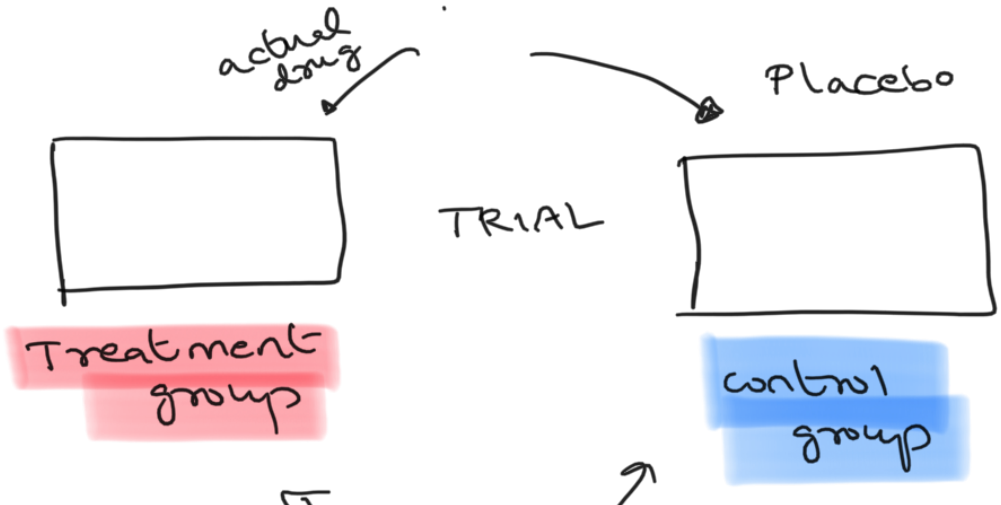
Day 1 – controlled experiments

Ref: Freedman, Pisani, Purves : Statistics

Drug trial

Comparison method to test efficaciveness



Double blinded experiment - neither subject nor doctor measuring responses should know which group subject belongs to

1916: Polio epidemic in US

1950s: Vaccine by Jonas Salk

1954: Ready for trials outside laboratory

How to check effectiveness of drug?

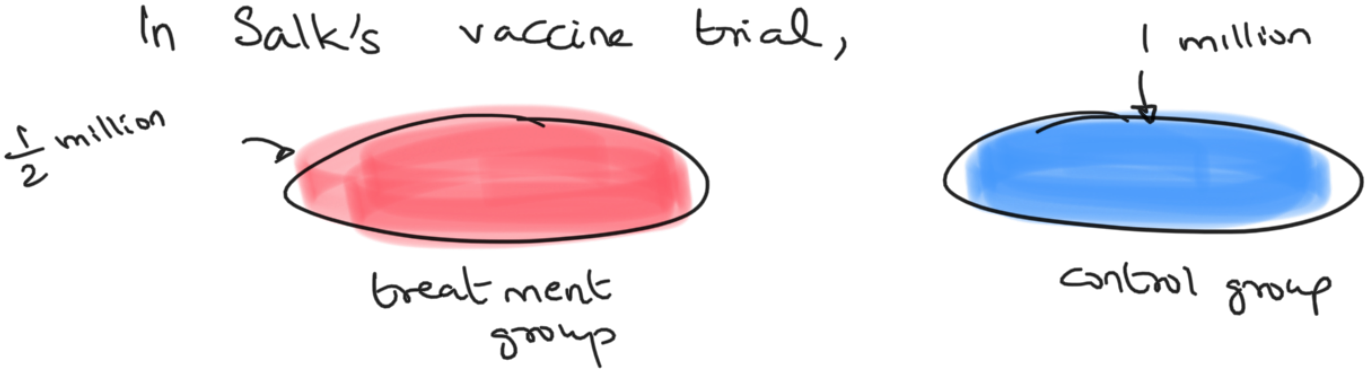
* Just give it to people and if low incidence of disease — is vaccine effective?

(Polio cases varied year to year ....)

* Do risks of vaccine > benefits ?

Need well controlled experiment to compare

In Salk's vaccine trial,



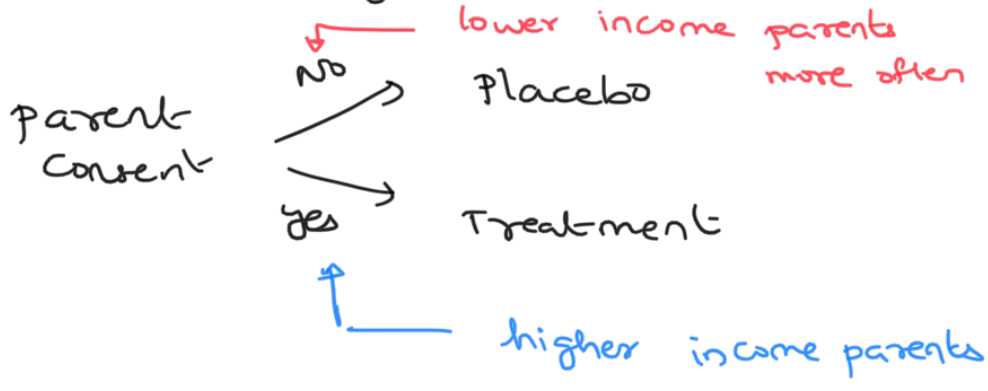
diff sizes

Compared rates instead of absolute # of cases

cases / 100,000

who gets treatment? who gets Placebo?

