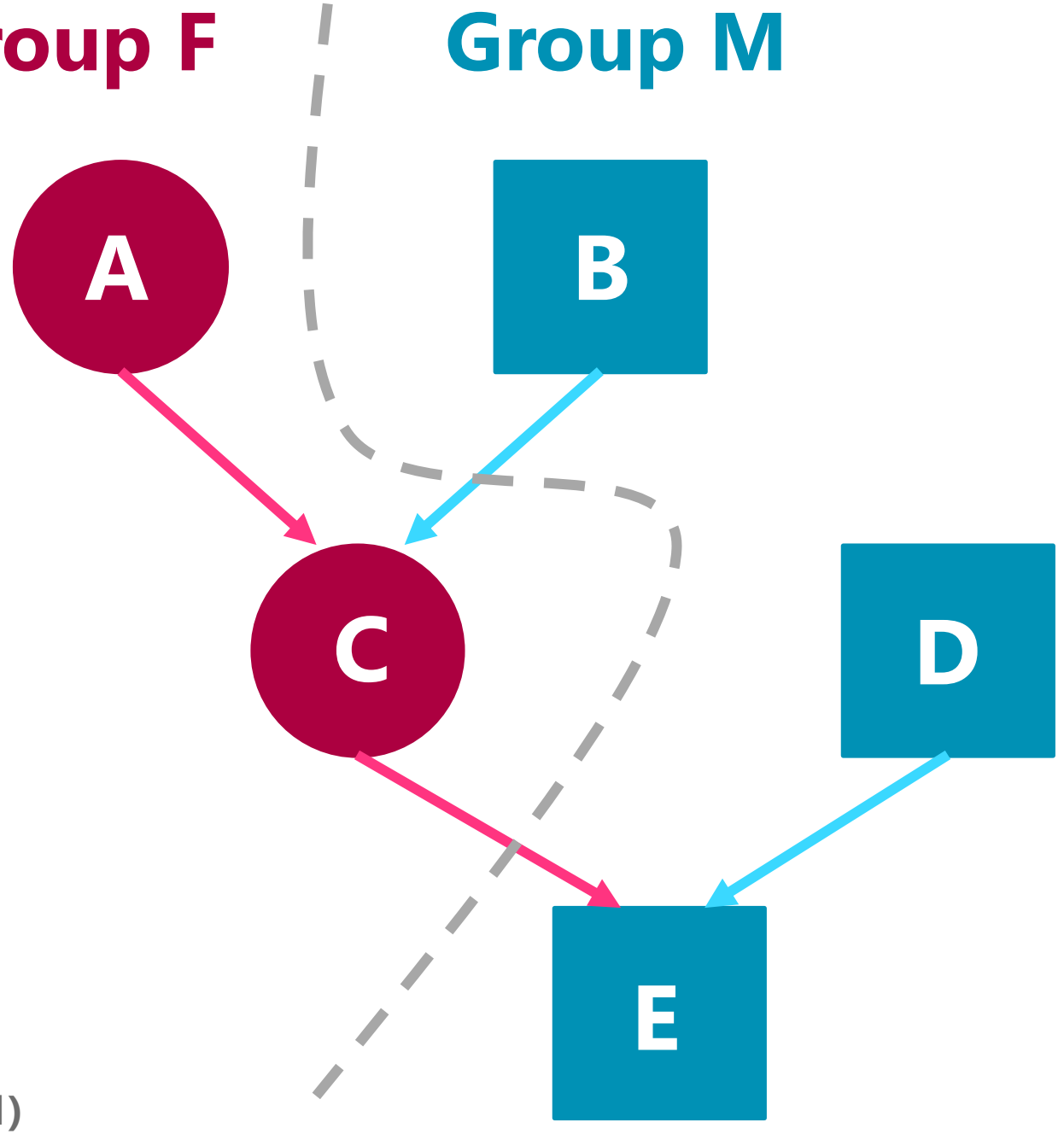
Partitioning of allele frequencies

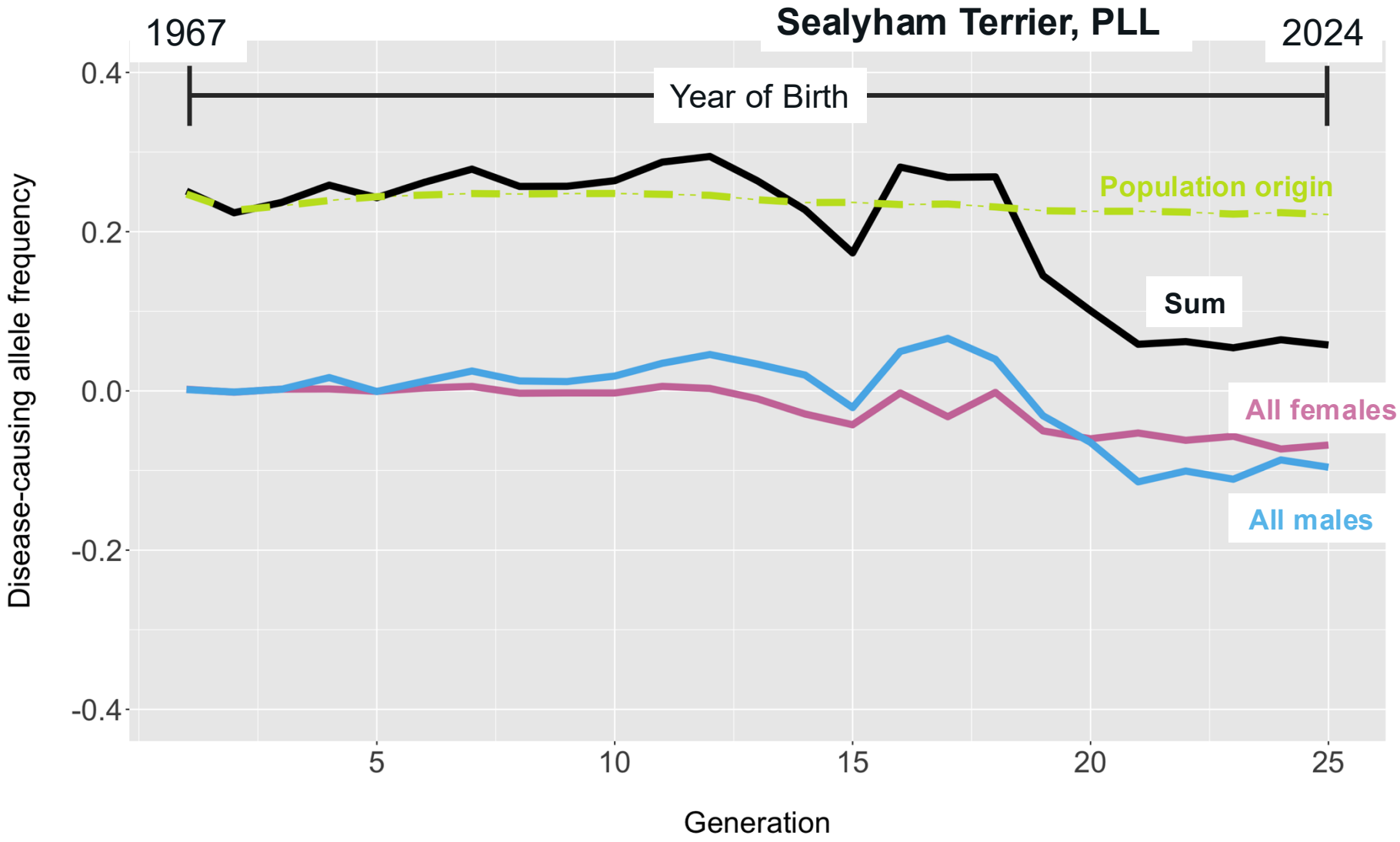
Partitioned by:

1. Sex
2. Individual sires
3. Presence of DNA test.



(García-Cortés *et al.*, 2008; Obšteter *et al.*, 2021)

