(Genetische) Epidemiologie van veroudering

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Genetische Epidemiologie, Erasmus MC
9 oktober 2013

Structuur

- Langlevendheid
- Doelstellingen
- Genetische associatie
- Genoomwijde associatie
- Kandidaat-gen associatie
- Telomeer lengte
- Conclusies

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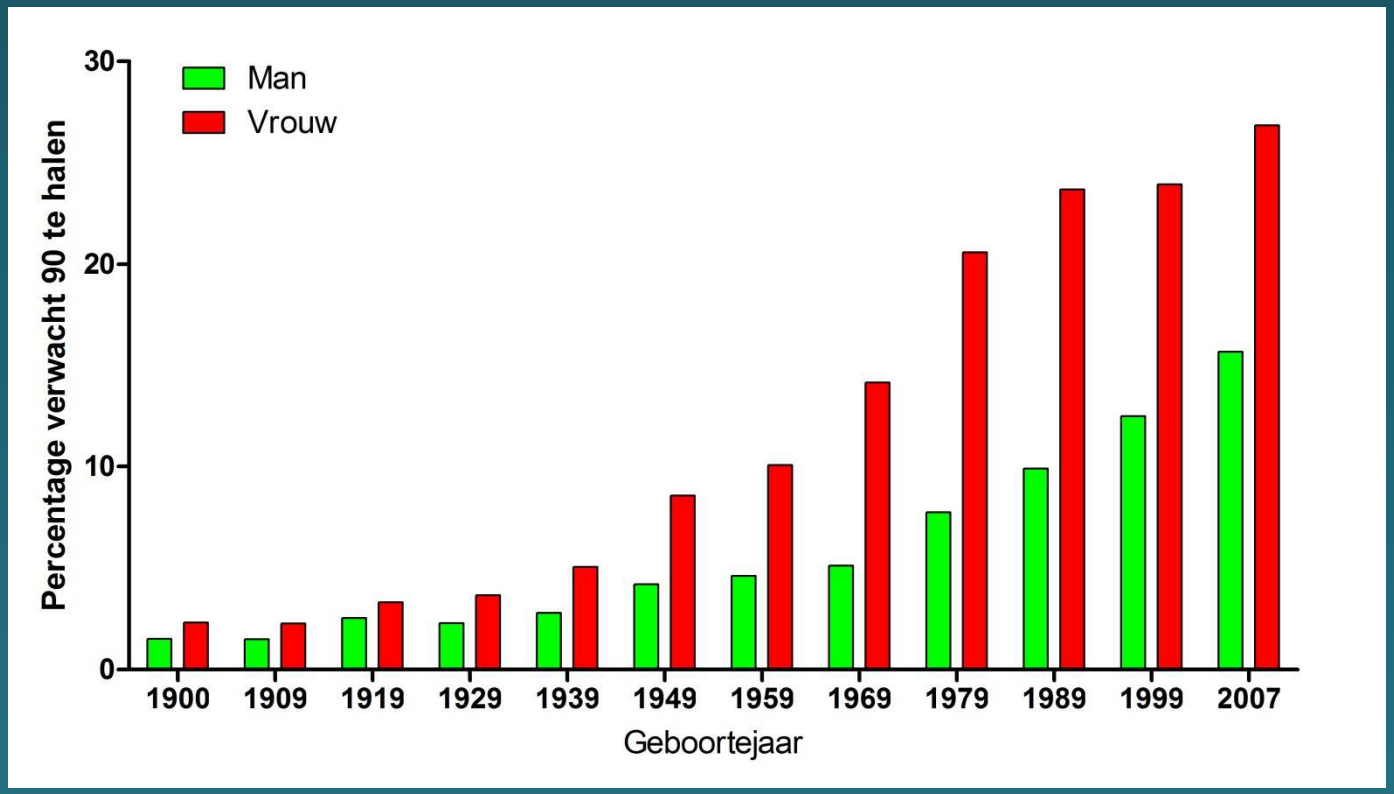
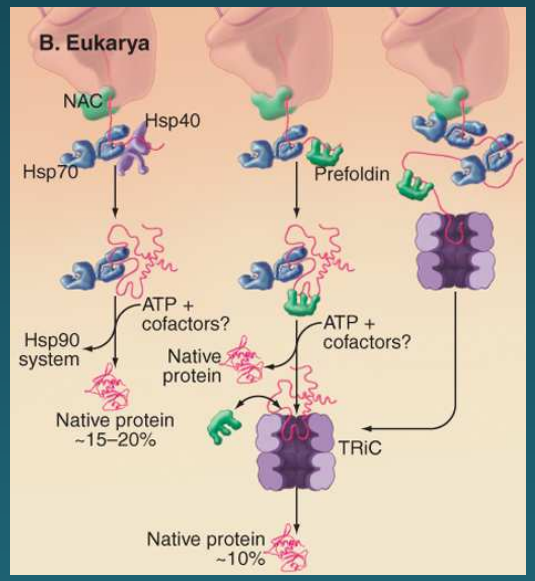
Langlevendheid

- Extreme levensverwachting
- Erfelijkheid ~ 20-40%



Experimentele Studies

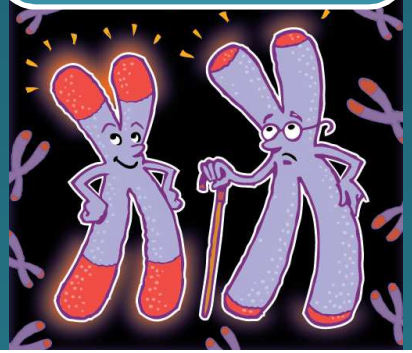
IGF-1 signaling



Telomeer lengte

Langlevendheid

Stress reactie



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Doelstellingen

- Welke genetische factoren zijn geassocieerd met langlevendheid:

1. Nog onbekende biologische processen
2. Stress reactie
3. Telomeer lengte

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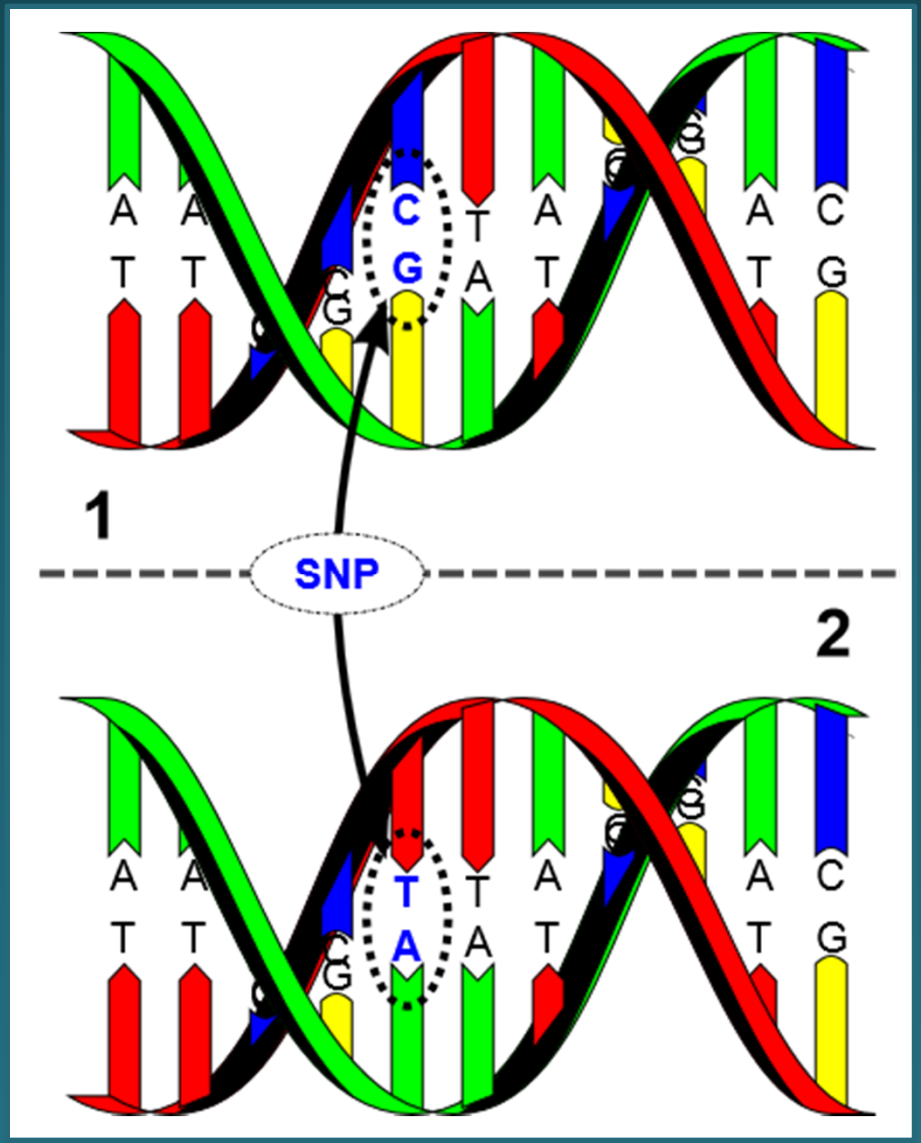
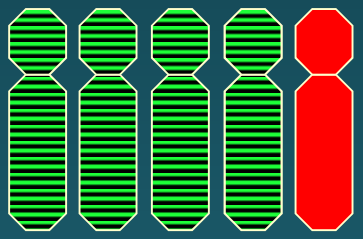
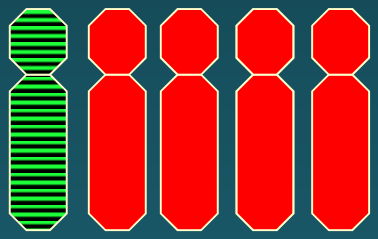
DNA



