

Additional file 1: A simple model for parameter estimations with and without constraint

[Setting]

We estimate parameters of “ $Y=AX+B$ ” as a simple pharmacological model. Three patients are prepared. Clinically observed data of X and Y in each patient are shown in Table 1. Parameter A is not influenced by individual varieties. On the other hand, parameter B is influenced.

Table S1 Individual clinical observed data of X and Y

	Patient 1	Patient 2	Patient 3
X1, Y1	2, 100	3, 200	4, 4
X2, Y2	7, 160	5, 300	8, 80
X3, Y3	18, 350	15, 500	20, 200

[Parameter estimation with and without constraint]

When we estimate parameter A and B without constraint, the estimated parameters are in Table 2; they are shown as points on the solid lines in Figure 1. The values of parameters A and B are determined by each other. Then, individual characteristics of parameter B may be masked.

After the parameter estimation without constraint, we calculate the median of the values of parameter A among all patients. Next, we estimate parameter B by using the median value as common parameter A, that is, parameter estimation with a constraint. The estimated parameters are in Table 1 and are illustrated as points on the dotted lines in Figure 1. The estimated parameter B significantly reflects individual varieties, since X and Y are individually observed data, and parameter A is common.

Table S2 Values of parameter A and B by parameter estimation with and without constraint

Parameter	Patient 1	Patient 2	Patient 3
Without constraint			
A	15.9	23.4	12.4
B	60.3	154.0	-34.3
With constraint of parameter A			
A (common)	17.2	17.2	17.2
B'	48.3	201.2	-85.8

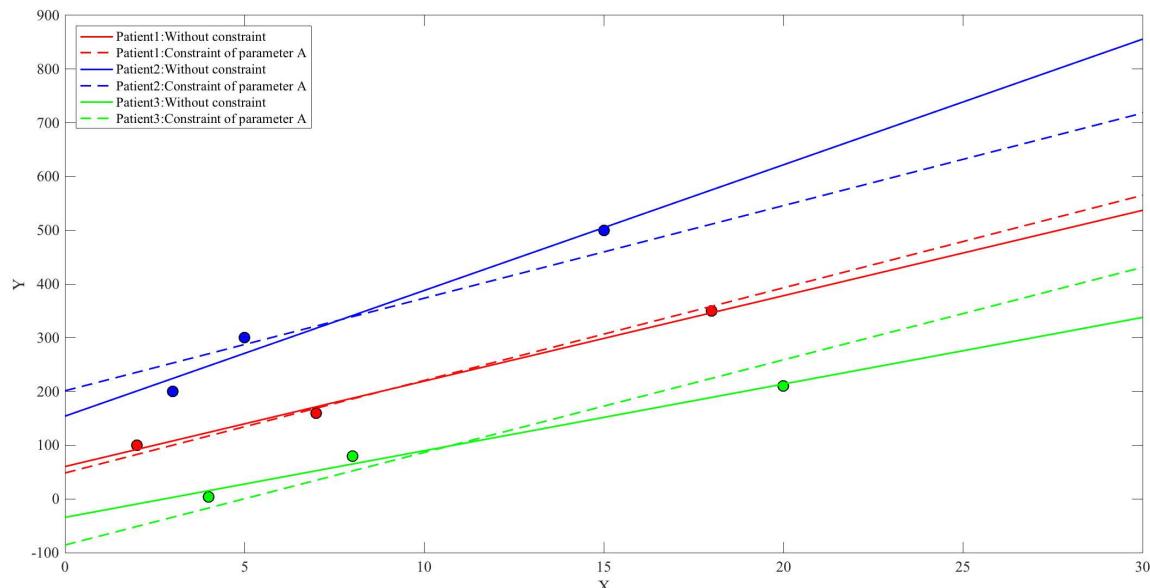


Figure S1 Parameter estimation with and without constraint