An introduction to statistical inference

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Course plan

- 2pm-3pm: lecture, "An introduction to statistical inference"
- 3.15pm-5pm: practical

Outline

1. The scientific process and statistics
2. Can statistics help to determine causation?
3. Estimating interesting quantities using regression
4. Model based thinking
5. Unpicking the signal from the noise

What is the aim of scientific inquiry?

Understand how the universe works.

What does it mean to understand the universe?

Why do we need data and statistics?

Question: can't we just use data we collect?

Nate Silver

"The numbers have no way of speaking for themselves. We speak for them. We imbue them with meaning."

But why do we need statistics?

- The universe is complex
- Its mechanisms are not directly observable
- Our data contain information both about the mechanisms and other nuisance factors

$\Longrightarrow$ we need to make assumptions that separate signal from noise

How statistics separates signal from noise?

$$\text{observations} = \text{signal} + \text{noise} \tag{1}$$

- Signal contains our interesting scientific mechanism
- Noise contains a bunch of things not of interest

Since we do not know or observe the exact noise processes, in statistics, it is assumed that the noise is represented as being *random*.

But random does not mean unstructured. In statistics, making assumptions about the nature of the random process allows us to bound its influence on the observed data.

Example 1: flipping a coin

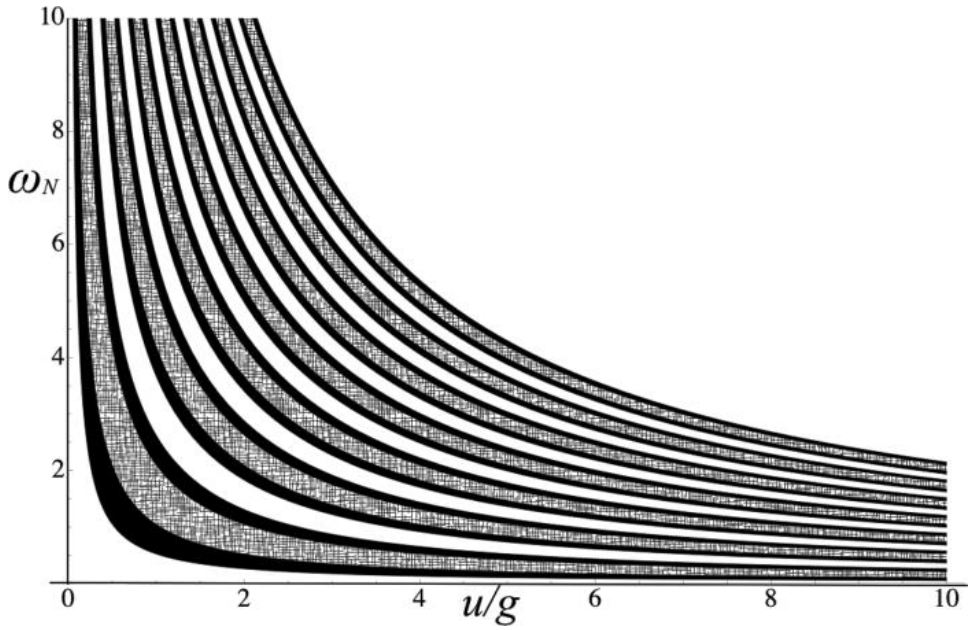
Suppose we flip a coin twice. We could obtain:

- Two tails
- One head; one tail
- Two heads

Why can we get different outcomes each time the coin is flipped?

Different initial conditions

Precessional frequency: ω_N; Magnitude of upward velocity, u.[1]



White indicates heads; hatched indicates lands on sides; black indicates tails.

[1] From Probability, geometry, and dynamics in the toss of a thick coin, Yong and Mahadevan (2011)

Coin flip dynamics: physics approach

Solve complex equations of motion (making assumptions about flipping process). One part of the system:

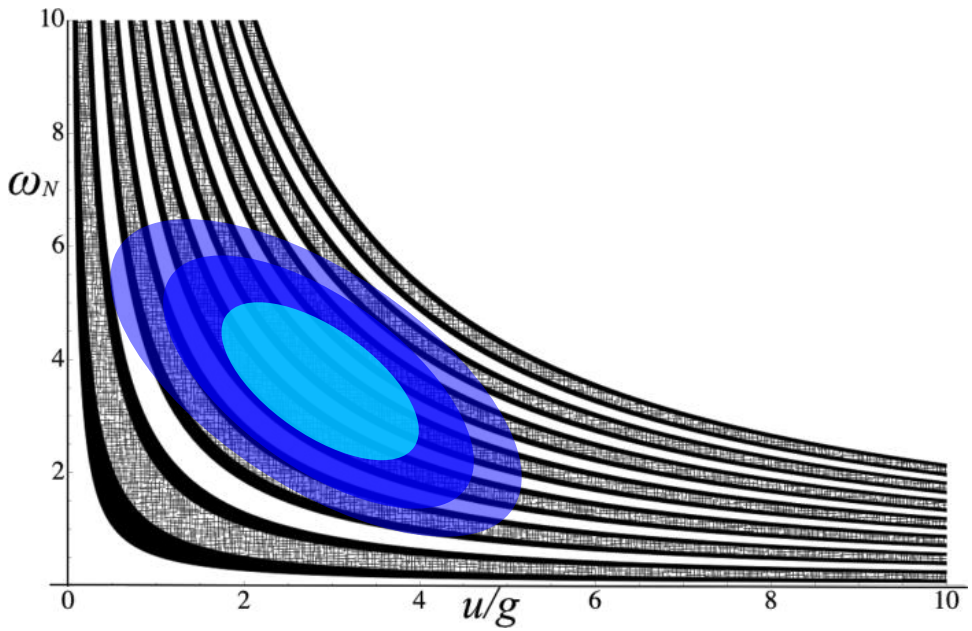
$$\frac{d\boldsymbol{N}}{dt} = \Omega \times \boldsymbol{N} \tag{2}$$

This system determines outcome given a set of initial conditions: precessional frequency and magnitude of upward velocity.

But we still don't know how different people throw a coin, so we'd need to measure this and likely represent this using randomness!

Coin flip dynamics: statistical approach

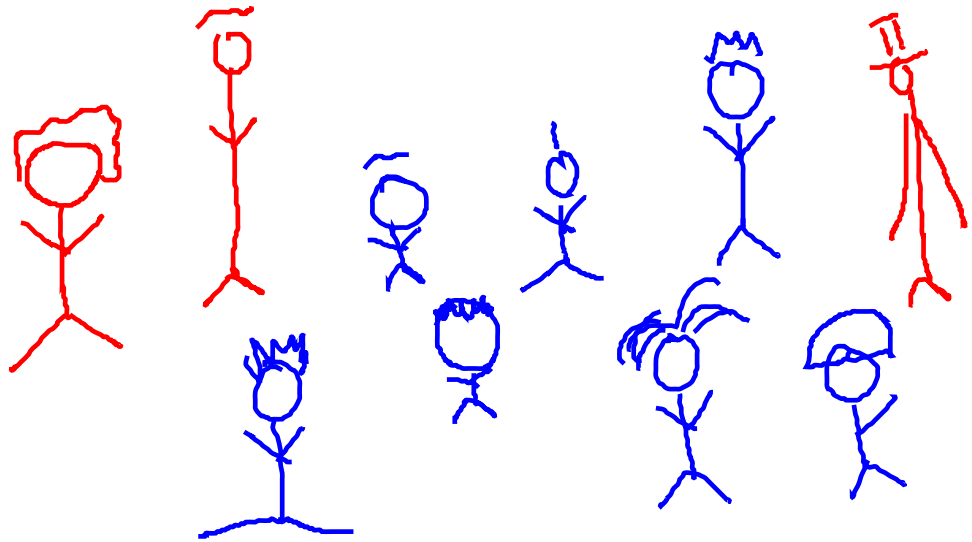
Assume outcome of a coin flip is a random variable with a probability of landing heads up (binomial distribution[2]). Implicitly:



[2] If we forget the landing on side situation.

Example 2: determining COVID-19 seropositivity

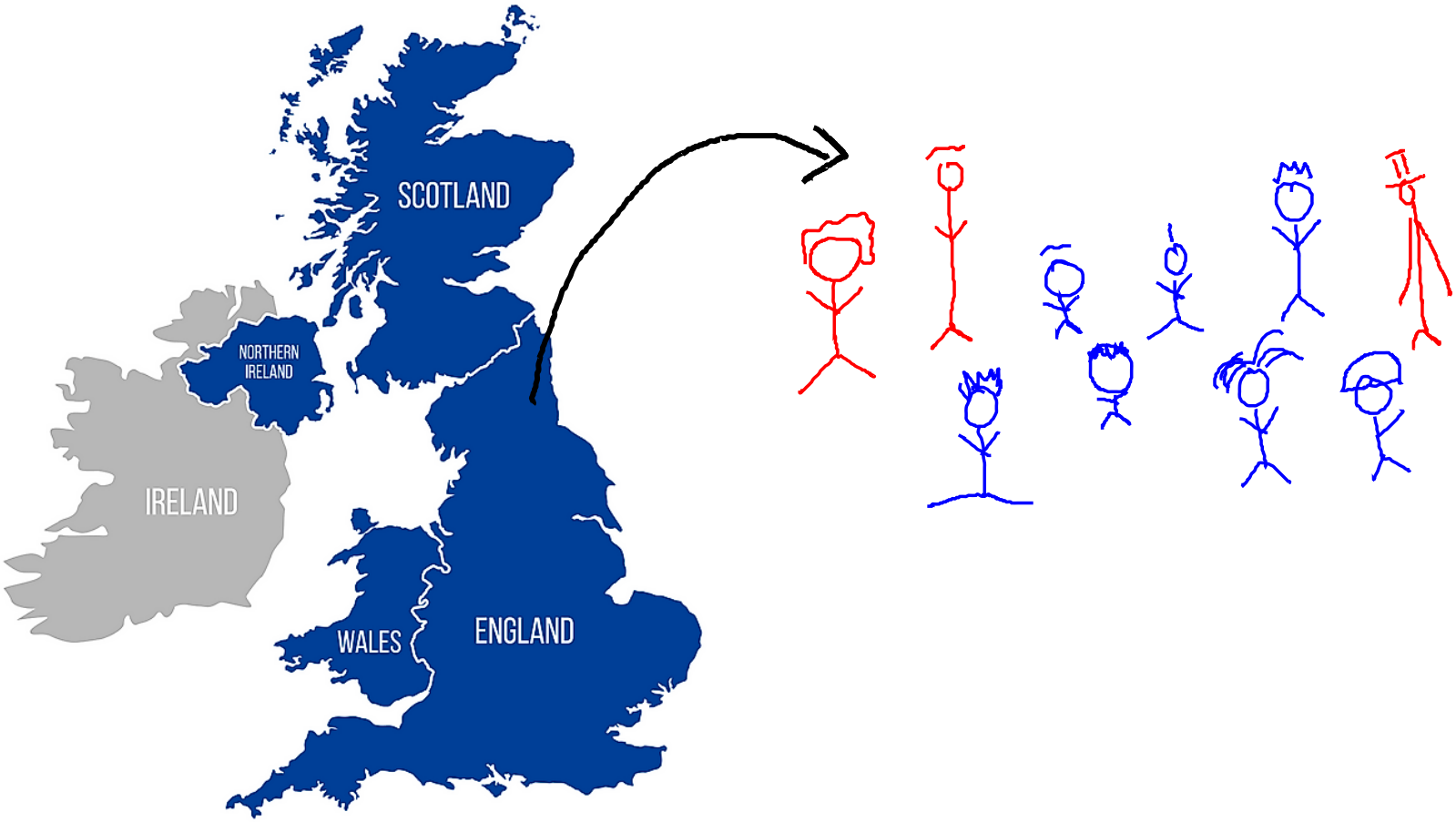
Imagine we want to determine the proportion of the UK population who have COVID-19 antibodies. To do this, we find 10 individuals and test their blood.



Does this mean $3/10 = 30\%$ of the UK population have these antibodies?

The sampling process yields variation in outputs

No.

