

“A profitable way to build understanding and confidence is through data simulation. **If you can create data sets** by sampling from a population for which you **know the ground truth** about the population parameters you are interested in (e.g., mean and standard deviation of each group), **you can check how often and under what circumstances a statistical model will give you the correct answer**”

(DeBruine et al., 2021)

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Understanding Mixed-Effects Models Through Data Simulation

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RECAP

```
> fit = lmer(Reaction ~ Days + (Days | subject), data = d)
> summary(fit)
Linear mixed model fit by REML. t-tests use Satterthwaite's
['lmerModLmerTest']
Formula: Reaction ~ Days + (Days | Subject)
Data: d

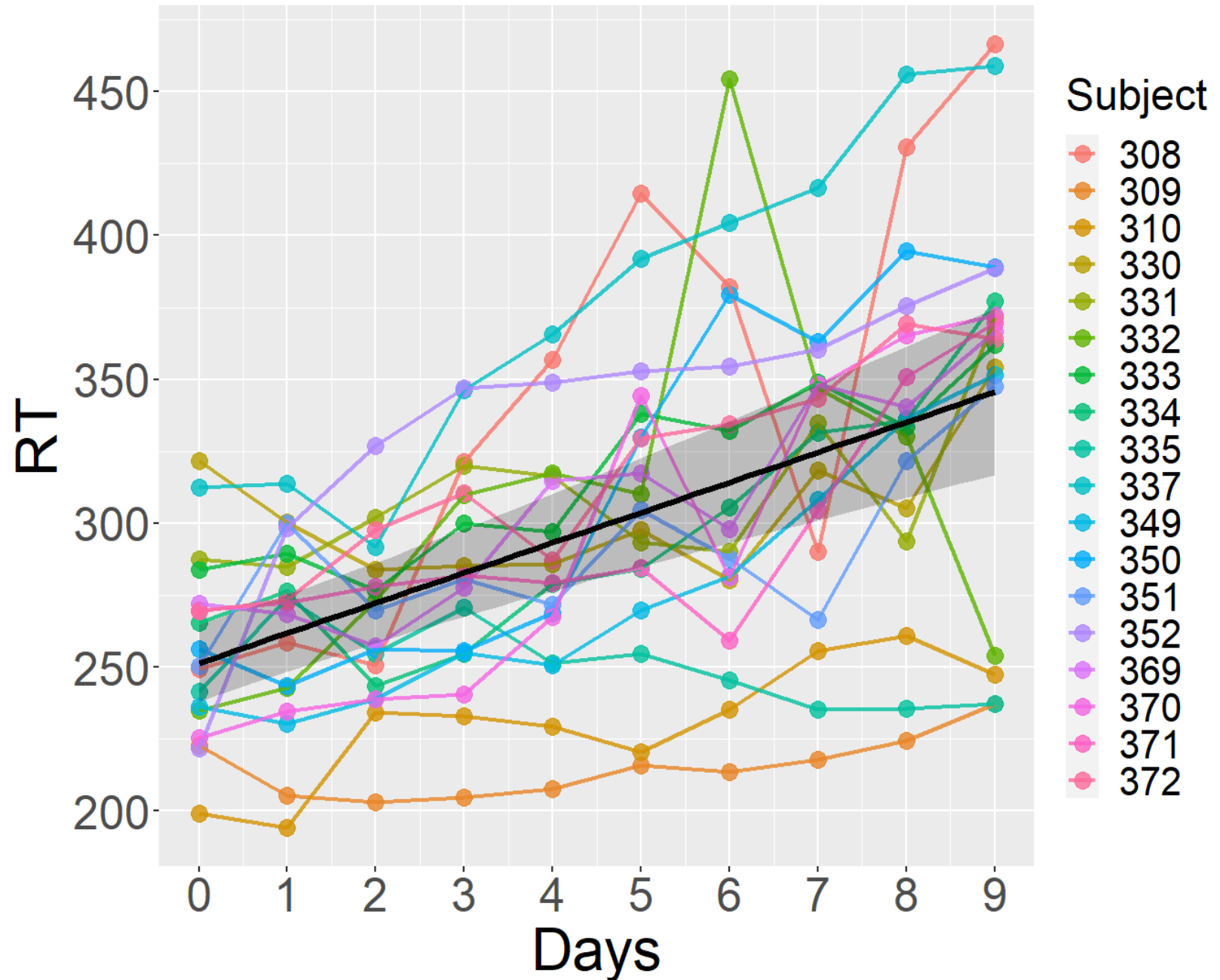
REML criterion at convergence: 1743.6

Scaled residuals:
  Min      1Q  Median      3Q      Max
-3.9536 -0.4634  0.0231  0.4634  5.1793

Random effects:
 Groups   Name      Variance Std.Dev. Corr
 Subject (Intercept) 612.10   24.741
          Days        35.07    5.922   0.07
 Residual              654.94   25.592

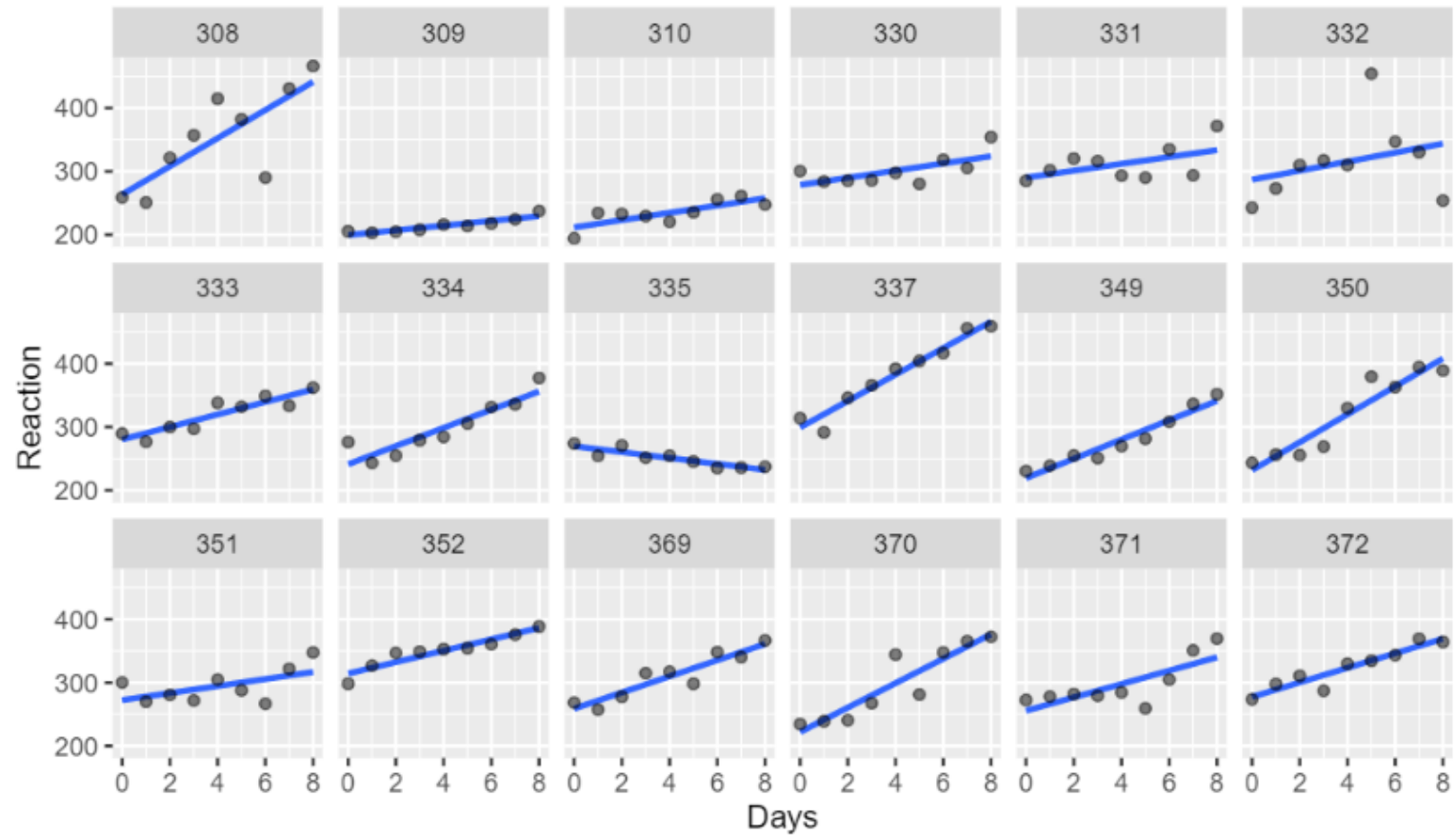
Number of obs: 180, groups: Subject, 18

Fixed effects:
      Estimate Std. Error    df t value Pr(>|t|)
(Intercept)  251.405     6.825  17.000  36.838 < 2e-16 ***
Days          10.467     1.546  17.000   6.771 3.26e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```



RECAP

```
> ggplot(data=d, aes(x=Days, y=Reaction)) + facet_wrap(~Subject, ncol=6)  
+ geom_smooth(method="lm", se=FALSE, formula="y~x") +  