Distinct trends within pedigrees when grouping by sex



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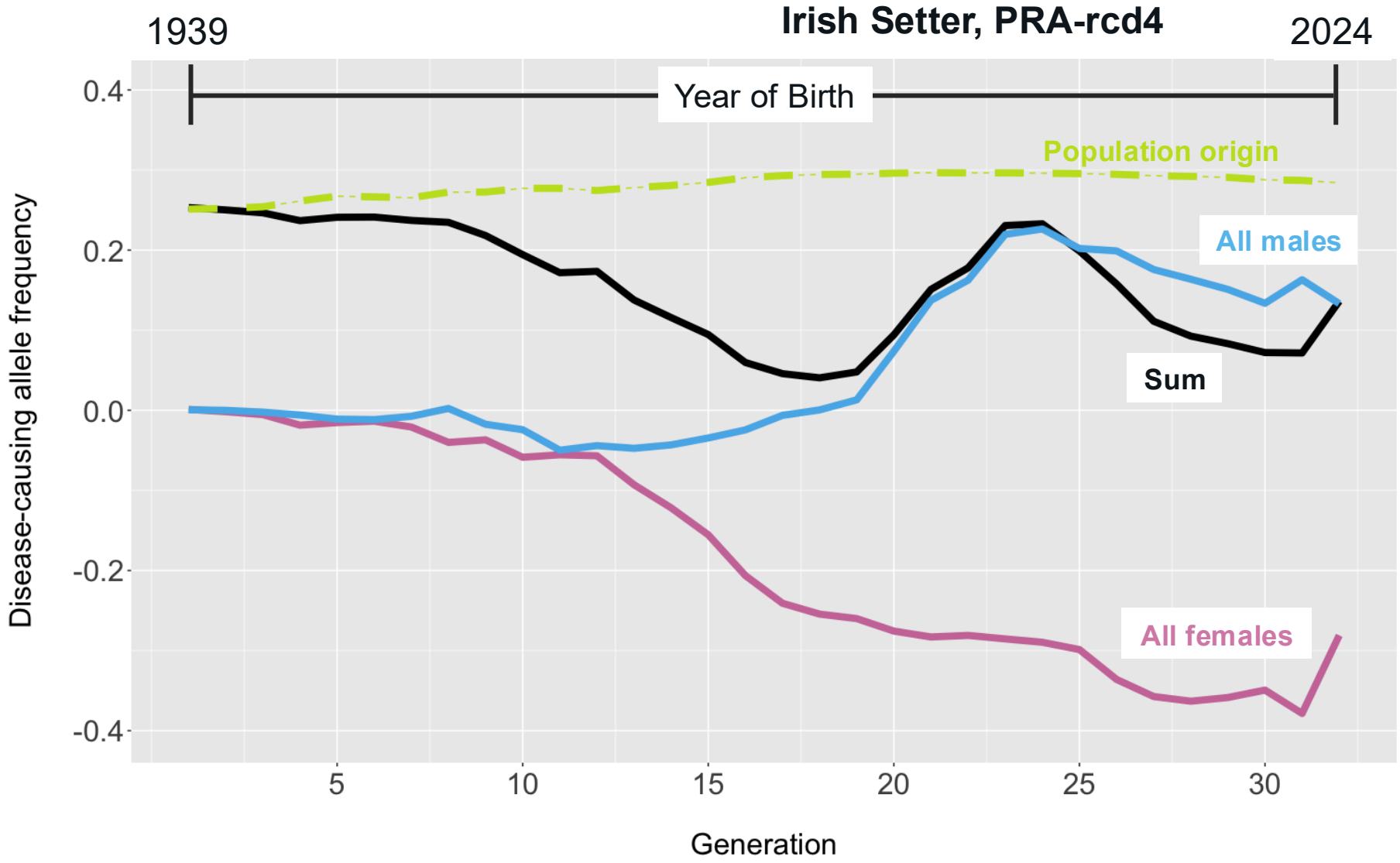