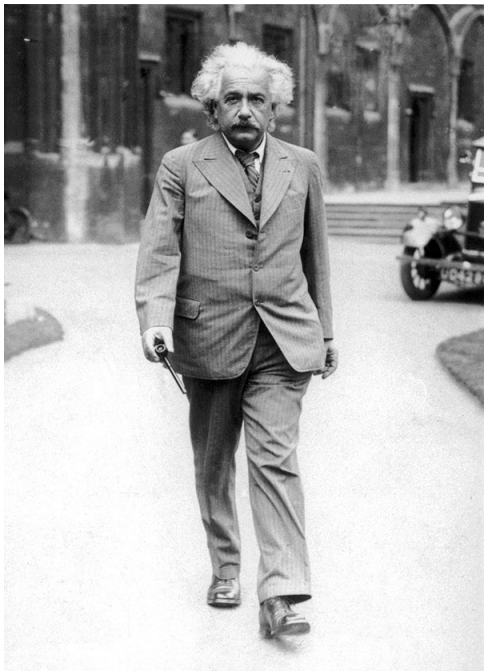


Correlation and causation

“”Correlation is not causation”. With good reason! The rooster’s crow is highly correlated with the sunrise; yet it does not cause the sunrise. Unfortunately, statistics has fetishized this commonsense observation. It tells us that correlation is not causation, but it does not tell us what causation is.”

Smoking and lung cancer: how did we get here?

Experiments: easier but immoral



"Development of Western science is based on two great achievements: the invention of the formal logical system (in Euclidean geometry) by the Greek philosophers, and the discovery of the possibility to find out causal relationships by systematic experiment (during the Renaissance)."

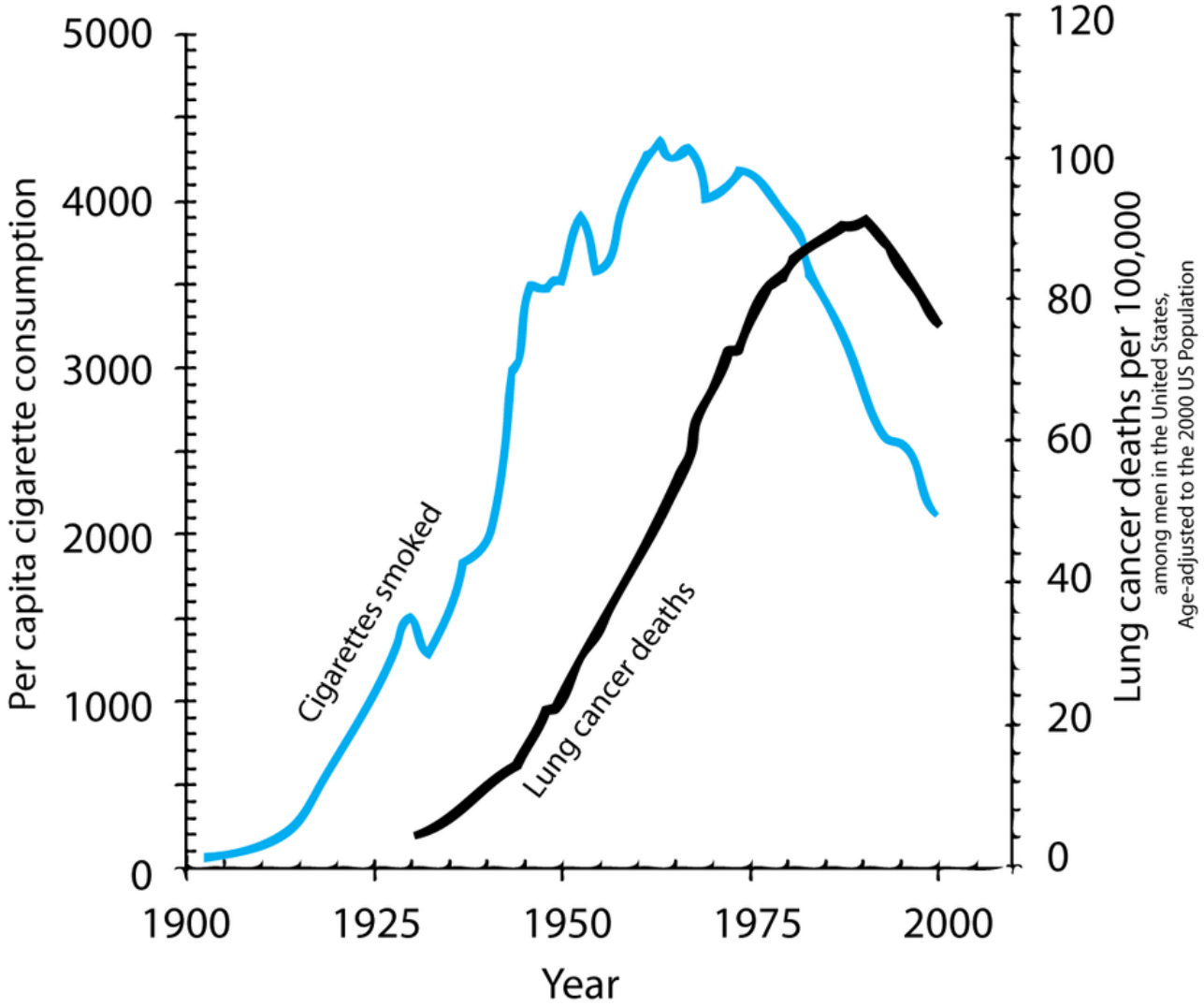
Occurrence of lung cancer: early on

Lung cancer was once a very rare disease, so rare that doctors took special notice when confronted with a case, thinking it a once-in-a-lifetime oddity.

Lung cancer was not even recognised medically until the 18th century, and as recently as 1900 only about 140 cases were known in the published medical literature.

Both taken from "The history of the discovery of the cigarette-lung cancer link: evidentiary traditions, corporate denial, global toll", Proctor, *Tobacco Control* 2012.

Correlation: early-mid twentieth century



Case-control: Doll and Hill, 1950

son is shown in Table IV.

TABLE IV.—*Proportion of Smokers and Non-smokers in Lung-carcinoma Patients and in Control Patients with Diseases Other Than Cancer*

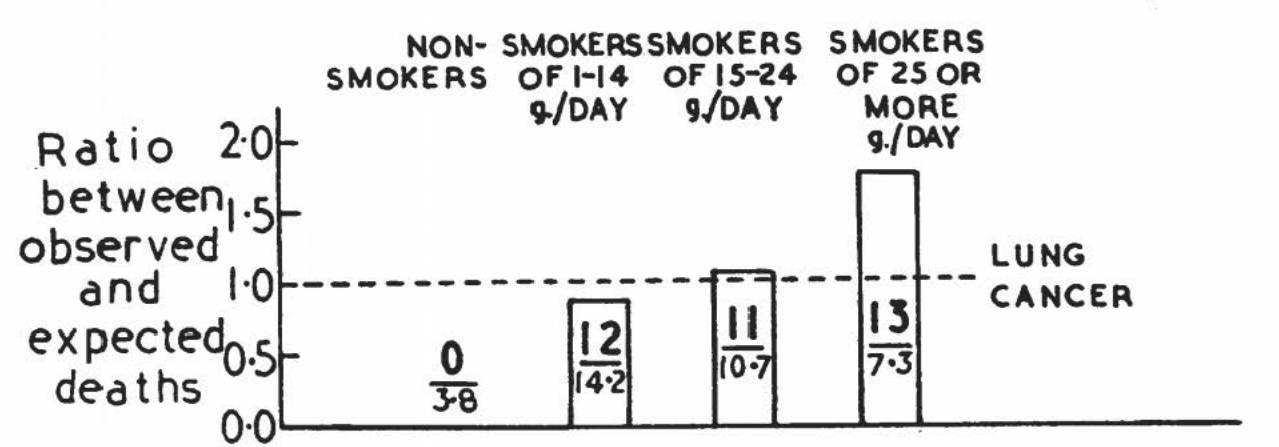
Disease Group	No. of Non-smokers	No. of Smokers	Probability Test
Males:			
Lung-carcinoma patients (649)	2 (0·3%)	647	P (exact method) = 0·00000064
Control patients with diseases other than cancer (649) ..	27 (4·2%)	622	
Females:			
Lung-carcinoma patients (60)	19 (31·7%)	41	$\chi^2 = 5{\cdot}76$; n = 1 0·01 < P < 0·02
Control patients with diseases other than cancer (60) ..	32 (53·3%)	28	

It will be seen that the vast majority of men have been

"Smoking and carcinoma of the lung", Doll and Hill, *BMJ* 1950.

Prospective cohort study: Doll and Hill, 1954

Study of over 40,000 doctors.



"The mortality of doctors in relation to their smoking habits", Doll and Hill, *BMJ* 1950.

Other sources of causal evidence

Animal studies:

- 1931: Roffo showed that smoke condensed from distillation of tobacco caused tumours when smeared on skins of rabbits
- 1953 Wynder, Graham and Croninger showed tumours could be generated by painting cigarette smoke tar onto backs of shaved mice

Cellular pathology:

- 1956: Hilding demonstrated that smokers experienced ciliastasis and that the cilia were being deadened at parts of lung wear cancers likely to develop

Other sources of causal evidence

Chemicals known to cause cancer in cigarette smoke:

- 1939: Roffo found polycyclic aromatic hydrocarbons in cigarette smoke, which had already been identified as carcinogenic components of coal tar
- 1952: Brown and Williamson identified benzpyrene in cigarette smoke
- End of 1950s: cigarette manufacturers had characterised several dozen carcinogens in cigarette smoke

Path to causal link between smoking and lung cancer

- Unethical to perform experiments on humans
- Statistical analysis of observational data played a key role
- Confluence of diverse forms of evidence

1954: a number of national health bodies advised that stopping smoking could prevent cancer

How to conclude causality from observational data

In 1965, Austin Hill set out a list of criteria to be considered before concluding that a causal link exists between an exposure and an outcome. Direct evidence:

- Effect size so large that can't be explained by confounders
- Appropriate temporal and/or spatial proximity
- Dose responsiveness and reversibility

Mechanistic evidence:

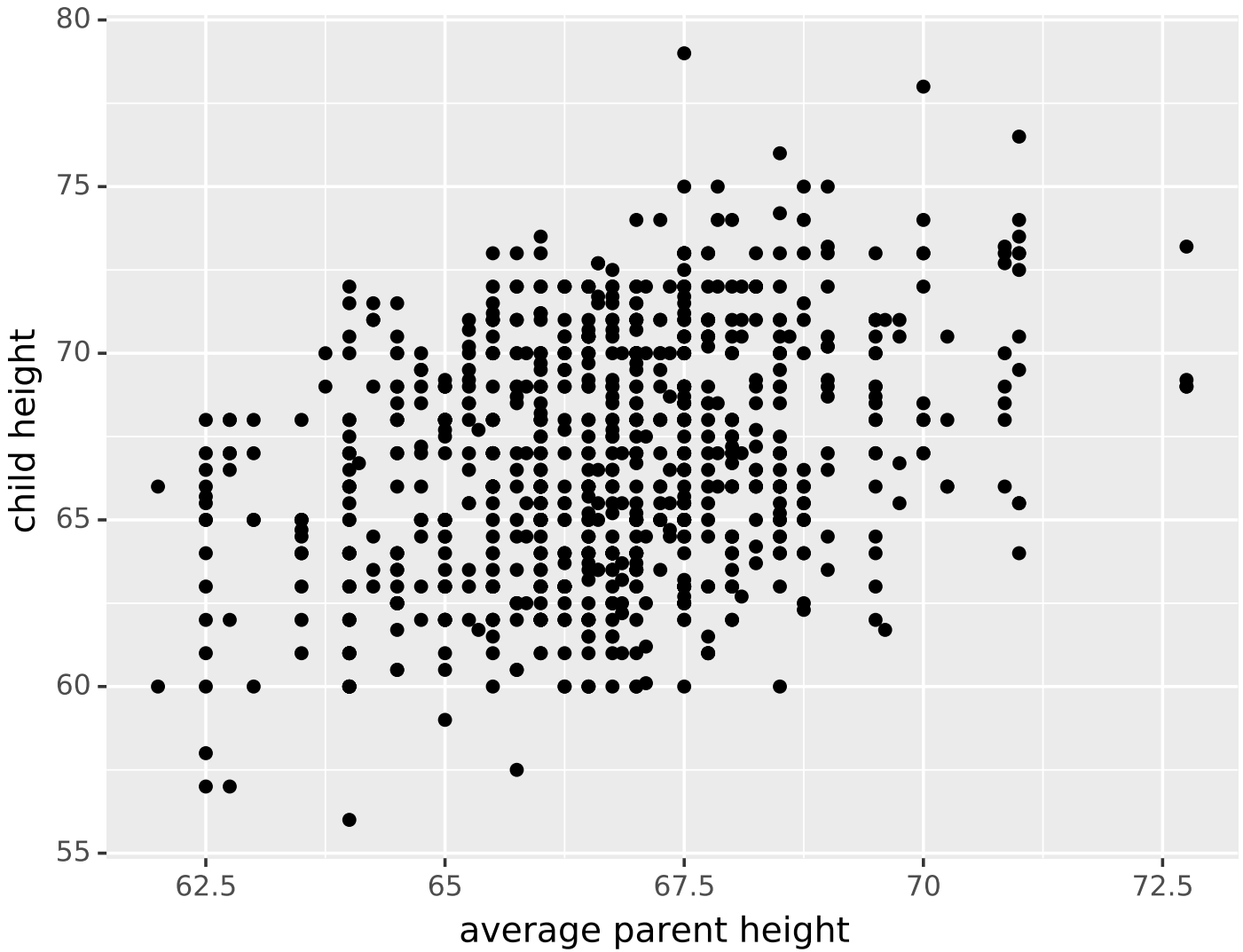
- There exists a plausible mechanism of action: biological, chemical, mechanical and so on

Parallel evidence:

- Fits with what is known already
- Effect found when study replicated
- Effect found in similar, but not identical studies

Example: Galton's 1885 study of 205 families (898 children)

Question: how inheritable is height from parent to child?



