study design vs. inference

A SOURCE OF CONFUSION

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why do statistics?

- Make a compelling argument about the world.
- Connect what's going on in the world (data) with a deductive framework (inference).
- If we control the process of data collection then we can have a better sense of how our deductive framework should behave.
- This leads to clearer reasoning about what the underlying structure of the world might be.

- This lecture: What if we don't control the way the data were actually generated? What if we didn't intervene?

study design vs. inference

- 90% of statistics classes are about inference
- Why?
  - It’s useful, getting you those confidence intervals and p-values.
  - The Math is pretty cool.
  - It feels hard.
  - Because many of us don’t really know much about the real world…

design

RANDOMIZATION AND SAMPLING

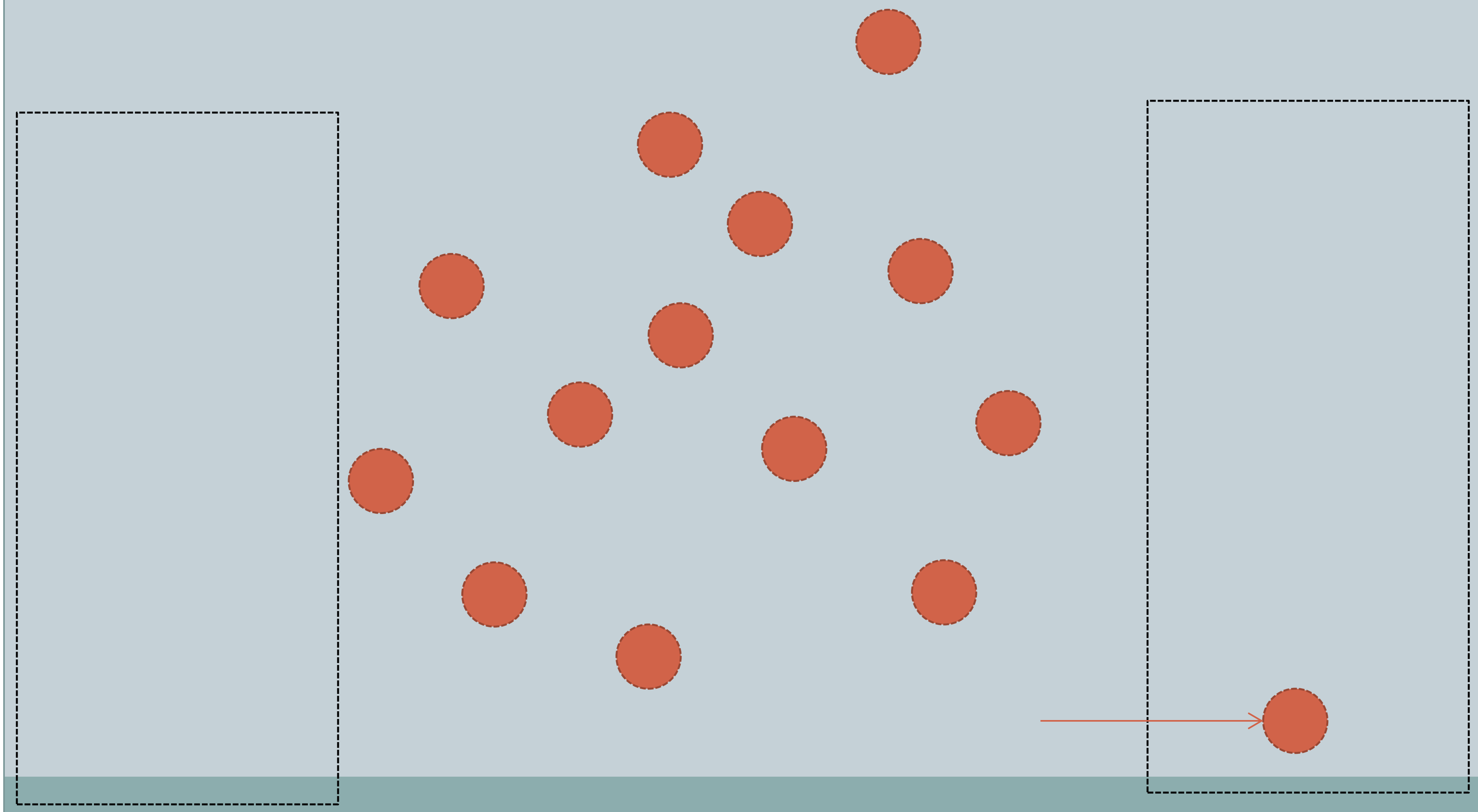
where does the data come from?

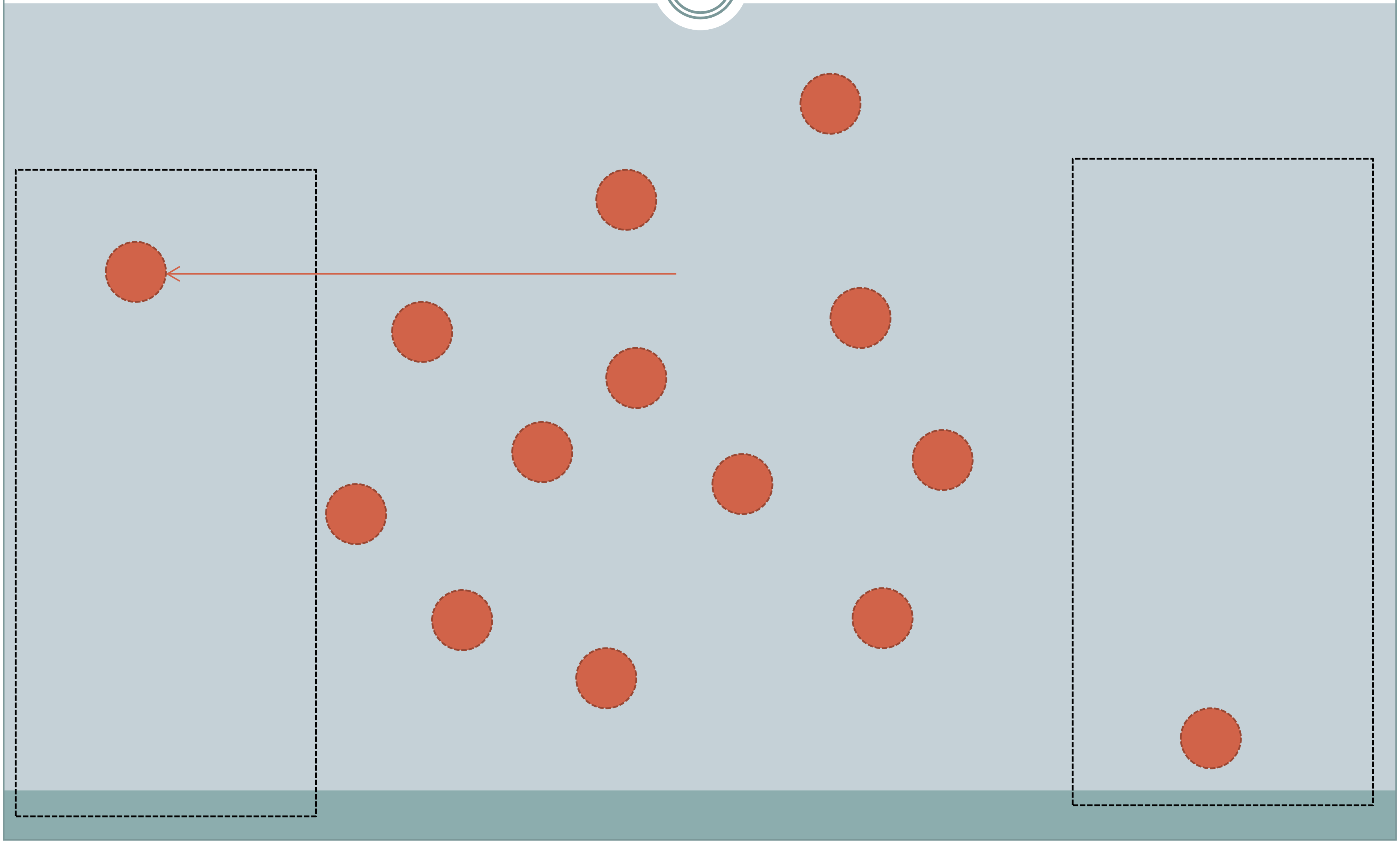
- We design trials.
  - Assign groups that are similar at baseline
  - Examine counterfactuals
- We also design surveys.
  - Representative groups
  - Understand population from subsets of those populations

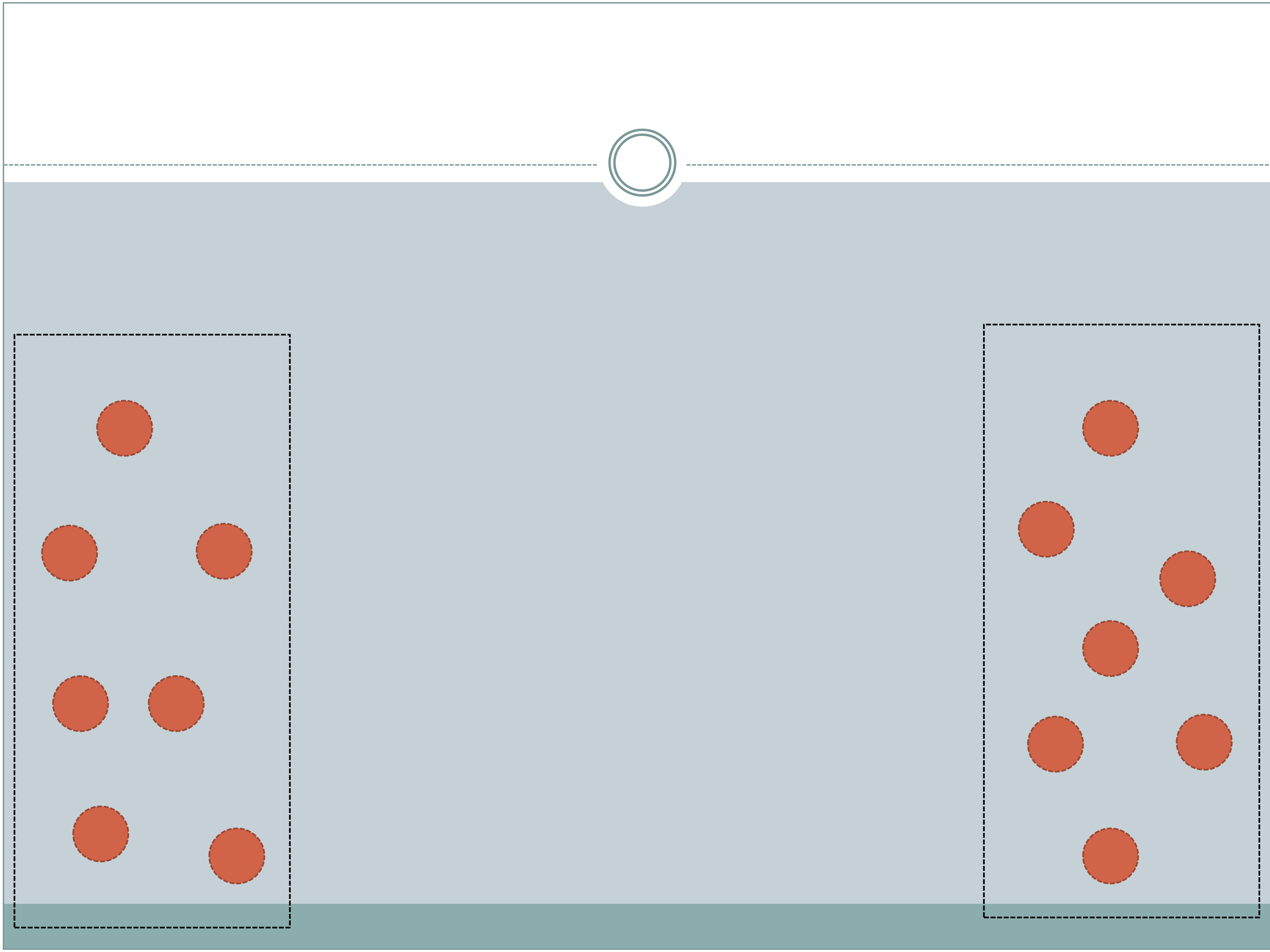
- Both use elements of control and randomness

