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Deductive Derivation and Computerization of Compatible Semiparametric Efficient Estimation

Constantine E. Frangakis[*] Tianchen Qian[†]

Zhenke Wu[‡] Ivan Diaz[**]

[*]Johns Hopkins University, cfrangak@jhsph.edu

[†]Johns Hopkins University, Tqiantianchen.thu@gmail.com

[‡]Johns Hopkins University, zhwu@jhu.edu

[**]Johns Hopkins University, ildiazm84@gmail.com

Deductive Derivation and Computerization of Compatible Semiparametric Efficient Estimation

Constantine E. Frangakis, Tianchen Qian, Zhenke Wu, and Ivan Diaz

Abstract

Researchers often seek robust inference for a parameter through semiparametric estimation. Efficient semiparametric estimation currently requires theoretical derivation of the efficient influence function (EIF), which can be a challenging and time-consuming task. If this task can be computerized, it can save dramatic human effort, which can be transferred, for example, to the design of new studies. Although the EIF is, in principle, a derivative, simple numerical differentiation to calculate the EIF by a computer masks the EIF's functional dependence on the parameter of interest. For this reason, the standard approach to obtaining the EIF has been the theoretical construction of the space of scores under all possible parametric submodels. This process currently depends on the correctness of conjectures about these spaces, and the correct verification of such conjectures. The correct guessing of such conjectures, though successful in some problems, is a nondeductive process, i.e., is not guaranteed to succeed (e.g., is not computerizable), and the verification of conjectures is generally susceptible to mistakes. We propose a method that can deductively produce semiparametric locally efficient estimators. The proposed method is computerizable, meaning that it does not need either conjecturing for, or otherwise theoretically deriving the functional form of the EIF, and is guaranteed to produce the result. The method is demonstared through an example.

1. Introduction

The desire for estimation that is robust to model assumptions has led to a growing literature on semiparametric estimation. Approximately efficient estimators can be obtained in general as the zeros of an approximation to the efficient influence function (EIF). Semiparametric estimation is useful, for example, for survival analysis (Cox, 1972), for estimating growth parameters in longitudinal studies (Liang and Zeger, 1986), and for estimating quantities under missing data, including treatment effects based on potential outcomes (Crump et al., 2009). Here, we focus on problems in which the distribution of the observed data is, in principle, unrestricted, but where estimability requires use of lower dimensional working models.

Theoretical derivation of the EIF in such problems can be challenging. If this task can be computerized, it can save dramatic human effort, which can then be transferred, for example, to designing new studies. The EIF for the unrestricted problem can be written, in general, as a Gateaux derivative (Hampel, 1974). However, if simple numerical differentiation is used to calculate the EIF by a computer to avoid theoretical derivations, then the EIF's functional dependence on the parameter of interest is not revealed. For this reason, the derivative approach has not been generally used. Instead, the standard approach to obtaining the EIF has been the theoretical construction of the space of scores under all possible parametric submodels (Begun et al., 1983). This process currently depends on the correctness of conjectures about these spaces and the correctness of their verification. The correct guessing of such conjectures can succeed in some problems, but is a nondeductive process, i.e., is not guaranteed to succeed (e.g., is not computerizable) and, as with their verification, is generally susceptible to mistakes.

We propose a method that can deductively produce semiparametric locally efficient estimators. In Section 2, we formulate the goal of a deductive method and show that it essentially requires numerical access to the functional dependence of the EIF on the parameter of interest. Section 3 shows how the concept of compatibility solves the functional dependence problem, and derives a deductive method. Throughout, we use the two-phase design as a test problem where the EIF is known theoretically, and we demonstrate our method with a study on asthma as an example. Section 4 discusses extensions, and Section 5 concludes with remarks.