Genetische associaties



Oud (>90)

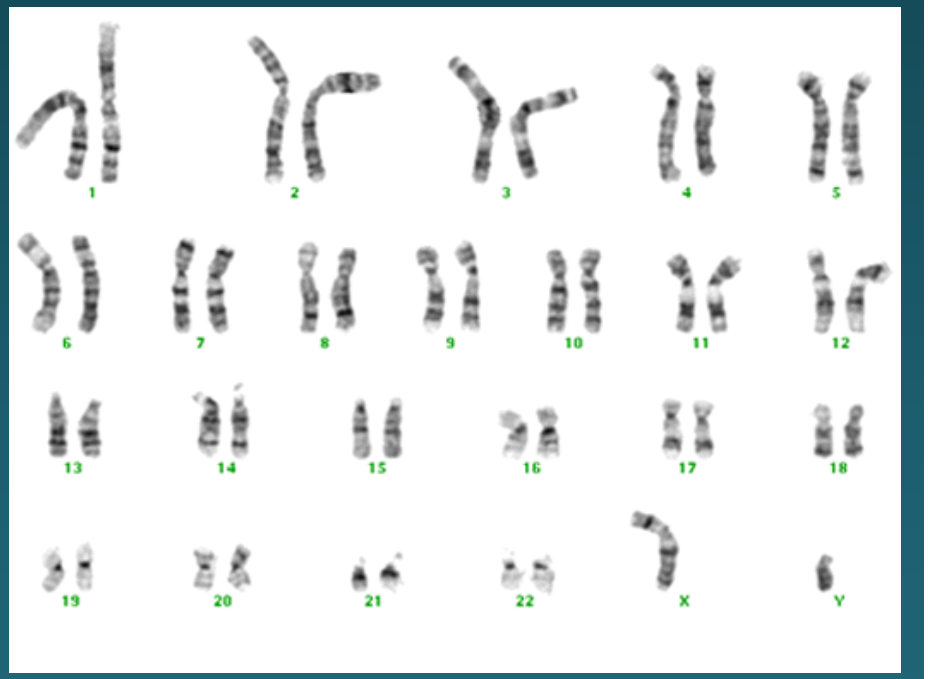


Overleden (<80)

Genoomwijde associatie

- 2.5 miljoen veelvoorkomende SNPs

- Rotterdam Studie
  - Ommoord, 55+
  - 20 jaar gevolgd
  - 1004: 90+
  - 1131: overleden voor 80

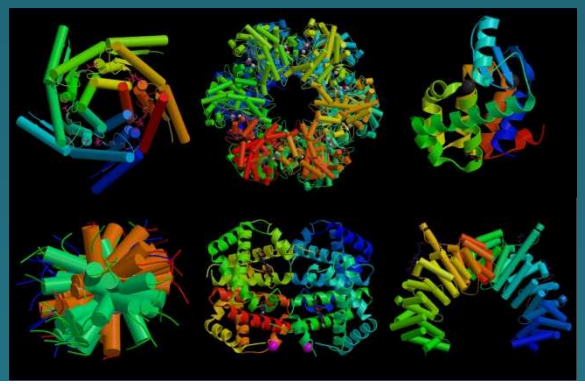


Exoomsequentiebepaling

DNA

mRNA

Eiwit



Exoomsequentiebepaling in de Rotterdam Studie

- 202 mensen van ouder dan 90
- 267 mensen overleden voor 80

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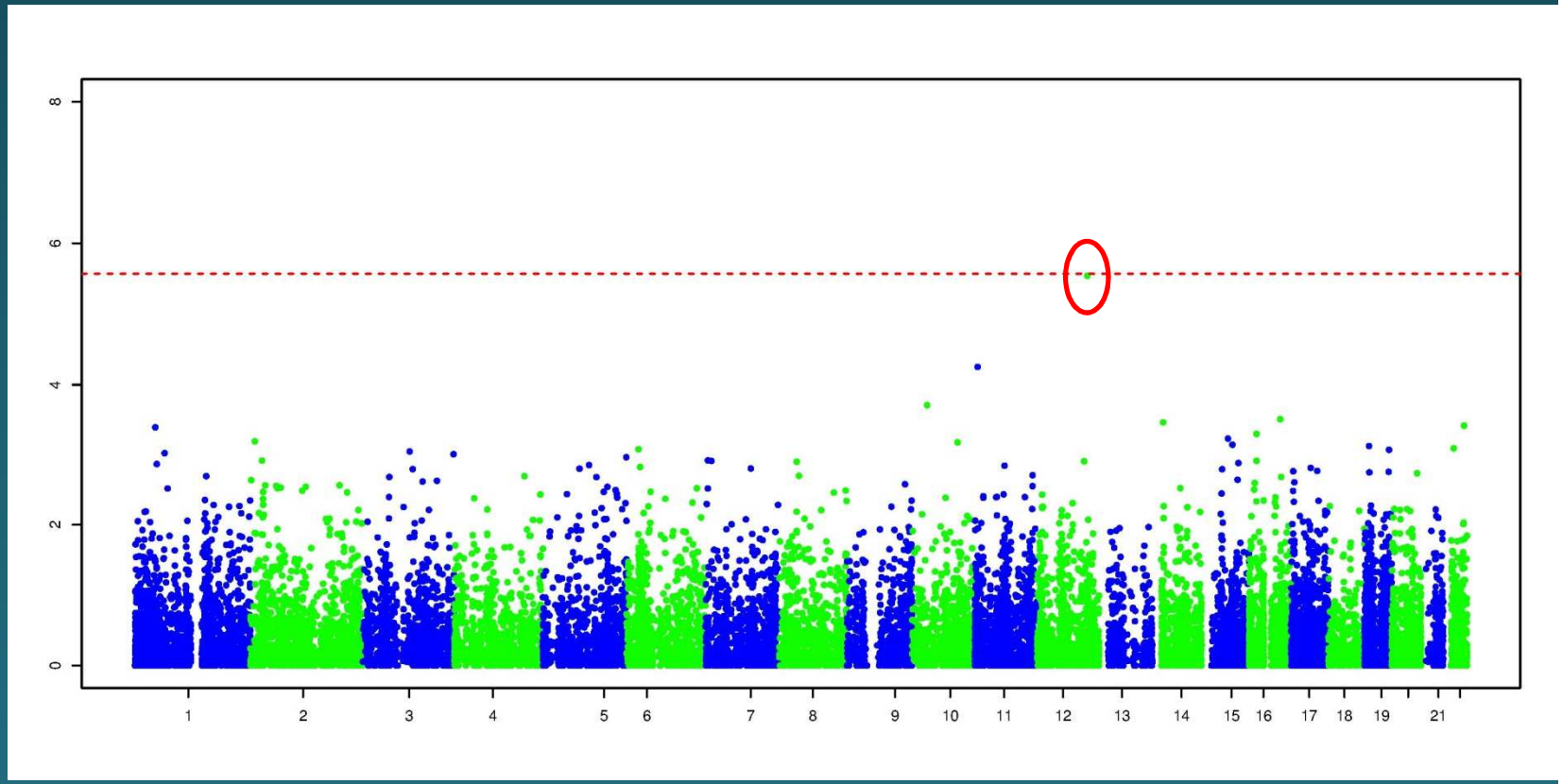
Hypothese