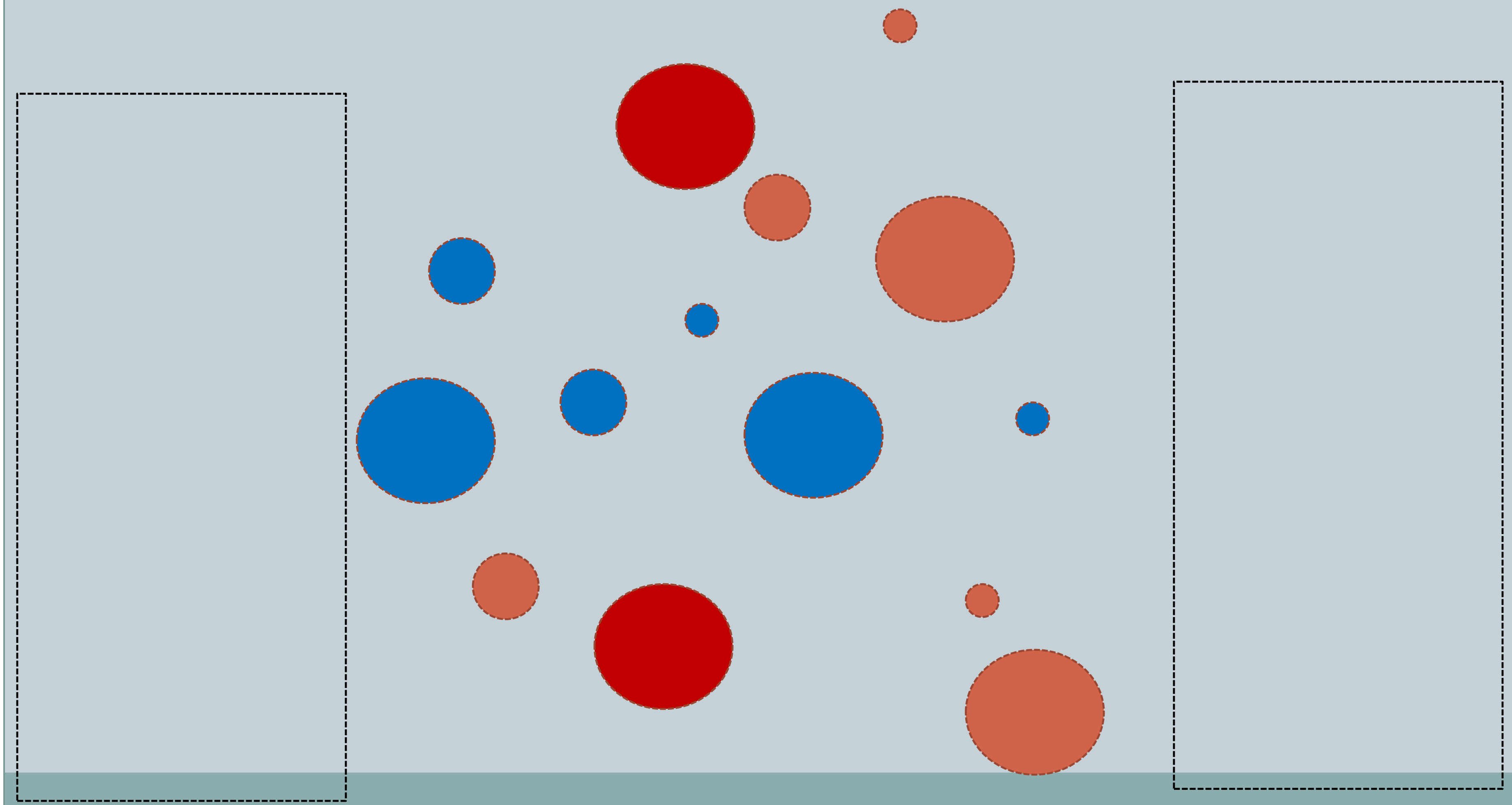
an example

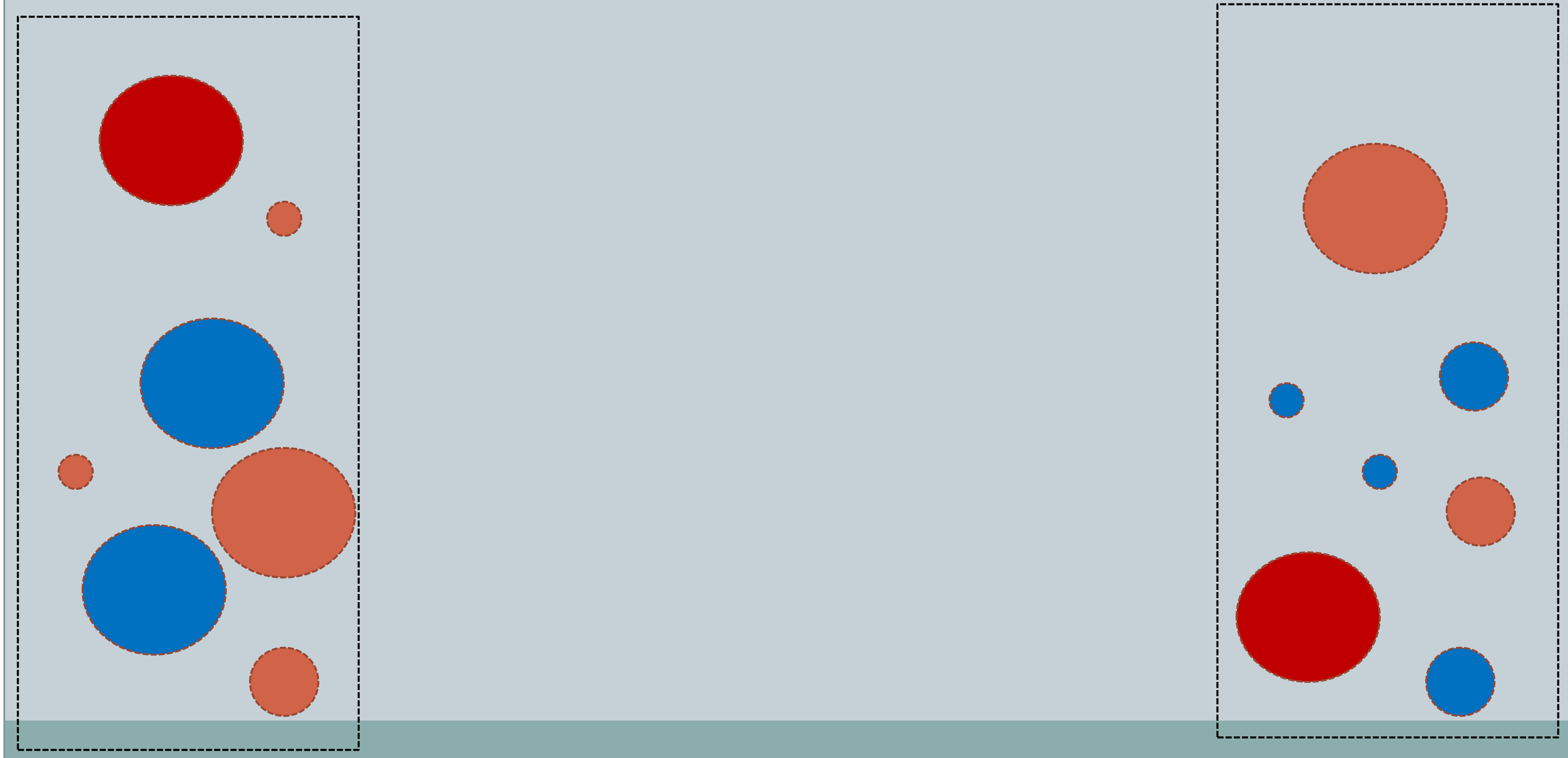
- Want to study a pill.
- Design the study
  - Uniform randomization
  - Matched pairs randomization
  - Crossover design
  - Cluster-randomized
- Inference
  - t-test
  - Matched-pairs t-test
  - Repeated measures model
  - Generalized linear mixed model
  - But… maybe all of those could be GLMM.