+ geom_point(alpha=.5)
```

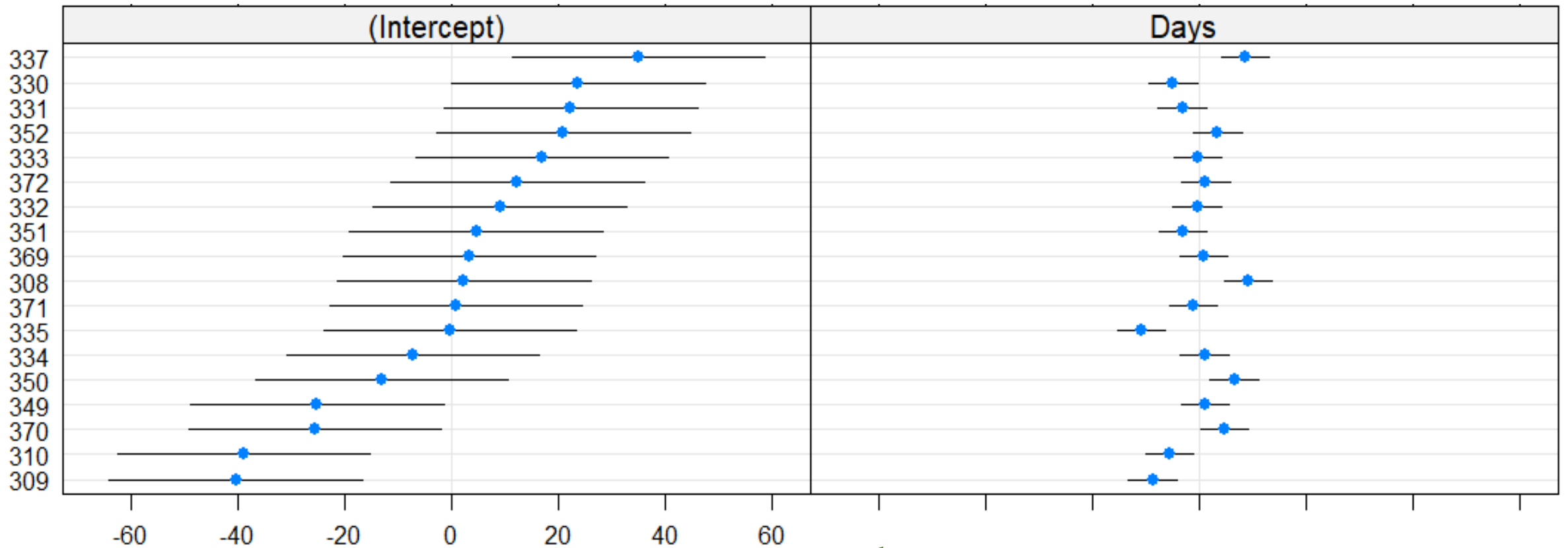


da slide del prof. Altoè (*PsicoStat*): <https://osf.io/b7tkp/>

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Distribuzione degli effetti random individuali

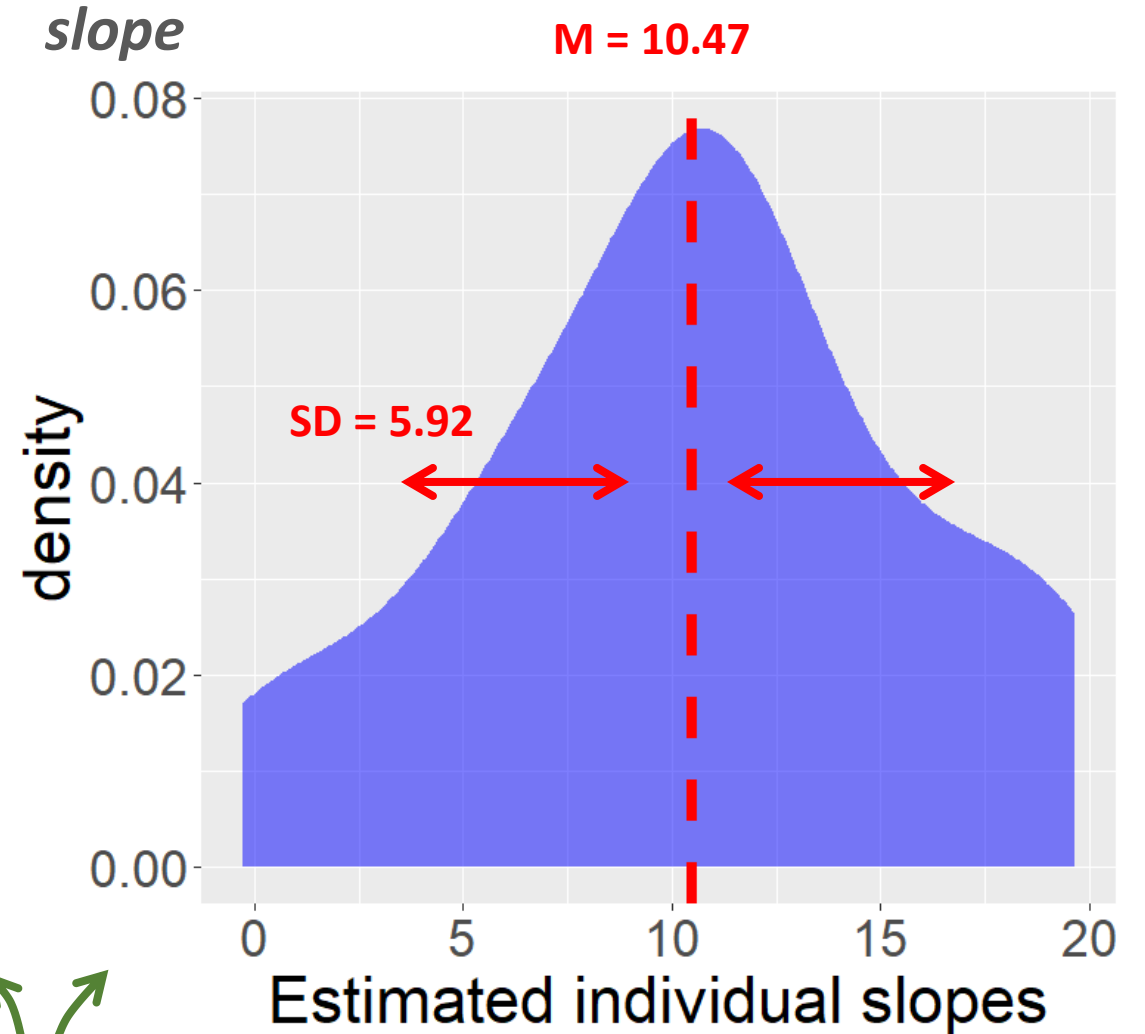
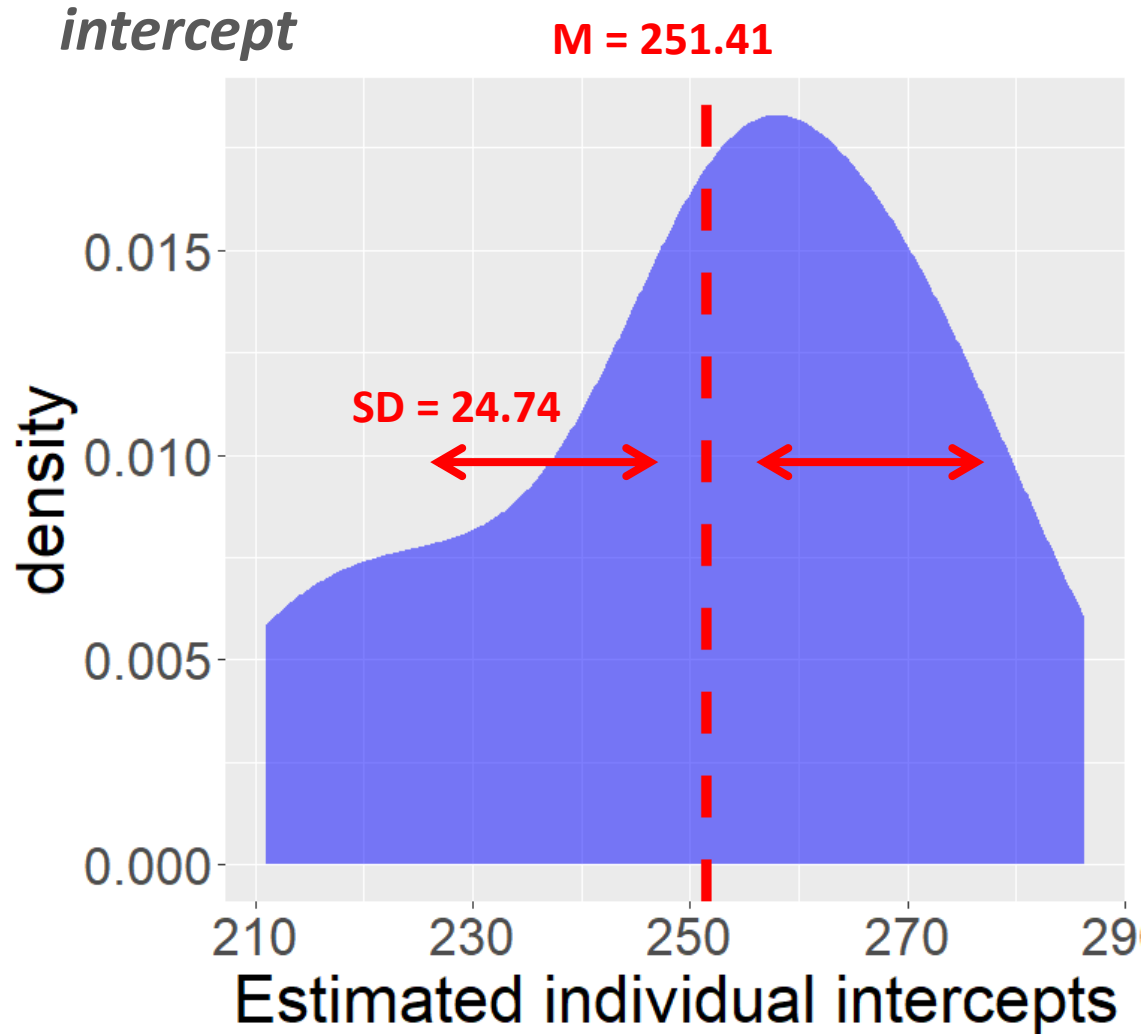
lattice :: dotplot(ranef(fit))



$r = 0.07$

RECAP

Distribuzione degli effetti random individuali



$r = 0.07$

Immaginiamo studio multilab come situazione analoga

- L'effetto random non è (per forza) il soggetto, ma il lab
- Invece di avere soggetti che hanno più giorni come misure ripetute, ho laboratori che hanno più soggetti come misure ripetute
- Invece di avere un effetto medio generale nel campione che varia di soggetto in soggetto, ho un effetto medio generale nel