Aspects of regression to the mean

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April 25, 2024

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Shrinkage of results can be seen to be a necessary fact of life.

(Stephen Senn)

1. Shrinkage is a fact of life

- Galton 1889: *Regression toward mediocrity*: Phenomenon where if one sample of a random variable is extreme, the next sampling of the same random variable is likely to be closer to its mean.

2. True and observed

Assume true diastolic blood pressure, τ, at baseline is measured with error ϵ so that

$$X = \tau + \epsilon \tag{1}$$

is the *observed* blood pressure. Let the *true* mean difference between patients be Δ and the *observed* mean difference D, then the expectation of D is

$$\mathrm{E}(D \mid \Delta = \delta) = \delta, \tag{2}$$

that is, we have "classical" *unbiasedness*, since $\beta_{D|\Delta} = \frac{\mathrm{Cov}(\Delta, D)}{\sigma^2_\Delta} = 1$.

However, the contrary is not true. We have for the expectation of Δ, given an observed difference d,

$$|\mathrm{E}(\Delta \mid D = d)| < |d| \,, \tag{3}$$

since $\beta_{\Delta|D} = \frac{\mathrm{Cov}(\Delta,D)}{\sigma_D^2} < 1$, and we have *regression to the mean*[1].

Reliability as upper bound The maximal possible correlation between Δ and D is $\sqrt{rel_D}$.

[1]

In a Bayesian approach, shrinking is *natural* and we have *inverse unbiasedness.* Most bayesians are rather unconcerned about unbiasedness (at least in the formal sampling-theory sense above) of their estimates. For example, Gelman et al (1995) write: "From a Bayesian perspective, the principle of unbiasedness is reasonable in the limit of large samples, but otherwise it is potentially misleading. Unbiasedness as conventionally understood is not a necessary property of good inferences". Assume without loss of generality $\mathrm{E}(\Delta) = 0$ and $\widehat{\Delta}$ an unbiased estimate of a given effect Δ and $\widehat{\Delta}_{shrunk}$ a shrunk estimate. Although $\widehat{\Delta}_{shrunk}$ is not unbiased in the classic forward sense, $\mathrm{E}(\widehat{\Delta}_{shrunk} \mid \Delta = \delta) \neq \delta$ it is unbiased in the Bayesian backward sense: $\mathrm{E}(\Delta \mid \widehat{\Delta}_{shrunk} = \widehat{\delta}_{shrunk}) = \widehat{\delta}_{shrunk}$.