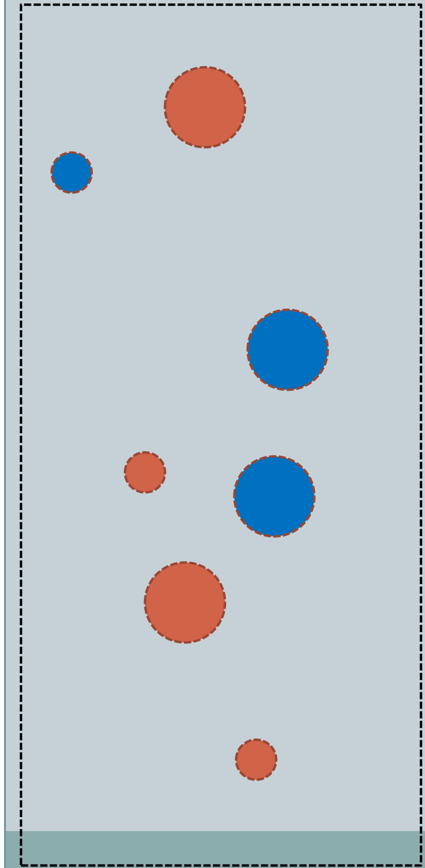




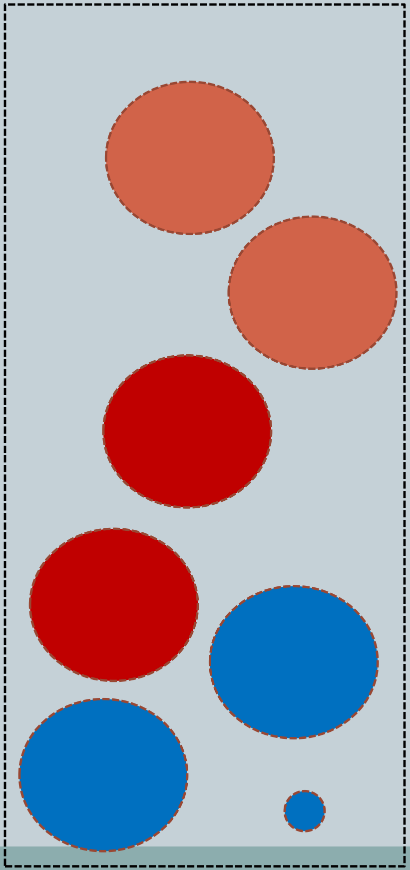


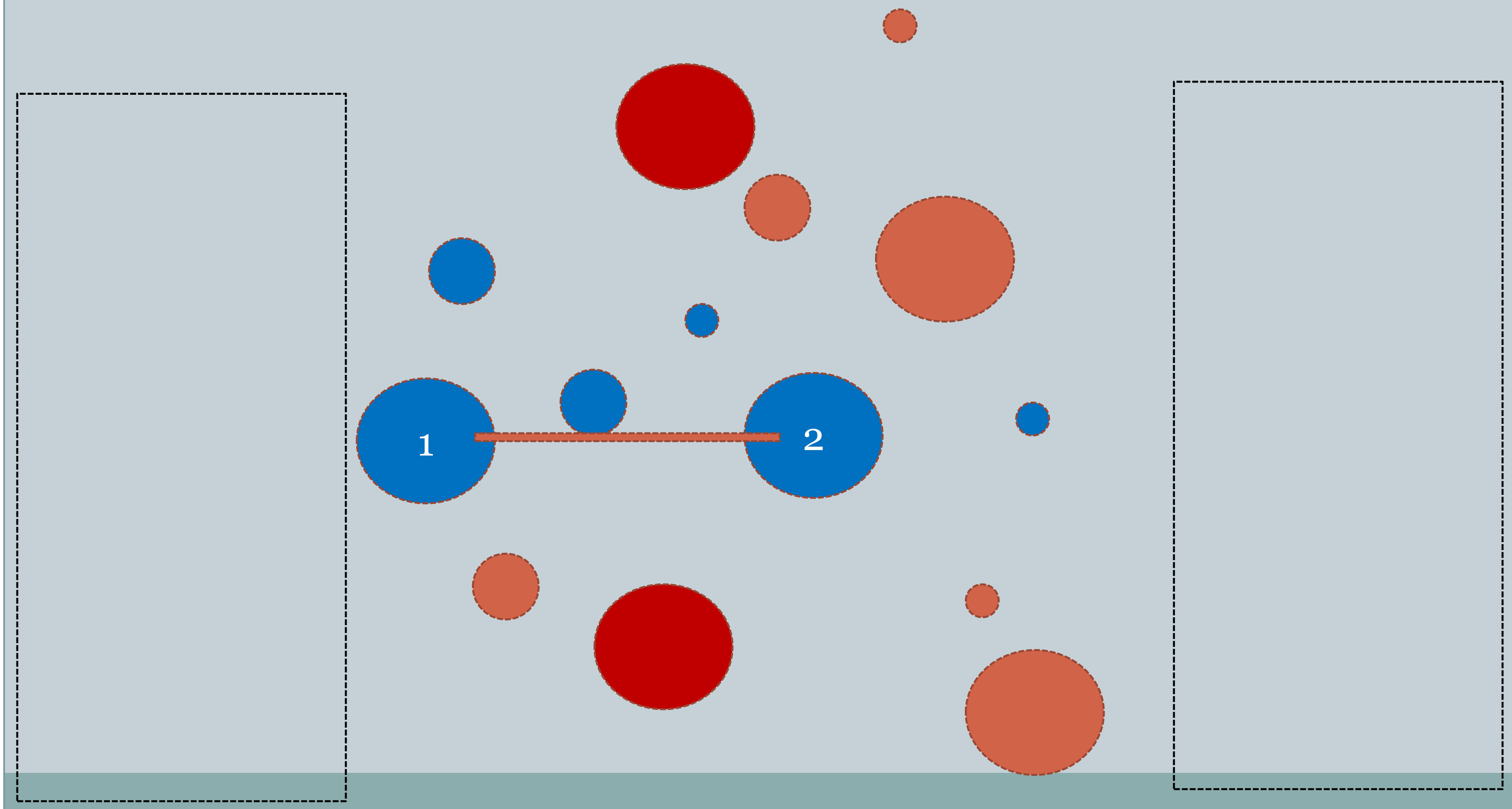






We’re off to a **bad** start.

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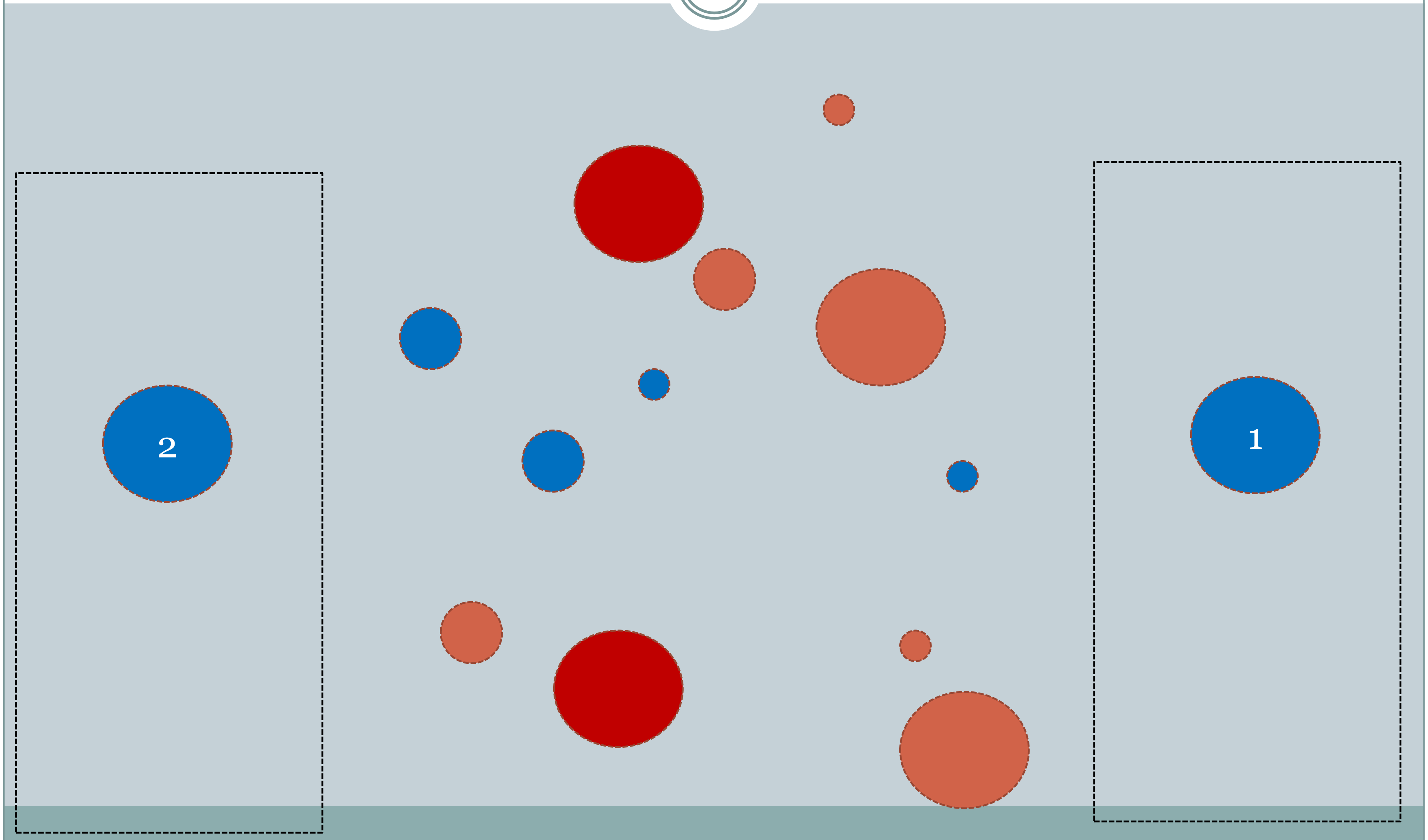
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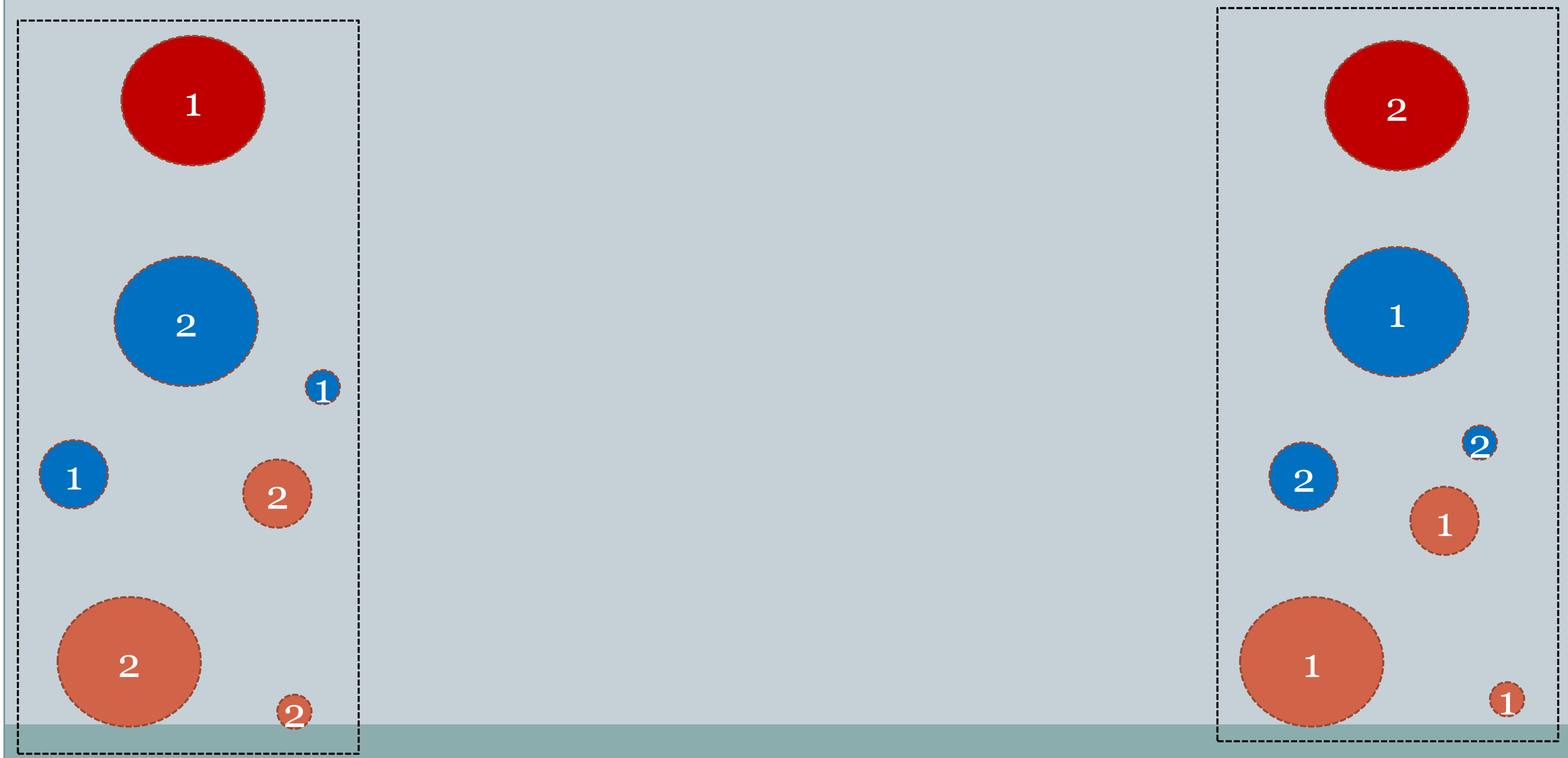
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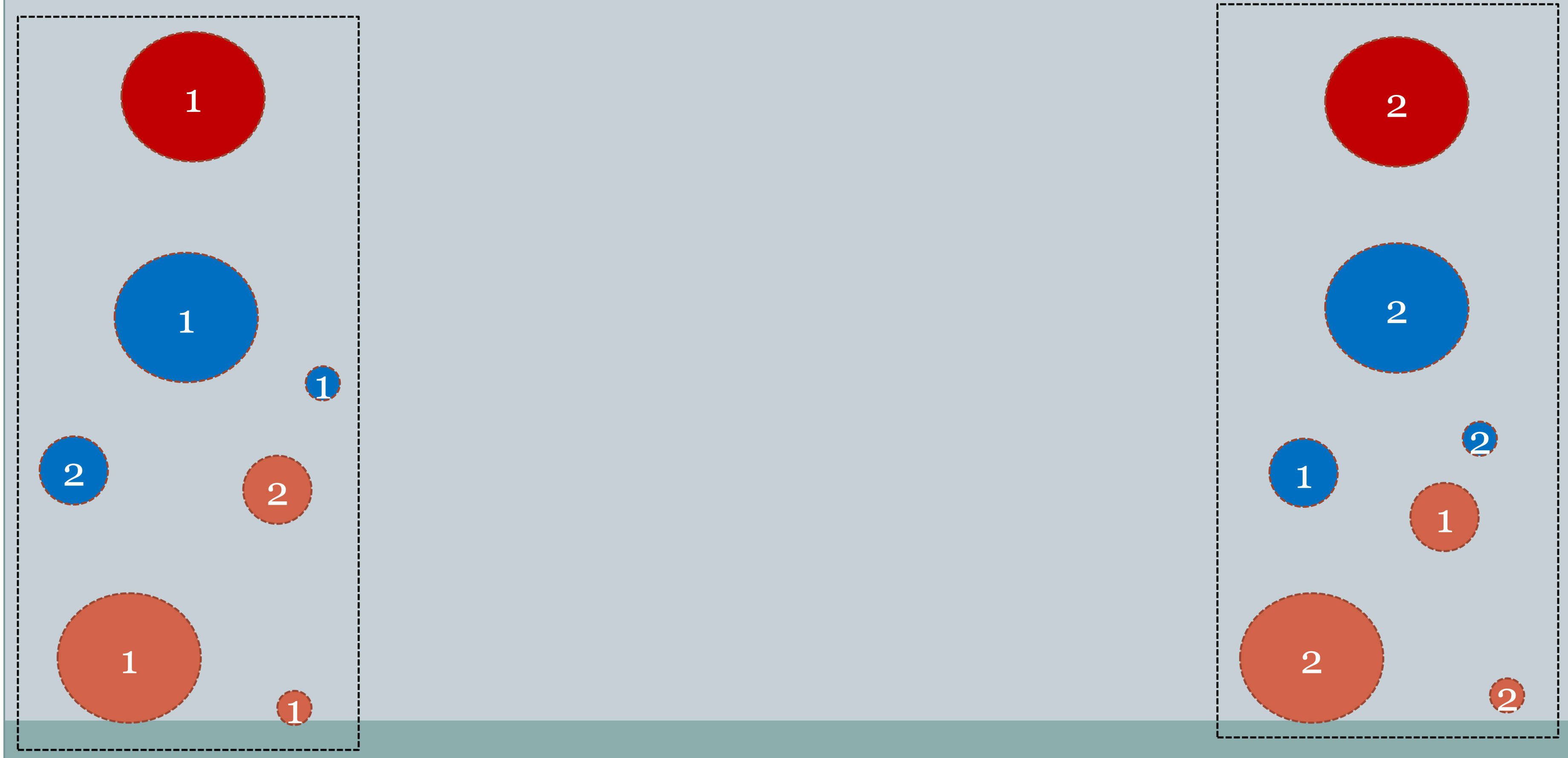
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the design limits what could have happened