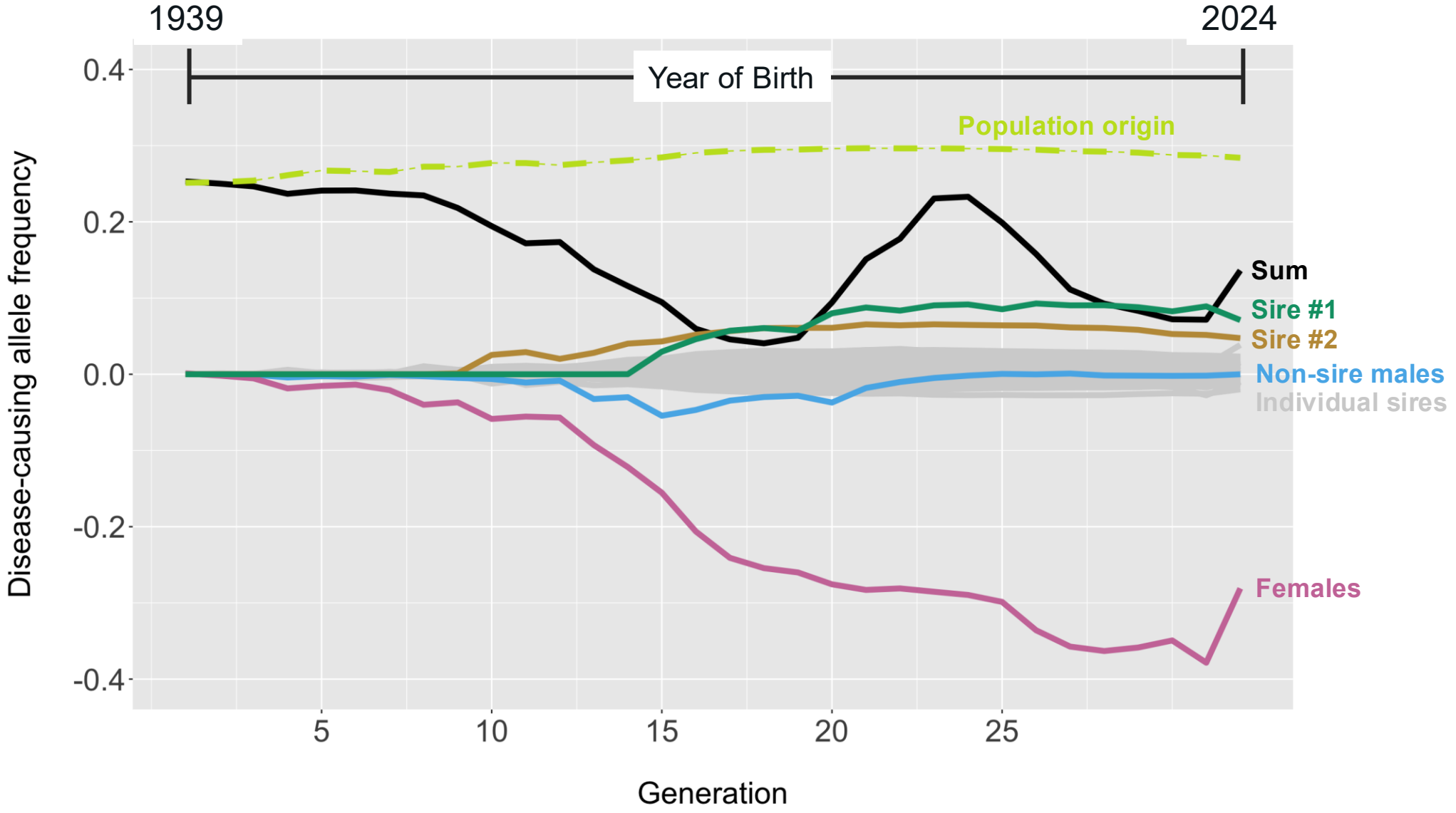
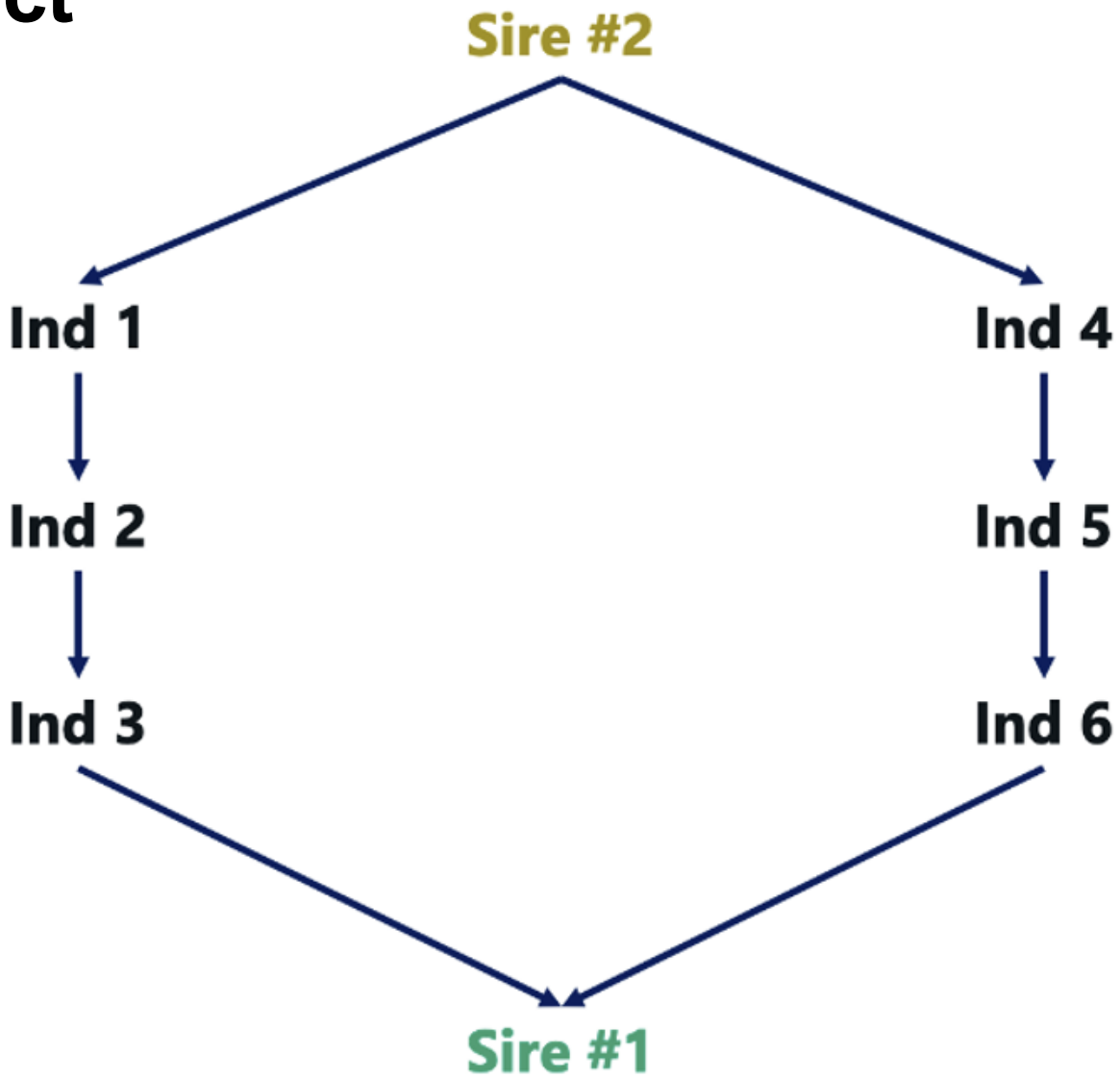


