

## Rate of *de novo* mutations and the importance of father's age to disease risk

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Nature, 2012

# Abstract

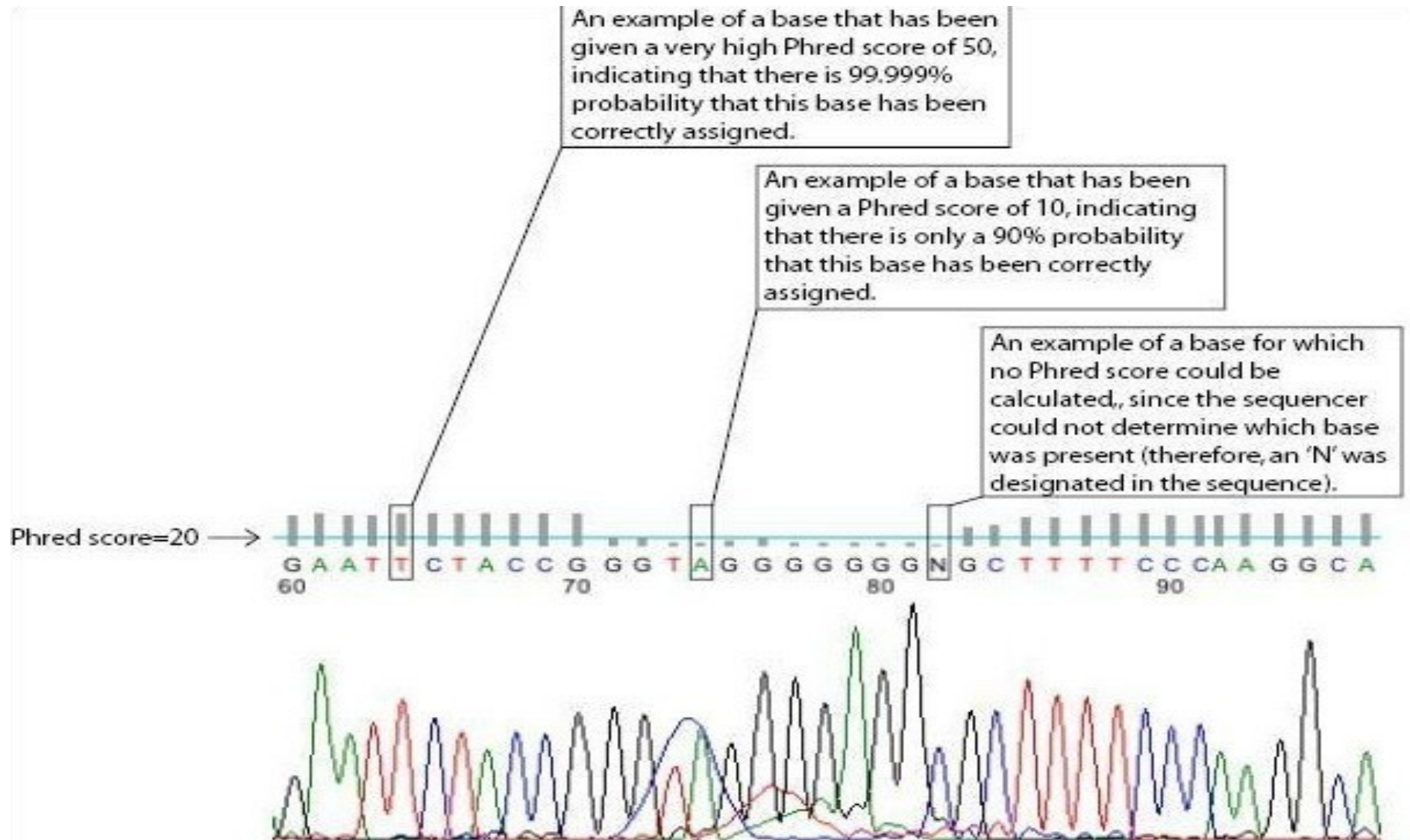
- Entire genomes of 78 Icelandic parent–offspring trios
- Average father's age 29.7 years
- Average new/*de novo* mutation rate **1.2e-8** per nucleotide per generation
- 2 *de novo* mutations for every year of the father
- Poisson blames the fathers

# Who participated?

- Some parents
- 44 children with autism
- 21 schizophrenic children
- 21 happy scientists

main conclusion: Schizophrenia and autism  
because of not freezing your sperm!

$$\text{Phred score} := -10 \cdot \log(P)$$



# Criteria for calling *a de novo* SNP mutation

Input: ~2'000 human genomes

where...

lik( $\cdot$ ) – likelihood based  
on Phred vals

**R** – reference allele

**A** – alternative allele

From all (**A**,**R**) pairs leave only:

1. (brand new mutation, not allele)

$\text{lik}(\text{AR})/\text{lik}(\text{RR}) < 10'000$  and  $\text{lik}(\text{AA})/\text{lik}(\text{RR}) < 10'000$

2. (Illumina lies?)