- Uniform randomization allows for quite different possibilities. $({}_nC_r)$
- Matched-pairs randomization limits the size, and range, of possible assignments. $(2^{(\frac{n}{2})})$
- In some sense, we're losing something when we go to matched-pairs…
- … but what are we losing? The "crazy" options that we know are going to lead us astray.

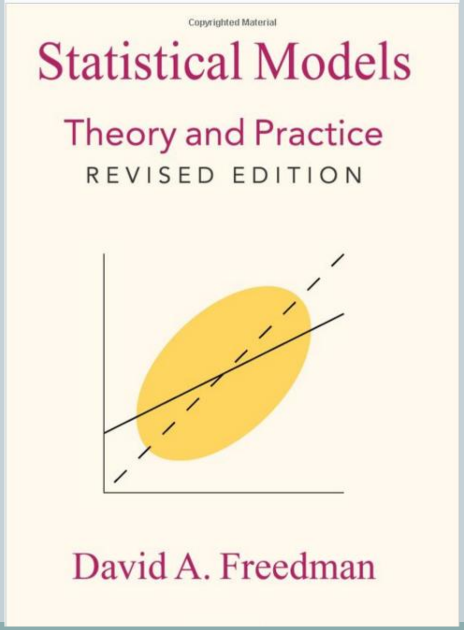
an example

- Want to study an election.
- Design the study
  - Simple random sample
  - Proportional sampling
  - Snowball sampling

- Inference
  - t-test
  - Inverse probability weighting
  - Generalized linear mixed model
  - But… maybe all of those could be GLMM.

different beliefs about where data come from

- RCT and survey
- Structural equation modeling
  - $y_i = \beta_0 + \beta_1 x_{1,i} + \cdots + \beta_p x_{p,i} + \varepsilon_i$
- If you want to be disabused of SEM spend some time reading



inference

picking inference

- Inference requires assumptions
- Linear regression:
  - Linearity and additivity
  - Independent errors
  - Homoskedastiticity
  - Normality of errors
- Permutation test:
  - No interference
- "Fancier" methods tend to have more assumptions… and thus leave you open to more lines of attack.
- These attacks can be obviated by careful preparation during the design phase.

picking inference

- Use the simplest method that gets the job done.
- If you want to accomplish more, collect more data or do additional analyses. ("If have to use something more complicated than a t-test then someone messed up…")

prospective study design

- A lot of the foundations have been worked out:
  - Experimental design
  - Survey sampling

- But, obviously, there are a lot of cool developments still going on:
  - Experimental design: adaptive trials, point-of-care randomization,
  - Sampling: active learning, explore exploit learning

observational (and retrospective) design

- This seems weird
- Usually a data set is in front of you, so you just analyze it
- It takes some thought to see this

Let’s do an example.

observational study design

NEONATAL INTENSIVE CARE UNITS

Application: Regionalization

- Hospitals vary in their ability to care for premature infants.
- The American Academy of Pediatrics recognizes levels: 1, 2, 3A, 3B, 3C, 3D and Regional Centers.
- ***Regionalization of care*** refers to a policy that suggests or requires that high-risk mothers deliver at hospitals with greater levels of capabilities.

Outcome

Outcome

The data

- Every baby delivered in a 10+ year period
  - California
  - Pennsylvania
  - Missouri
- Mothers' information
  - ICD9 codes
    - Delivery
    - Post-delivery complications
    - Some pre-delivery
  - Some SES information
  - Zip code of residence
- Birth/death certificates
- Census information
  - PA and MO have zip code level
  - CA will have block group

Pre-delivery Severity?

	Variable Type	High NICU	Low NICU	sd	Δ/sd
Mortality	Outcome	2.26%	1.25%	13.33%	0.08
Difference in Travel Time	Instrument	4.57	19.00	17.18	-0.84
% attending high level NICU	Treatment	100.0%	0.0%	49.7%	2.01
Birth weight	Preemie covariates	2,454.07	2,693.24	739.27	-0.32
Gestational age		34.61	35.69	2.80	-0.39
GI	% of preemies with type of congenital disorders	0.9%	0.6%	8.7%	0.04
GU		0.9%	0.8%	9.0%	0.01
CNS		0.9%	0.4%	8.3%	0.05
Pulmonary		0.8%	0.7%	8.8%	0.01
Cardio		1.4%	0.7%	10.5%	0.06
Skeletal		0.7%	0.9%	9.0%	-0.02
Skin		0.0%	0.0%	0.0%	0.00
Chromosomes		0.4%	0.3%	6.3%	0.02
Other_Anomaly		0.8%	0.1%	7.0%	0.09
Gestational_DiabetesM	Mother covariates	4.9%	4.3%	21.0%	0.03
Mother's education		3.76	3.58	1.19	0.16
Insurance - Fee for service		24.0%	24.5%	42.8%	-0.01
Insurance - HMO		32.3%	27.8%	46.0%	0.10
Insurance - Government		23.5%	24.2%	42.6%	-0.02
Insurance - Other		16.8%	21.4%	39.1%	-0.12
Uninsured		2.2%	1.6%	13.7%	0.04
Prenatal care		2.51	2.37	1.30	0.11
Single birth (y/n)		79.0%	86.1%	38.3%	-0.18
Parity		2.08	2.09	1.31	-0.01
Mother's age		28.41	27.71	6.25	0.11
Median income	Census level covariates	41,484.25	40,258.92	14,587.24	0.08
Median home value		97,663.00	95,083.15	48,762.43	0.05
% completed high school		79.9%	80.0%	9.7%	-0.01
% completed college		22.2%	19.4%	13.1%	0.21
% renting		31.4%	27.9%	12.8%	0.28
% below poverty line		13.4%	11.8%	9.9%	0.16

