P9185 - Project 3: Protocol of a Cluster-randomized trial for Asthma-PASS

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Background

Our interest is in persistent asthma in minority children.

- Comprehensive school-based interventions in collaboration with communities to reduce asthma morbidity and promote physical activity in urban areas.
- A pilot cluster RCT was conducted exploring this intervention in Bronx elementary schools
  - **Goal:** whether Children in schools receiving Asthma-PASS intervention may experience a greater improvement in the number of SFD at 6 **or** 12 months follow up than the children in the comparison group.
  - 4 Bronx elementary schools were recruited into the pilot study.
  - A total of 108 children recruited including ages 4-11 years with physician-diagnosed persistent or uncontrolled asthma attending kindergarten to 5th grades

Overview

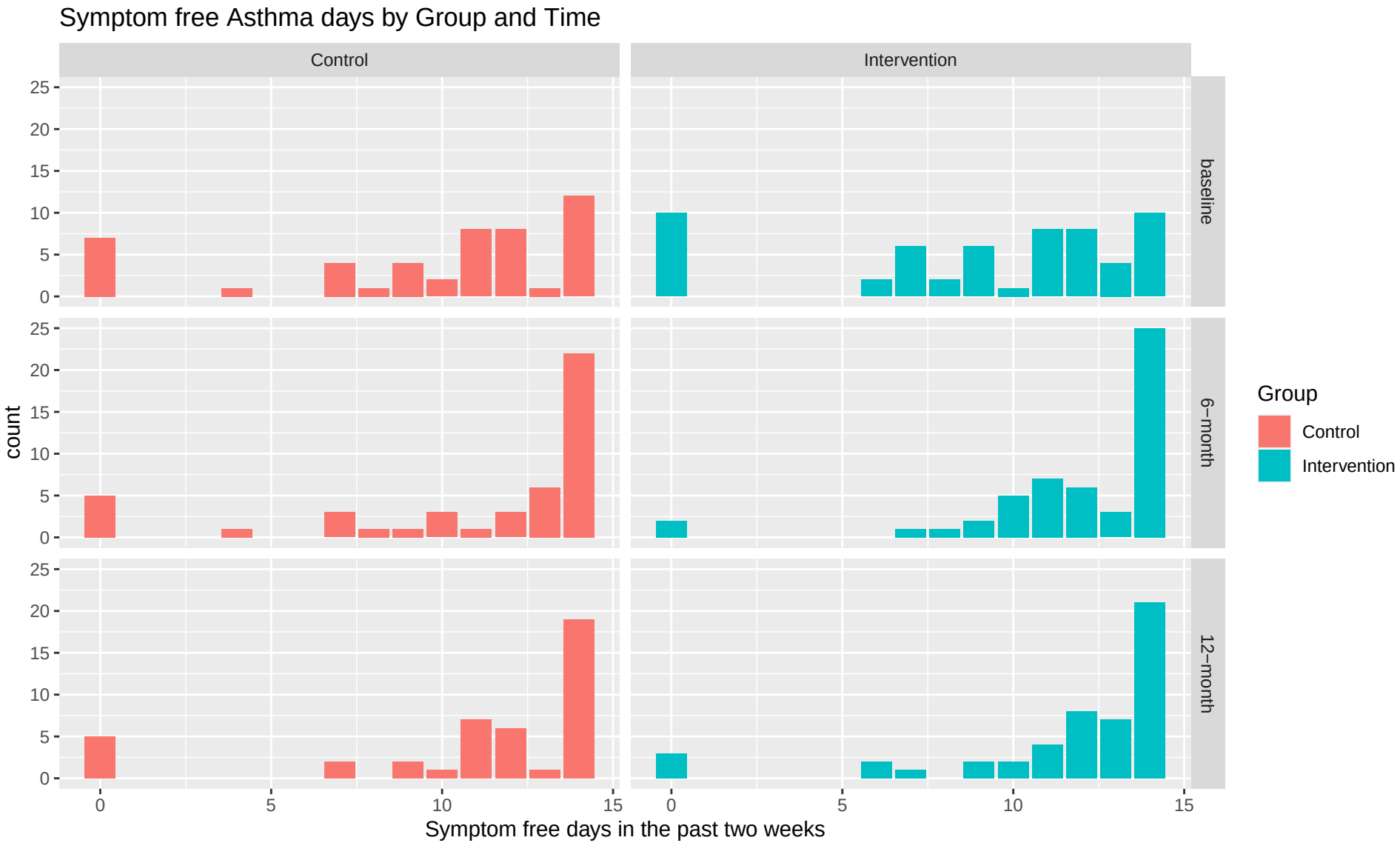
1. Data Overview
2. Exploration into Pilot Study data
   - Model Specifications
   - Results
3. Phase III Proposal
   - Model Specifications
   - Sample Size Suggestions

