Shrinkage and regression to the mean

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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

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 $\beta_{\Delta|D} = \frac{\mathrm{Cov}(\Delta,D)}{\sigma^2_D} < 1$, 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: $\mathrm{E}(\Delta \mid \widehat{\Delta}_{shrunk} = \widehat{\delta}_{shrunk}) = \widehat{\delta}_{shrunk}$.

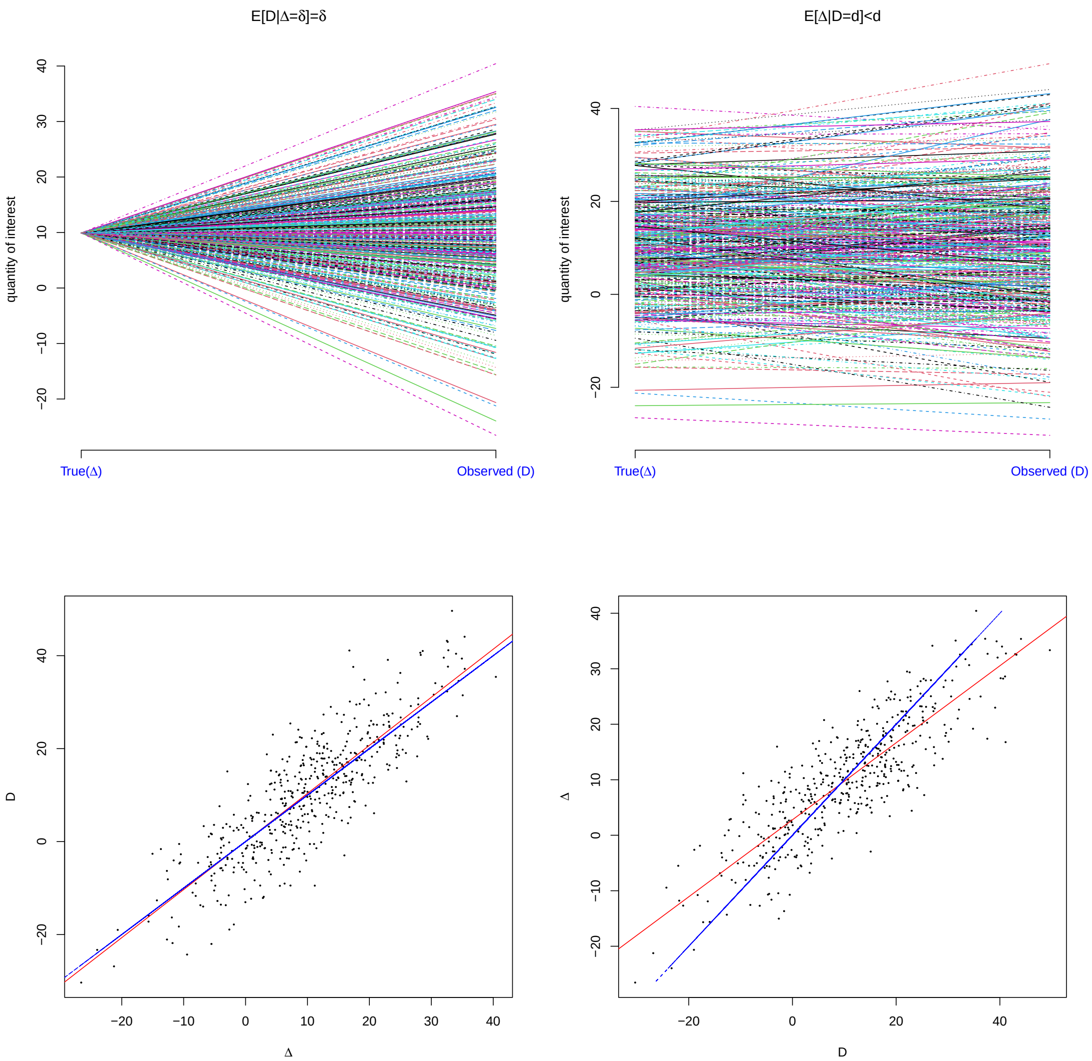


Figure 1: Shrinkage as a fact of life

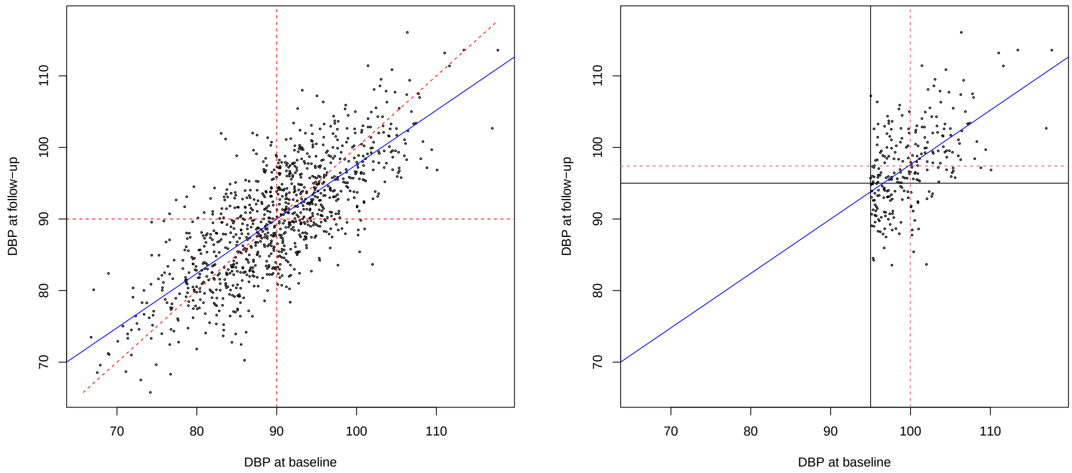