2. The problem of deductive computerization of semiparametric estimators

2.1 The goal of a deductive method

Suppose we conduct a study to measure data D_i, $i = 1, ..., n$, independent and identically distributed (iid) from an unknown distribution F, in order to estimate a feature of the distribution

$$\tau(F). \tag{1}$$

Suppose τ has a nonparametric EIF denoted by $\phi(D_i, F - \tau, \tau)$, where $F - \tau$ denotes the remaining components of the distribution, other than τ. The goal is to find a deductive method that can derive ϕ and can compute estimators $\hat{\tau}$ that solve

$$\sum_i \phi\{D_i, (F - \tau)_w, \tau\} = 0 \tag{2}$$

for working estimators of $(F - \tau)_w$. In general, estimators solving (2) are consistent and locally efficient if the working estimators of $(F - \tau)_w$ are consistent with rates larger than $n^{1/4}$ (Van der Vaart, 2000). Our specific requirement that the method be "deductive and computerizable", means that the method should need neither conjecturing for, nor otherwise theoretically deriving the functional form of ϕ, and should be guaranteed to produce the result, in the sense of Turing (1937).

2.2 Conjecturing and functional form as limitations to a deductive method

A test problem: estimating the mean in a two-phase design. To help make arguments concrete, we consider he following example where the EIF is known. Suppose that in order to estimate the mean $\tau = E(Y)$ in a population, first the study obtains a simple random sample of individuals and records an easily measured covariate X_i. Then, the study is to measure the main outcome Y_i only for a subset denoted with $R_i = 1$, where the missing data mechanism is ignorable given X, i.e., $\text{pr}(R_i = 1 \mid Y_i, X_i) = \text{pr}(R_i = 1 \mid X_i)$. The final data D_i are $(X_i, R_i, Y_i R_i)$, $i = 1, ..., n$, iid from a distribution F, and, by ignorablity, the parameter τ is identified from F as

$$\tau(F) = \int y(x)p(x)dx, \tag{3}$$

where $p(x)$ is the density of X_i; and $y(x)$ is the conditional expectation $E(Y_i \mid R_i = 1, X_i = x)$. For this problem, the EIF is known (e.g., Robins and Rotnitzky (1995) and Hahn (1998)) to be

$$\phi\{D_i, (F - \tau), \tau\} = \frac{R_i \cdot \{Y_i - y(X_i)\}}{e(X_i)} + y(X_i) - \tau, \tag{4}$$

where $e(x)$ is the propensity score $\text{pr}(R_i = 1 \mid X_i = x)$. The derivation has, so far, been nondeductive because it is first based on conjectures on the score space over all submodels, which are then verified to be true (e.g., Hahn (1998)).

Current estimation methods need the functional form of EIF. Most existing approaches to using (2), first isolate a dependence of ϕ on τ, then replace the remaining dependence on F with a working model, and finally solve $\sum_i \phi$ for τ. In the test problem above, the most common approach to using (4) to estimate τ first obtains working functions $y_w(X_i)$ and $e_w(X_i)$, for example using parametric MLEs, and estimates τ as the zero of the empirical sum of (4), to obtain:

$$\hat{\tau}_{\text{nonde-ductive}} = \frac{1}{n} \sum_i \frac{R_i \cdot \{Y_i - y_w(X_i)\}}{e_w(X_i)} + y_w(X_i); \tag{5}$$

see, for example, Robins et al. (1994), Davidian et al. (2005), and Kang et al. (2007). While there also exist modified estimators like the targeted minimum loss estimator (TMLE) (van der Laan and Rubin, 2006), all methods that have been presented so far have advocated that it is critical to know the functional form dependence of ϕ on F, and so are nondeductive, hence, noncomputerizable without prior knowledge of the functional form.

The Gateaux derivative approach to EIF. For a general parameter τ, the EIF evaluated at an observation d' can be obtained as the Gateaux derivative

$$\phi(d', F) = \lim_{\epsilon \to 0} \frac{\tau(F_{d',\epsilon}) - \tau(F)}{\epsilon} \text{ where} \tag{6}$$

$$F_{d',\epsilon} = (1-\epsilon)F + \epsilon \cdot 1 < d' > \tag{7}$$

where $1 < d' >$ denotes a point mass at d' (Hampel, 1974). Calculating this derivative at a given d' and F is a deductive and computerizable operation. To demonstrate the ease of its derivation, consider again the test problem with missing data.