Data Overview

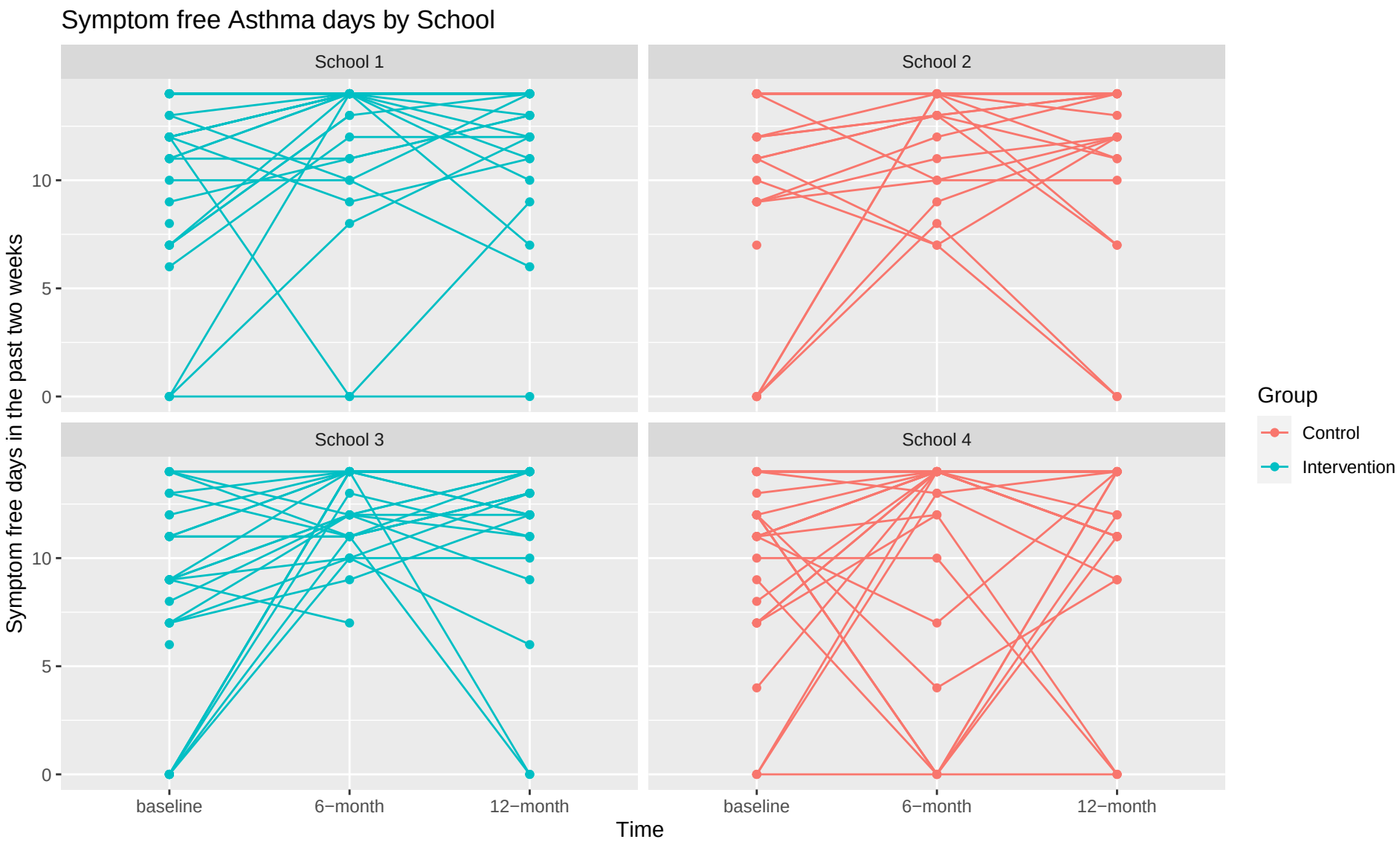
Variable	Definition
ID	Participant's ID
Time	Follow up time (Baseline, 6 months, 12 months)
Group	Intervention group (control or Intervention)
SFD	Symptom free days in the past two weeks
School	School recruited for the study