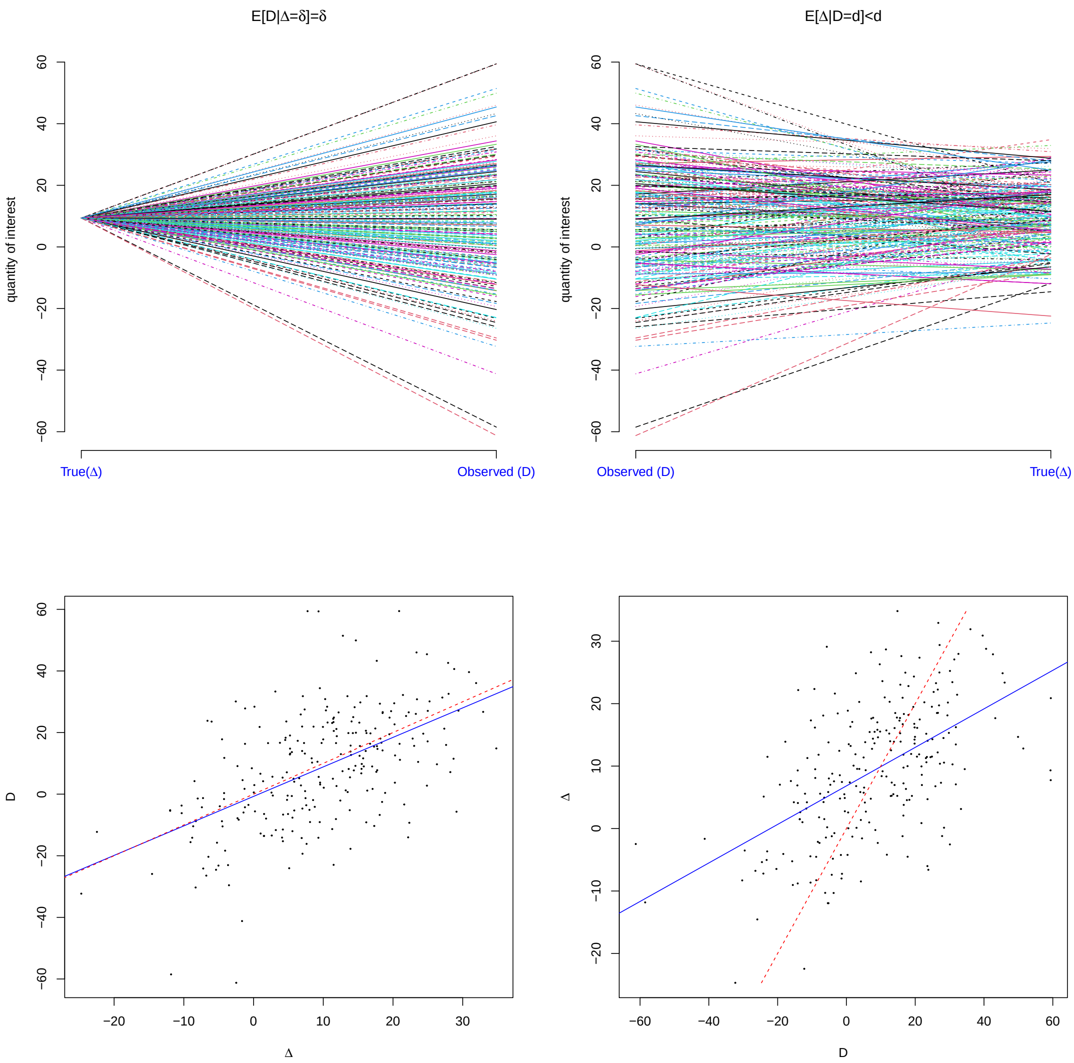


Figure 1: Shrinkage as a fact of life

3. Placebo as a statistical phenomenon

Placebo effects can often be interpreted as a purely statistical – not a psychological – phenomenon.

Assuming no true change. We simulate correlated pre-post diastolic blood pressure data assuming *no change* from baseline to follow-up: simulations from parameters: $\rho_{BL,FU} = 0.76, \mu_{BL} = \mu_{FU} = 90, \sigma_{BL} = \sigma_{FU} = 8$. Then let us look at the *subgroup* of "hypertensive at baseline" only. We have regression to the mean, since $\beta_{FU|BL} = \frac{\sigma_{FU,BL}}{\sigma^2_{BL}} = r \leq 1$.

```
library(RegToMeanExample)
args(DBP.RTM)

## function (mu = 90, sigma = 8, r = 0.76, n = 1000, limit = 95,
##     TrueChange = 0, show.plot = TRUE, show.out = FALSE)
## NULL

res <- DBP.RTM(show.plot = FALSE)
```

```
res$ttestall$p.value

## NULL

res$ttestextrem$p.value

## NULL
```

```r
DBP.RTM(show.plot = TRUE)
```

