

Exercise walk-through

6.5

# Population genetics

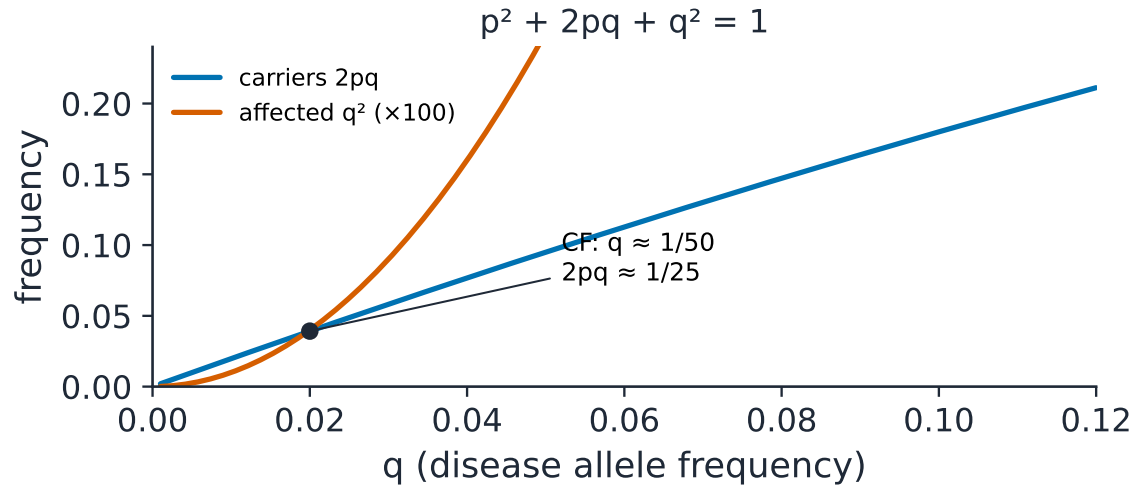
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University Medicine

# Population genetics: one equation does the work

- 1 **Equation**  $p^2 + 2pq + q^2 = 1$ ; carriers are  $2pq$ , NOT  $q^2$ .
- 2 **CF**  $q^2 = 1/2500 \rightarrow q = 1/50 \rightarrow 2pq \approx 1/25$  - the 4% **carrier** rate from a disease rate.
- 3 **Screening** Couple risk  $1/25 \times 1/300$  (residual after negative screen)  $\times 1/4 \approx 1/30\,000$  - quoted residuals, never zero.

# Population genetics - the figure



**Carrier**  $2pq$  and affected  $q^2$  curves against  $q$ .

## Exercises 2.1-2.3

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**2.1** A recessive disease at 1/10 000: compute  $q$  and the carrier rate. [3]

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**2.2** Tay-Sachs carrier frequency in Ashkenazi Jews (about 1/30): what is  $q$  approximately? [3]

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**2.3** Why does sickle heterozygosity stay common in malarial regions? [3]

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**2.1**

- $q = \sqrt{(1/10\,000)} = 1/100$ ; carriers  $2pq \approx 1/50$  ✓.

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**2.2** Tay-Sachs carrier frequency in Ashkenazi Jews (about 1/30): what is  $q$  approximately? [3]

**2.2**

- $q \approx 1/60$  ( $2pq \approx 1/30 \rightarrow q \approx 1/60$ ).

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**2.3** Why does sickle heterozygosity stay common in malarial regions? [3]

**2.3**

- Heterozygote advantage against malaria (selection).

## Exercise 3.1

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**3.1** CF carrier screening (fictional): the woman is a known carrier (1/1); her partner tests negative (panel detection ~95 %; population carrier rate 1/25).

Compute the partner's residual carrier risk after the negative test. Compute the affected-child risk. Explain why the answer is not zero. [7]

## Exercise 3.1

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### 3.1

- Residual =  $(1/25 \times 0.05) / (1/25 \times 0.05 + 24/25 \times 1) \approx 0.002 \approx 1/500$  ✓ (Bayes).
- Child risk =  $1 \times 1/500 \times 1/4 = 1/2000$  ✓.
- Not zero: no panel detects every variant (CNVs, regulatory, rare missense).

## Exercise 3.2

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**3.2** A population screens newborns for a recessive disease at  $q^2 = 1/40\,000$ .

Compute  $q$  and the carrier frequency. Compute the chance two unrelated carriers marry (from carrier frequencies). State how a founder effect changes the arithmetic. [7]

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### 3.2

- $q = \sqrt{1/40\,000} = 1/200$ ; carriers  $\approx 1/100$  ✓.
- Two carriers meeting:  $(1/100)^2 = 1/10\,000$ ; with the  $1/4$  affected-child factor that IS the  $1/40\,000$  disease rate ✓.
- A founder effect concentrates the allele in a subgroup: carriers  $1/30 \rightarrow q^2$ -based expectations rise orders of magnitude.