Table 1: Data Descriptions

Data Exploration



Data Exploration



Data Exploration

Current outcome: SFD (Count data)

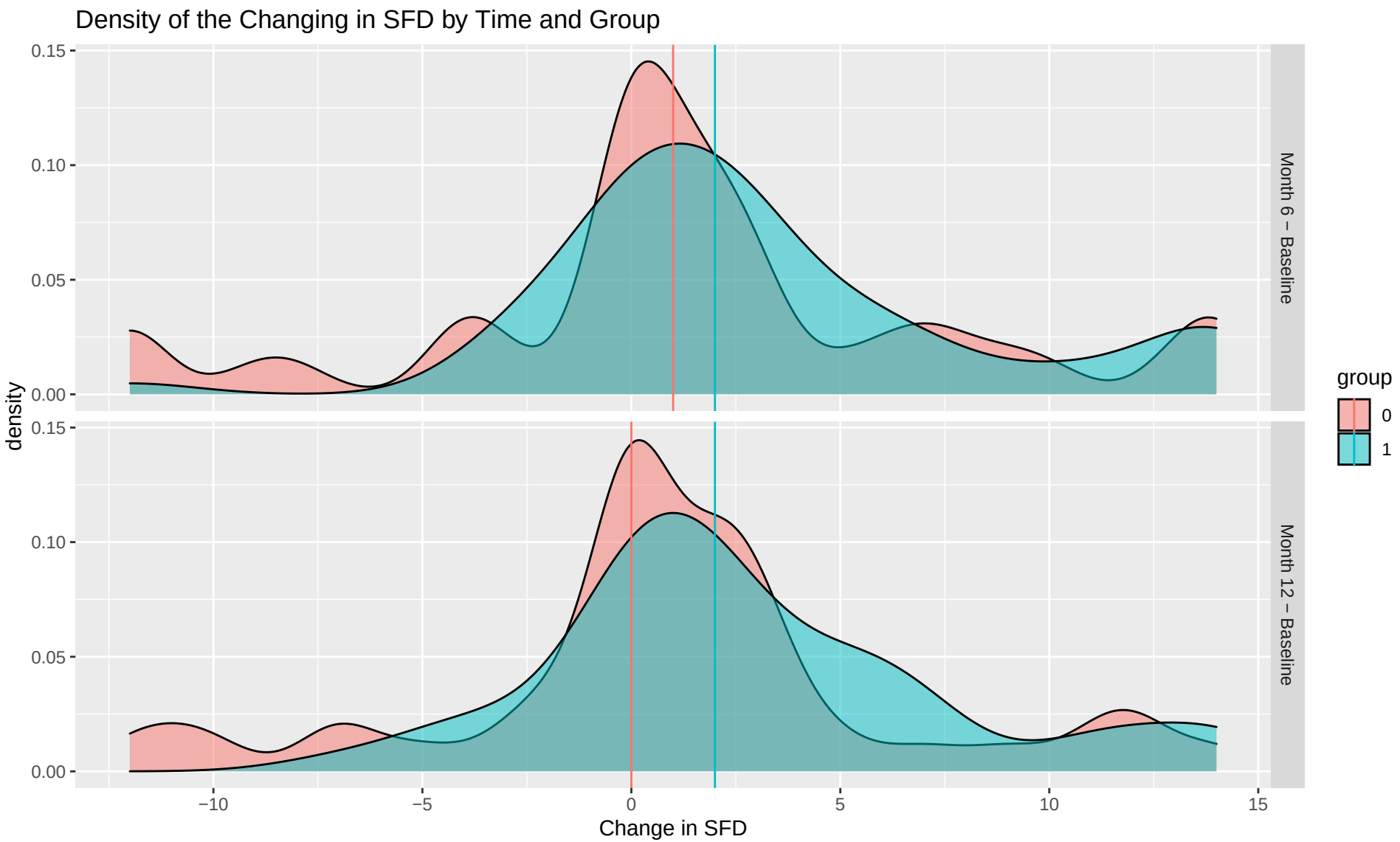
- Due to the skewed distribution towards higher values a poisson model will not fit our data well
- Outcome does not seem linear over the time observations.