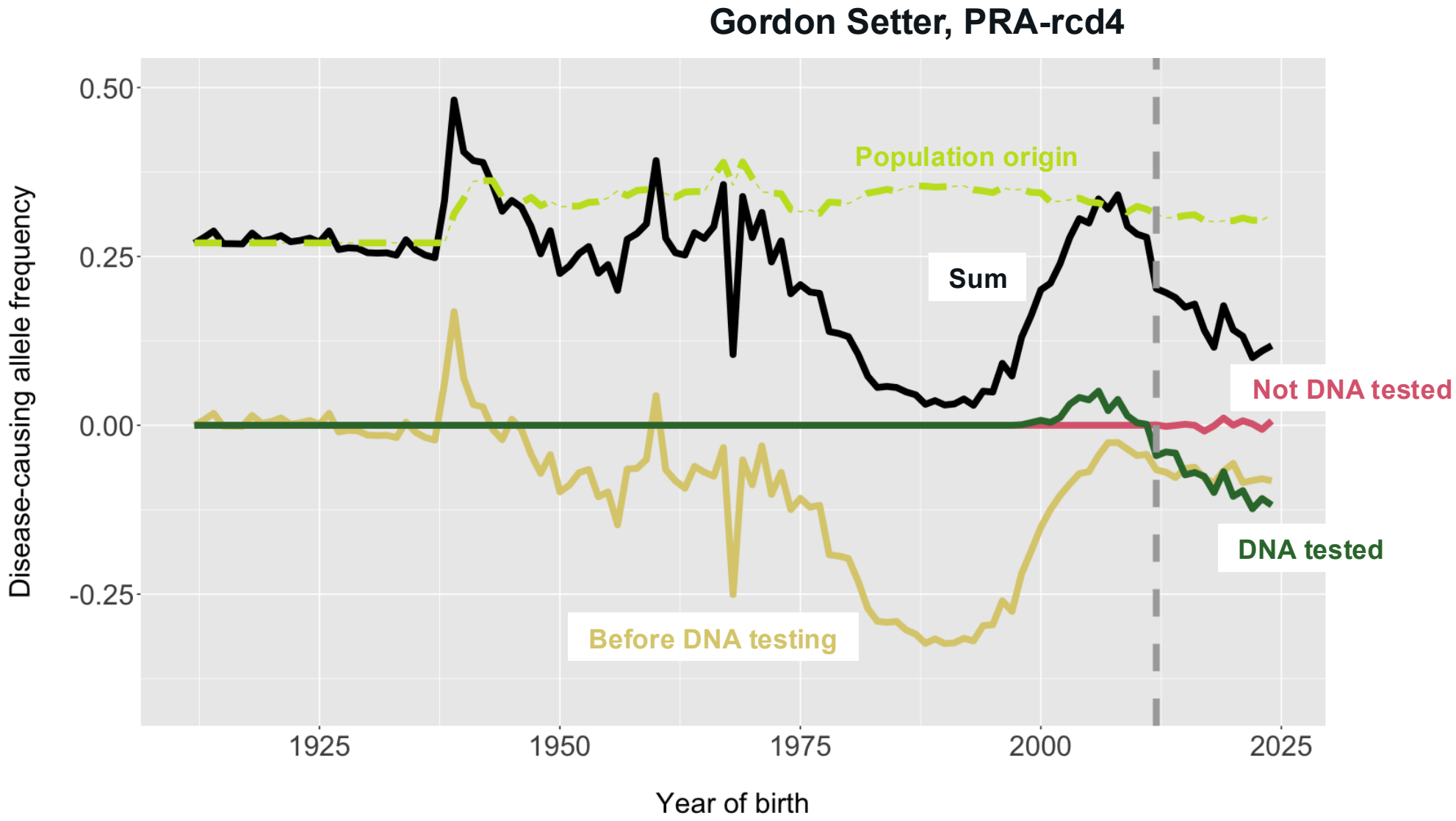
Two male dogs play a key role in segregating the disease-causing allele in Irish Setters