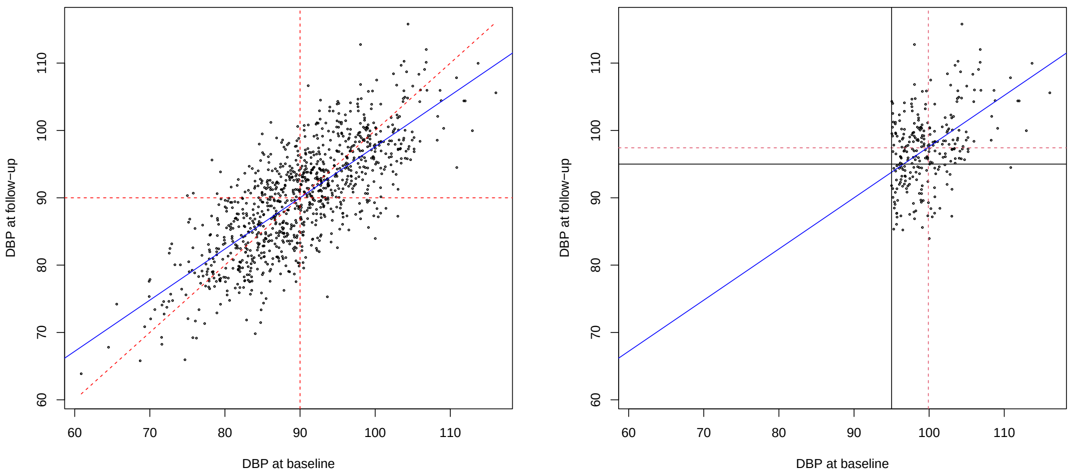
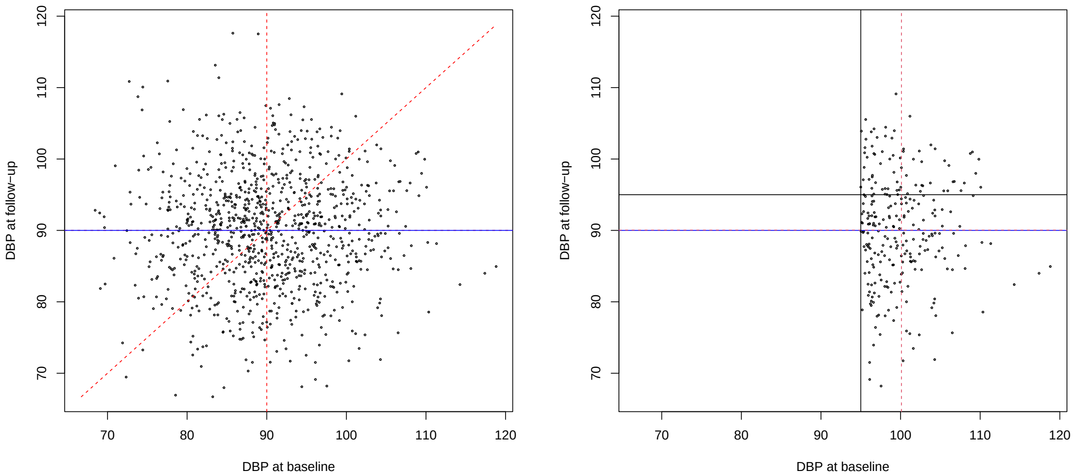


Figure 2: Simulation of diastolic blood pressure data. Simulations from parameters: $\rho_{BL,FU} = 0.76, \mu_{BL} = \mu_{FU} = 90, \sigma_{BL} = \sigma_{FU} = 8$. Left panel: Baseline versus Follow-up for diastolic blood pressure: no change in the mean. Right panel: Baseline versus Follow-up for "hypertensive at baseline" only. We observe an apparent change due to regression to the mean (Solid line: Regression of follow-up on baseline-measure (that is, by fixing baseline)). Dashed lines: mean values and equality lines.