Interested in the change from baseline to observation times.

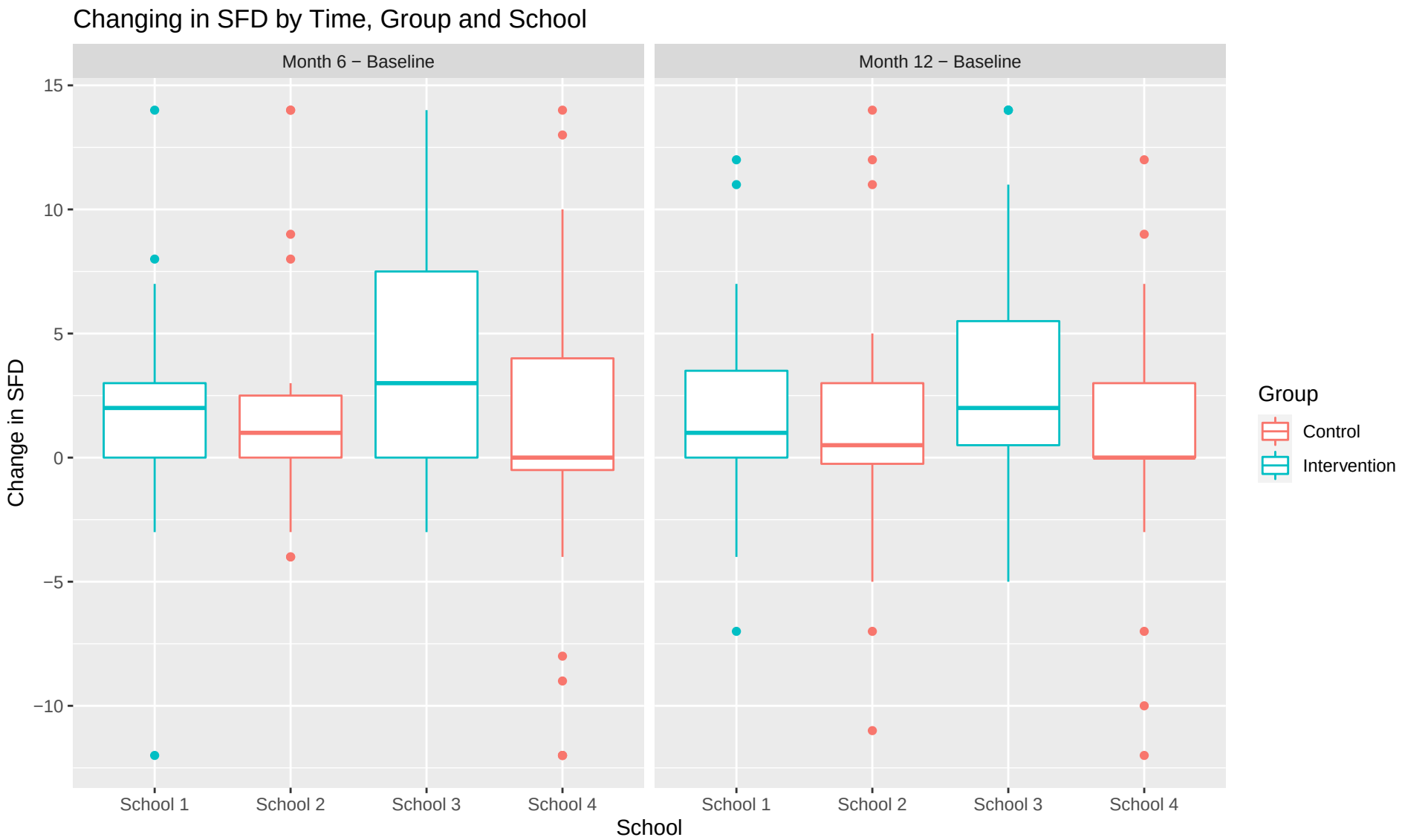
New outcome: Change in SFD (Continuous Data)