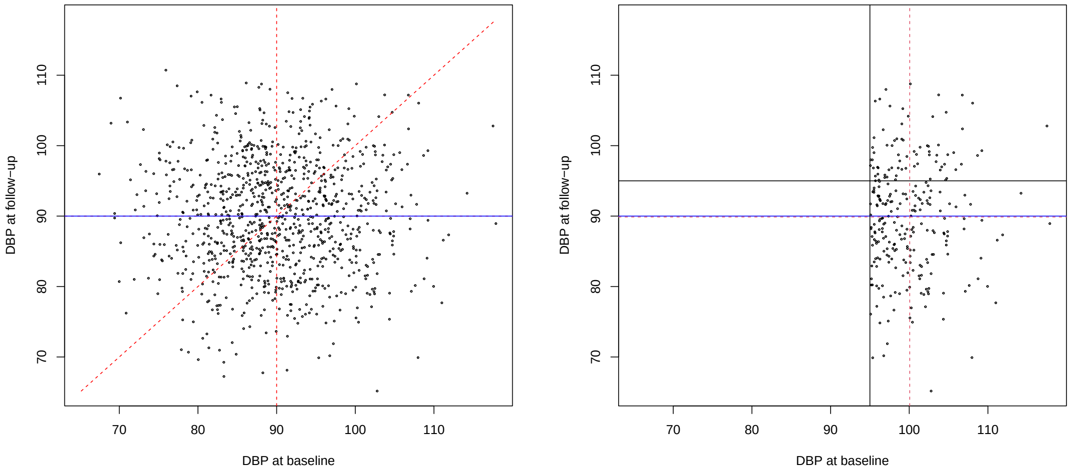
Figure 2: Simulation of diastolic blood pressure data. Simulations from parameters: $\rho_{BL,FU} = 0.76, \mu_{BL} = \mu_{FU} = 90, \sigma_{BL} = \sigma_{FU} = 8$. Left panel: Baseline versus Follow-up for diastolic blood pressure: no change in the mean. Right panel: Baseline versus Follow-up for "hypertensive 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.

2. Placebo as a statistical phenomenon

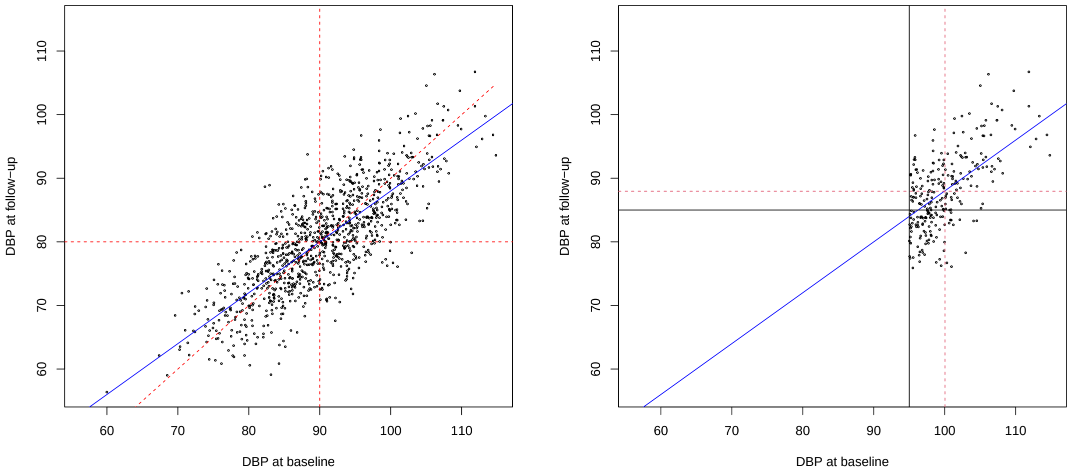
Placebo effects can often be interpreted as a purely statistical – not a psychological – phenomenon.