>15 quality reads at the mutated site

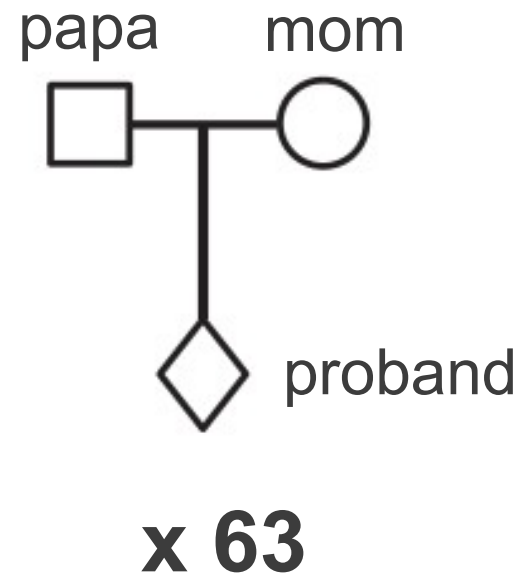
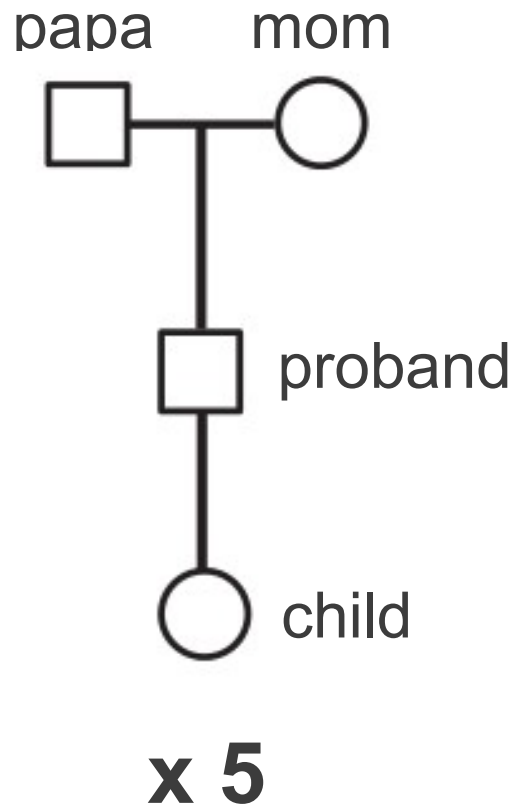
3.  $\text{lik}(\text{AR})/\text{lik}(\text{RR}) > 1e10$  ???

4. for both parents, the ratio  $\text{lik}(\text{RR})/\text{lik}(\text{AR})$  is above 100

5. the number of A allele calls is above 30%

Output: ~5'000 candidate mutations.