Suppose :



so trial will be biased....

AGAINST VACCING

Infact, children of higher income parents more susceptible to Polio [mild cases of polio in poor children → got antibodies early on while still having antibodies from mother... prevented more severe cases later]

① So treatment, control groups should be similar, except for treatment

if not, other factors effects CONFOUNDED with treatment effects.

② RANDOM ASSIGNMENT TO CONTROL / TREATMENT GROUP OF CHILDREN WHOSE PARENTS HAD CONSENTED FOR VACCING

(coin toss)

Randomized controlled experiment

③ Placebo given to control group

④ Doctors and subjects not told who was vaccinated, who wasn't.

↑

(borderline cases detection not influenced..)

Double blinding

	Size	Rate / 100,000
Treatment	200,000	28
Control	200,000	71
Refused consent	350,000	46

71 → 28

sharp drop

Another experiment

	Size	Rate / 100,000
Grade 2 (vaccine)	225,000	25
Grade 1, 3 (control)	725,000	54
Grade 2 (no consent)	125,000	44

parents consented → and Grade 2

all children in grade 1, 3 with / without consent

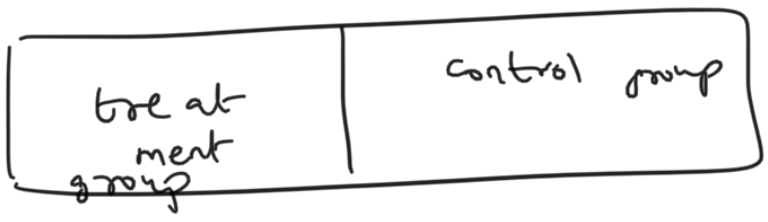
54 → 25
not that much of a jump

CONFOUNDING,
as treatment, control groups not comparable

Also randomized controlled double blinding

→ suppose vaccine has no effect

→



polio cases: 50% chance in treatment group,
50% chance is control group

→ so roughly equal # of polio cases in each group

→ if observe disparity ----→ with high prob, vaccine is having some effect
...

Another experiment

→ Porta caval shunt for cirrhosis of liver

to prevent bleeding

→ but surgery is long and hazardous

Benefits > risks ?