Specifically, for a given observation $d' = [x', r', y'r']$ and a distribution F, it follows from (3), (7), and Bayes rule, that

$$\tau(F_{d',\epsilon}) = \int y_{d',\epsilon}(x) p_{d',\epsilon}(x) dx$$

$$\text{where } p_{d',\epsilon}(x) = (1-\epsilon)p(x) + \epsilon 1(x = x')$$

$$\text{and } y_{d',\epsilon}(x) = \frac{\epsilon \cdot 1(x = x', r' = 1) \cdot y' + (1-\epsilon) \cdot p(x)e(x)y(x)}{\epsilon \cdot 1(x = x', r' = 1) + (1-\epsilon) \cdot p(x)e(x)}.$$

Then, (6) becomes

$$\phi(d', F) = \int \left[\frac{\partial y_{d',\epsilon}(x)}{\partial \epsilon} p_{d',\epsilon}(x) \right]_{\epsilon=0} dx + \int \left[y_{d',\epsilon}(x) \frac{\partial p_{d',\epsilon}(x)}{\partial \epsilon} \right]_{\epsilon=0} dx$$

The first and second terms of the above are $\frac{r'\{y' - y(x')\}}{e(x')}$ and $y(x') - \tau$, respectively, which is the result (4) above.

The problem with the derivative operation is that if simple numerical differentiation is used to calculate the EIF by a computer to avoid theoretical derivations, then the EIF's functional dependence on the parameter of interest is not revealed.

3. A deductive estimation method

Method

A start to finding a deductive method is to appreciate from a new perspective a problem that nondeductive estimators such as (5) have. Specifically, nondeductive estimators are usually constructed from a dependence of the EIF ϕ on τ that is different from the variation-independent partition into $[(F-\tau), \tau]$ (this is probably because of the limitations of closed-form expressions). For example, the estimator $\hat{\tau}_{\substack{\text{nonde-}\\ \text{ductive}}}$ of (5) is a sample analogue of (a) the expression of the last appearance "τ" in the right hand side of (4), using (b) a working expectation $y_w(x)$; and (c) the empirical estimator for $p(x)$ to average over quantities of X_i. However, the parameters underlying (a) (namely, τ), (b) (namely, $y(x)$) and (c) (namely, $p(x)$) are not variation-independent, because τ is the average of $y(x)$ over $p(x)$. This creates an incompatibility: the value of the estimator $\hat{\tau}_{\substack{\text{nonde-}\\ \text{ductive}}}$ from this method differs (almost surely) from its defining expression $\tau(F)$ if for F we use the estimates in (b) and (c) that are used to produce $\hat{\tau}_{\substack{\text{nonde-}\\ \text{ductive}}}$.

The problem of incompatibility has been noted before as a nuisance and has motivated compatible estimators like the TMLE (e.g., van der Laan and Rubin (2006)). Here, we show that, more fundamentally, the concept of incompatibility together with the Gateaux derivative create a solution to the problem of deductive estimation. In particular, the previous section noted that evaluation of the Gateaux derivative at a working distribution F_w masks the dependence on τ. However, the same evaluation does contain evidence of whether parts of the working distribution F_w are misspecified, if the empirical sum of the Gateaux derivative is not zero. This evidence of misspecified F_w can be turned, by "εις άτοπον απαγωγή" [1], into

[1] "Reduction to the absurd".

estimation for τ, where plausible values of τ are values $\tau(F)$ for distributions F for which the empirical sum of the Gateaux derivative eliminates any evidence of misspecification.

Based on the above argument, we have devised the following method that solves the deductive computarization problem by addressing the above compatibility problem.

(step 1) Extend the working distribution F_w to a parametric model, say, $F_w(\delta)$, around F_w (i.e., so that $F_w(0) = F_w$), where δ is a finite dimensional vector. In this extension, we can keep unmodified the part of F_w that is known to be most reliably estimated (e.g., a propensity score elicited by physicians).

(step 2) Using the Gateaux numerical difference derivative

$$\mathsf{Gateaux}\{\tau, F_w(\delta), D_i, \epsilon\} := \left[\tau\{F_{w(D_i,\epsilon)}(\delta)\} - \tau\{F_w(\delta)\}\right]/\epsilon$$

for a machine-small ϵ, to deduce the value of $\phi\{D_i, F_w(\delta)\}$ for arbitrary δ, find

$$\hat{\delta}^{opt} \text{ that minimizes the empirical variance of } \tau\{F_w(\hat{\delta})\} \tag{8}$$

among all roots $\{\hat{\delta}\}$ that are subject to the condition

$$\sum_i \left[\phi\{D_i, F_w(\hat{\delta})\} \longleftarrow \mathsf{Gateaux}\{\tau, F_w(\hat{\delta}), D_i, \epsilon\}\right] = 0. \tag{9}$$