- Zeldzame eiwitcoderende varianten bepalen langlevendheid
- Veelvoorkomende varianten bepalen langlevendheid

Zeldzame varianten

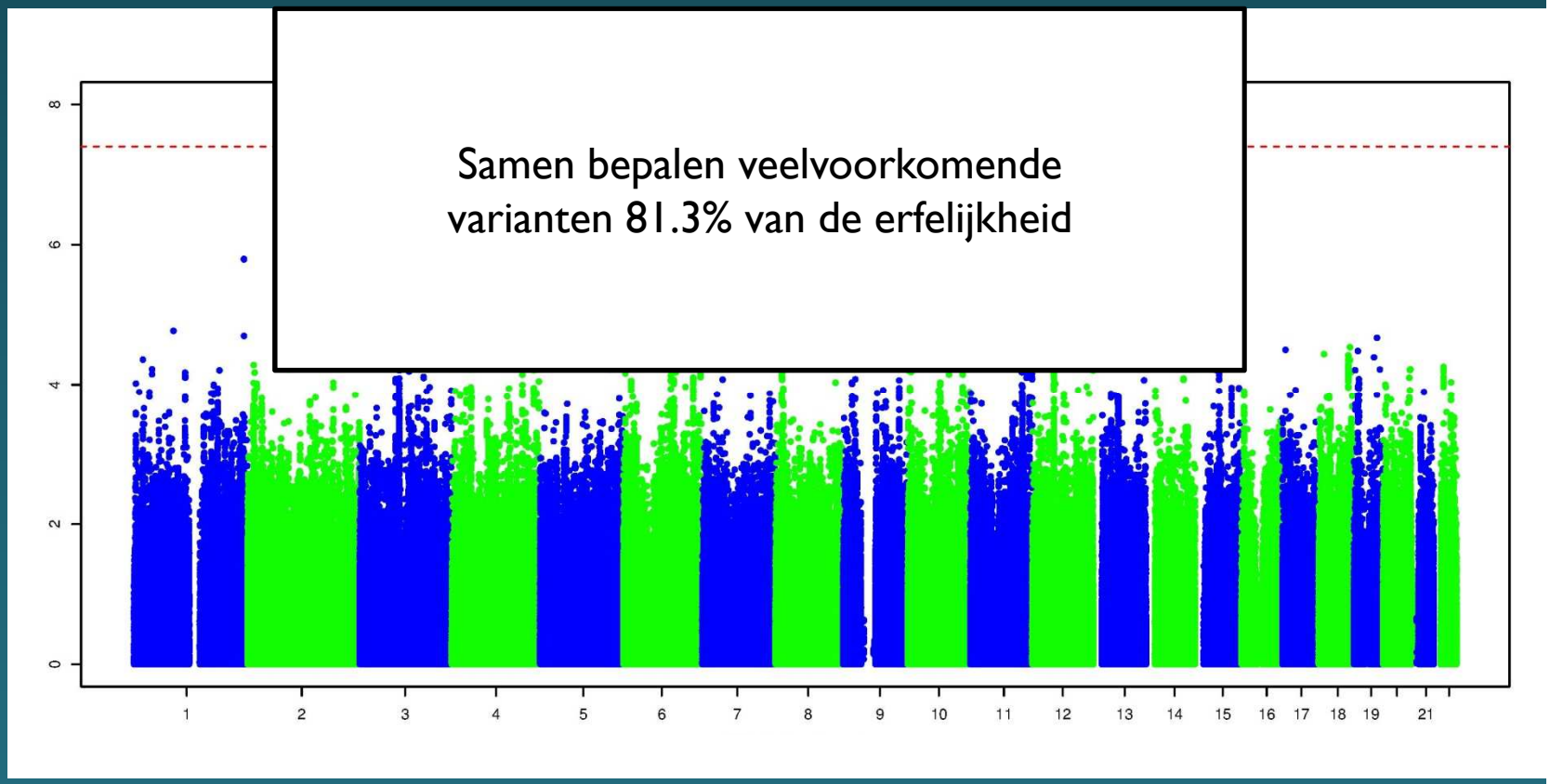
Significantie



Chromosoom

Veelvoorkomende varianten

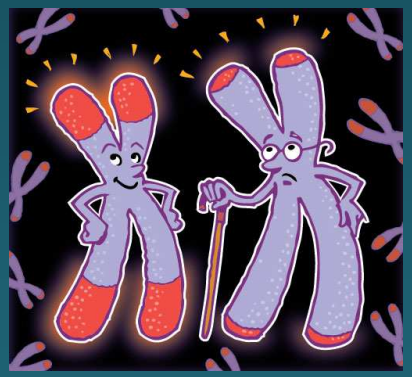
Significantie



Chromosoom

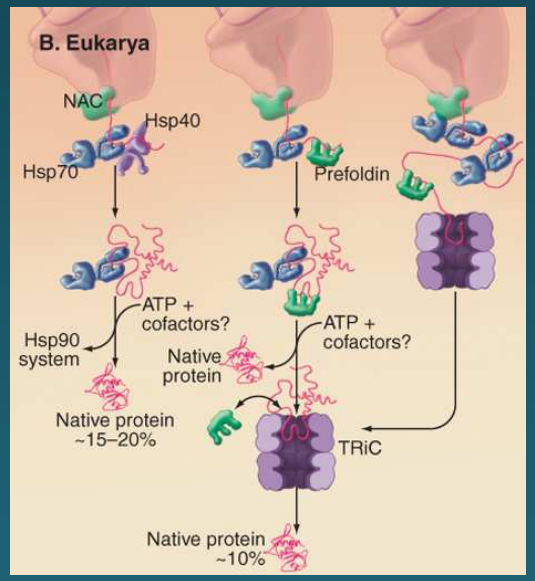
Vervolgonderzoek

IGF-1 signaling



Telomeer lengte

Langlevendheid



Stress reactie

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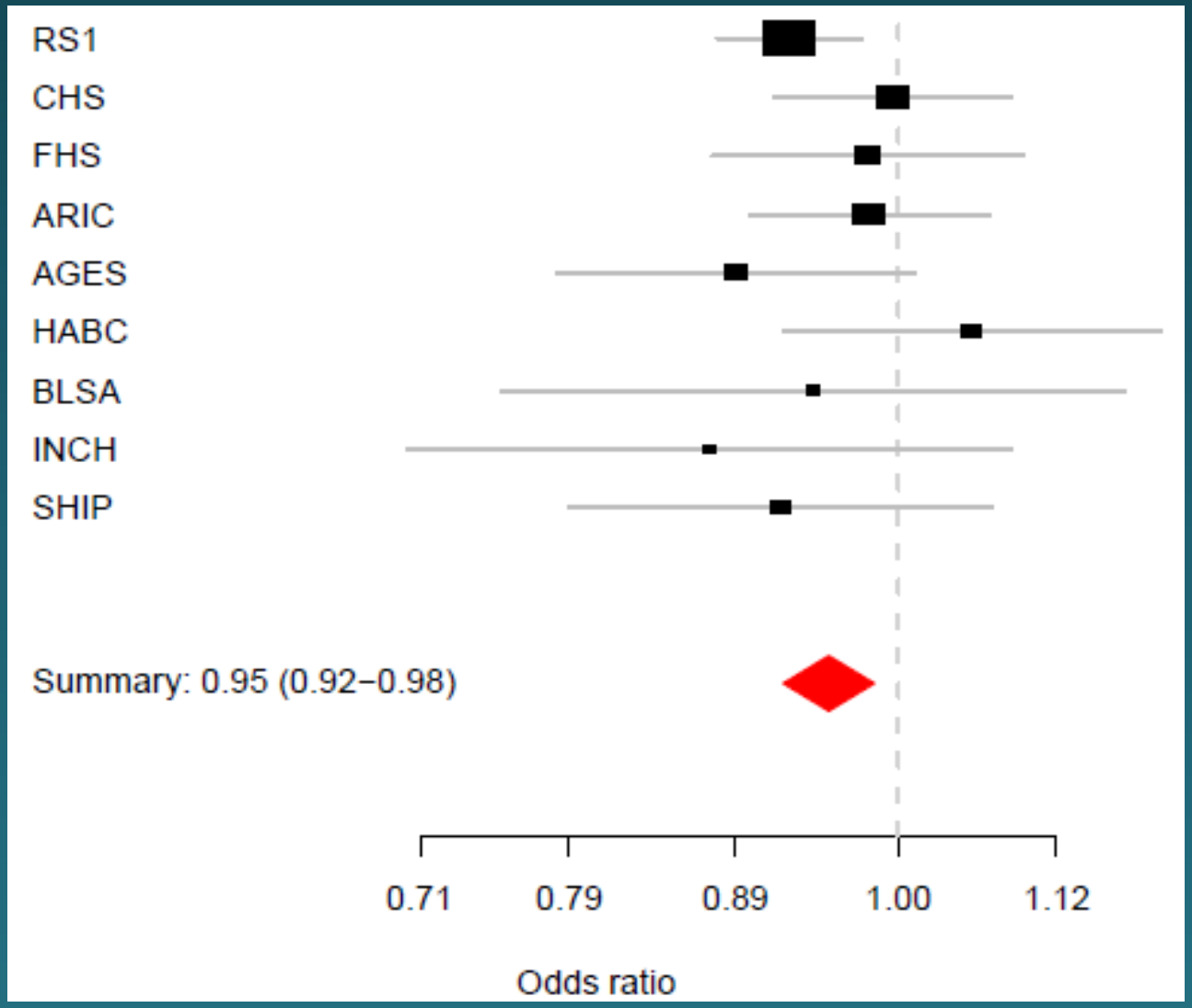