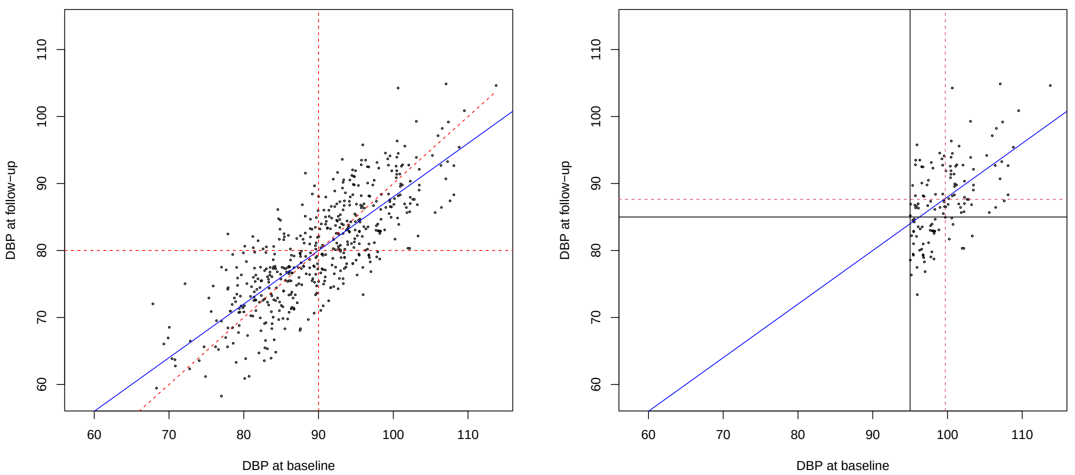
Extreme case: ρ=0

```r
DBP.RTM(r = 0, show.plot = TRUE)
```



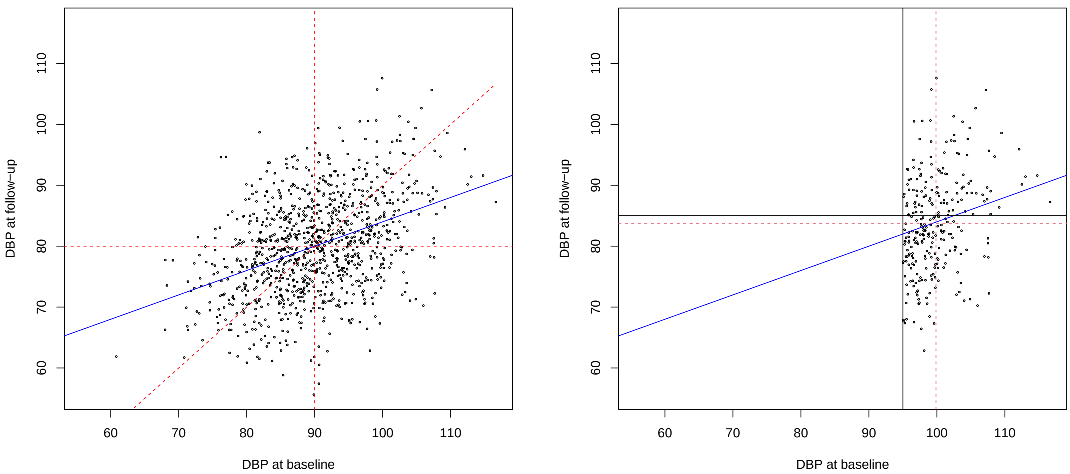
Including a true change of -10 and ρ=.8

```r
DBP.RTM(n = n, r = 0.8, TrueChange = -10, show.plot = TRUE)
```



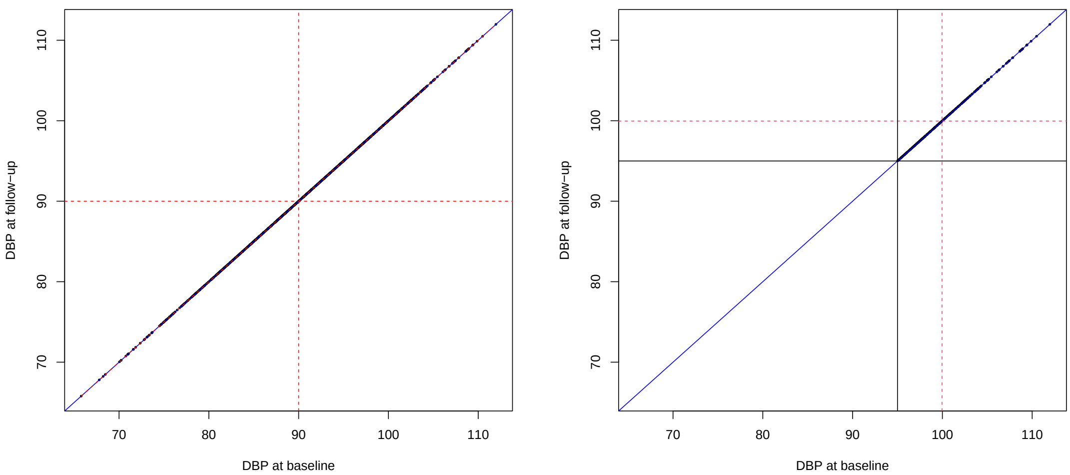
Including a true change of -10 and ρ=.4

```
DBP.RTM(r = 0.4, TrueChange = -10, show.plot = TRUE)
```