multilab study (cruciale per l'inferenza) che varia di lab in lab (comunque importante per capire l'eterogeneità e variabilità degli effetti nei contesti)
- **ESEMPIO: ho uno studio multilab che coinvolge k laboratori, ciascuno dei quali raccoglie n casi vs n controlli e li confronta calcolando una *Standardized Mean Difference* (e.g., Cohen's d) sulla variabile y**

ESEMPIO: MULTILAB

$k = 10$ laboratori, ciascuno raccoglie $n = 100$ casi clinici vs $n = 100$ controlli (N totale = 2000)

Parametri «*ground truth*» della simulazione: intercetta fissa = 0.0; slope fissa = -0.5;

SD intercetta random = 0.3; SD slope random = 0.2; SD residui = 1.0

```
> fit = lmer(y ~ clinicalstatus + (clinicalstatus | lab), data=d)
> summary(fit)
Random effects:
  Groups      Name                Variance Std.Dev. Corr
lab          (Intercept)         0.10956  0.3310
            clinicalstatus      0.02807  0.1676  -0.04
Residual                            0.98949  0.9947
Number of obs: 2000, groups: lab, 10

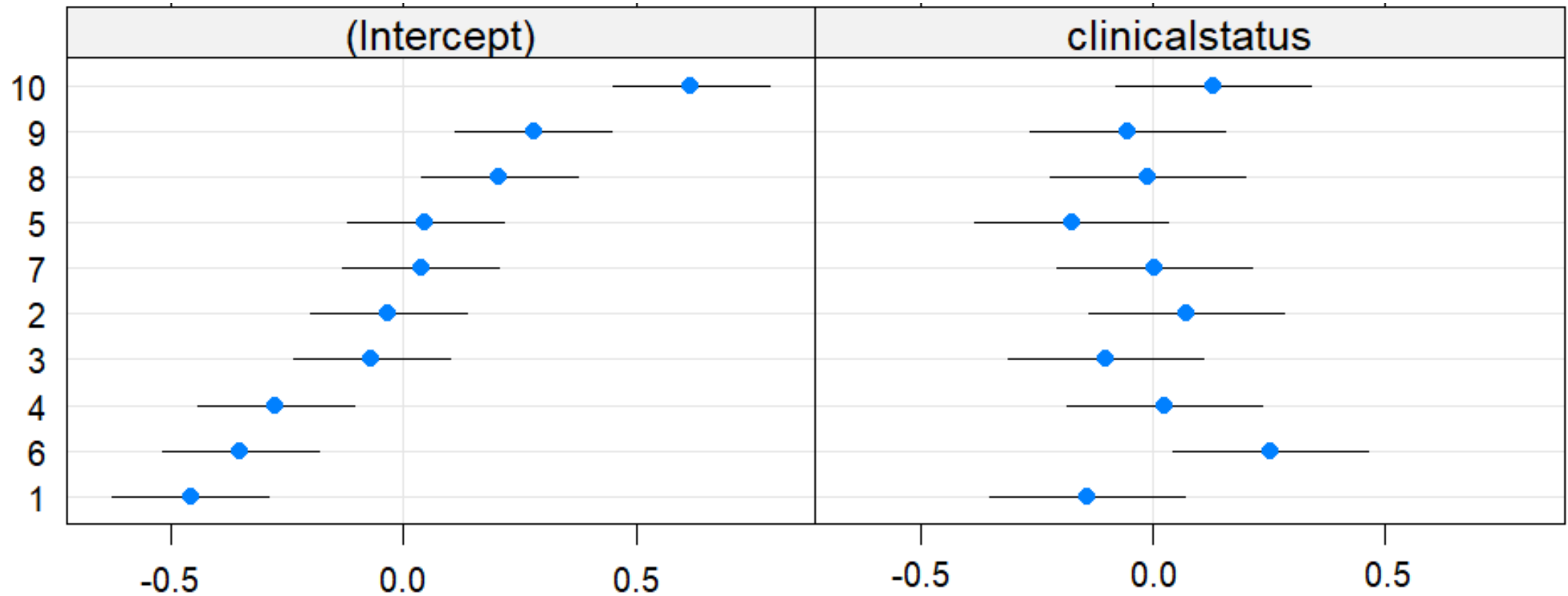
Fixed effects:
              Estimate Std. Error      df t value Pr(>|t|)
(Intercept)    0.05426   0.10930  8.99998   0.496   0.631
clinicalstatus -0.52172   0.06918  8.99996  -7.541 3.54e-05 ***
```

ESEMPIO: MULTILAB

$k = 10$ laboratori, ciascuno raccoglie $n = 100$ casi clinici vs $n = 100$ controlli (N totale = 2000)

Parametri «*ground truth*» della simulazione: intercetta fissa = 0.0; slope fissa = -0.5;

SD intercetta random = 0.3; SD slope random = 0.2; SD residui = 1.0



ESEMPIO: MULTILAB

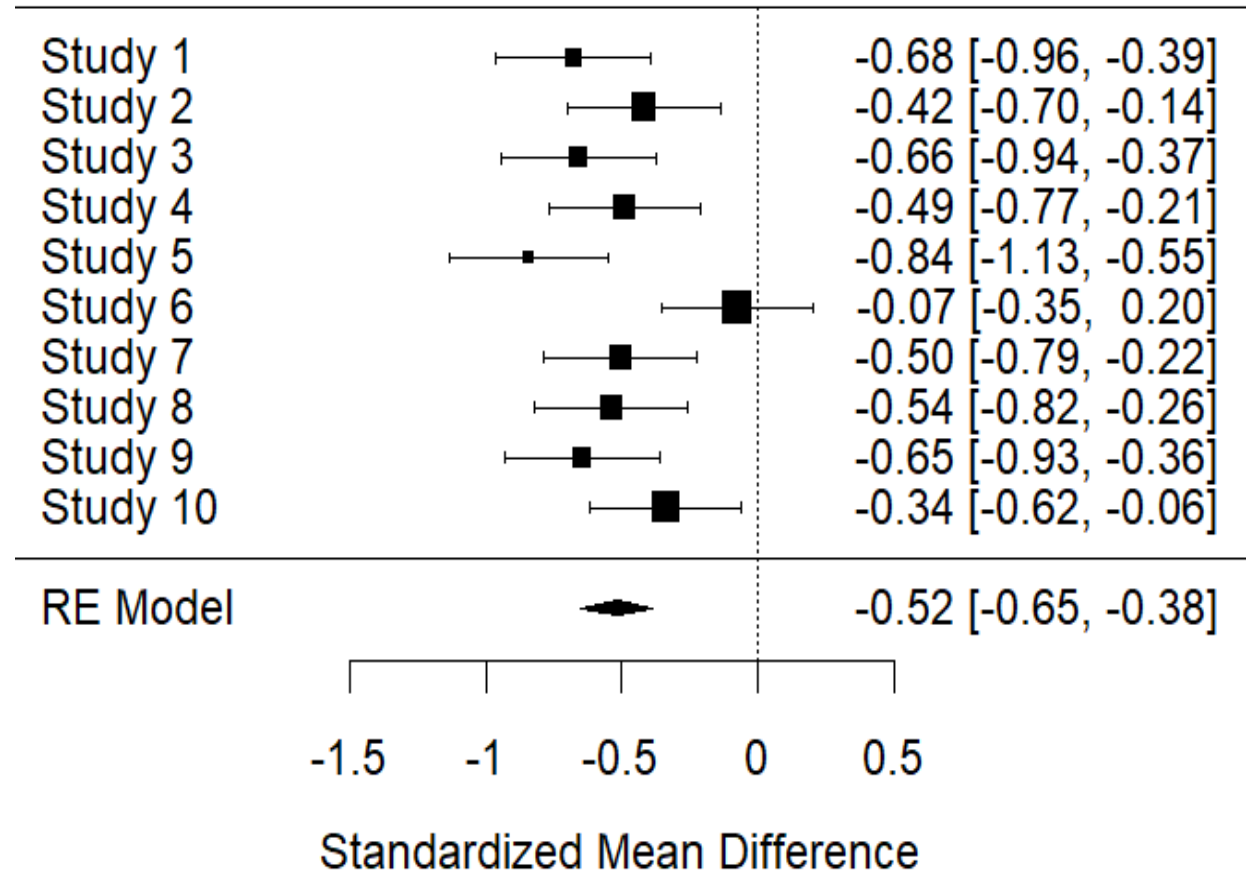
Rianalizzato come una meta-analisi a effetti random