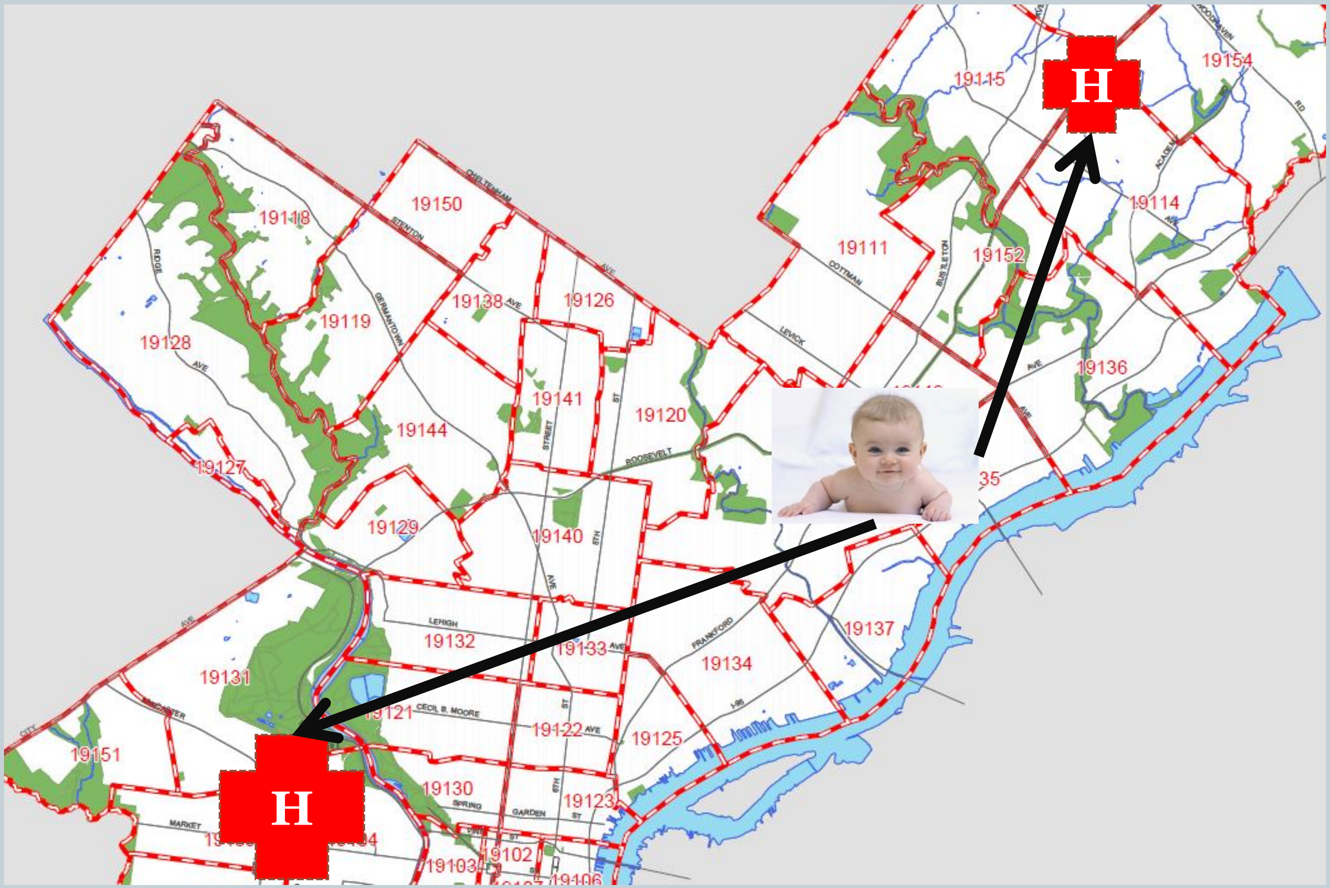
Summary of Problem

- Want to quantify effect of level of NICU on rate of death
- Observational data
- Sorting bias
- Some sorting variables are **unobserved**

real world randomness

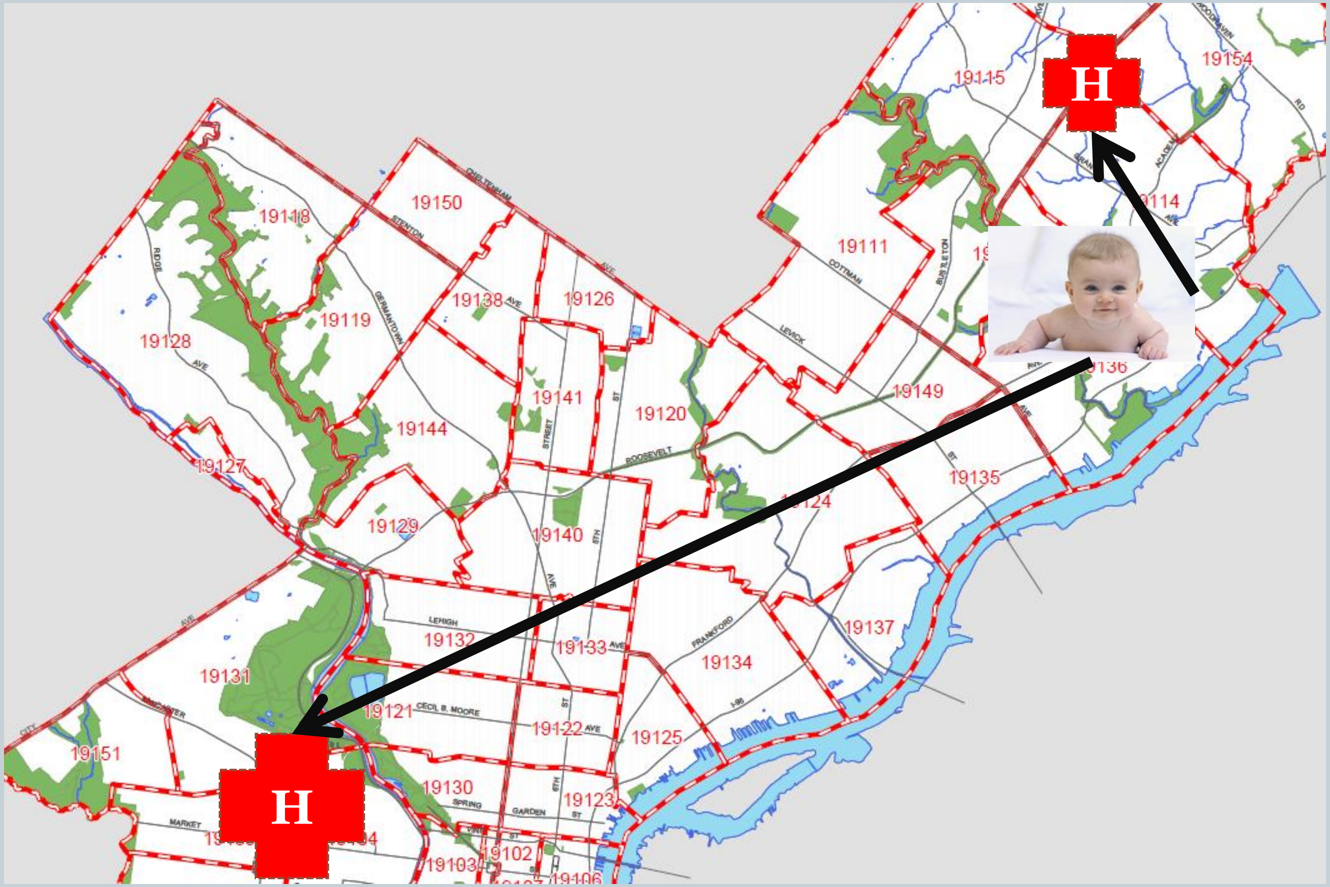
(MAYBE)

Instrument: Excess Travel Time



Excess Travel Time

Instrument: Excess Travel Time



Excess Travel Time

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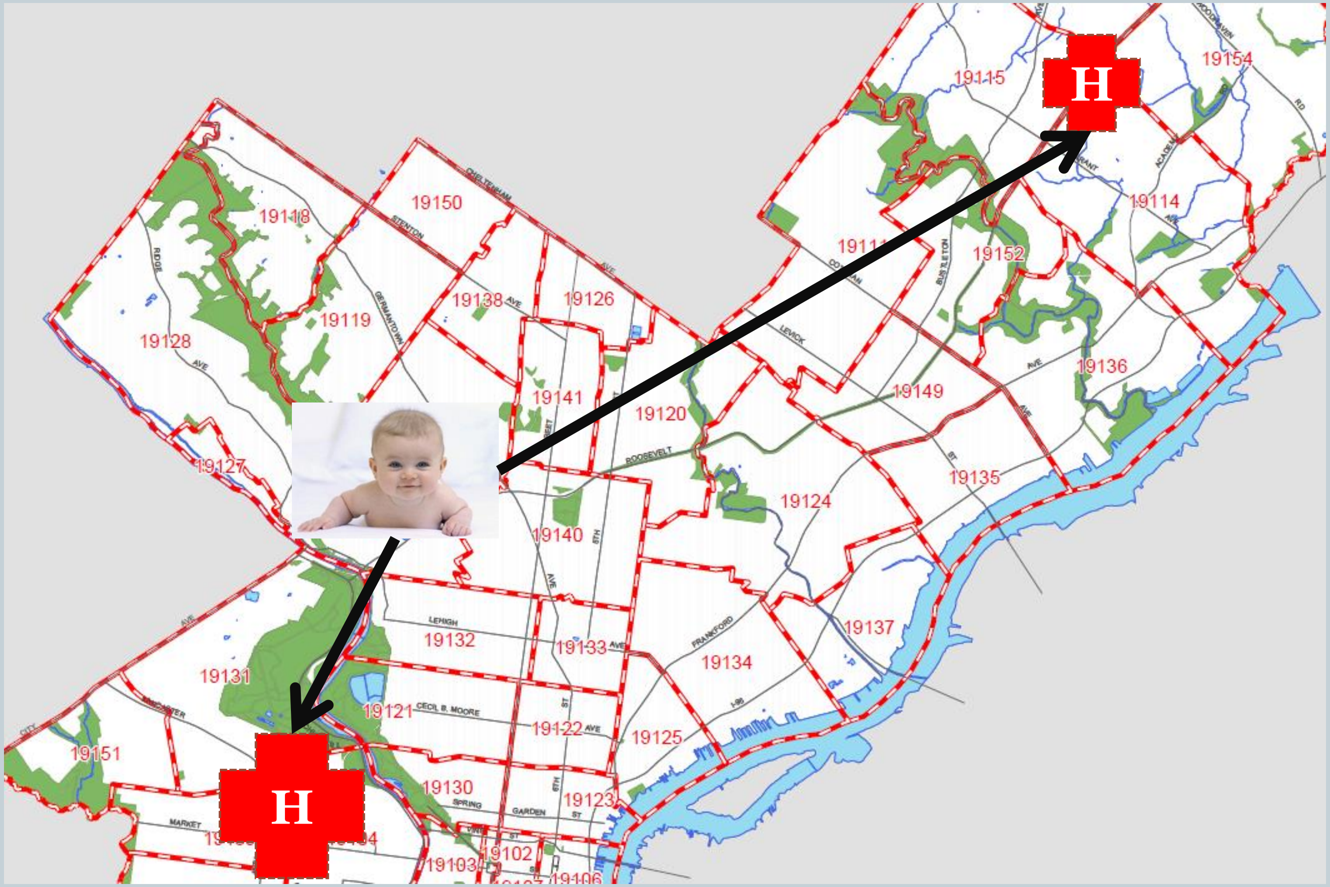