Potential model

Suppose child height linearly related to parent height:

$$\text{child}_i = a + b * \text{parent}_i. \tag{3}$$

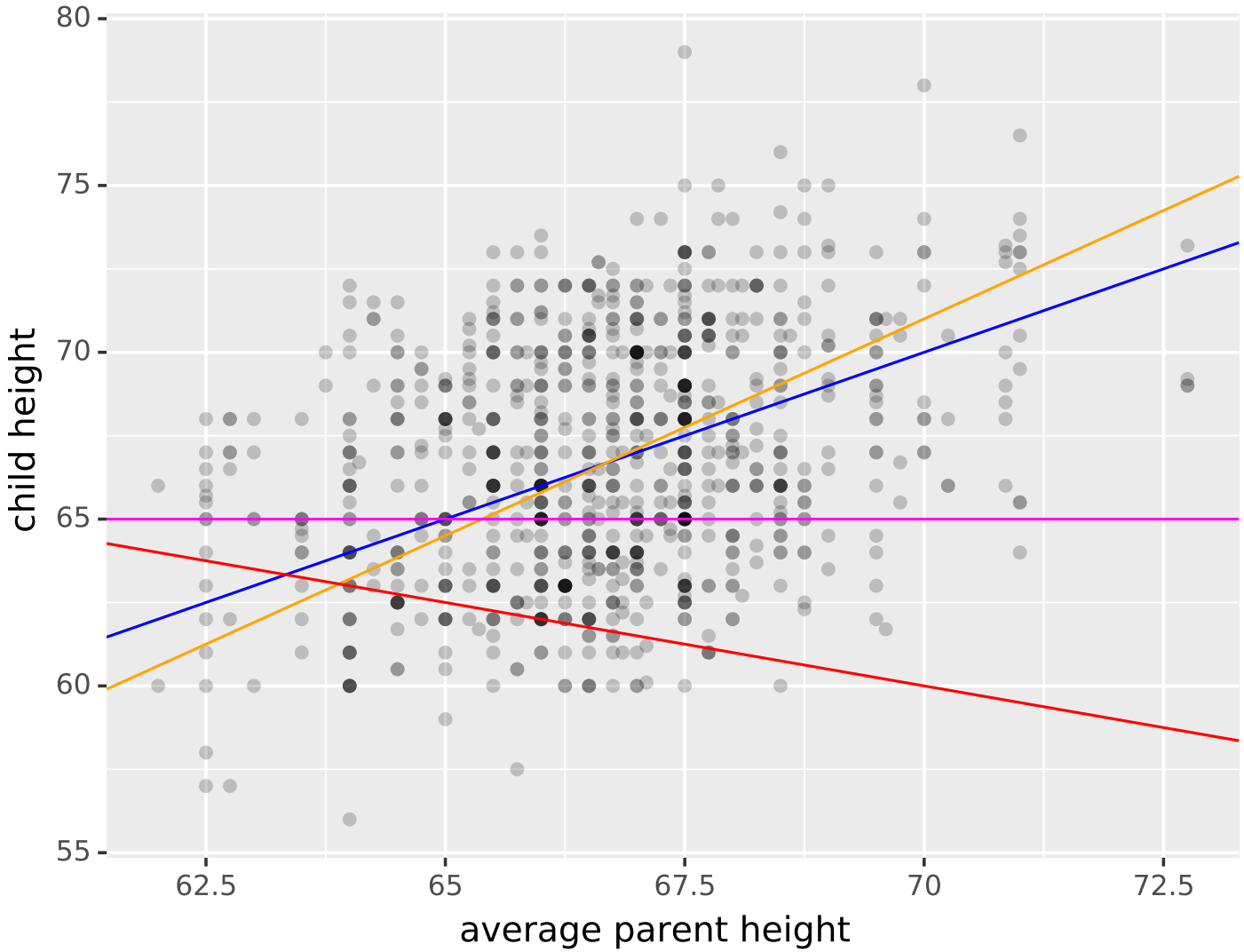
Here, b represents the effect of interest:

- $b = 1 \implies$ a 1 inch increase in average parent height is associated with a 1 inch increase in child height.
- $b = 0 \implies$ no relationship.

This isn't a causal model, so doesn't directly answer our heritability question. But it is still useful.

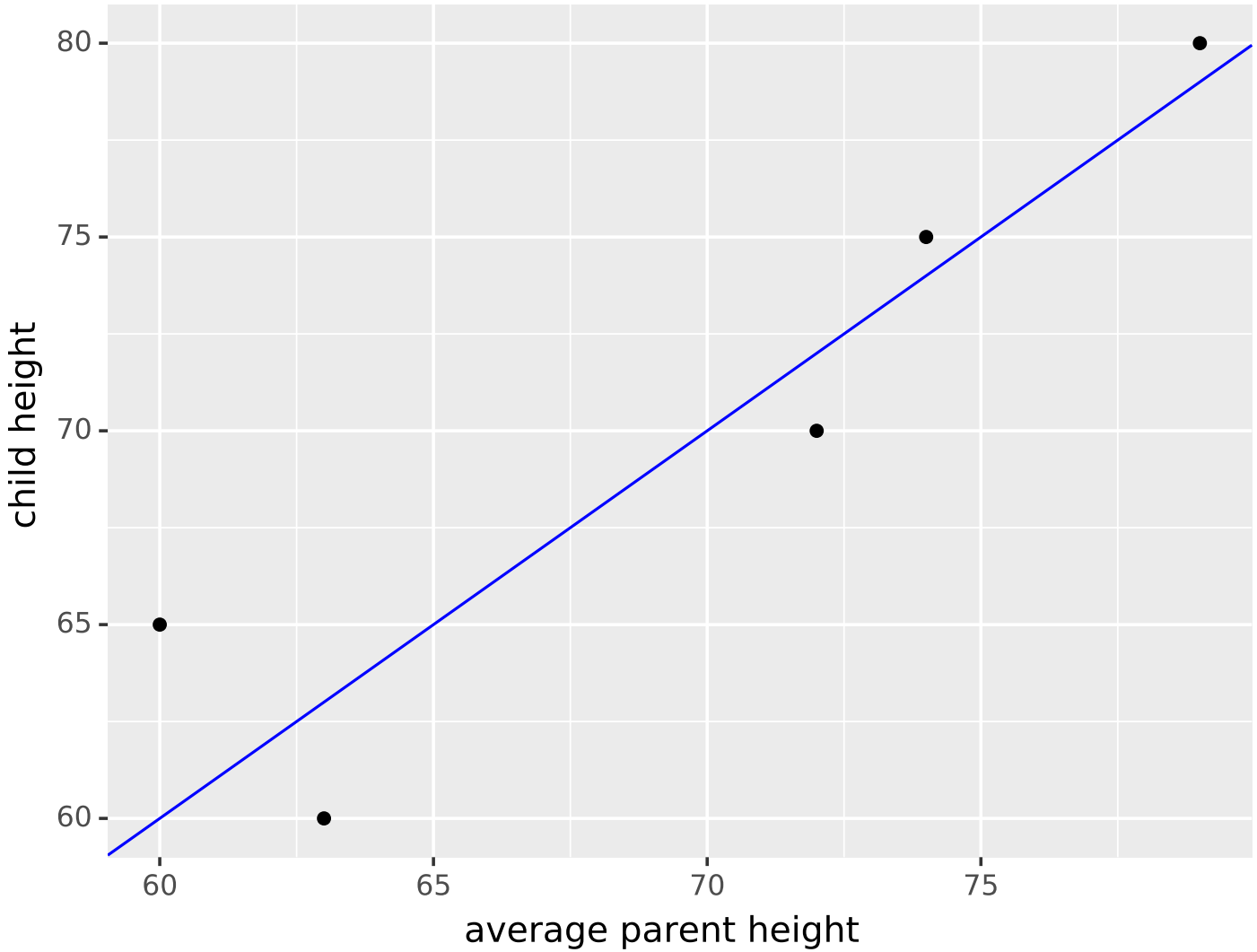
Important: this is a model: a simplified version of reality. It embodies a number of assumptions.

Example models



What's the problem with this model?

It doesn't provide a mechanism to exactly hit data.

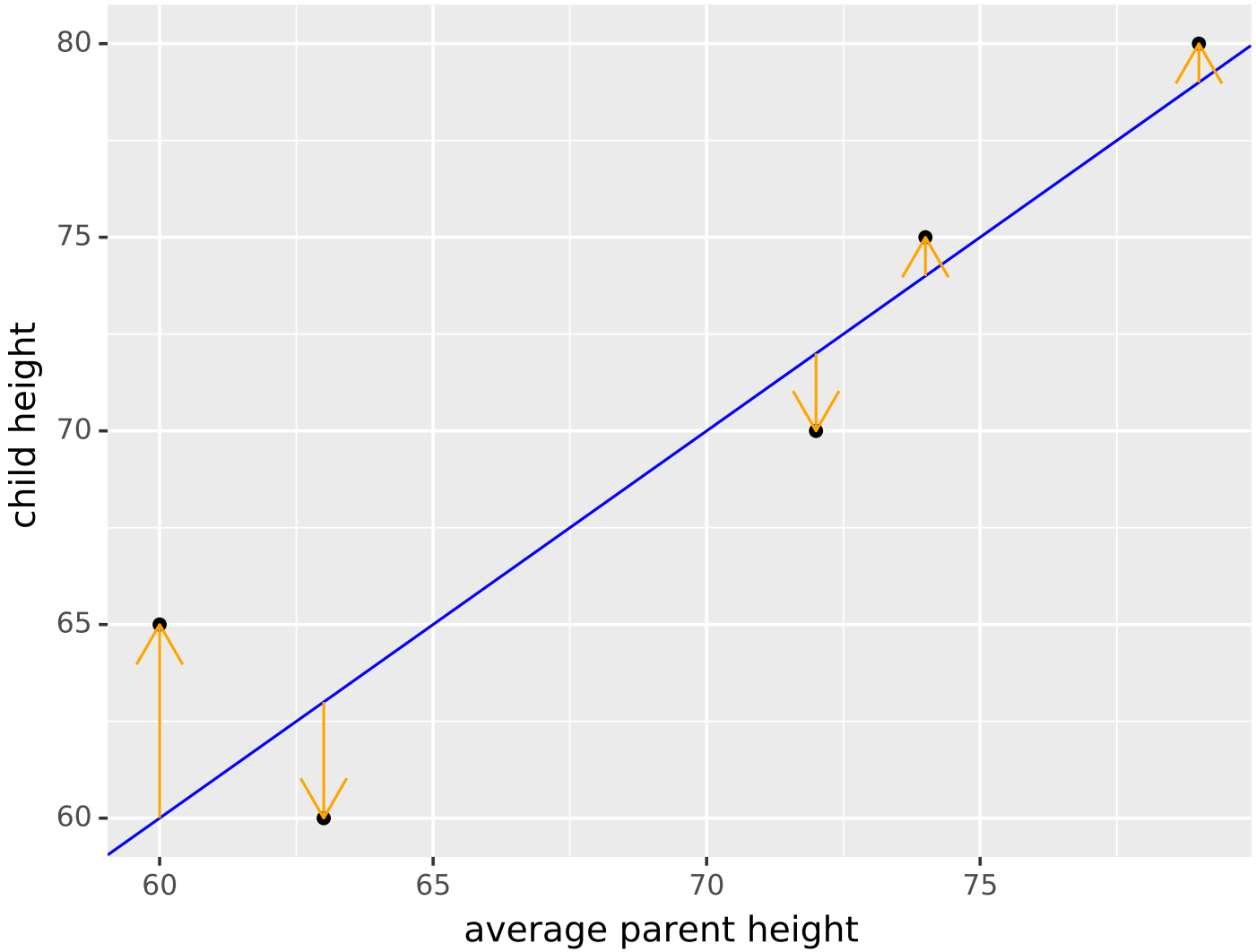


How to modify the model

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i. \tag{4}$$

where ϵ_i is a random error term representing the myriad of other factors not captured by the other parts of the model.