CHARGE consortium

Heat Shock Factor 2 (*HSF2*)



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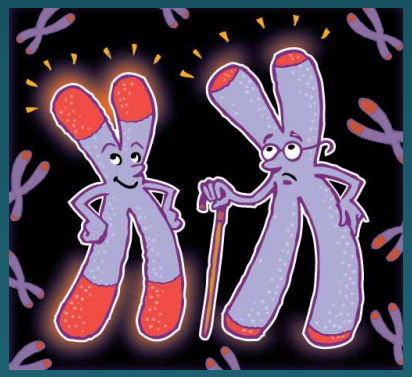
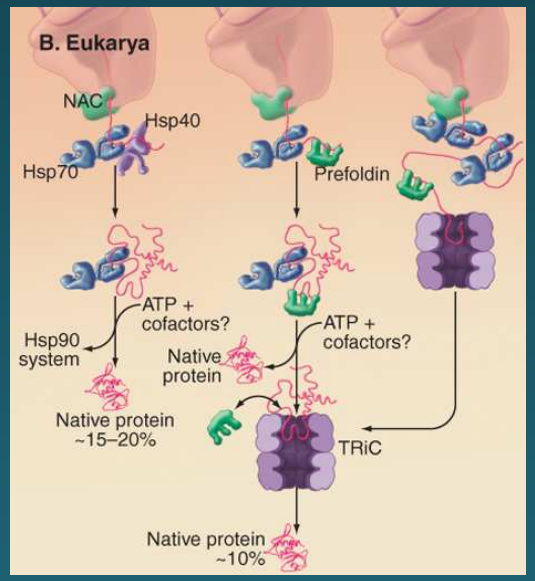
IGF-1 signaling



Telomeer lengte

Langlevendheid



Stress reactie

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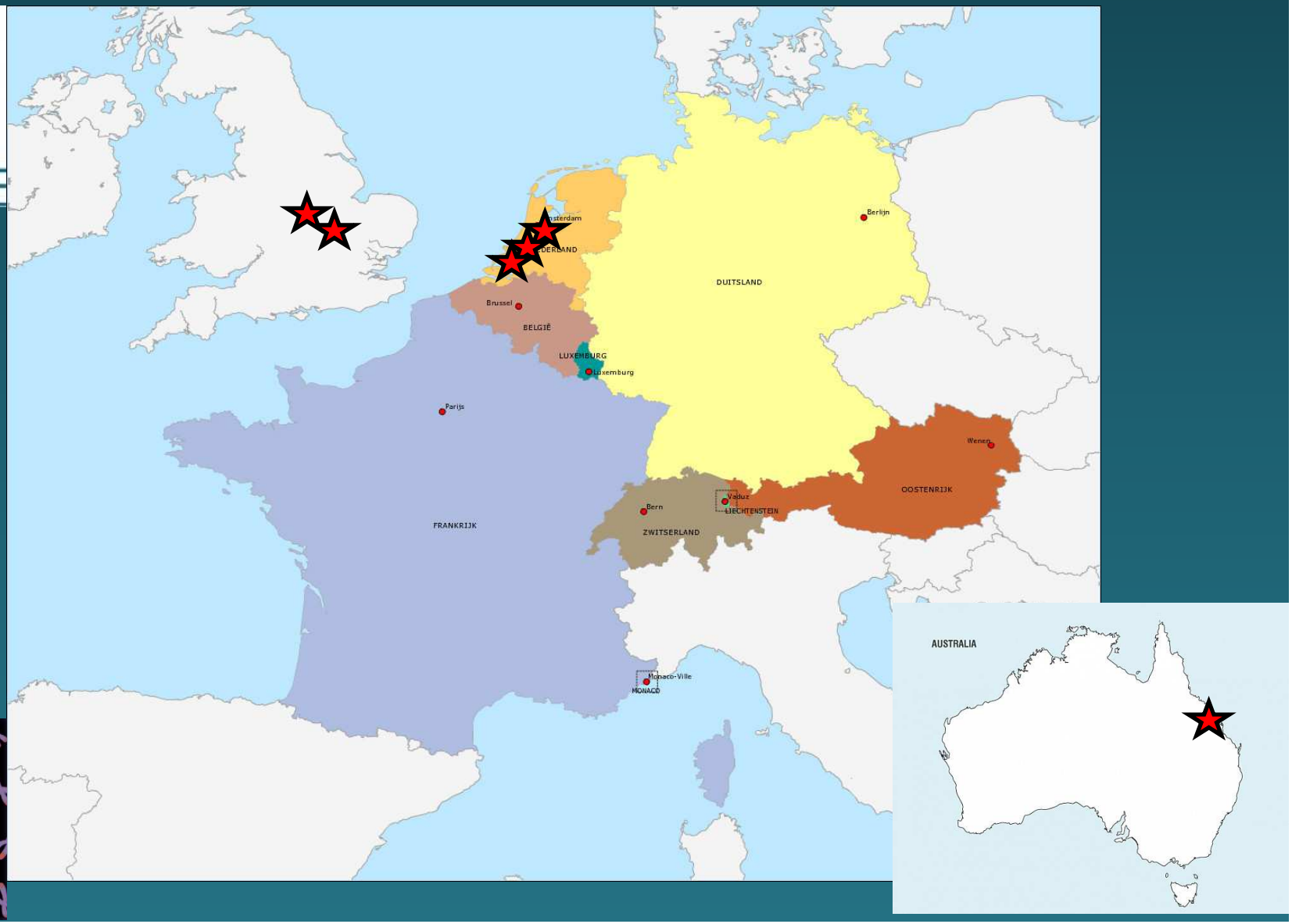
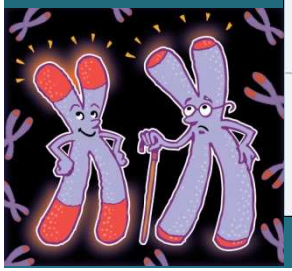
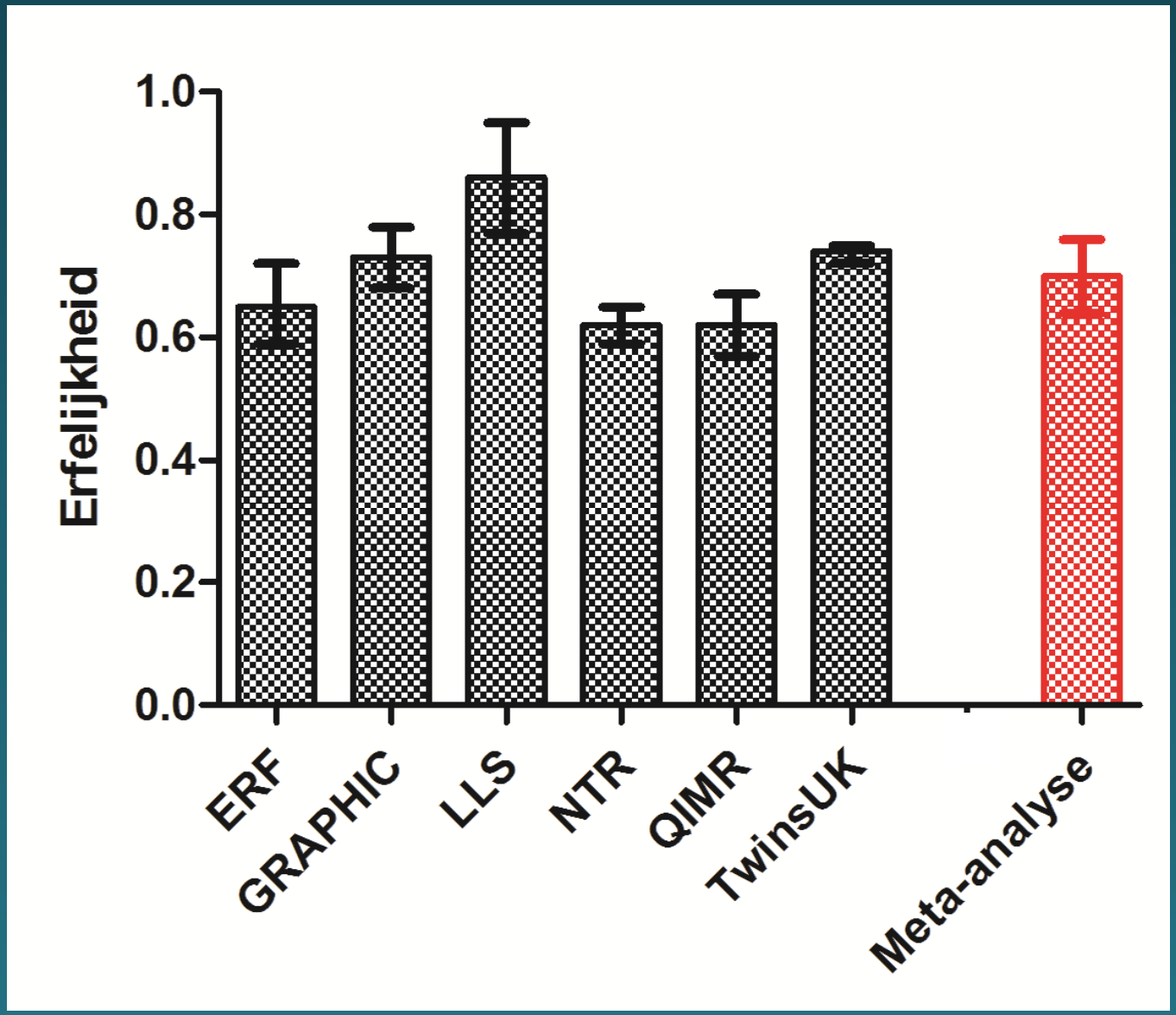
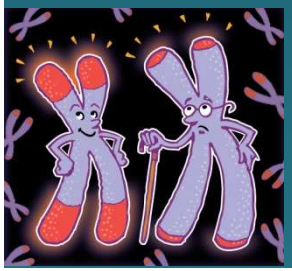
Studiepopulaties