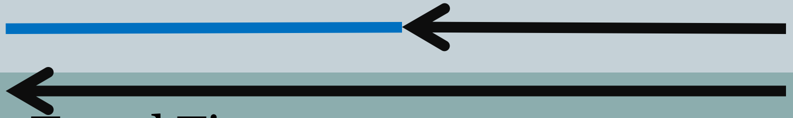

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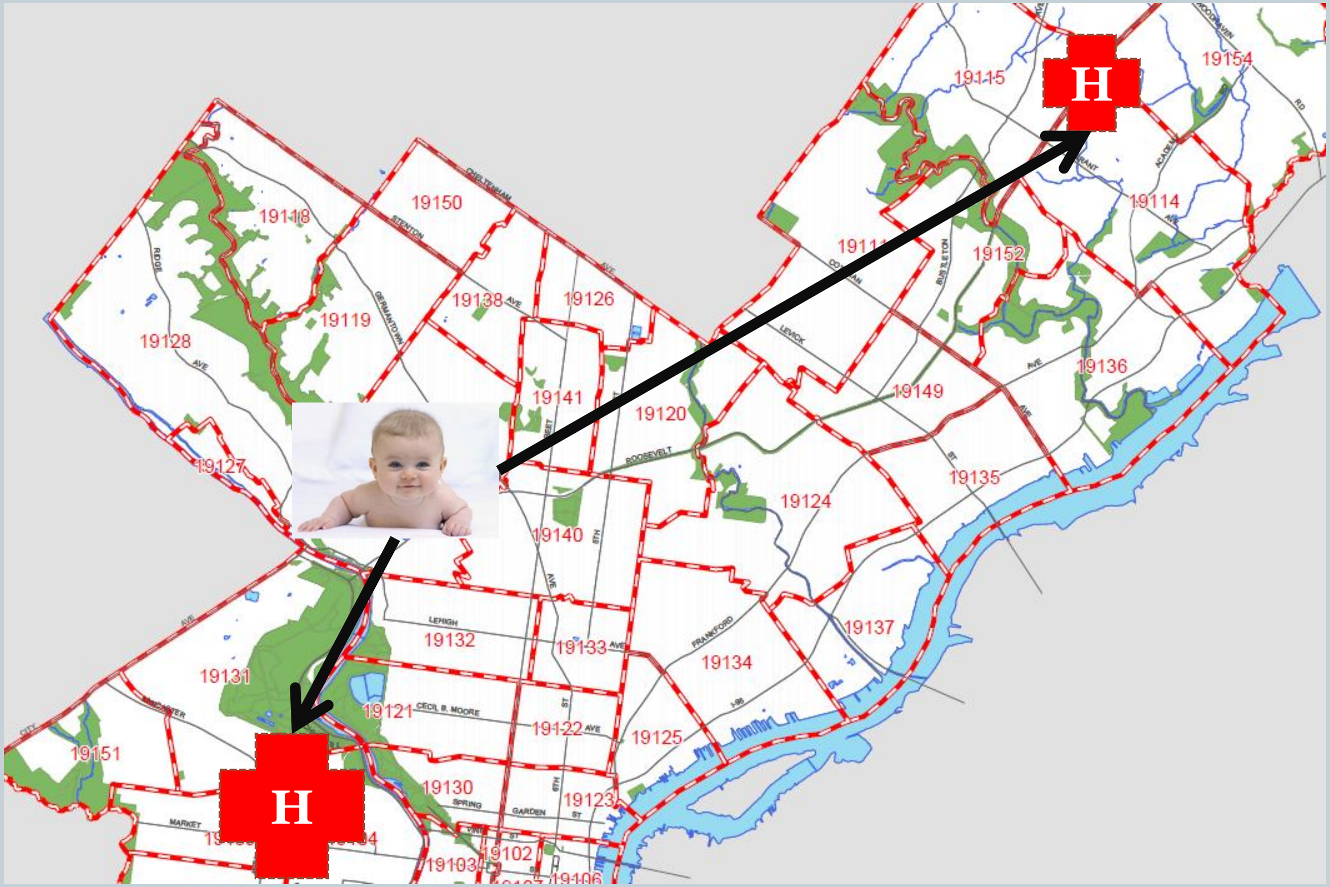

McClellan, McNeil & Newhouse; "**Does more intensive treatment of acute myocardial infarction reduce mortality?**" *JAMA*. 272(11): 859-66, September 1994

revised design

NEAR-FAR MATCHING

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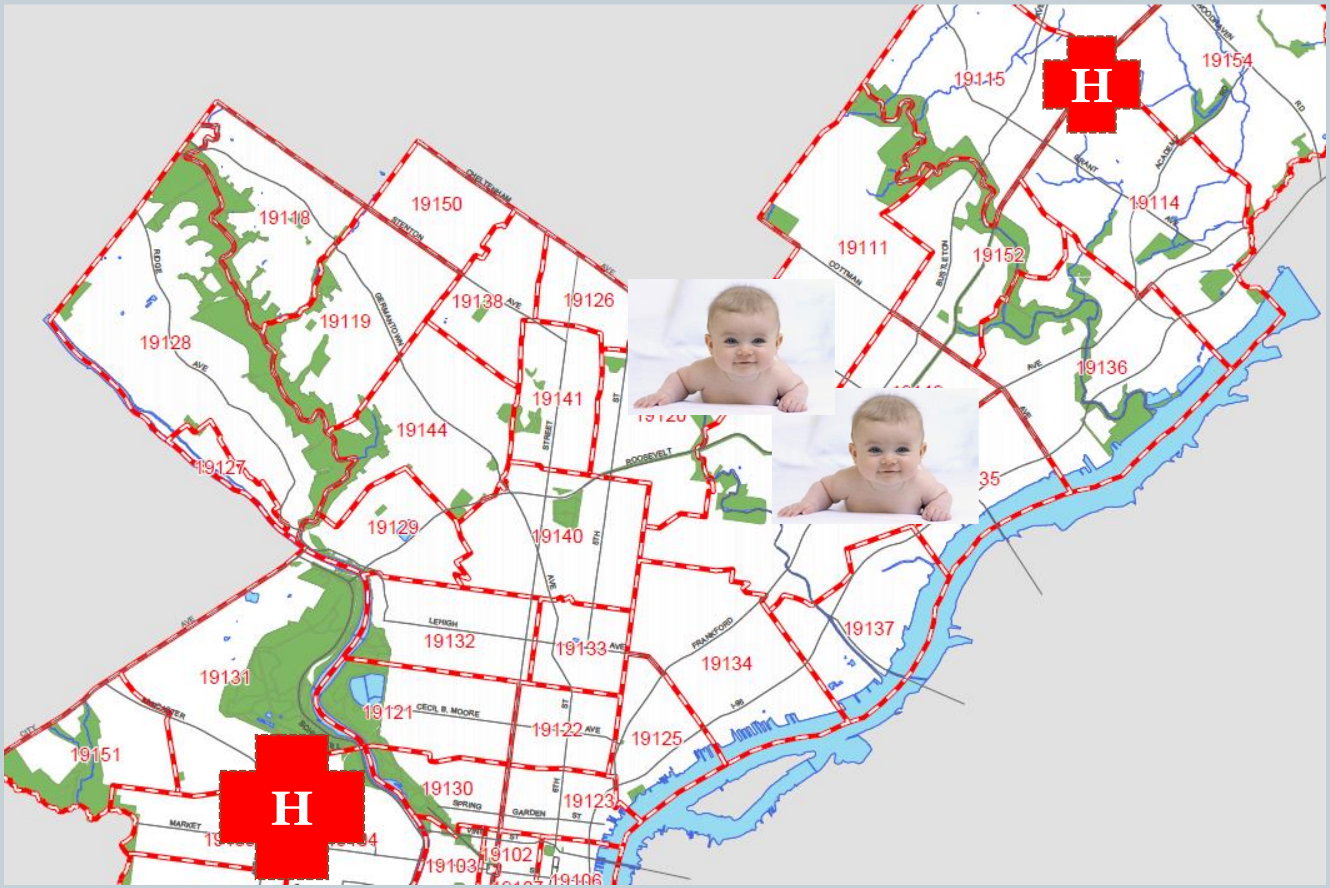
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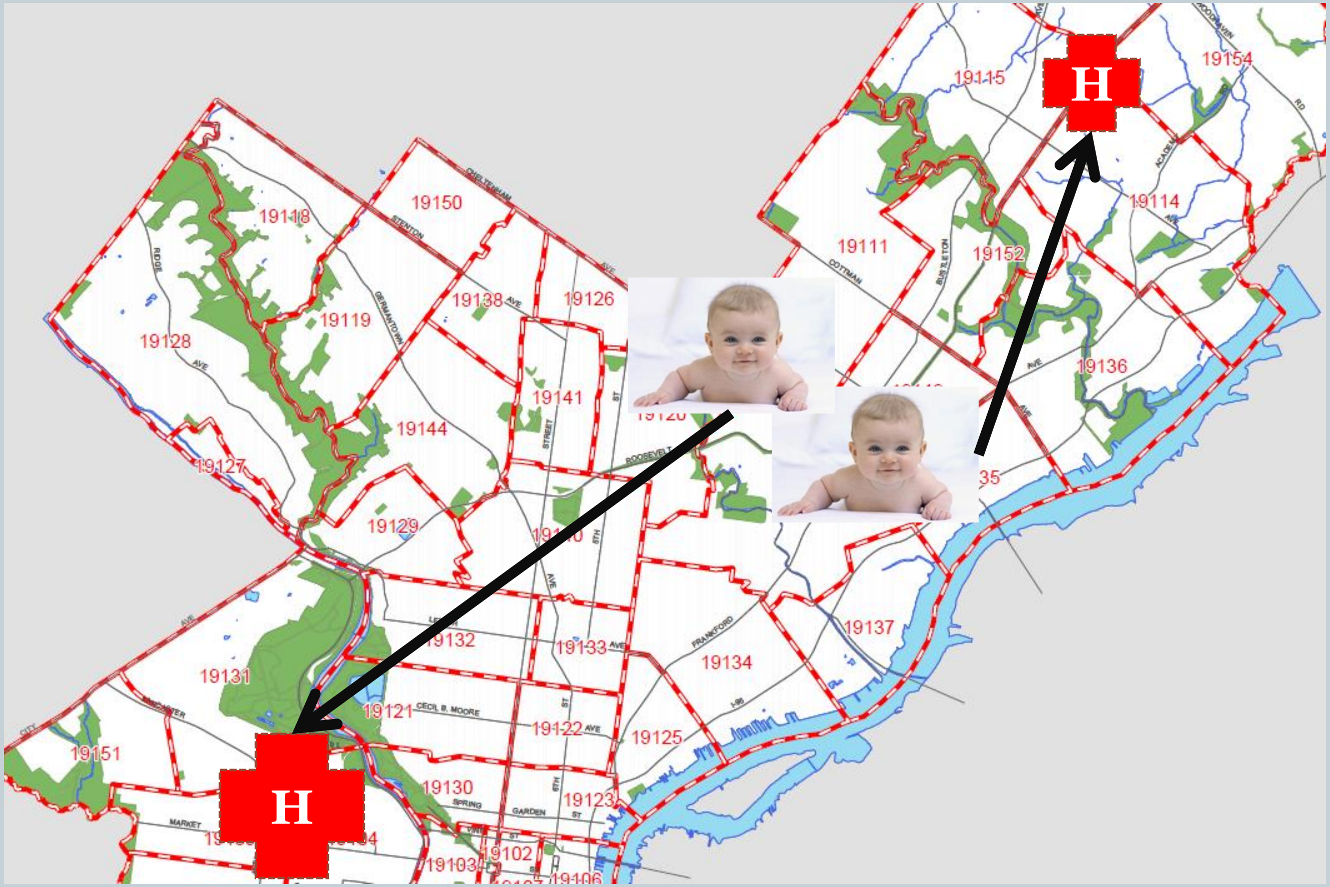