What does this model look like?



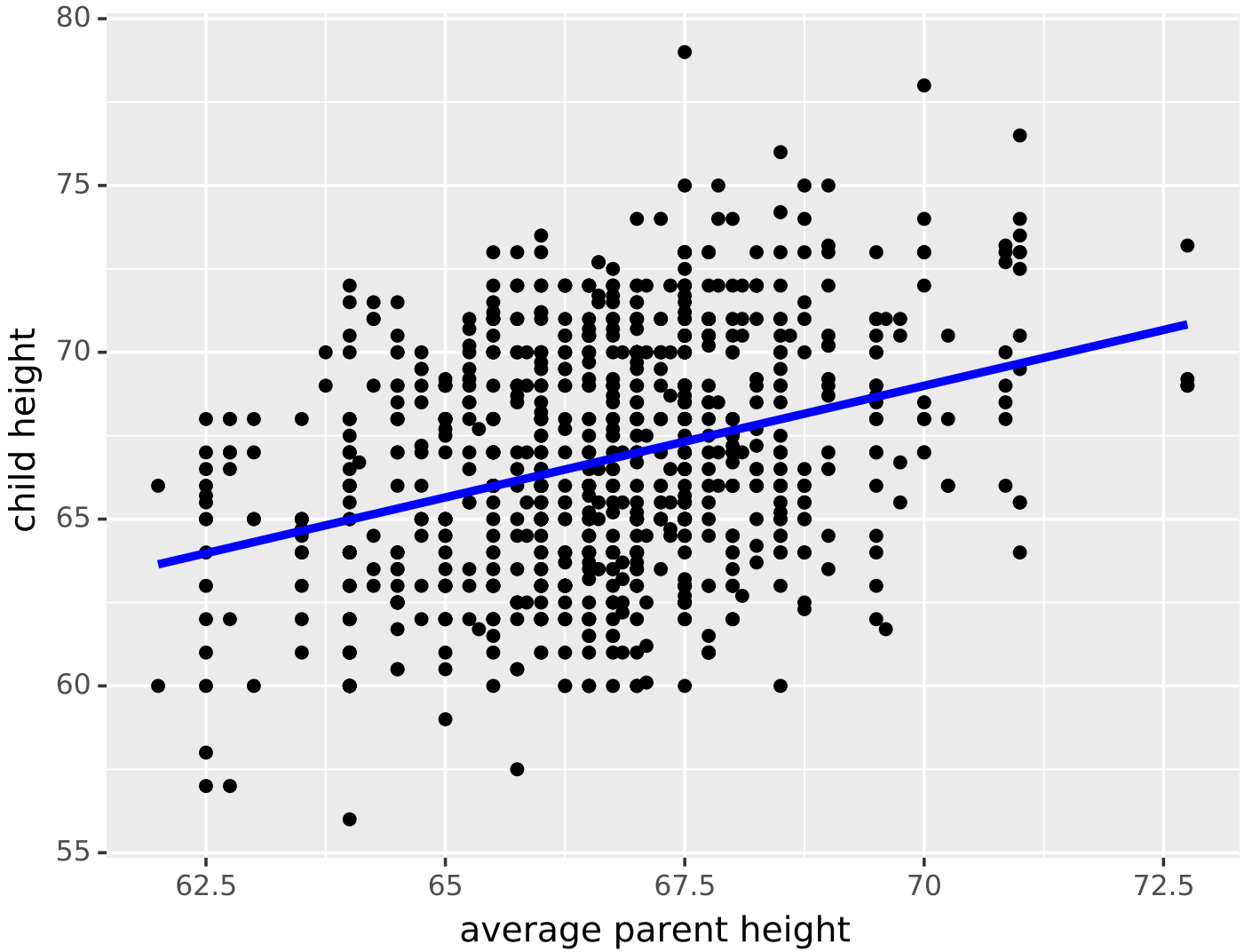
How to estimate the model's parameters from data?

Want the non-random parts of the model to explain most variation.

So, choose (a, b) so that they minimise some measure of distance between points and line. For example, sum of squared errors:

$$d = \sum_{i=1}^{N} (\text{child}_i - a - b * \text{parent}_i)^2 \tag{5}$$

Sum of squared errors fit



Other distance measures

Could have chosen the sum of absolute distances instead:

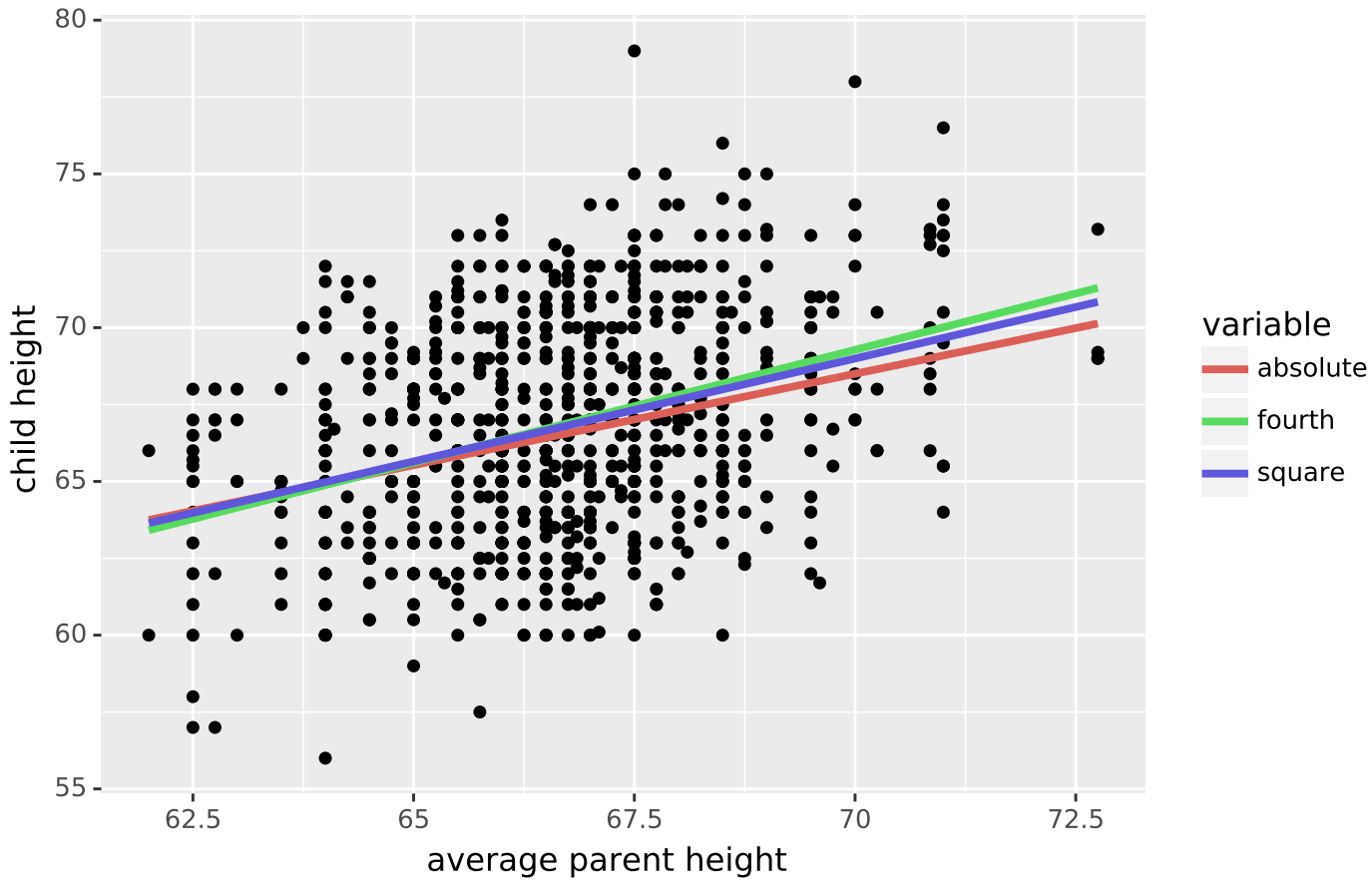
$$d = \sum_{i=1}^{N} |\text{child}_i - a - b * \text{parent}_i| \tag{6}$$

Or of fourth power:

$$d = \sum_{i=1}^{N} (\text{child}_i - a - b * \text{parent}_i)^4 \tag{7}$$

Question: how would these choices affect the fit?

Various fits



Conclude: subjective choice of 'distance' affects our estimates.

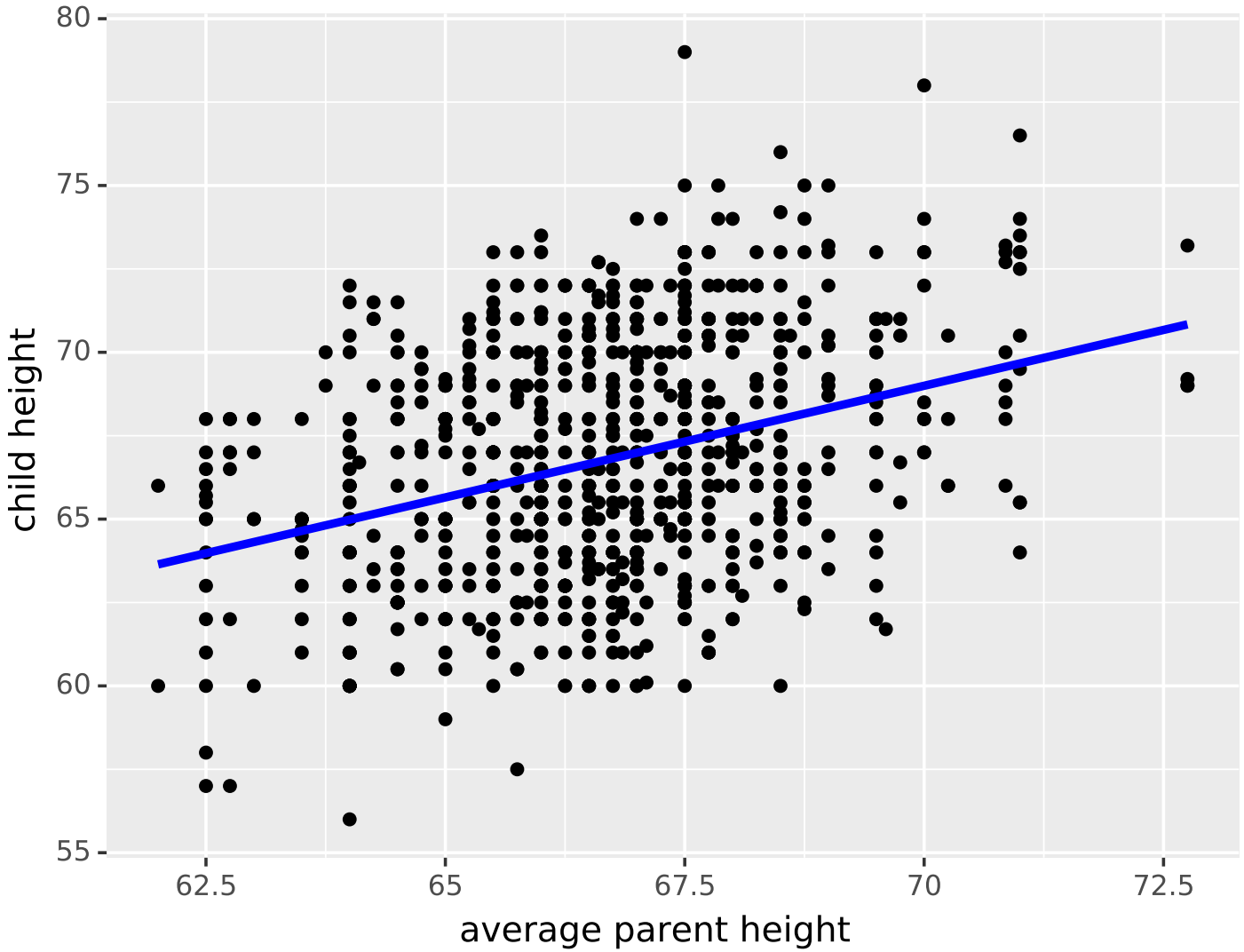
A more principled probability-based approach

Assume:

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i, \tag{8}$$

where $\epsilon_i \sim \text{normal}(0, \sigma)$.