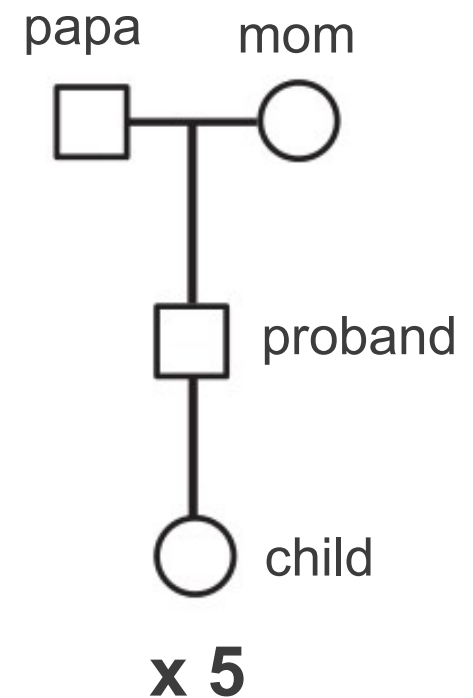
# Two different approaches



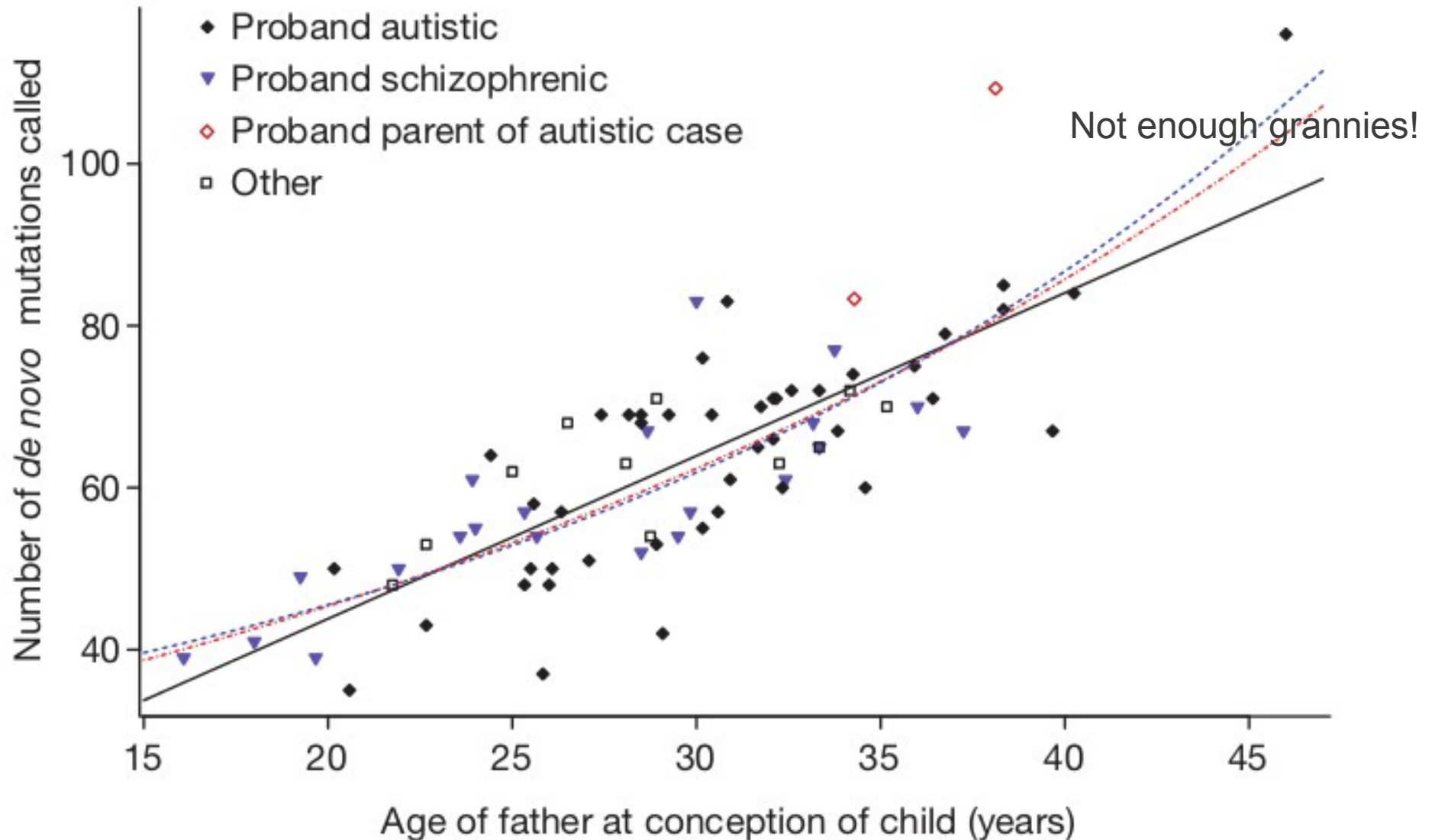
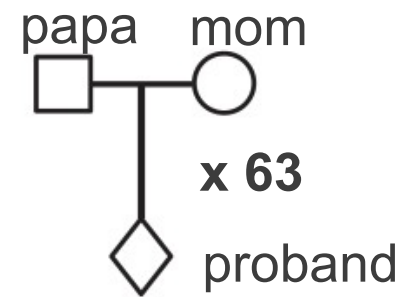
# First approach: Parent of origin is clear

**Table 1 | *De novo* mutations observed with parental origin assigned**

	Father's age (yr)	Mother's age (yr)	Number of <i>de novo</i> mutations in proband		
			Paternal chromosome	Maternal chromosome	Combined
Trio 1	21.8	19.3	39	9	48
Trio 2	22.7	19.8	43	10	53
Trio 3	25.0	22.1	51	11	62
Trio 4	36.2	32.2	53	26	79
Trio 5	40.0	39.1	91	15	106
Mean	29.1	26.5	55.4	14.2	69.6
s.d.	8.4	8.8	20.7	7.0	23.5
Variance	70.2	77.0	428.8	48.7	555.3



# Second approach: Who is the parent?





# Three fitting models

- Linear
- Exponential
- Exponential with mother's de novo mutation rate fixed at the mean value (14.2)

# Mutations

- 5000 mutations
  - 73 exonic (2 stop and 60 non-synonymous)
  - 1800 intron
  - 2500 intergenic
- 18 times higher CpG transition rate ( $A \leftrightarrow G$ ,  $C \leftrightarrow T$ )
- 2.5 times higher CpG transversion rate ( $A \leftrightarrow C/T$ ,  $G \leftrightarrow C/T$ )
- transition/transversion ratio is independent on age

# Advertisement



Transhumanism



Success rates depending on the age of the woman:

- under 35, the success rate is around 19%
- 35–39, the success rate is around 15%
- 40–42, the success rate is around 7%

# Open science

I donated my 23andme genotyping  
to the general public  
(<https://opensnp.org/users/637>)

What about you? :")