where "$\longleftarrow$" means "computed as". Property (9) is the empirical analogue of the central, mean-zero property if the evaluated ϕ at $F_w(\hat{\delta})$ is the true influence function of τ. An average of the EIF at a $F_w(\delta)$ that deviates from zero is evidence that the working distribution is incorrect. This step finds a distribution $F_w(\hat{\delta})$ that eliminates such evidence. Technically, there may be no zeros, in which case $\hat{\delta}$ can be defined as the minimizer of the absolute value of (9), although a better solution would be to make the model $F_w(\delta)$ more flexible (see below). More realistically, for a working model $F_w(\delta)$, we can expect as many zeros as the dimension of δ, and so condition (8) selects the best one.

(step 3) Calculate the parameter at the EIF-fitted distribution $F_w(\hat{\delta})$ as

$$\hat{\tau}^{\text{deductive}} := \tau\{F_w(\hat{\delta}^{opt})\} \tag{10}$$

Properties

The above method is deductive because step 2 does not need the functional form of ϕ, but deduces it by the numerical Gateaux derivative (6). If δ is 1-dimensional, then (9) is expected to have one root, and this can be found by numerical root-finding methods such as in Brent (1973) or Newton-Raphson. If δ has more dimensions, then $\hat{\delta}^{opt}$ can be found by numerical Lagrange multipliers, where (8) can be coded as the jackknife variance. Also, the above estimates for τ and the remaining model parameters are compatible, by construction.

The deductive estimator shares useful properties of so-far known, nondeductive estimators that take ϕ as given. Notably, if the actual expectation of $\phi(D_i, F_w)$ is zero for a working distribution when, say $\text{part}_1(F_w) = \text{part}_1(F)$, or,...,or $\text{part}_K(F_w) = \text{part}_K(F)$, then the deductive estimator above will be consistent as would be usual, nondeductive estimators (e.g., Scharfstein et al. (1999)). Also, the deductive estimator above shares with the TMLE the idea of extending the working model (Chaffee and van der Laan (2011)), and with other estimators the idea of empirical maximization (e.g., Rubin and van der Laan (2008)). However, to our knowledge, all such existing work for local efficiency has considered it critical to have the theoretically derived form of the EIF based on the score theory. The contribution of the proposed method above is to show that this theory can be translated to estimation that can be computerized in general, by combining model extension with the Gateaux derivative.

The extension in step 1 can take different forms. For example, for the two-phase problem, suppose an original working function $y_w(x)$ has been obtained as the OLS fit $x'\hat{\beta}^{ols}$ of a linear regression model $x'\beta$ for $E(Y \mid R=1, X=x)$. Then, a simple model extension is to free-up (again) the intercept of $x'\hat{\beta}^{ols}$ and let it be the parameter δ. This, as well as any analogous such extension, results in an estimator, as defined by the above method, that is consistent if the propensity score model is correct, and locally efficient under the working model with parameter δ.

Feasibility evaluations

To evaluate the feasibility of our method, we applied it to the study reported by Huang et al. (2005), as an example of the two-phase design. The goal of that study was to compare rates of patient satisfaction for asthma care as the outcome (yes/no) among different physician groups (treatments). Physician groups differed in their distribution of patient covariates. So, in order to compare between, say, two physician groups, we set the goal to estimate the average (3) of patient satisfaction for each group, standardized by the distribution of patient covariates in the combined population of the two groups. The following covariates X were considered: age, gender, race, education, health insurance, drug insurance coverage; asthma severity; number of comorbidities, and SF-36 physical and mental scores.

We tested feasibility of the above method for the comparison within two pairs of groups, denoted in Table 1 as a_1 vs. b_1 and a_2 vs. b_2 (actual ids omitted). We chose (a_1, b_1) as a pair for which the usual estimator $\hat{\tau}^{\text{nonde-}}_{\text{ductive}}$ produces values diverging from the unadjusted rates for a_1 and b_1; and we chose (a_2, b_2) as a pair for which the usual estimator produces values shrinking from a_1 and b_1. The nondeductive estimator used as propensity score the quintiles of the logistic regression of group membership conditionally on X; and a working expectation y_w as the prediction from the logistic regression of patient satisfaction conditionally on X within each group. The deductive estimator uses the same propensity score, and, for step 1 of the method, extended the working expectation y_w by including back the intercept in the logistic regression for each group as a free parameter δ. The computation of ϕ for each δ in (9) was obtained by straight-forward numerical differentiation for the Gateaux derivative; and the root $\hat{\delta}$ was found by the method of Brent (1973) implemented by the function "uniroot" in R.