```
> fitMeta = rma(yi,vi,data=d_agg)
> fitMeta
Random-Effects Model (k = 10; tau^2 estimator: REML)

tau^2 (estimated amount of total heter.): 0.0247 (SE=0.0214)
tau (square root of estimated tau^2 value): 0.1571
I^2 (total heterogeneity / total variability): 54.31%
H^2 (total variability / sampling variability): 2.19

Test for Heterogeneity:
Q(df = 9) = 19.7086, p-val = 0.0198

Model Results:
estimate      se      zval      pval      ci.lb      ci.ub      ***
-0.5161      0.0674     -7.6559     <.0001     -0.6482     -0.3840
```



DALLA FORMULA ALLA SIMULAZIONE

$$y_{ij} = \beta_0 + \beta_1 * X_{ij} + T_{0j} + T_{1j} * X_{ij} + \varepsilon_{ij}$$

dato osservato nel
soggetto i-esimo del
j-esimo lab

intercetta fissa
(stimata per la
popolazione)

slope fissa
(stimata per la
popolazione)

valore del
predittore X per
l'i-esimo soggetto
del j-esimo lab

intercetta
random (stimata
per il j-esimo
lab)

slope random
(stimata per il
j-esimo lab)

residuo (termine di errore
per il soggetto i-esimo del
j-esimo lab)

$$T_0 \sim N(0, \tau_0)$$

$$T_1 \sim N(0, \tau_1)$$

$$\varepsilon \sim N(0, \sigma)$$

Quando guardiamo `> summary(fit)` vediamo:

$$\hat{\beta}_0, \hat{\beta}_1, \hat{\tau}_0, \hat{\tau}_1, \hat{\sigma}$$

con `> ranef(fit)` vediamo anche:

$$\hat{T}_{0j}, \hat{T}_{1j}$$

DALLA FORMULA ALLA SIMULAZIONE

lab (j)	sub (i)	clinicalstatus (X_{ij})	β_0	β_1	T_{0j}	T_{1j}	ε_{ij}	Y_{ij}
1	11	0	0.00	-0.50	0.46	0.23	0.24	0.70
1	12	0	0.00	-0.50	0.46	0.23	-0.81	-0.35
1	13	1	0.00	-0.50	0.46	0.23	0.23	0.42
1	14	1	0.00	-0.50	0.46	0.23	0.05	0.24
2	21	0	0.00	-0.50	-0.36	0.02	0.90	0.54