What does this model look like? Draw

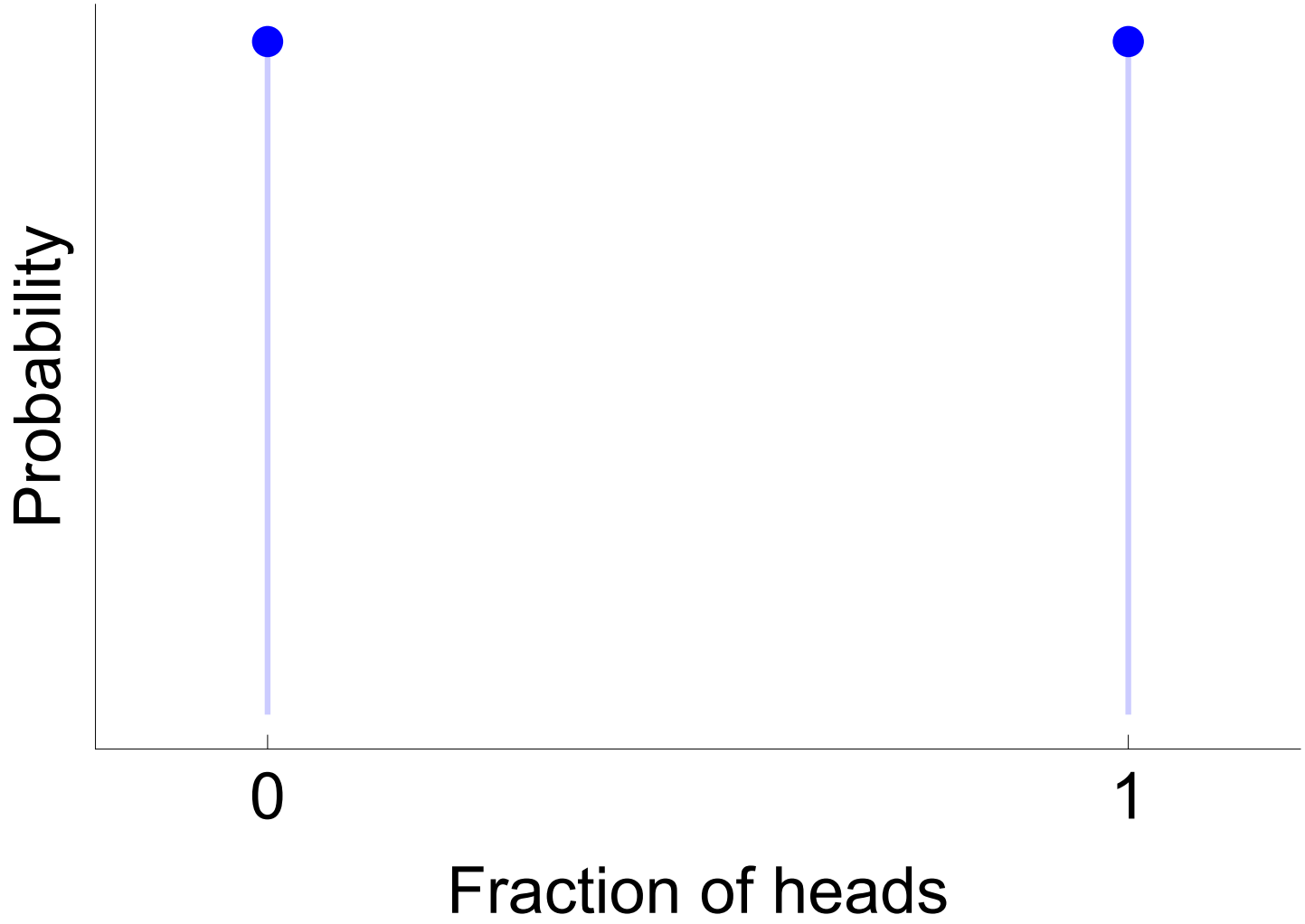


But isn't a normal distribution also arbitrary?

No! Why? The central limit theorem.

Suppose we flip a fair coin once. What does its probability distribution look like?

One coin flip

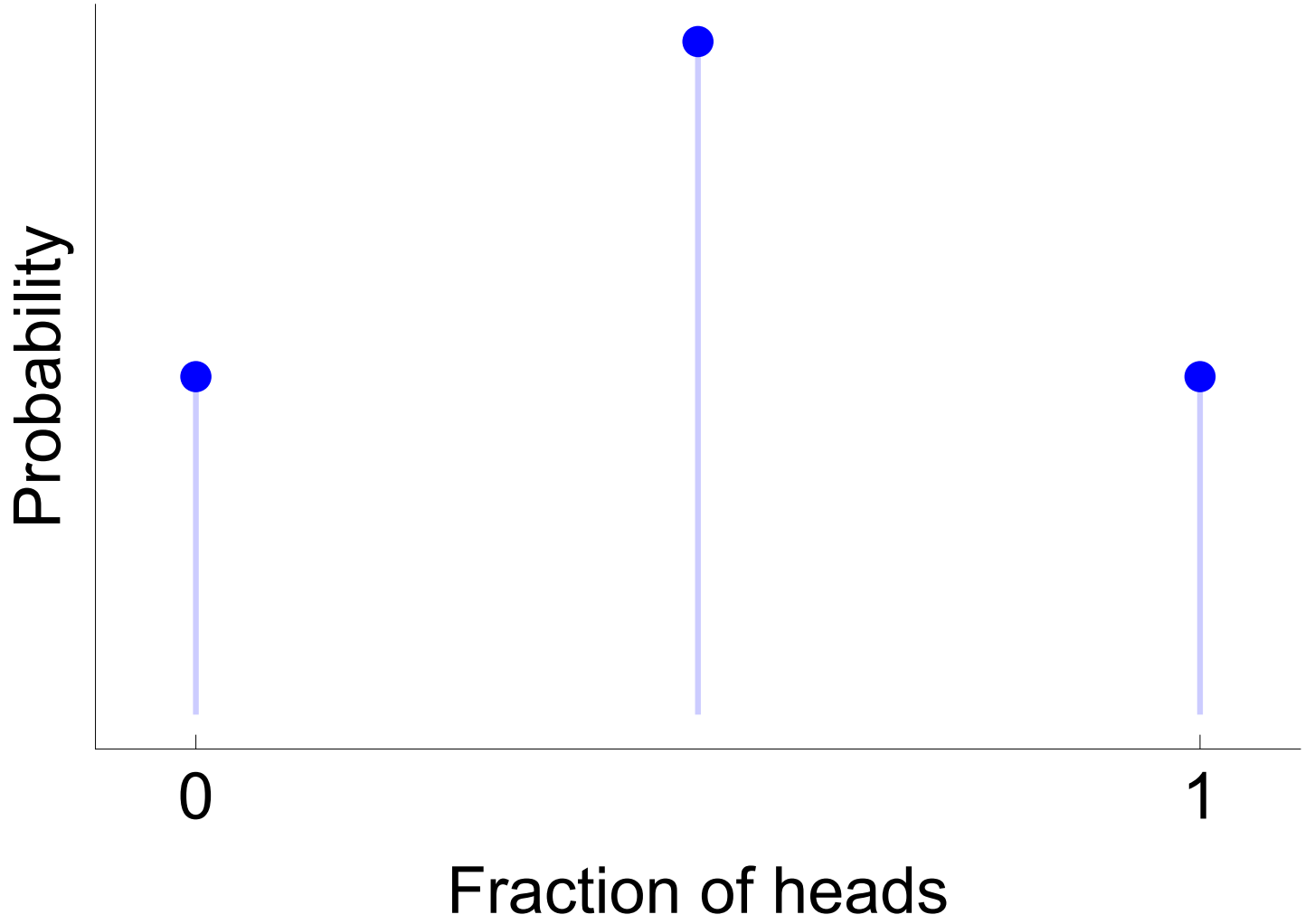


Two flips

I now flip the coin 2 times.

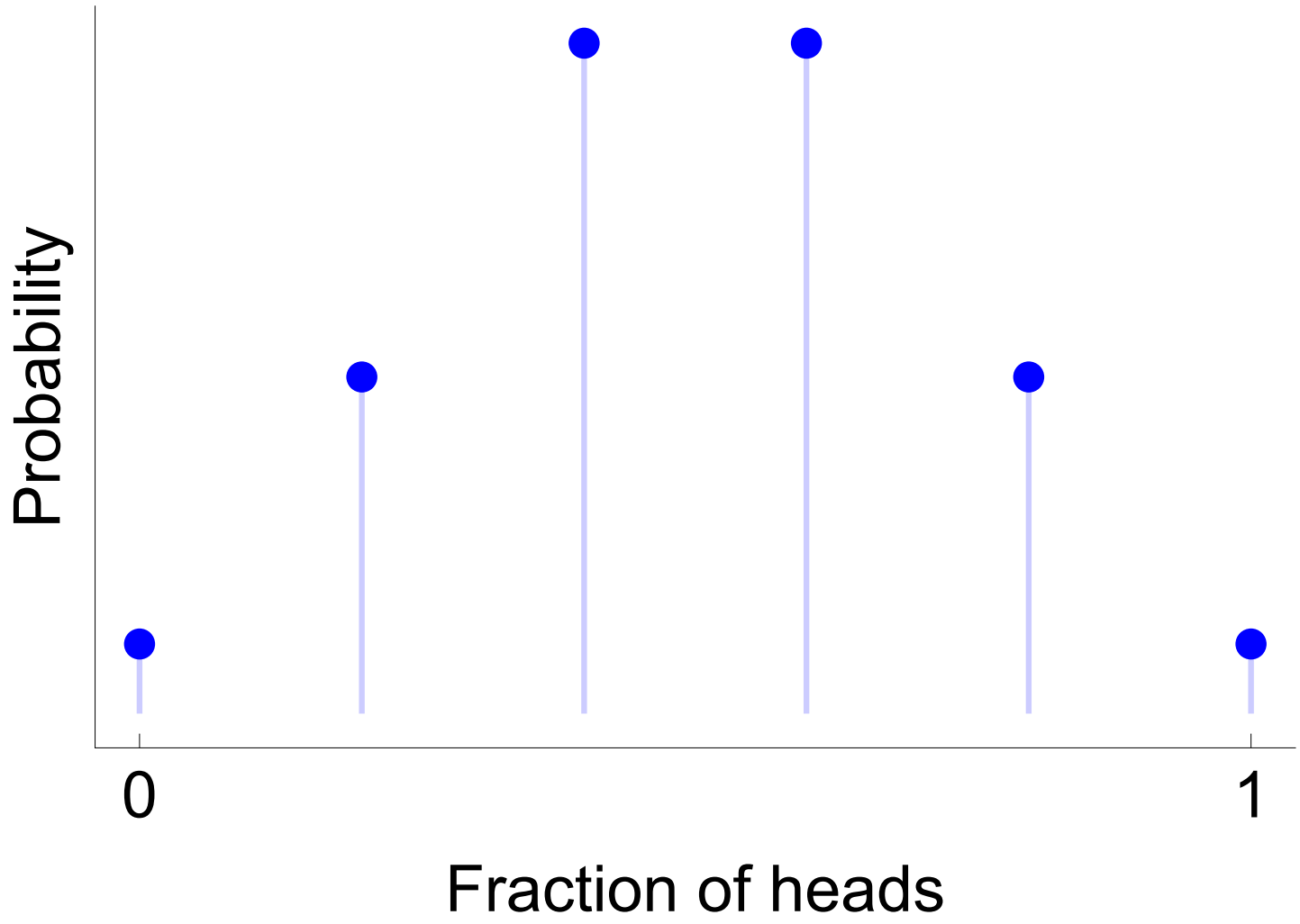
Question: What does the distribution look like now?