In all cases, the deductive estimator gives answers close to the nondeductive estimator. Moreover, as discussed earlier, both are doubly-robust for the same model. Both estimators produced their answers in less than a second for each group, although the nondeductive estimator used the a-priori knowledge of the closed form expression (4) for ϕ, whereas the deductive estimator did not. Finally, the standard errors (based on jackknife) are also comparable. A guarantee that the deductive estimator be more precise can be incorporated by extending δ to two dimensions (two coefficients) and minimize the empirical variance as in step 2.

4. Extensions

In complex problems, it is possible that standard root finding methods for (9) are unstable. In this section we show that the Gateaux numerical derivative may still be used to construct a deductive estimation method that does not rely on solving an estimating equation.

Suppose that the parameter $\tau(F)$ depends on F only through a set of variation independent parameters $q_j(F) : j = 1, \ldots, J$. Such is the case of parameter (3) in our example, with $q_1(F;x) = y(x)$ and $q_2(F;x) = p(x)$. In an abuse of notation, let $\tau(q_1(F), \ldots, q_J(F)) := \tau(F)$. Since the parameters q_j are variation independent, the Gateaux derivative expression of ϕ in (6) reduces to

$$\phi(d', F) = \sum_{j=1}^{J} \lim_{\epsilon \to 0} \frac{\tau(q_1(F), \ldots, q_j(F_{d',\epsilon}), \ldots, q_J(F)) - \tau(F)}{\epsilon}. \tag{11}$$

This expression provides the decomposition $\phi(d', F) = \sum_{j=1}^{J} \phi_j(d', F)$, where ϕ_j is the non-parametric efficient score associated to q_j. Once the Gateaux numerical derivatives ϕ_j have been computed, it is possible to implement a standard TMLE. We only provide a brief recap of the TMLE template since extensive discussions are presented elsewhere van der Laan and Rubin (2006); van der Laan and Rose (2011). For each q_j, consider a loss function $L_j(q_j; D)$ whose expectation is minimized at the true value of q_j. Consider also a working model q_{jw} and a parametric extension $q_{jw}(\delta)$ satisfying

$$\frac{d}{d\delta} L(q_{jw}(\delta); d')\bigg|_{\delta=0} = \phi_j(d').$$

In our example, since q_j are components of the likelihood, the negative log-likelihood loss function and the exponential family may be used in this step:

$$\begin{aligned} L(q_j; d) &= -\log q_j(d) \\ q_{jw}(\delta; d) &\propto \exp(\delta \phi_j(d)) q_{jw}(d). \end{aligned} \tag{12}$$

The TMLE is then defined by an iterative procedure that, at each step, estimates δ by minimizing the expected sum of the loss functions $L_j(q_{jw}(\delta); \cdot)$. An update of the working model is then computed as $q_{jw} \leftarrow q_{jw}(\hat{\delta})$, and the process is repeated until convergence. The TMLE is defined by $\hat{\tau} = \tau(q^\star_{1w}, \ldots, q^\star_{Jw})$, where $q^\star_{jw}$ denotes the estimate obtained in the last step of the iteration. Like the estimator presented in Section 3, the TMLE is a compatible estimator, and solves the EIF estimating equation. Unlike the estimator of Section 3, the TMLE does not require direct solution of that equation. However, the TMLE may be computationally more intensive, as it is iterative and may require numerical integration for computation of the proportionality constant in (12).

5. Remarks

We proposed a deductive method to produce semiparametric estimators that are locally efficient. The method does not rely on conjectures of tangent spaces and is not susceptible to possible errors in the verification of such conjectures. Instead, the new method relies on computability of the estimand τ for specified working distributions of the observed data F, and on numerical methods for differentiation and for root finding.