2	22	0	0.00	-0.50	-0.36	0.02	0.95	0.59
2	23	1	0.00	-0.50	-0.36	0.02	-0.57	-1.41
2	24	1	0.00	-0.50	-0.36	0.02	1.57	0.73
3	31	0	0.00	-0.50	0.12	-0.18	-1.73	-1.61
3	32	0	0.00	-0.50	0.12	-0.18	0.90	1.02
3	33	1	0.00	-0.50	0.12	-0.18	1.70	1.14
3	34	1	0.00	-0.50	0.12	-0.18	-0.87	-1.43

\nearrow
 $N(0, 0.30)$
 τ_0

\uparrow
 $N(0, 0.20)$
 τ_1

\nwarrow
 $N(0, 1.00)$
 σ

DALLA FORMULA ALLA SIMULAZIONE

```
> fit = lmer(y ~ clinicalstatus + (clinicalstatus | lab), data=d)
> summary(fit)
```

Random effects:

Groups	Name	Variance	Std.Dev.	Corr
lab	(Intercept)	0.09000	0.3000	
	clinicalstatus	0.04000	0.2000	0.00
Residual		1.00000	1.0000	

Number of obs: xxxxx, groups: lab, xxxxx

Fixed effects:

	Estimate	Std. Error	df	t value	Pr(> t)
(Intercept)	0.00	xxxxx	xxx	xxxxx	xxxxx
clinicalstatus	-0.50	xxxxx	xxx	xxxxx	xxxxx