ρ=1 (Perfect reliability)

```
DBP.RTM(r = 1, TrueChange = 0, show.plot = TRUE)
```



A. Maths

Definition for bivariate normal distribution If (X, Y) follows a bivariate normal distribution, then $E(Y \mid X)$ is a linear function of X. The correlation ρ between X and Y determines:

$$\boxed{\frac{\mathrm{E}(Y \mid X) - \mathrm{E}(Y)}{\sigma_Y} = \rho \frac{X - \mathrm{E}(X)}{\sigma_X}}, \tag{4}$$

where $E(X)$ and $E(Y)$ are the expected values of X and Y, respectively, and σ_X and σ_Y are the standard deviations of X and Y, respectively.

The conditional expected value of Y, given that X is t standard deviations above its mean (and that includes the case where it is below its mean, when $t < 0$), is ρt standard deviations above the mean of Y .

Since $|\rho| \leq 1$, Y is no farther from the mean than X is, as measured in the number of standard deviations. Hence, if $0 \leq \rho < 1$, then (X, Y) shows regression toward the mean, that is, $Z_{Y|X} = \rho Z_x$, leading to $Z_{Y|X} - Z_X = (\rho - 1)Z_x$. The amount of RTM is

$$\boxed{\left|z_{Y|X} - z_x\right| = (1 - \rho) z_x}. \tag{5}$$

The estimated fraction of RTM is given by $1 - \rho$, the fraction of variance that is due to within-subject variability. This quantity represents *unreliability.*

Attenuation Spearman 1904: *The proof and measurement of association between two things.*

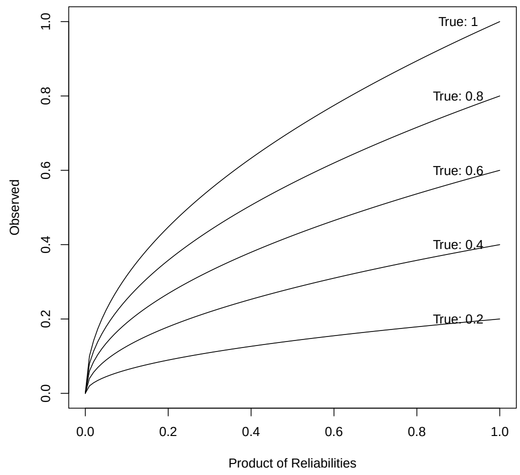
- *Reduced reliability* of X and Y will always *attenuate* the *observed correlation*
- attenuation

$$r_{X,Y} = r_{X_T,Y_T} \times \sqrt{r_{XX'} \times r_{YY'}} \tag{6}$$

- dis-attenuation:

$$r_{X_T,Y_T} = \frac{r_{X_T,Y_T}}{\sqrt{r_{XX'} \times r_{YY'}}} \tag{7}$$

- The *maximal possible observable correlation* between X and Y is the square root of the product of their reliability


True: 1
True: 0.8
True: 0.6
True: 0.4
True: 0.2
Observed
0.0
0.2
0.4
0.6
0.8
1.0
Product of Reliabilities