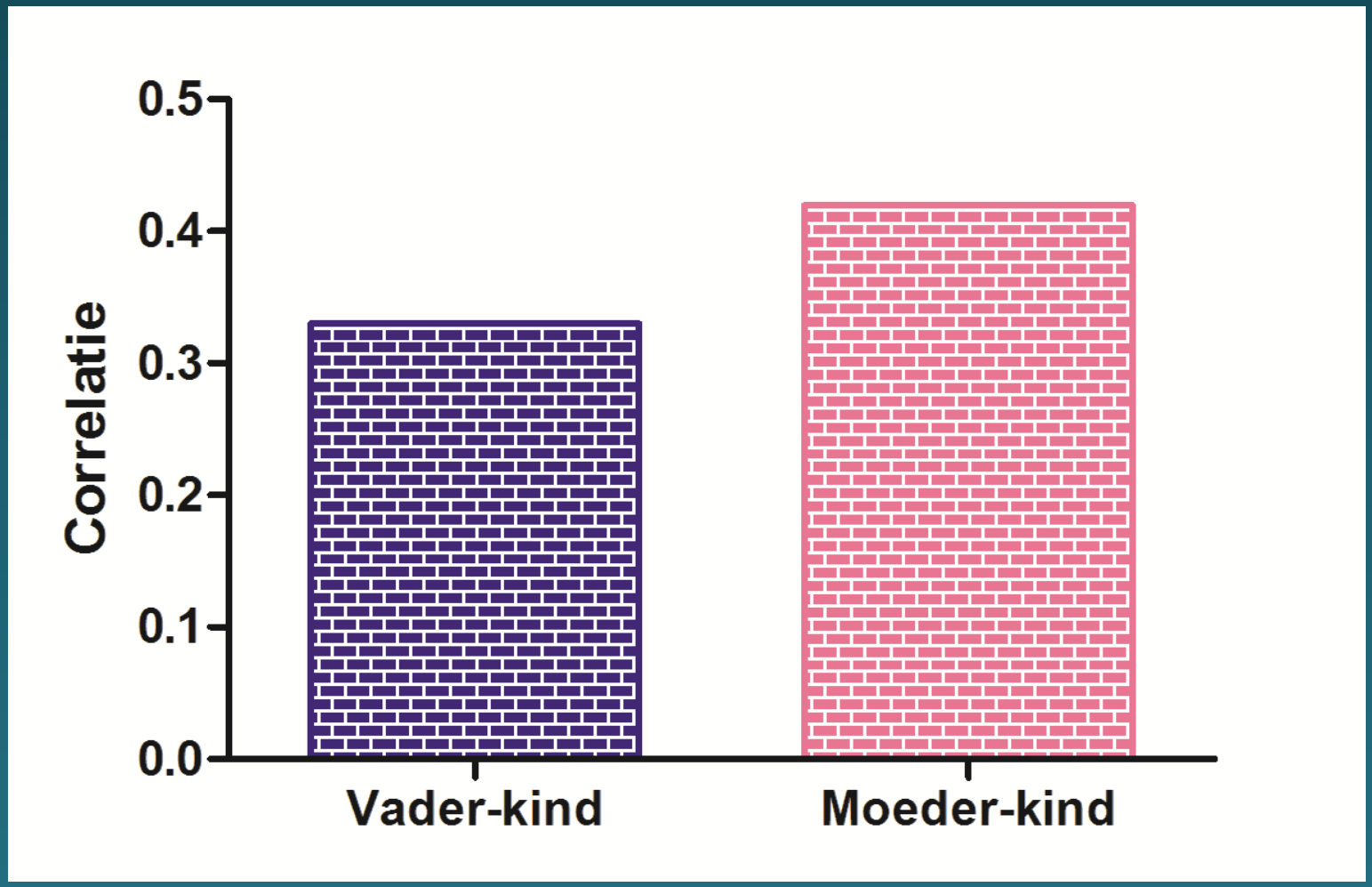


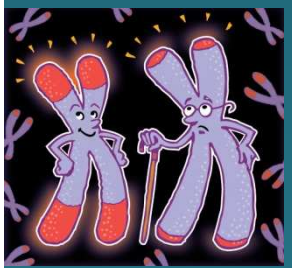
Erfelijkheid van telomeer lengte





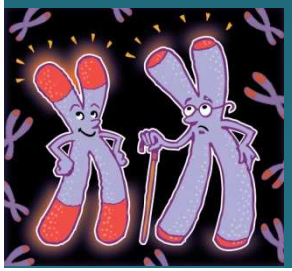
Overerving door vader of moeder?