Two flips flips

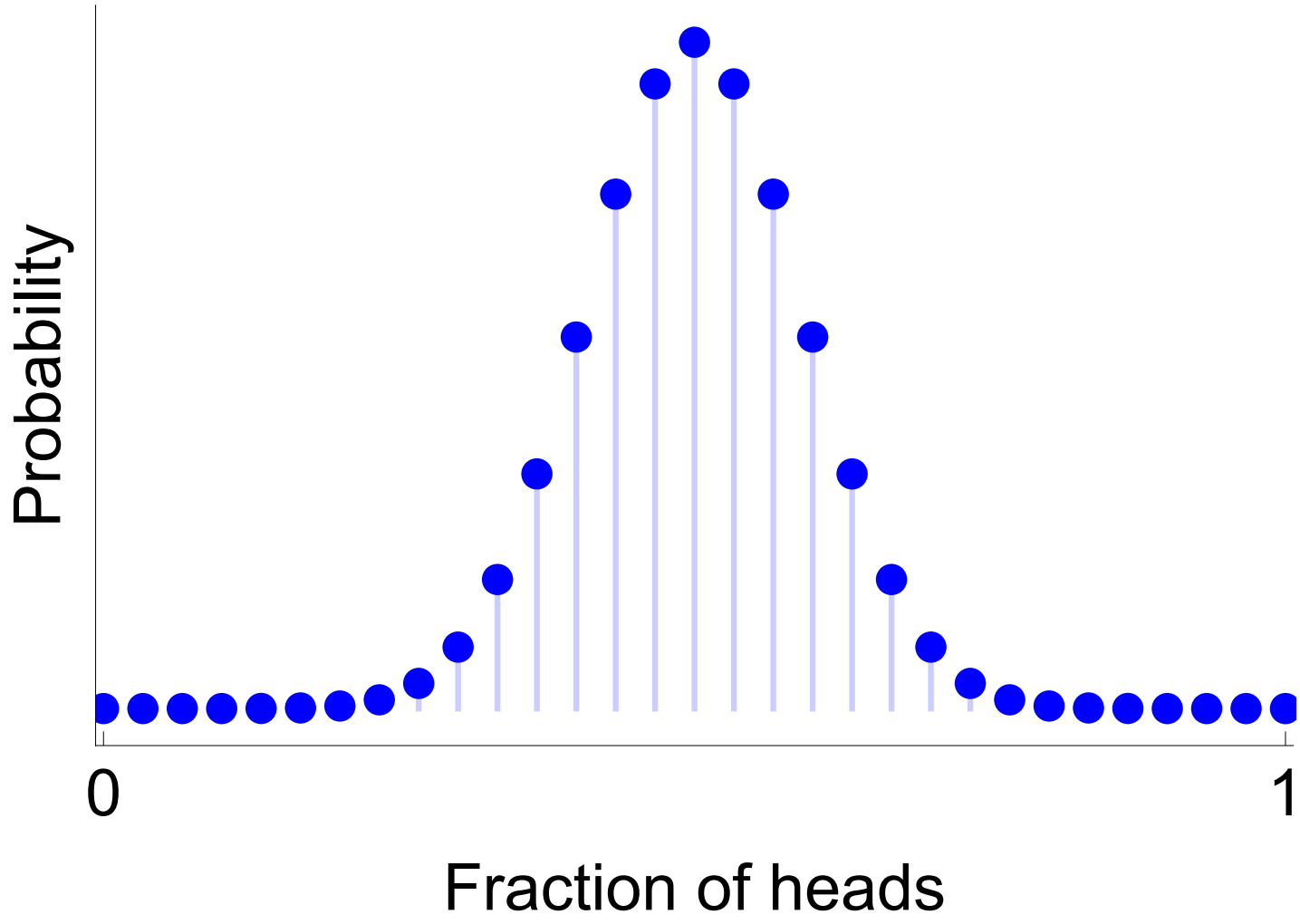


What about five flips?

What about five flips?



What about 30 flips?



What's going on?

The Central Limit Theorem (CLT) says that under general conditions:

"The distribution of the average of a large number of weakly dependent random variables is approximately normal."

In the coin flipping case, we effectively calculated the average number of independent coin flips landing heads up $\Longrightarrow$ CLT applies.

Back to our regression example

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i, \tag{9}$$

where $\epsilon_i \sim \text{normal}(0, \sigma)$.

Large number of weakly dependent factors – genetic, environmental and so-forth – likely influence a person's height.

$\Longrightarrow$

CLT applies, so normal distribution may be appropriate.

Likelihood based inference

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i, \tag{10}$$

and

$$\epsilon_i \sim \text{normal}(0, \sigma), \tag{11}$$

means that:

$$\text{child}_i - a - b * \text{parent}_i \sim \text{normal}(0, \sigma). \tag{12}$$

This provides us with a way of writing down the overall probability (density) of observations.

Likelihood

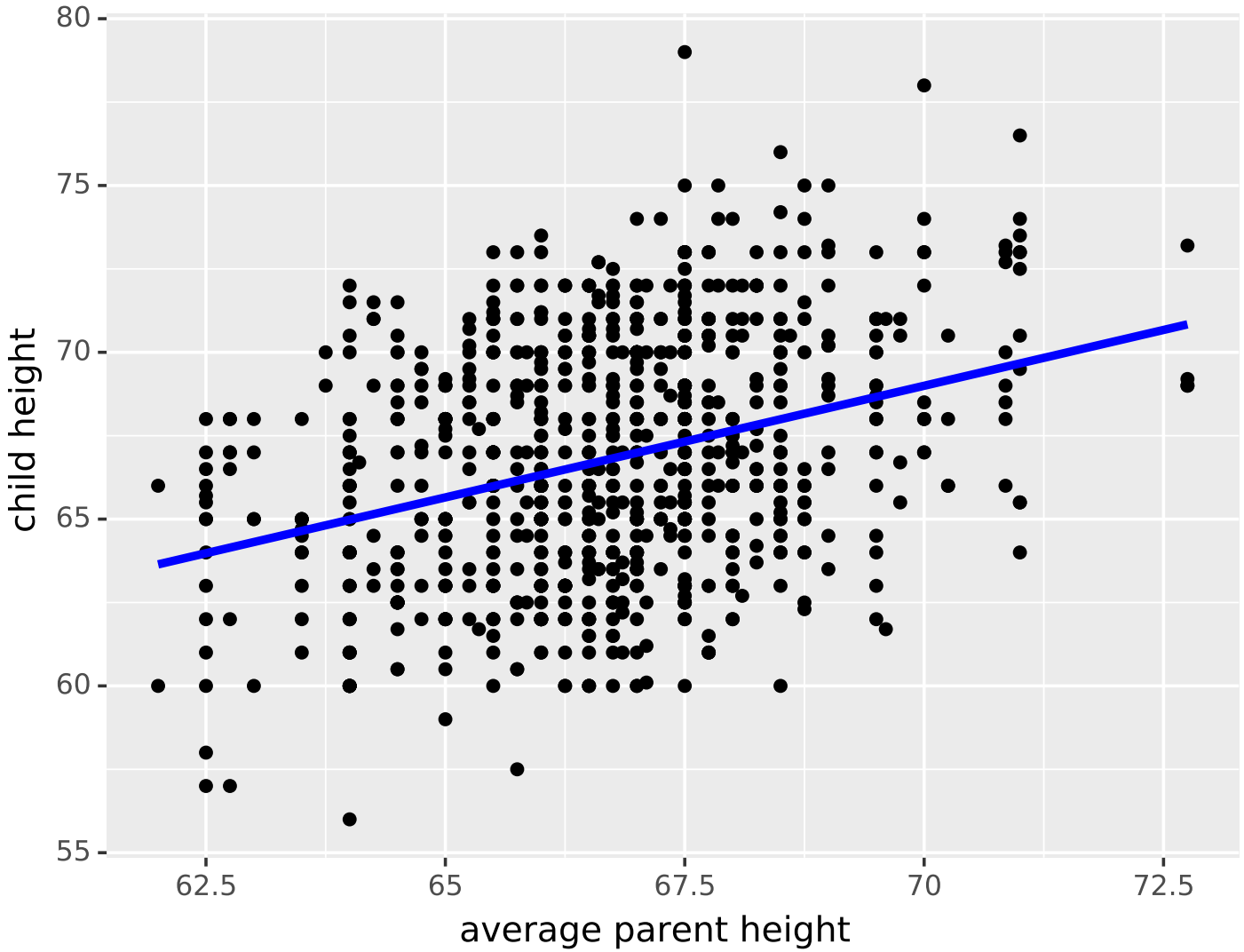
Due to independence of observations:

$$\begin{aligned}
\mathcal{L} =& \mathbb{P}(\epsilon_1) \times \mathbb{P}(\epsilon_2) \times ... \times \mathbb{P}(\epsilon_n) && (13)\\
=& \text{normal}(\text{child}_1 - a - b * \text{parent}_1 | 0, \sigma) \times && (14)\\
& \text{normal}(\text{child}_2 - a - b * \text{parent}_2 | 0, \sigma) && (15)\\
& ... && (16)\\
& \text{normal}(\text{child}_n - a - b * \text{parent}_n | 0, \sigma) && (17)\\
& && (18)
\end{aligned}$$

This object is a function of the parameters of our model: a and b. So choose a and b values to maximise $\mathcal{L}$.

This is known as the method of *maximum likelihood*.

Likelihood estimated model



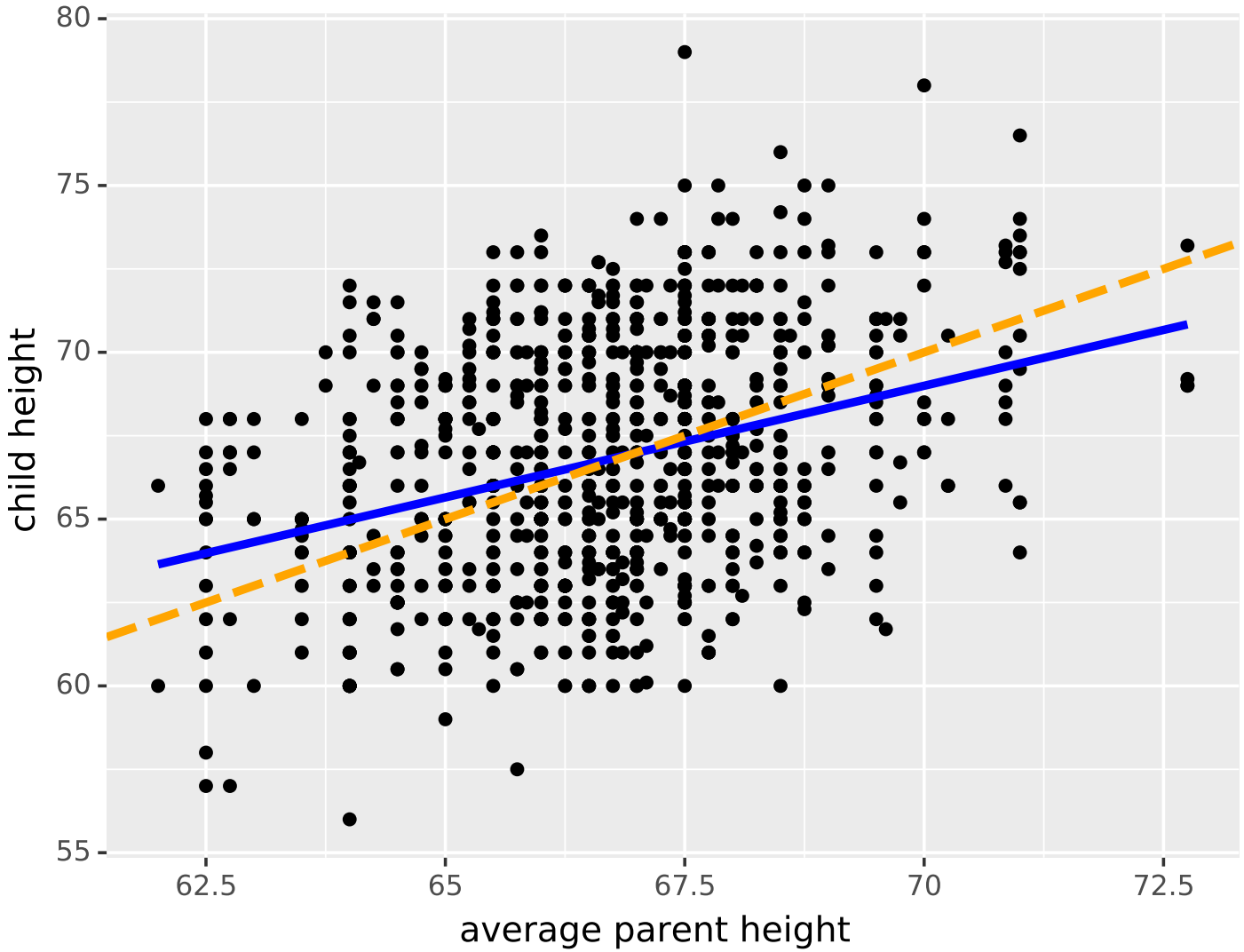
Strength of association between parent and child heights

Estimates of regression coefficient:

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i, \tag{19}$$

- Least squares / maximum likelihood: $b = 0.67$
- Absolute deviance: $b = 0.57$
- Fourth power: $b = 0.73$

Regression to mean



Questions?