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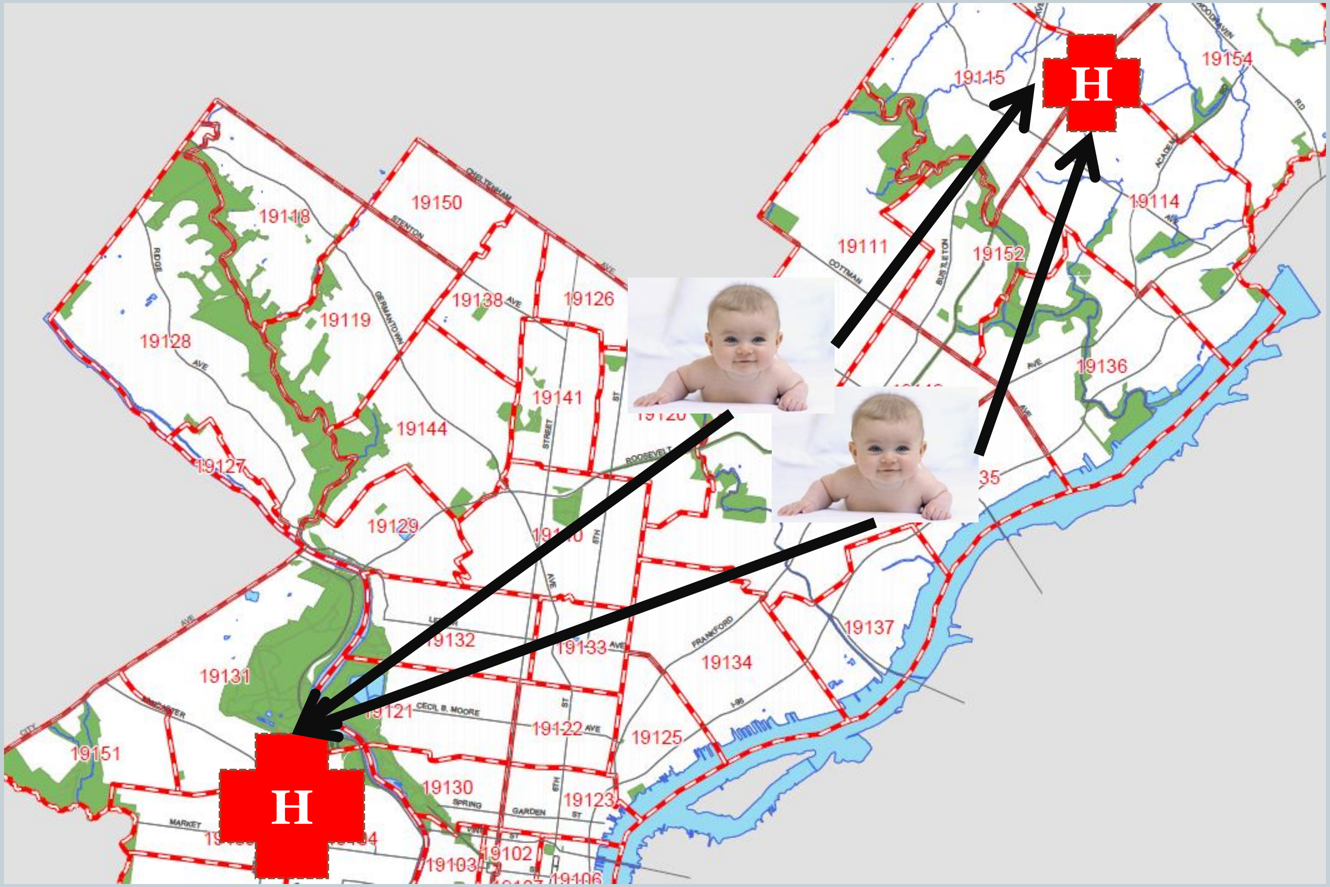
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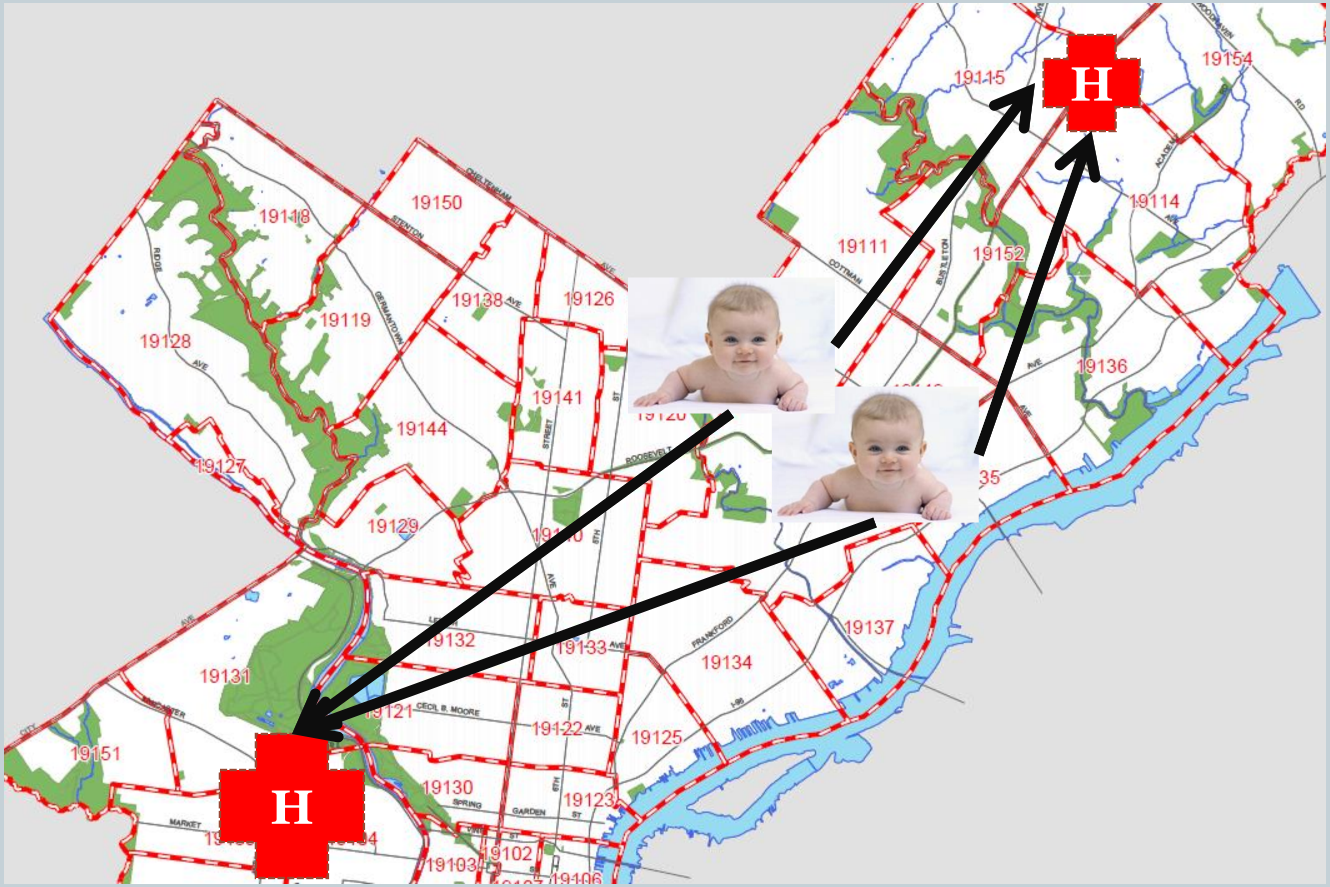
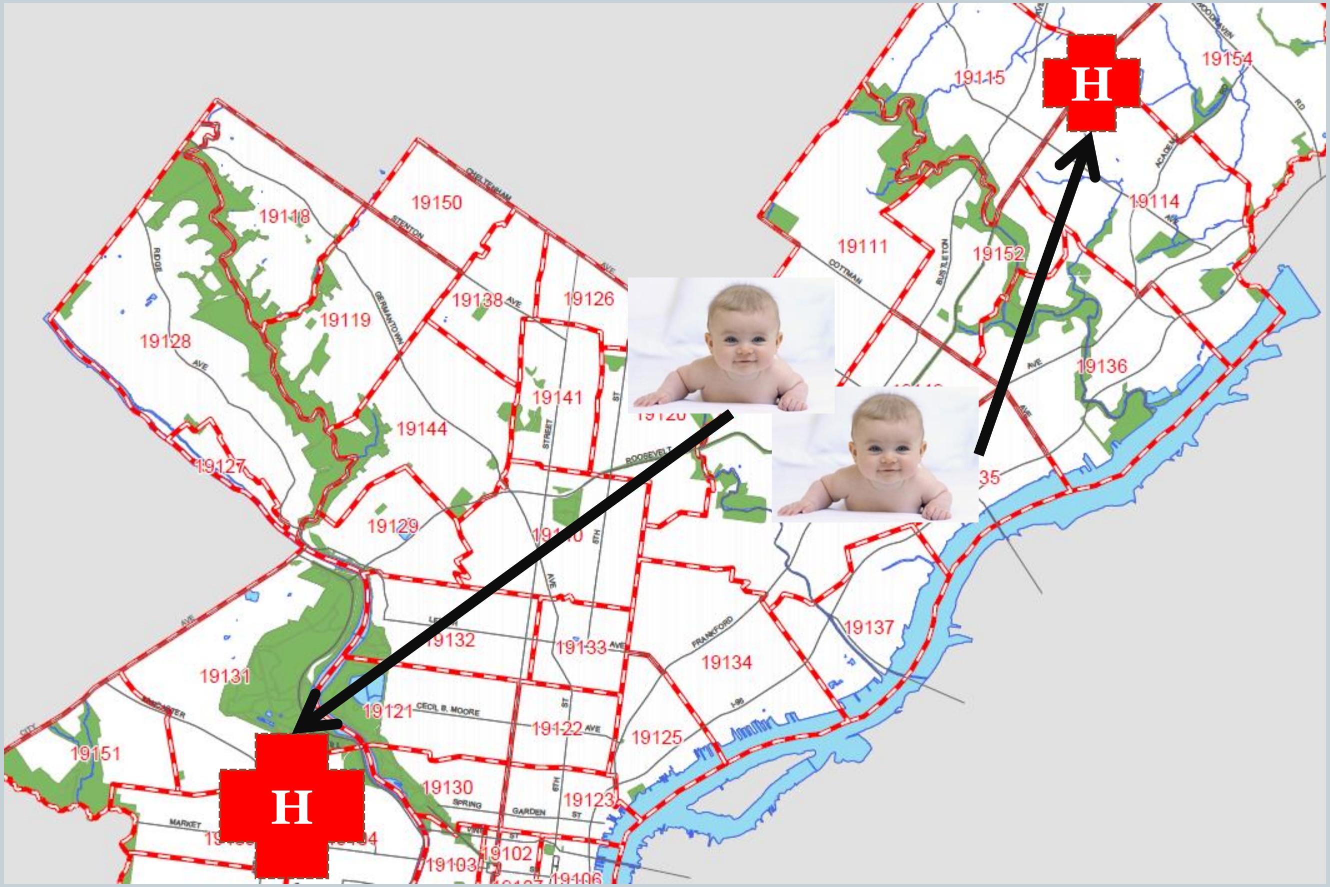