Telomeer lengte en sterfte

- Relatie telomeer lengte en sterfte onduidelijk
- Geen studies met lange follow-up
- In familiestudie (ERF) te benaderen



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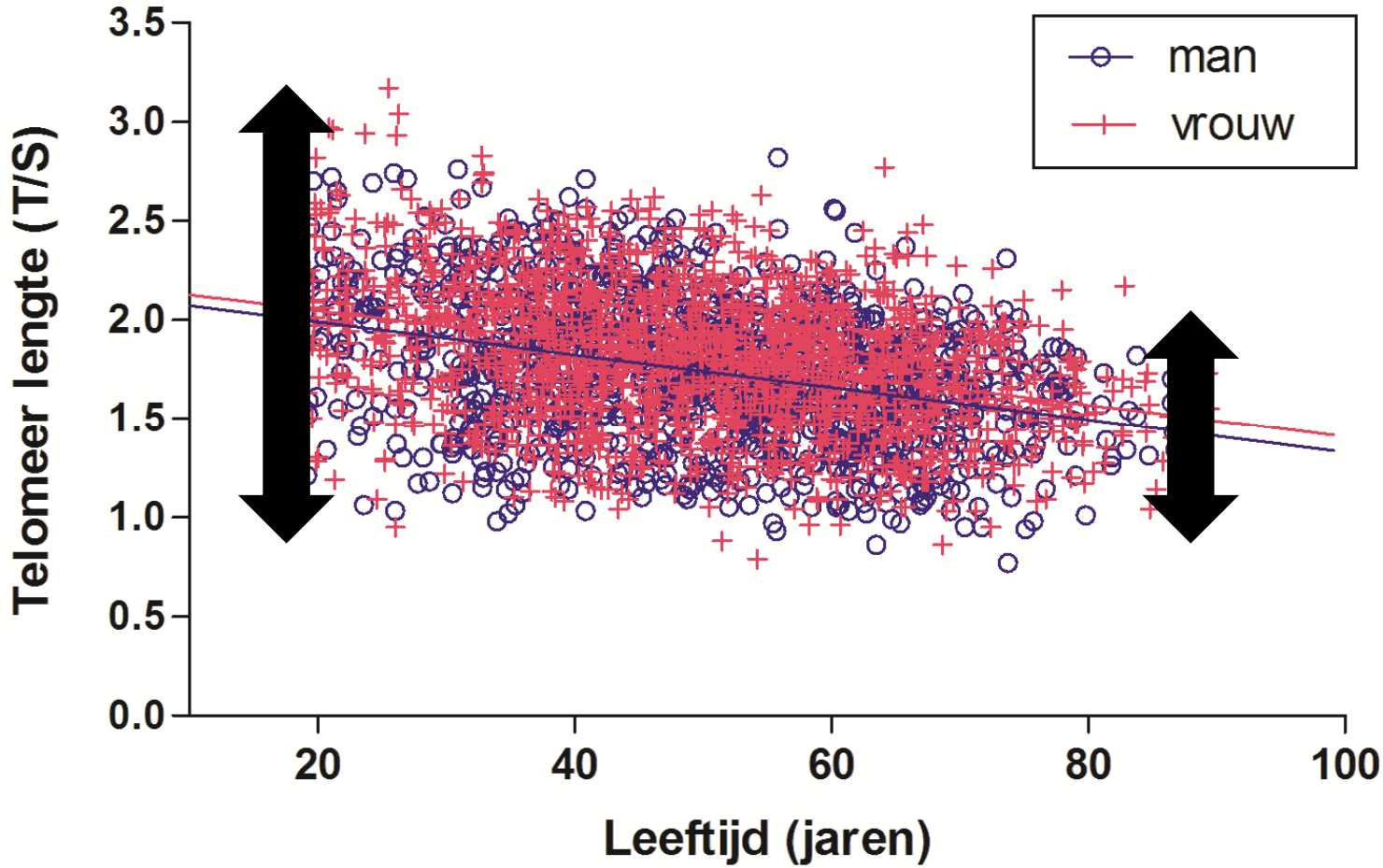
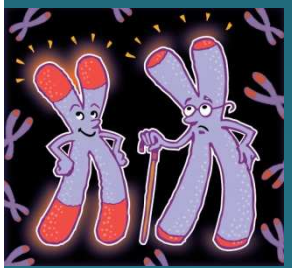
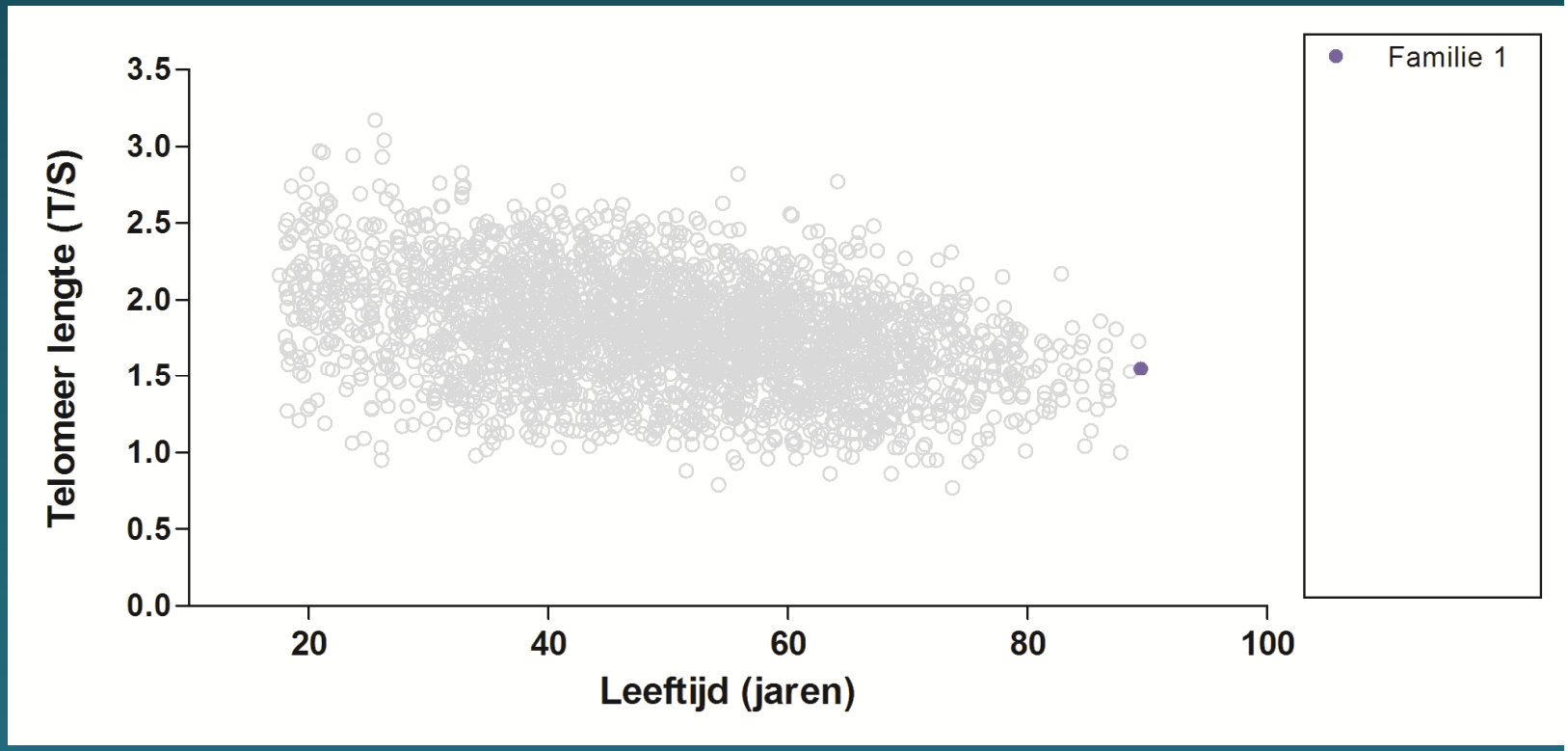
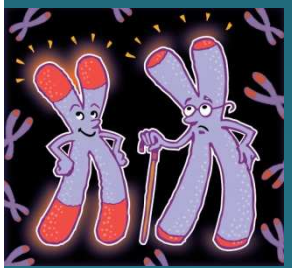