Regression is a model

$$\text{child}_i = a + b * \text{parent}_i + \epsilon_i, \tag{20}$$

and

$$\epsilon_i \sim \text{normal}(0, \sigma), \tag{21}$$

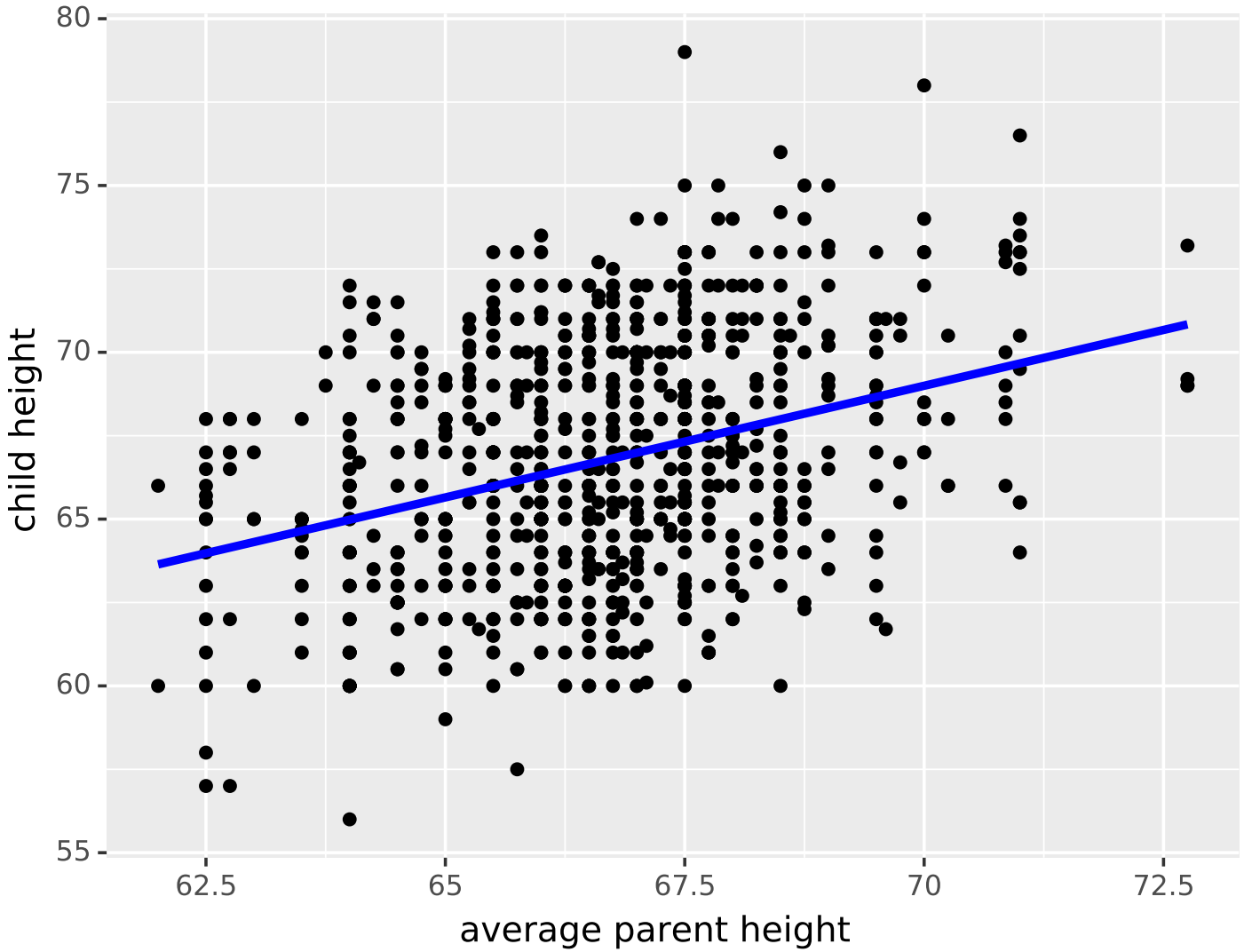
is a model: an idealised version of reality.

Assumptions

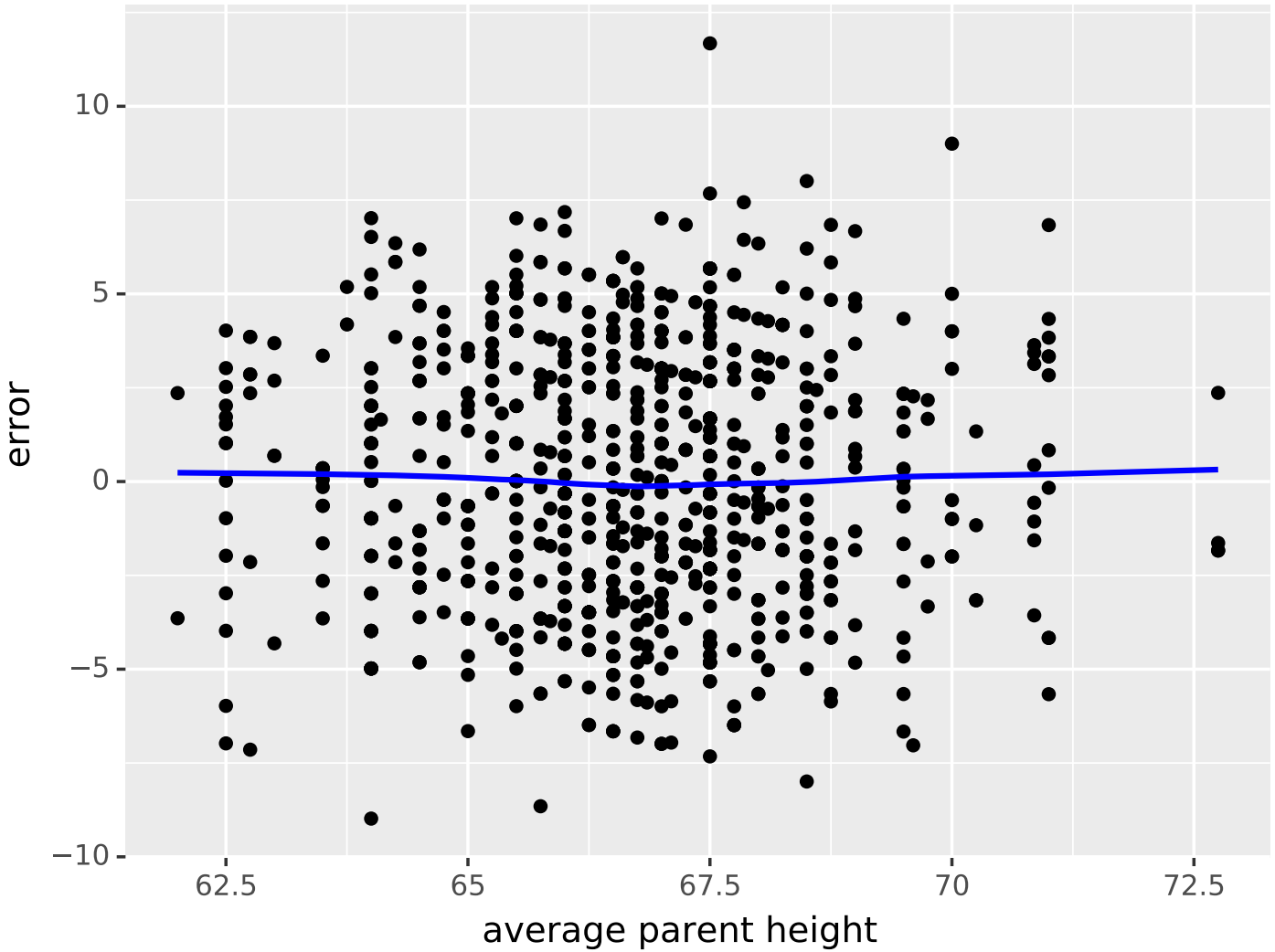
Some of these:

- Linear association of average parental height with child height
- Variance of points around line is constant
- Normality of errors
- Male / female parent heights not separately important
- Sex of child unimportant in relationship

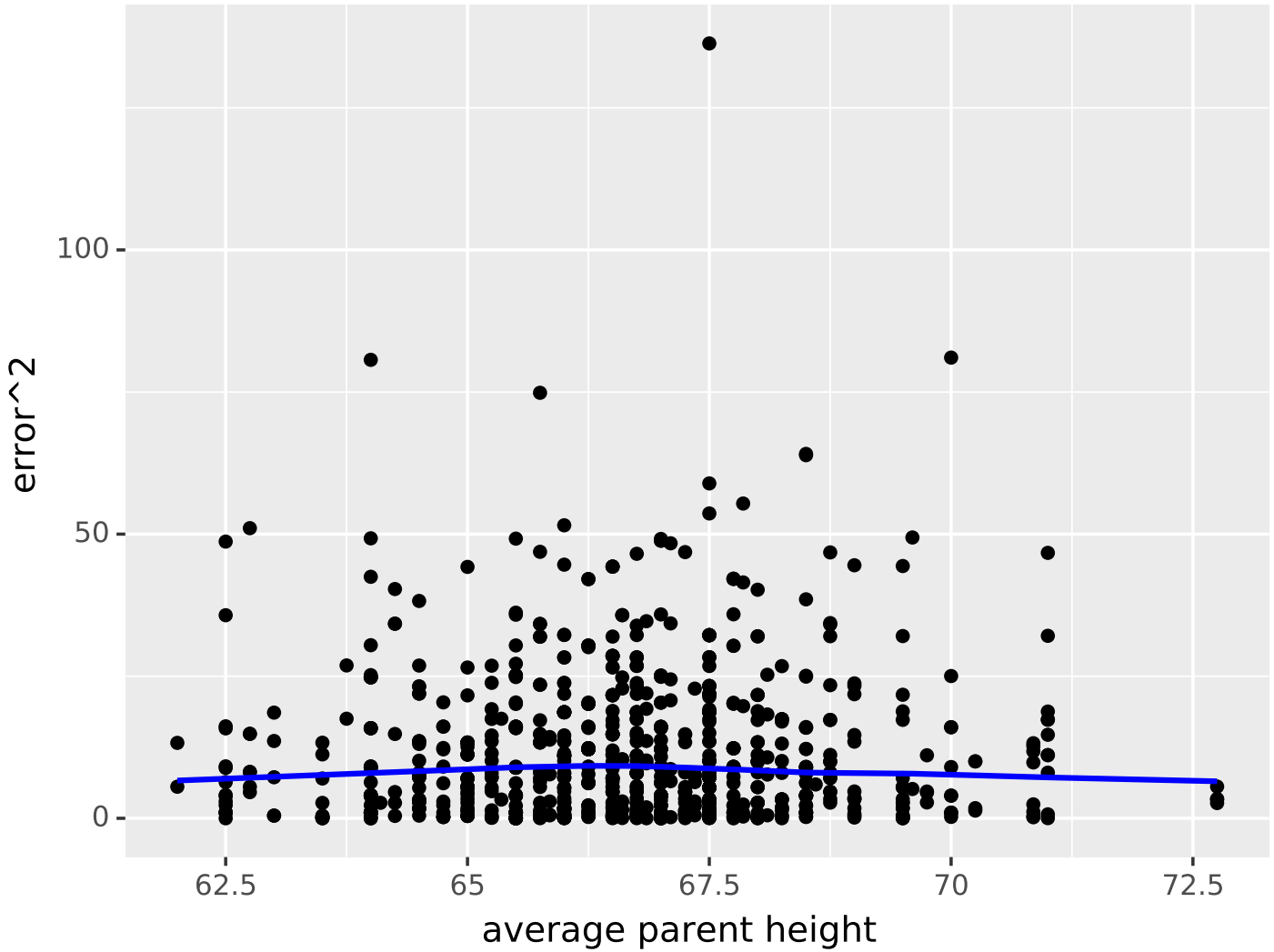
Calculate errors: draw



Checking linearity



Checking variance homogeneity



Questions?

How uncertain are we?

Least squares / maximum likelihood estimates:

$$\text{child}_i = 22.15 + 0.67 * \text{parent}_i + \epsilon_i, \tag{22}$$

How representative are these of the population as a whole?

Gauging uncertainty: draw

Imagine:

- Repeatedly sampling from the population
- Each time calculating an estimate

$\Longrightarrow$ variability in estimates dictates uncertainty.

Circularity

- If we knew variability in estimates, we'd know how accurate they were
- But to do so, we need exact details of the population

How to resolve this ambiguity?