Sorting is potentially biased!



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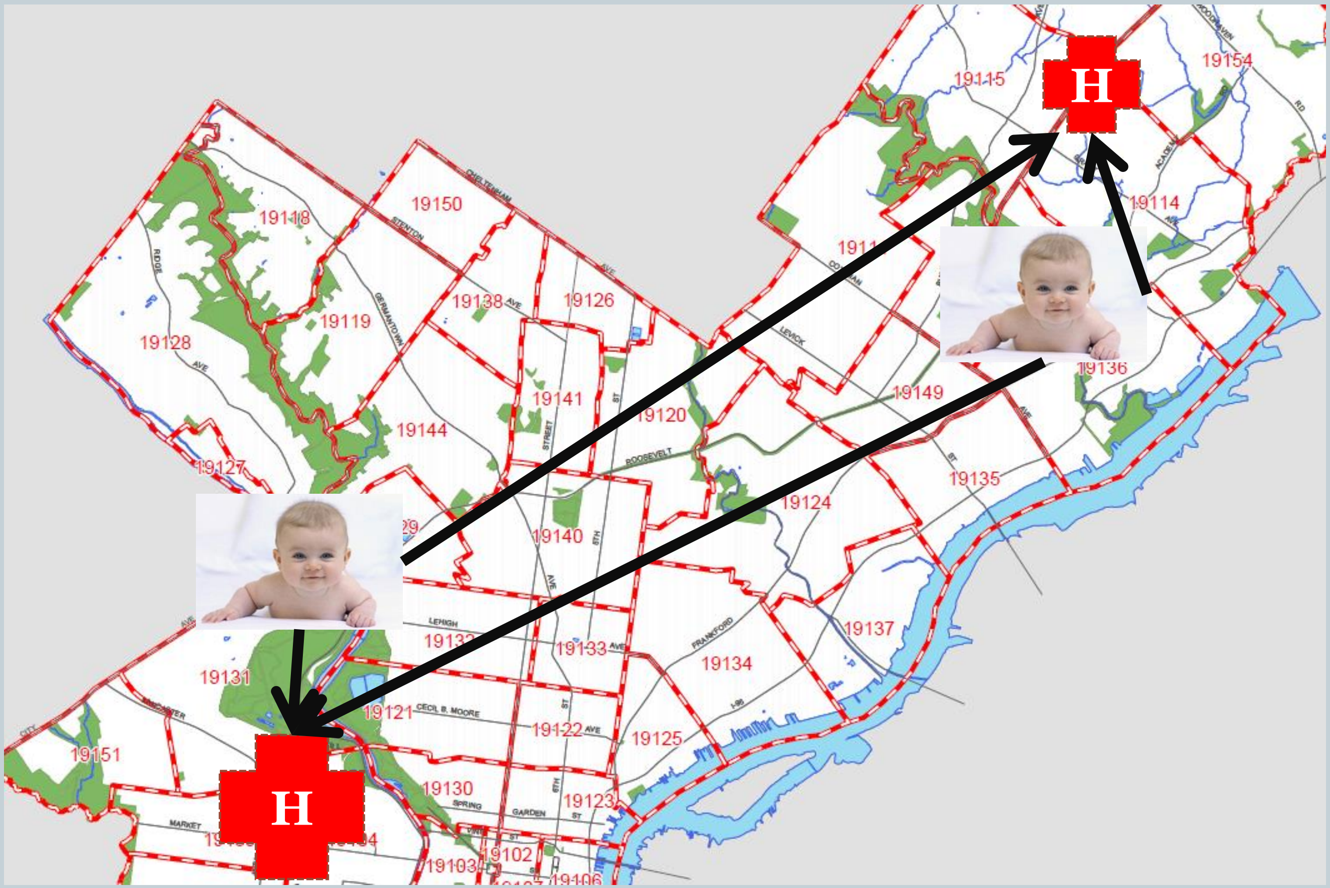
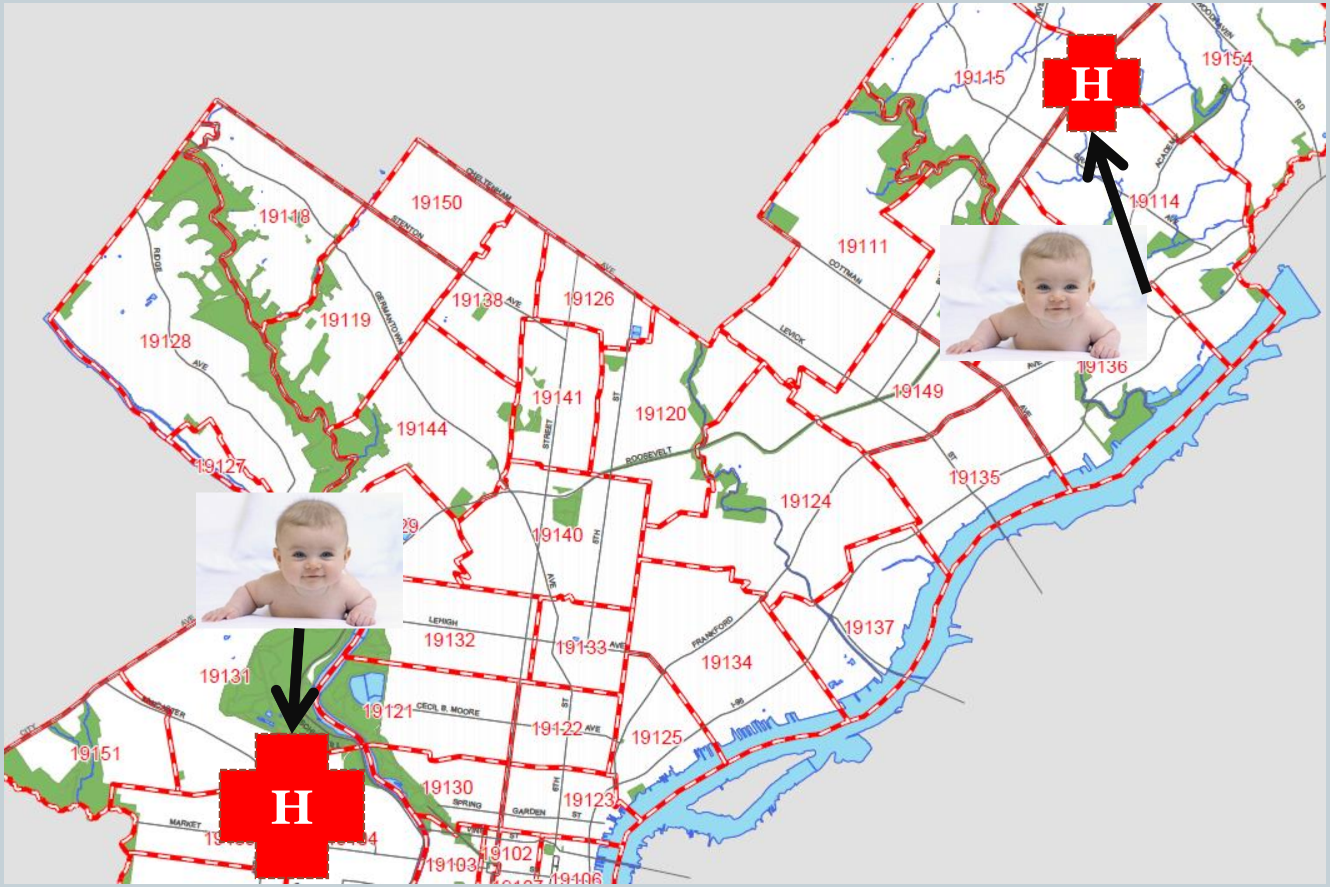


Sorting largely due to the randomness!



Sorting largely due to the randomness!

linking to inference

the fundamental form

- For RCTs, the fundamental form of inference is based on permutation tests (a.k.a. randomization tests)
- For survey, the fundamental form of inference is bootstrap (debatable)
- Everything else are necessary concessions to the particularities of a given problem
- Connect the structure of the data to your form of inference

takeaways

takeaways

- Design comes it two flavors
  (actually, three… but the third one is not very healthy)
- In prospective studies
  - design is an obvious consideration
  - and one that MUST be passed through in order to obtain data
- In retrospective studies,
  - design is a less obvious consideration
  - but one that MUST be passed through… unfortunately without much attention paid