no controls : 32 studies

- 24 — benefits > risks
- 7 — benefits ~ risks
- 1 — benefits < risks

75%

controls, but assignment to treatment/control not randomized : 15 studies

- 10 — benefits > risks
- 3 — benefits ~ risks
- 1 — benefits < risks

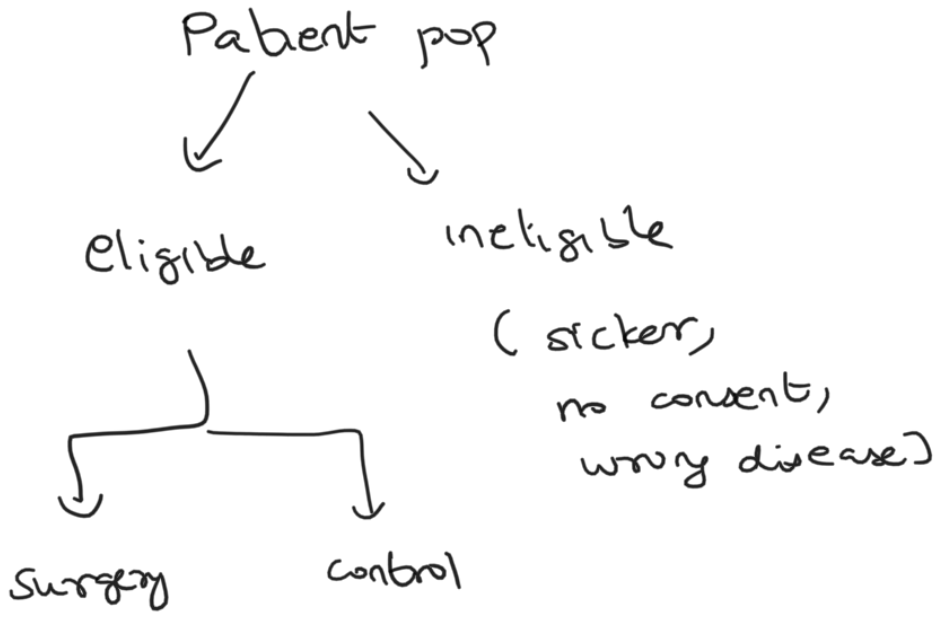
67%

randomized control : 4 studies

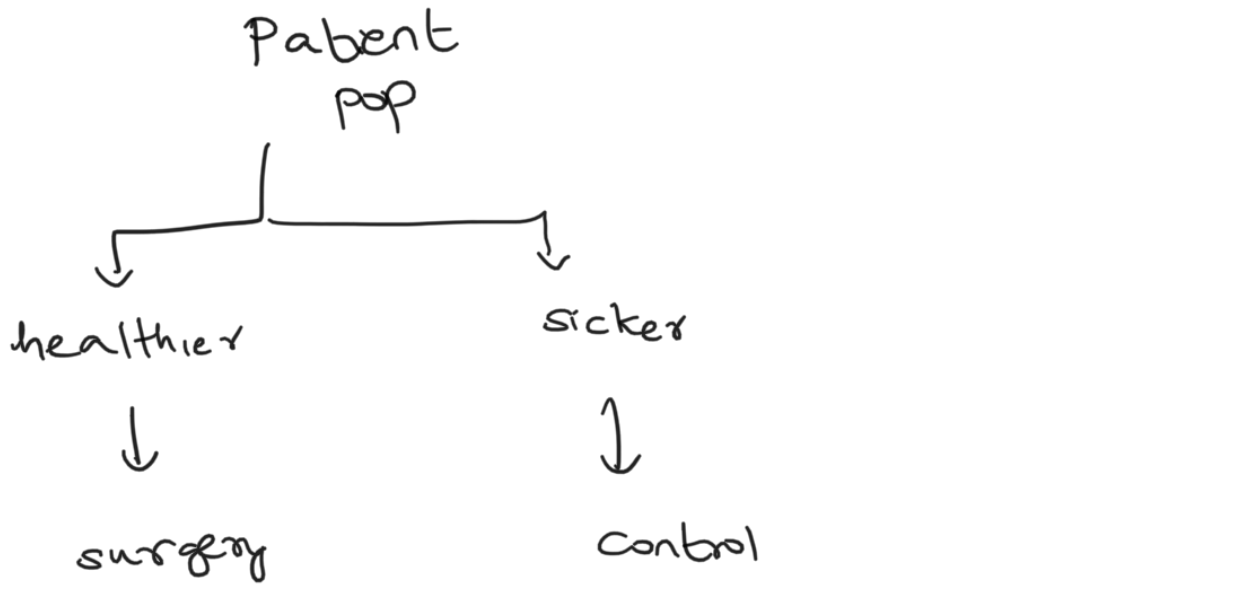
- 0 — benefits > risks
- 1 — benefits ~ risks
- 3 — benefits < risks

0%

Randomized controlled exp in this context ?



non randomized Poorly controlled experiment



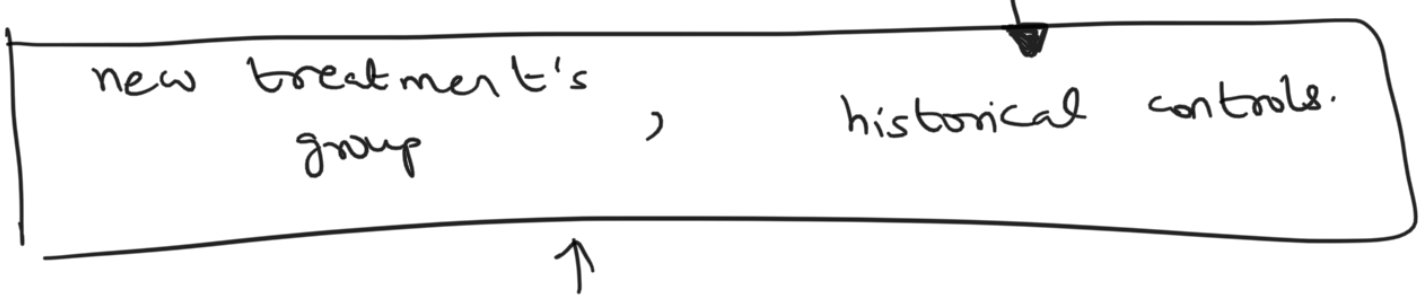
percentage ∧ patients who survived after 3 years

	Randomized exp	non randomized exp
Surgery	60%	60%
Control	60%	45%

biased in favour of surgery → if control group was already made ∧ sicker patients, not comparable to surgery group.

Randomized controlled experiment hard to do in medical context

old treatment's group, old controls



but historical controls are not is same time period as new treatment's group

non - contemporaneous controls

Coronary by pass surgery

randomized controlled contemporaneous studies

negative about value of operation

historically controlled etc..

badly designed studies more enthusiastic about value of operation

Similarly drug "DES" (1960s)

diethylstilbestrol to

prevent "spontaneous abortion". Randomized

trials: negative about drug. Historically

controlled trials: positive about it

1971: banned. Found to cause

cancer in daughters in their adulthood.