Although we have focused on local efficiency of originally unrestricted problems, one can see a path towards finding a deductive method also for problems with restrictions set a priori. Such a path can explore, first, nesting the restricted problem within an unrestricted one, and then, making use of the proposed deductive method for the unrestricted problem, modified to impose numerically the nested restrictions. Such deductive methods can save dramatic amounts of human effort on essentially computerizable processes, and allow the transfer of that effort to other statistically demanding parts of the scientific process such as the efficient design of new studies.

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References

Begun, J. M., Hall, W., Huang, W.-M., and Wellner, J. A. (1983). Information and asymptotic efficiency in parametric-nonparametric models. *The Annals of Statistics* **11,** 432–452.

Brent, R. (1973). Algorithms for minimization without derivatives. *Englewood Cliffs, NJ: Prentice-Hall* .

Chaffee, P. and van der Laan, M. J. (2011). Targeted minimum loss based estimation based on directly solving the efficient influence curve equation. *UC Berkeley Division of Biostatistics Working Paper Series* .

Cox, D. R. (1972). Regression models and life tables. *Journal of the Royal Statistical Society, Ser. B* **34,** 187–220.

Crump, R. K., Hotz, V. J., Imbens, G. W., and Mitnik, O. A. (2009). Dealing with limited overlap in estimation of average treatment effects. *Biometrika* **96,** 187–199.

Davidian, M., Tsiatis, A. A., and Leon, S. (2005). Semiparametric estimation of treatment effect in a pretest–posttest study with missing data. *Statistical science: a review journal of the Institute of Mathematical Statistics* **20,** 261.

Hahn, J. (1998). On the role of the propensity score in efficient semiparametric estimation of average treatment effects. *Econometrica* pages 315–331.

Hampel, F. R. (1974). The influence curve and its role in robust estimation. *Journal of the American Statistical Association* **69,** 383–393.

Huang, I., Frangakis, C., Dominici, F., Diette, G., and Wu, A. (2005). Application of a propensity score approach for risk adjustment in profiling multiple physician groups on asthma care. *Health Services Research* **40,** 253–278.

Kang, J. D., Schafer, J. L., et al. (2007). Demystifying double robustness: A comparison of alternative strategies for estimating a population mean from incomplete data. *Statistical science* **22,** 523–539.

Liang, K.-Y. and Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika* **73,** 13–22.

Robins, J. M. and Rotnitzky, A. (1995). Semiparametric efficiency in multivariate regression models with missing data. *Journal of the American Statistical Association* **90,** 122–129.

Robins, J. M., Rotnitzky, A., and Zhao, L. P. (1994). Estimation of regression coefficients when some regressors are not always observed. *Journal of the American Statistical Association* **89,** 846–866.

Rubin, D. B. and van der Laan, M. J. (2008). Empirical efficiency maximization: improved locally efficient covariate adjustment in randomized experiments and survival analysis. *The International Journal of Biostatistics* **4,**.

Scharfstein, D. O., Rotnitzky, A., and Robins, J. M. (1999). Adjusting for nonignorable drop-out using semiparametric nonresponse models. *Journal of the American Statistical Association* **94,** 1096–1120.

Turing, A. (1937). On computable numbers, with an application to the entscheidungs problem. *Proceedings of the London Mathematical Society* **42,** 230–265.

van der Laan, M. and Rose, S. (2011). *Targeted Learning: Causal Inference for Observational and Experimental Data*. Springer, New York.

van der Laan, M. J. and Rubin, D. B. (2006). Targeted maximum likelihood learning. *The International Journal of Biostatistics* **2,** 1–40.

Van der Vaart, A. W. (2000). *Asymptotic statistics*, volume 3. Cambridge University Press.

Table 1: Feasibility of the deductive method for estimating the probability of patient satisfaction adjusted for covariates for two physician group pairs of the asthma study of Huang et al. (2005)

physician		unadjusted	estimates of $\tau(F) = \int y(x)p(x)dx$			
group g	n	$pr(Y \mid G)$ (%)	$\hat{\tau}^{\text{nonde-ductive}}$ (%)	se (%)	$\hat{\tau}^{\text{deductive}}$ (%)	se (%)
a_1	177	60.5	63.1	4.5	64.3	4.1
b_1	86	59.3	52.0	8.8	51.4	9.1
a_2	110	78.2	72.1	8.2	69.4	7.9
b_2	194	48.5	49.4	4.5	48.8	4.3