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 $\beta_{FU|BL} = \frac{\sigma_{FU,BL}}{\sigma^2_{BL}} = r \leq 1$.

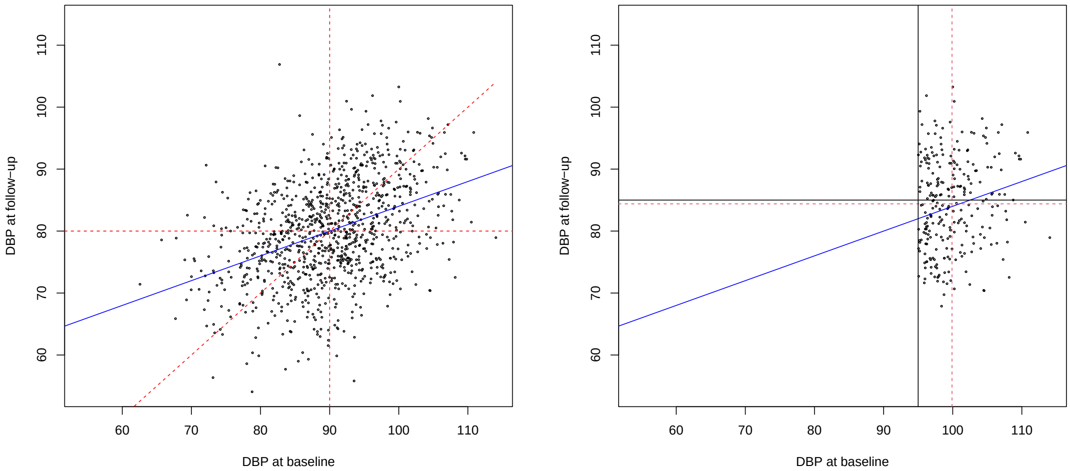
Extreme case: ρ=0



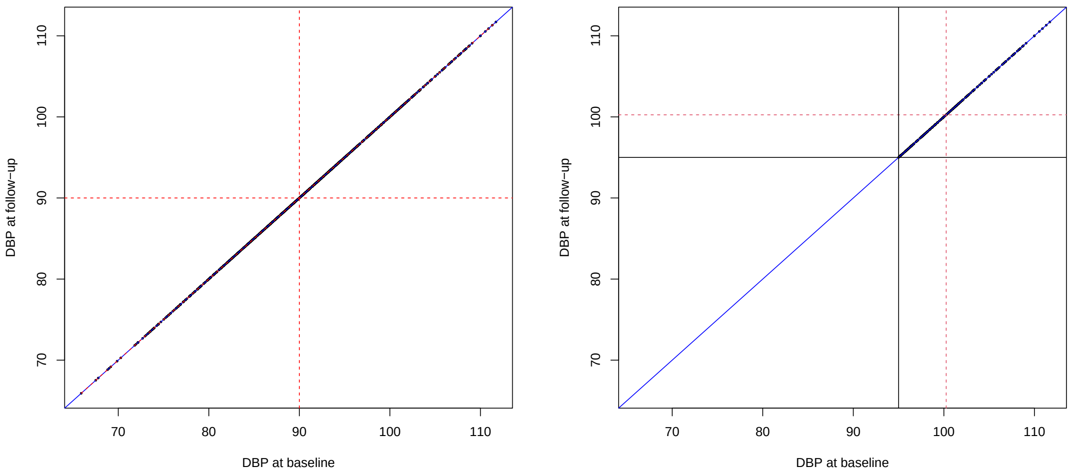
Including a true change of -10 and ρ=.8



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



ρ=1 (Perfect reliability)



A. Maths

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.

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

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*.