- Transform the SFD by calculated:
  - 6 month observation - baseline
  - 12 month observation - baseline
- Baseline with become covariate

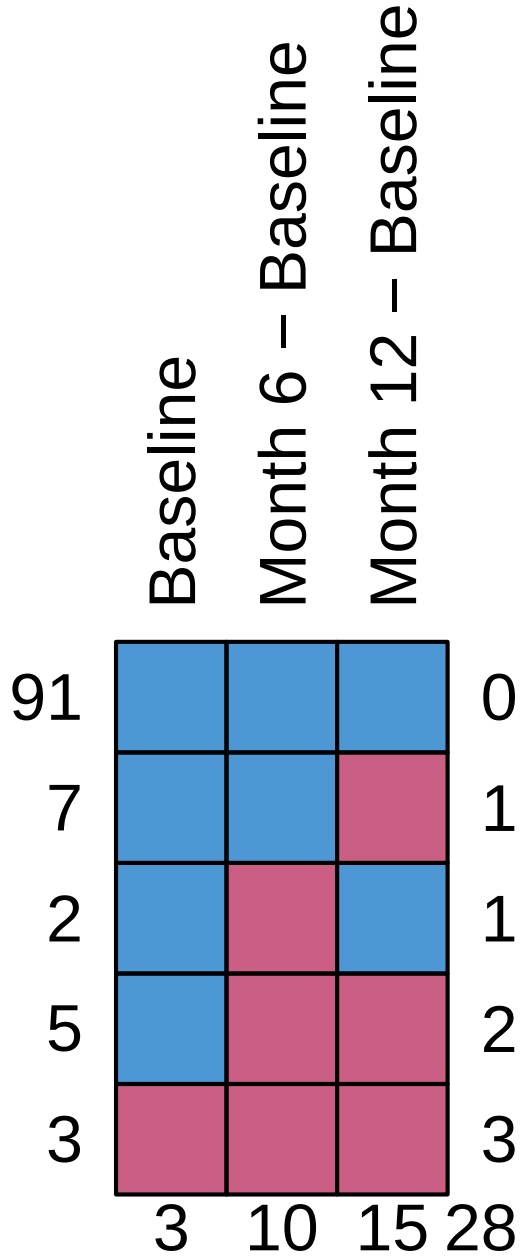
New Continous Outcome



Exploring variation between school and within school



Missing Data



Model Specifications

To model change in SFD let school $i \in (1, 2, 3, 4)$, individual j, time interval $k \in (1, 2)$.