Telomeer lengte in families van langlevende mensen





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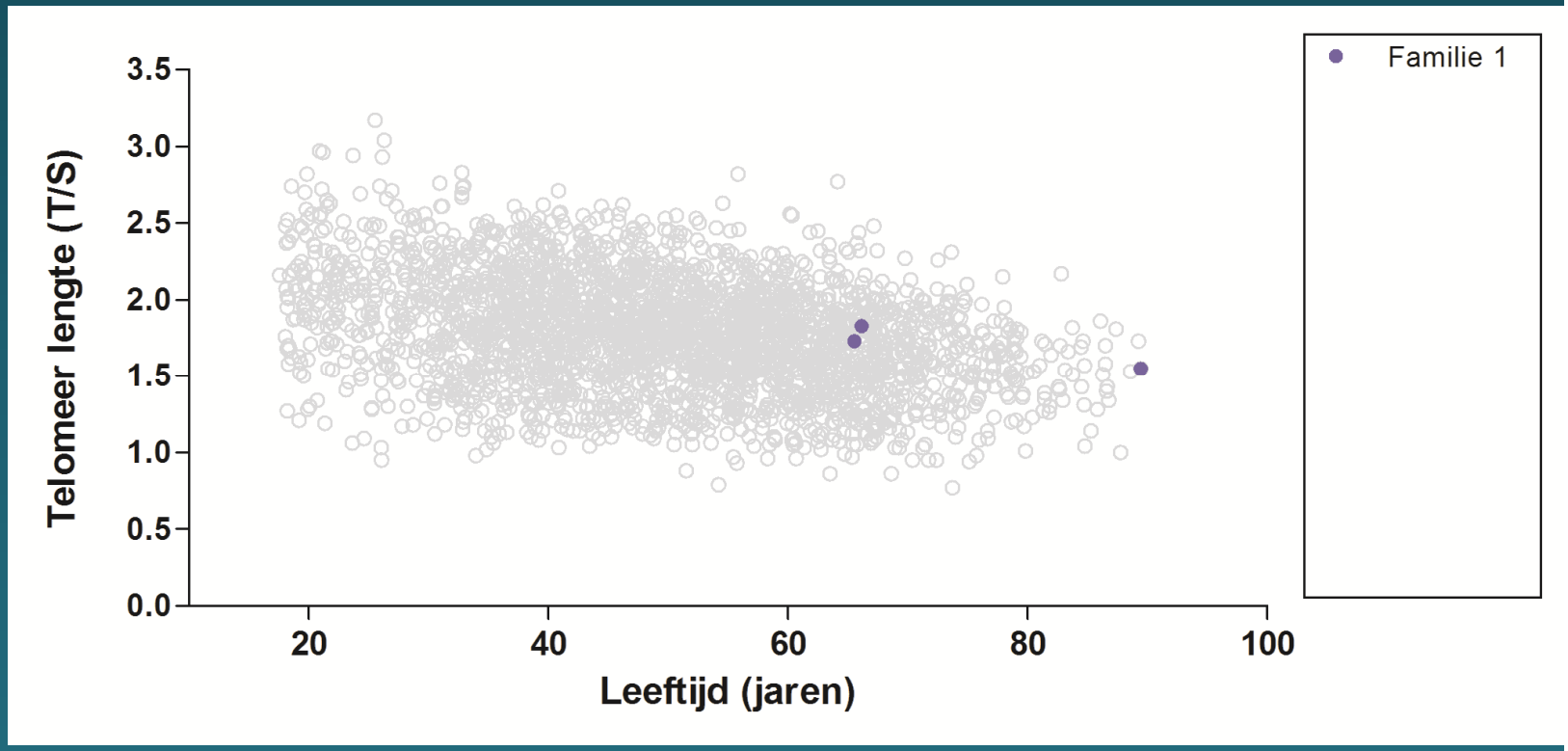

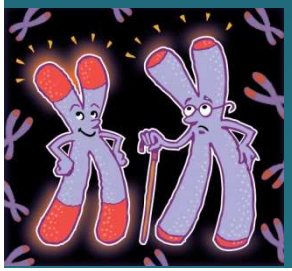

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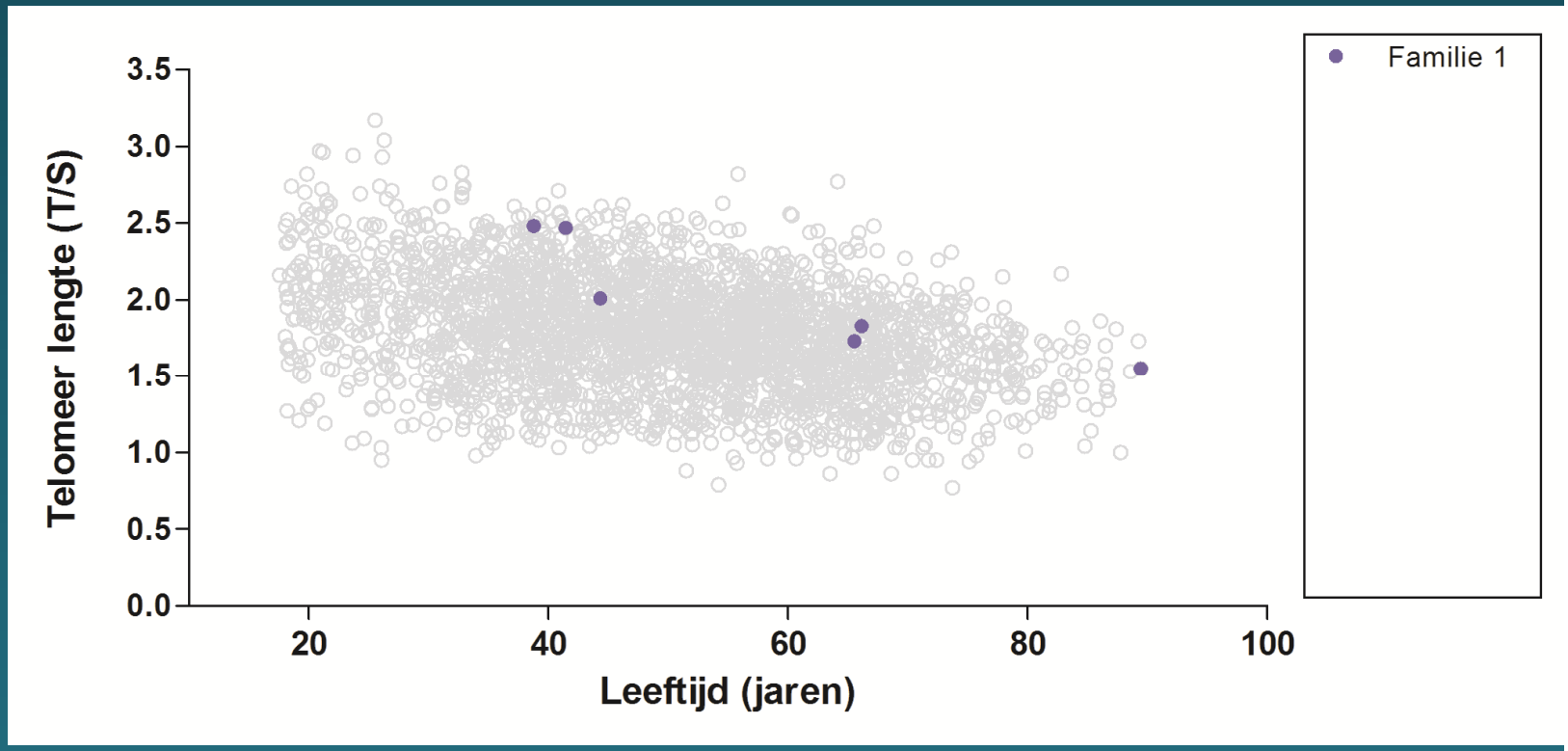