Two resolutions

- Make mathematical assumptions about nature of population distribution. e.g. use CLT to determine normality
- Bootstrap sampling

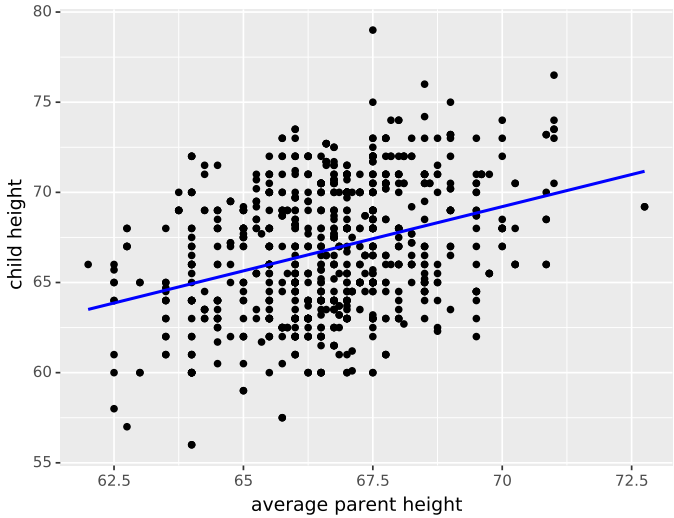
Bootstrap sampling

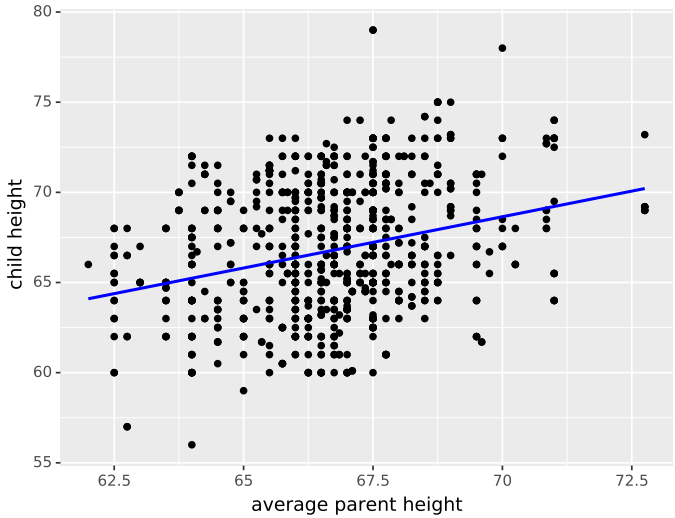
Since sample is drawn from the population, it should mirror it.

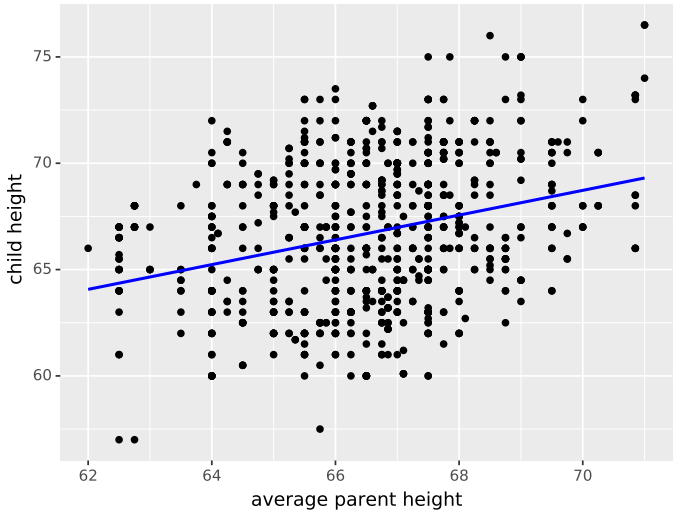
$\Longrightarrow$ repeatedly draw new samples from our sample! And perform estimation on each.

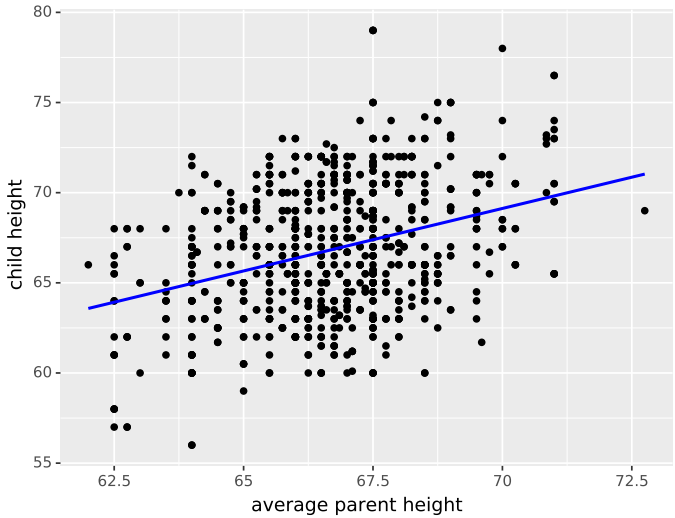
Note sampling done with replacement.

Bootstrapped Galton samples

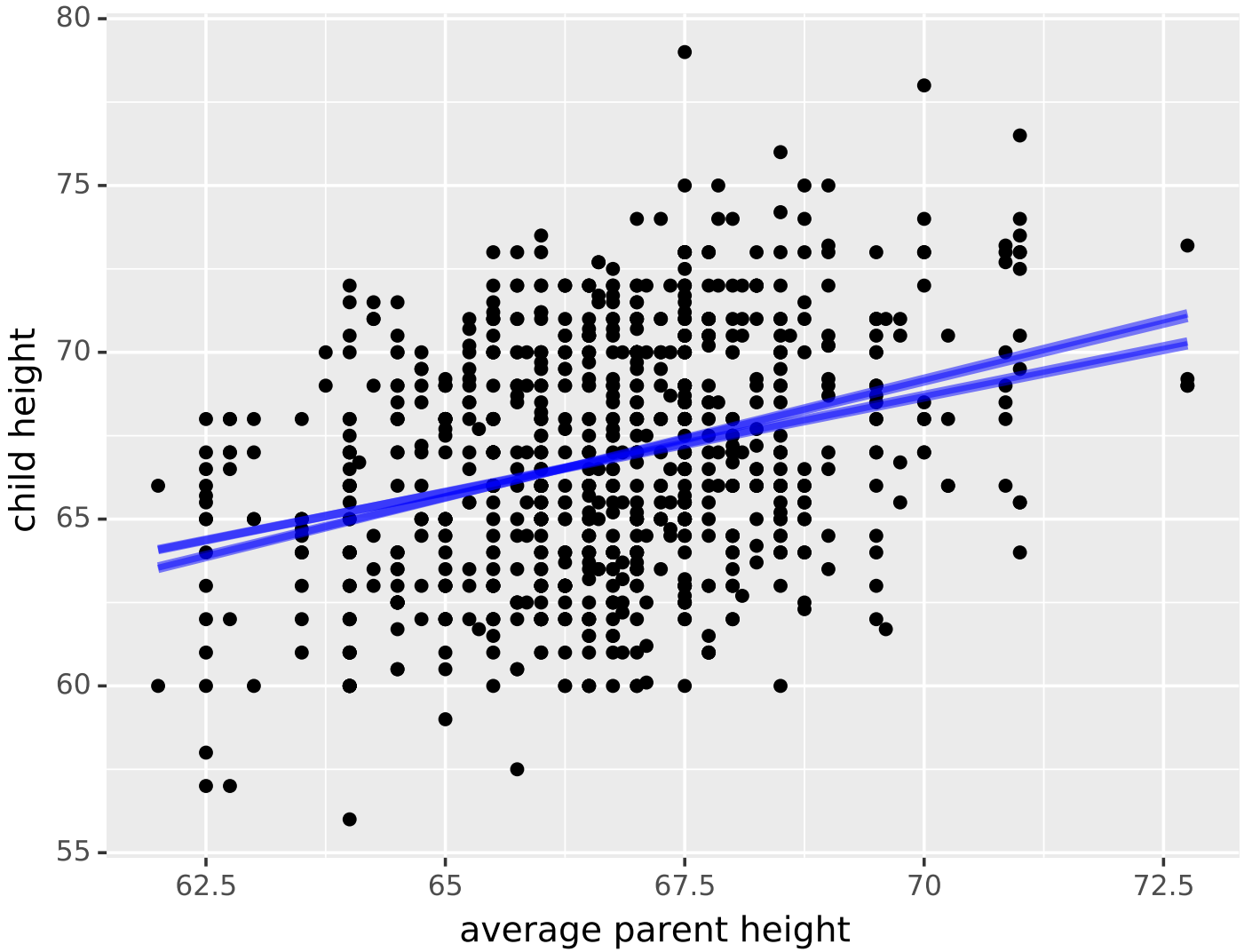




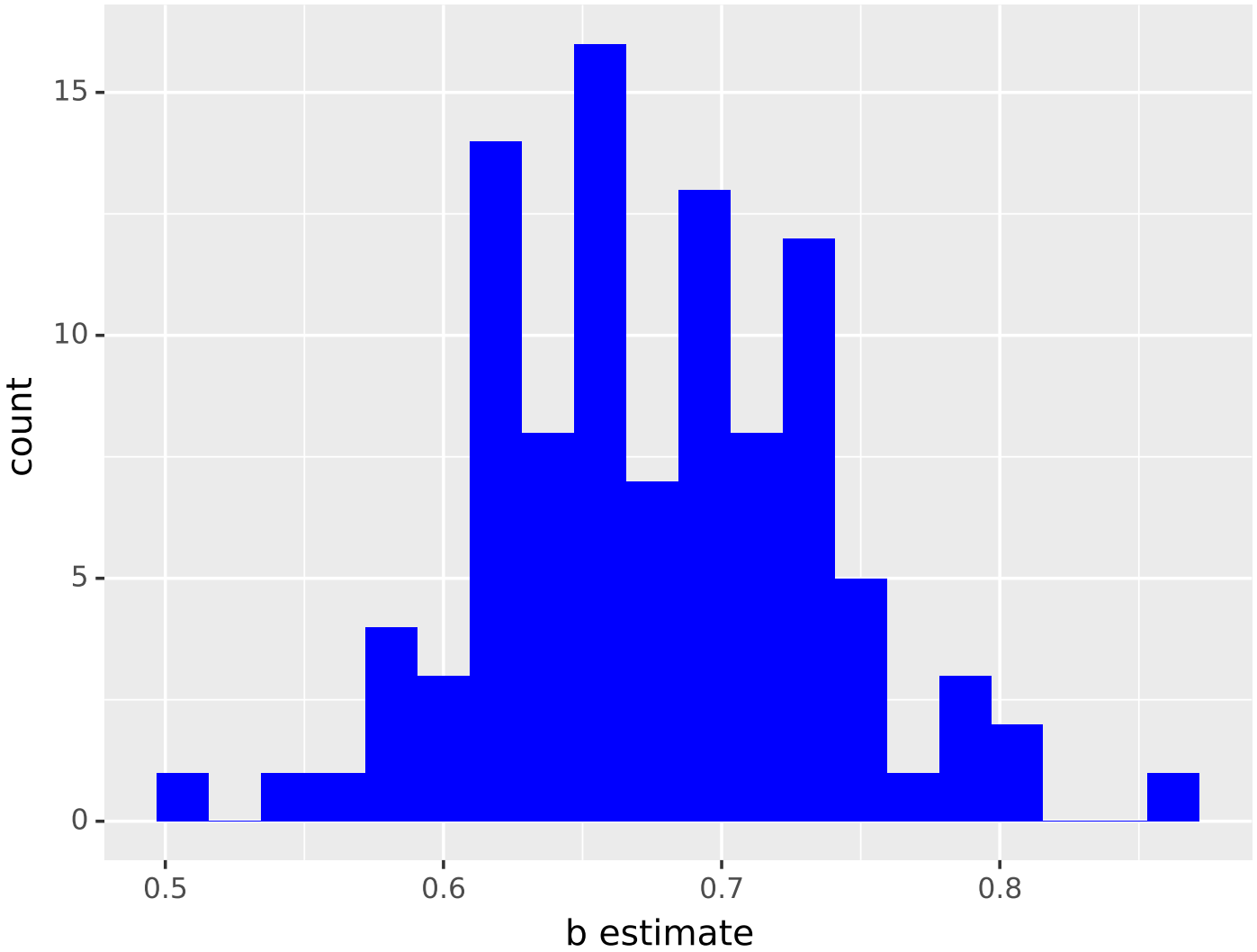




Bootstrapped Galton estimates: 4 bootstrapped samples



Bootstrapped Galton estimates: 100 bootstrapped samples



When doesn't bootstrapping work?

- Complex, highly structured data: for example, time series
- Large data $\Longrightarrow$ too expensive

$\Longrightarrow$ probability model based approach less cumbersome in these cases.

Conclusions

- Data does not contain enough information about signals
- In statistics, we augment data with assumptions (embodied in randomness) $\Longrightarrow$ separate signal from noise
- Simple associations are non-causal but shouldn't dampen our ambition
- Linear regression allows for quantification of relationships between two variables
- Linear regression, like all statistical assumptions, is a model which can be fallible
- Uncertainty in estimates can be obtained by bootstrap sampling

That's it!

Questions?

Further material