We will used mixed effect model.

$$\begin{aligned} Y_{ijk} = \beta_0 &+ \beta_1 Baseline_{ij} \\ &+ \beta_2 Group_{ij} + \beta_3 Compare_{ijk} \\ &+ \beta_4 Group_{ij} \times Compare_{ijk} \\ &+ \alpha_{0i} + \alpha_{0j} + \epsilon_{ijk} \end{aligned}$$

where $\alpha_{0i} \sim N(0, \sigma_w^2)$, $\alpha_{0j} \sim N(0, \sigma_b^2)$, and $\epsilon_{ijk} \sim N(0, \sigma^2)$.

Missing Data Assumptions

We will be assuming data is missing at random (MAR)[1].

- MAR assumption: $R \perp\!\!\!\perp Y_{mis} | X, Y_{obs}$
- Separable parameter assumption
- Ignorability condition

$$
\begin{aligned}
L_i^{\mathrm{O}}(\theta, \psi) &\propto f_{\theta,\psi}\left(Y_{\mathrm{obs},i}, R_i, X_i\right) \\
&= f_{\psi}\left(R_i \mid Y_{\mathrm{obs},i}, X_i\right) f_{\theta}\left(Y_{\mathrm{obs},i} \mid X_i\right)
\end{aligned}
$$

Model Result

Fixed Effects Estimates:

Characteristic	Beta	95% CI[1]	p-value
baseline	-0.82	-1.0, -0.69	<0.001
group			
0	—	—	
1	1.1	-0.46, 2.6	0.2
compare			
m6_m0	—	—	
m12_m0	-0.05	-1.4, 1.3	>0.9
group * compare			
1 * m12_m0	-0.27	-2.2, 1.6	0.8

[1] CI = Confidence Interval

Random Effects Estimates:

group	Std.Dev	Variance
id	2.055	4.221
school	0.000	0.000
Residual	3.250	10.560

Model Interpretations:

1. interpretations
2. interpretations
3. interpretations

Note: This model is singular

Analysis for the pilot study

- Paired proportion test (binomial) / Paired T test (continuous, normal)
- For 6 months v.s. baseline, compair pass v.s. control
- For 12 months v.s. baseline, compair pass v.s. control
- Multiple adjustment
- Describe and comment on the effect sizes.
- Estimate intra class variation

Cluster RCT design

- The investigators wish to propose a **cluster-randomized clinical trial (RCT)** in 30 Bronx schools to evaluate the effectiveness of their intervention program.
- Primary hypothesis: compared to the control group, children in schools randomized to intervention group will experience a greater improvement in the number of SFD at **any of the 3, 6, 9, and 12 months** assessment.
- The investigators would like to have at **80% probability** to declare the trial is successful if the true effect size in **improvement of SFD over time** is **at least 1/3 standard deviation**.

Study design proposal:

3 level structure:[1]

$$y_{ijk} = \beta_0 + \delta_{(3)} X_{ijk} + \mu_i + \mu_{j_i} + e_{ijk}$$

- i for school, j for subjects, k for measures
- $\mu_i \sim N(0, \sigma_3^2)$ random intercept for school
- $\mu_{j_i} \sim N(0, \sigma_2^2)$ random intercept for school random intercept for subject
- randomize on school level, $X_{ijk} = X_i = 0/1$ indicating the control/intervention
- Hypothesis: $H_0 : \delta_{(3)} = 0, H_1 : \delta_{(3)} \neq 0$
  - **Q**: $H_1 : \delta_{(3)} > 0$?
- calculate N based on normal distribution, with multiple adjustment: $\alpha* = \alpha/4 = 0.025/4$ for the 4 comparison;
  - **Q**: Need multiple adjustment or not?
- $\beta = 0.2$

Resources

[1] Hogan, J. W., Roy, J., & Korkontzelou, C. (2004). Handling drop-out in longitudinal studies. Statistics in Medicine, 23(9), 1455–1497. https://doi.org/10.1002/sim.1728