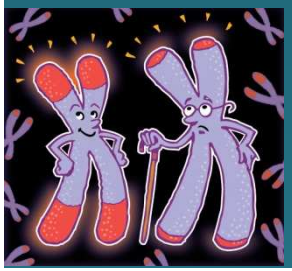

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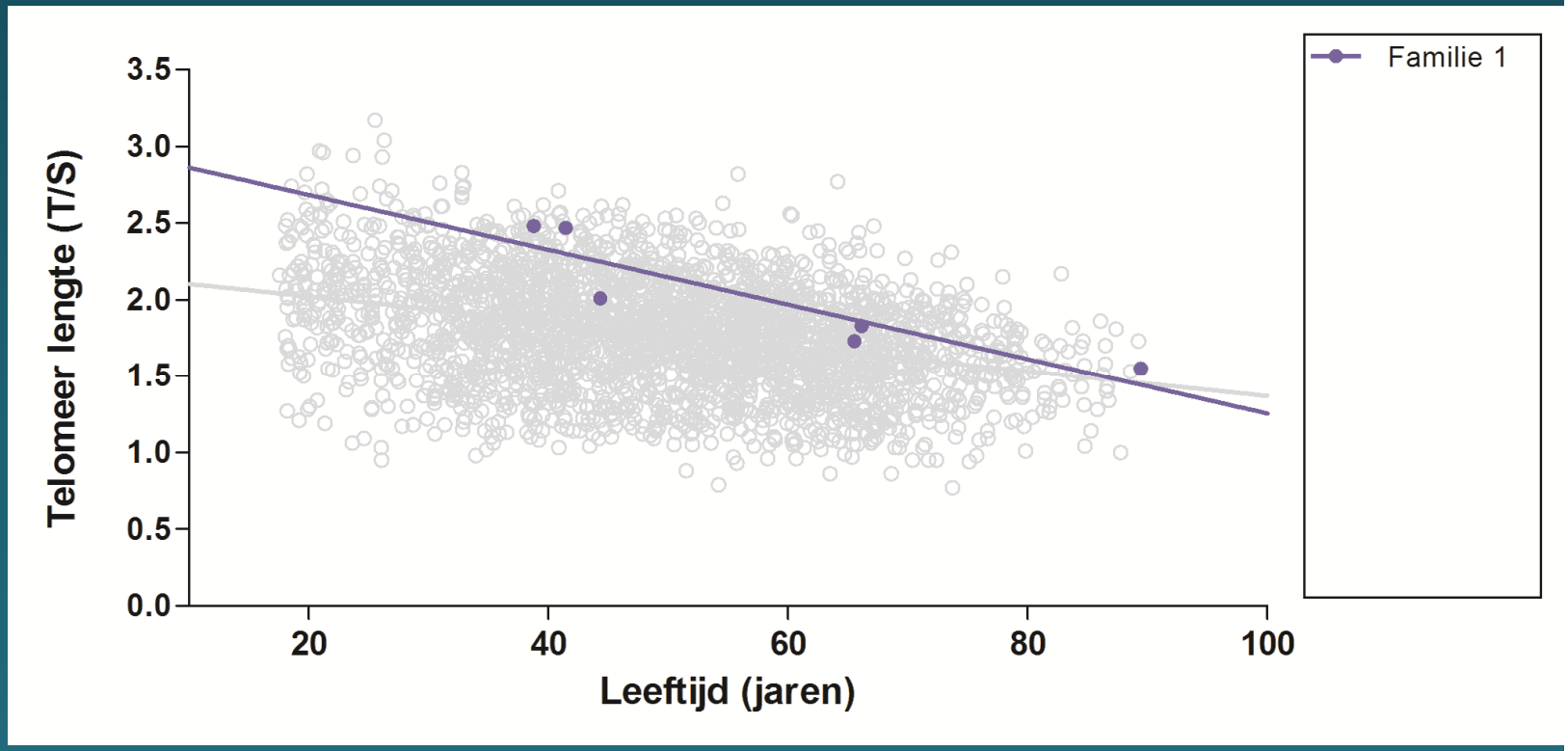

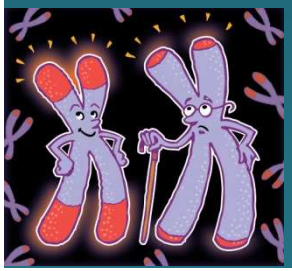

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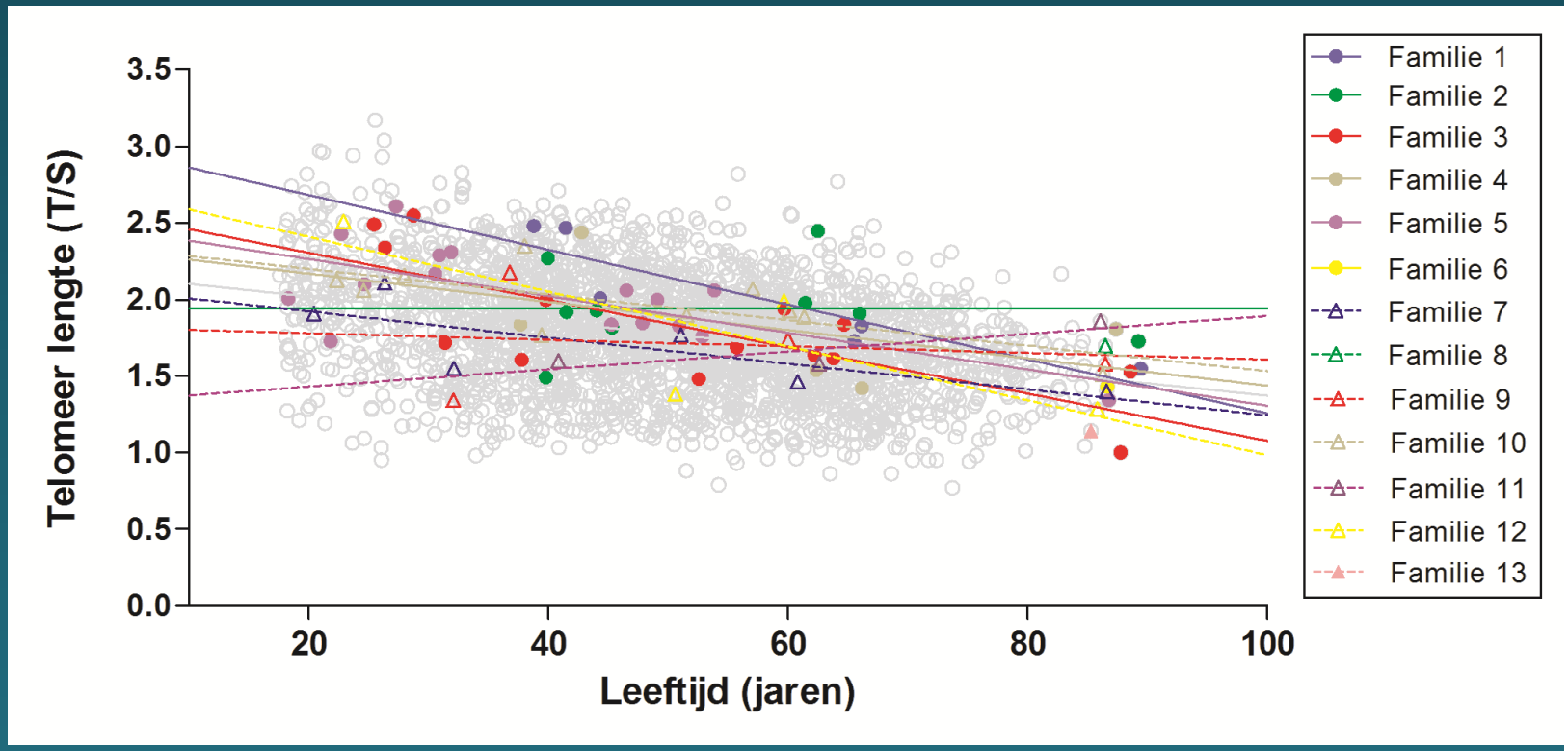

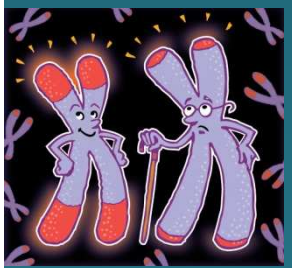

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Conclusies

- Langlevendheid voor meer dan 80% bepaald door veelvoorkomende varianten
- *HSF2* is geassocieerd met langlevendheid
- Relatie tussen telomeer lengte en sterfte moet in jongeren onderzocht worden

Dank U