Due to inbreeding and the popular sire effect



DNA testing used successfully to select against the disease-causing allele



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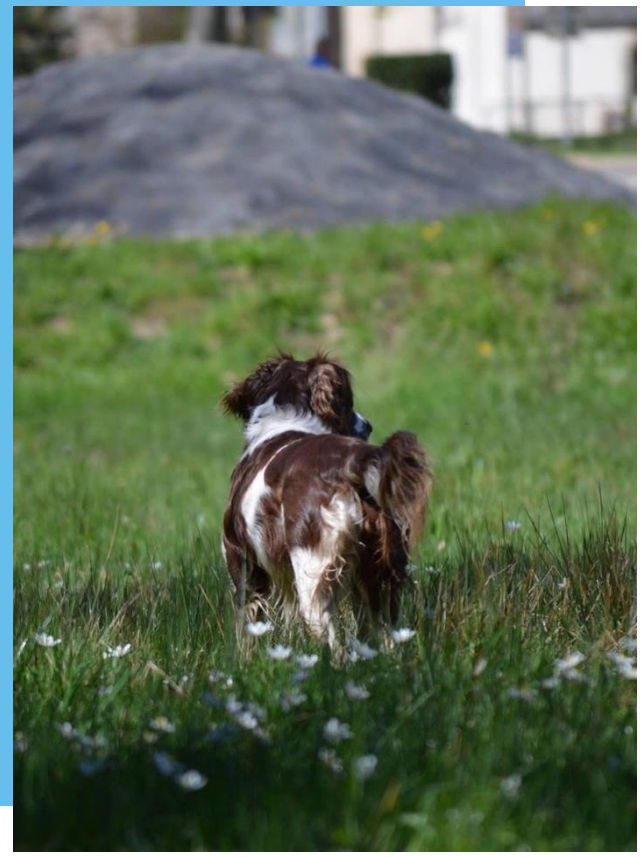
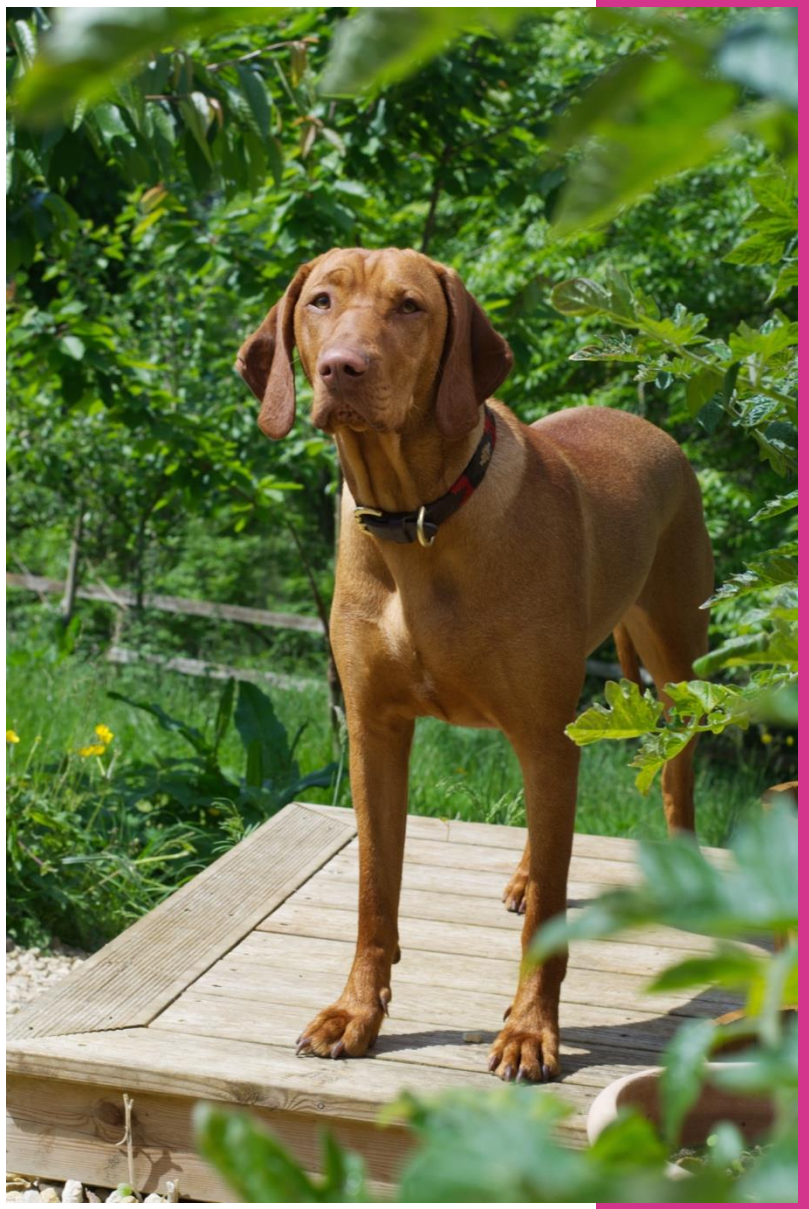
Conclusions

Estimated disease-causing allele frequencies were **improved** by considering the whole pedigree through **genotype probabilities**

The **popular sire effect** and **inbreeding** have **increased** disease-causing allele frequencies.

DNA-tested dogs have driven the **reduction** in disease-causing allele frequencies.





Thank you

Special thanks to The Kennel Club Charitable Trust and The University of Edinburgh for supporting this research.

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