BST260 final project

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1 Introduction

Nowadays, food frequency questionnaires (FFQs) have been the primary method of dietary assessment in large cohort studies of diet and health outcomes, because they can be self-administered, efficiently processed, and provide data on individual intakes of both foods and nutrients over an extended period (1). However, FFQ estimates rely on memory and hence prone to recall bias. Other sources of error in FFQ estimates include misinterpretation about portion size, omitting food, and so on. Therefore, it is is critical to document the validity of FFQ estimates (nutrients, foods, and dietary scores) and quantify the impact of these measurement errors in the diet and disease associations.

In this project, we first evaluated the reproducibility and validity of a FFQ in measuring three dietary scores: overall plant-based diet indices (PDI), healthful plant-based diet index (hPDI), and unhealthful plant-based diet index (uPDI) and their scoring components: healthful plant foods (hplant), unhealthful plant foods (uplant), total plant foods (tplant), and animal foods (animal) (2). The scoring methods of these plant-based indices were shown in the **Figure 1**. This analysis included 742 participants from the Women's Lifestyle Validation Studies (3, 4). Participants completed a 152-item FFQ at the beginning of the study (FFQ1) and one year later (FFQ2) and completed two weighed 7-day dietary records (DR_wk1 and DR_wk2) six-month apart between FFQ assessments (**Table 1**). The reproducibility of the FFQs was evaluated by rank intraclass correlation coefficients (ICC) with two repeated FFQ assessments (5). The validity was assessed by comparing FFQ2-derived DQSs to those from the average of two 7DDRs (DR_avg) using Spearman rank correlation coefficients (rs), because we are more interested in ranking the population correctly (6, 7). Calibration coefficients were obtained as slopes from linear regression models with FFQ estimates as independent (predictor) variables and estimates from the average of the two 7DDRs as dependent (outcome) variables (8-10).

We also conducted a simulation analysis to assess the effect of measurement error in FFQ estimates on diseases risk estimation and applied the linear approximation to correct the measurement errors (11) . We would simulate a main study with 5,000 participants where FFQ-derived exposures with error (Z) and outcome status (D) were collected. Then, would sample an internal validation (n=500) from the main study where the exposure estimates from FFQ (Z) and dietary records (X) were collected (**Figure 2**). We assumed FFQ estimates with within-person errors: $Z = \lambda X + \alpha + \epsilon_r$, where $\epsilon_r \sim N(0, \sigma)$. The exposure-diseases associations would be represented by a logistic model: $logit(P(D = 1|X)) = \alpha + \beta X$. With FFQ-derived exposures, the observed exposure-diseases associations would be $logit(P(D = 1|X)) = \alpha_{obs} + \beta_{obs} Z$.

For the analysis part,
1. The uncorrected coefficients $\hat{\beta_{obs}}$ and $Var(\hat{\beta_{obs}})$ would be obtained from the main study
2. The $\hat{\lambda}$ and $Var(\hat{\lambda})$ would be obtained from the validation study
3. We would apply the Linear approximation to correct the $\hat{\beta_{obs}}$:

$$\hat{\beta_{cor}} = \hat{\beta_{obs}}/\hat{\lambda}$$

4. Variance of corrected coefficients would be obtained by delta method.

$$Var(\hat{\beta_{cor}}) = \frac{1}{\hat{\lambda}^2} Var(\hat{\beta_{obs}}) + \frac{\hat{\beta_{obs}}^2}{\hat{\lambda}^4} Var(\hat{\lambda})$$

We would consider several scenarios with different degree of measurement error (λ), prevalence of diseases (CI), as well as strength of associations (odds ratio (OR)). For each combination of parameters, we would iterate the simulation process 1,000 times to assess the RMSE of the uncorrected and corrected β estimates and its convergency probability of the true β. We would also assess the direction and degree of bias in estimated odds ratio by calculating the percentage of bias.

2 Results

2.1 PART 1. Validation study on FFQ derived dietary indices.

We observed weak correlations between PDI and the other two plant-based diet indices (rs=0.20 with hPDI and -0.10 with uPDI. Because higher hPDI represented higher dietary quality and higher uPDI represented lower dietary quality, the hPDI is inversely associated with uPDI as expected (rs=-0.39) . The strength of correlations between plant-based diet indices and their scoring components ranges from 0 for animal food and PDI to 0.80 for total plants and PDI (**Figure 3**).

The FFQ-derived estimates from two assessments taken one year apart demonstrated moderate to high reproducibility (ICC_FFQs =0.54 to 0.77) that are slightly higher than the reproductivity of two dietary records (ICC_DRs=0.50 to 0.68; **Table 2**). Using the average estimates of two dietary records as the comparison method, FFQ-derived three plant-based diet indices showed relatively high validity (rs=0.47 to 0.63), whereas FFQ were less valid to estimate their scoring components (rs= 0.30 to 0.63; **Table 3**). We also visualized the validity results in the **Figure 4** where we plotted the estimates from the average of the two dietary records against FFQ estimates. Here, we found the calibration coefficients (slopes) and R^2 were generally higher for three plant-based diet indices than their scoring components, suggesting the FFQ-derived plant-based diet indices were more comparable with their true estimates from dietary records.

2.2 PART 2. Simulation analysis on measurement error in FFQ estimates

In the simulation procedure,
* We first assumed a standardized normally distributed true intake X_i $N(0,1)$ within the overall study population.
* Then, we derived the FFQ estimates with systematic and random error $Z_i = X_i + E_i + \epsilon_i$ where half of the population over-report with $E_i \sim N(1,(1-\lambda)/\lambda)$ and the other half of the population under-report with $E_i \sim N(-1,(1-\lambda)/\lambda)$. All study participants followed the same random error distribution: $\epsilon_i \sim N(0,0.001)$.
* Next, we simulated the diseases status according to the binominal distribution

$$P(D=1|X_i) = \frac{\exp(\alpha+\beta X_i)}{1+\exp(\alpha+\beta X_i)}$$

where $\alpha = logit(CI)$ and $beta=log(OR) $ * The 500 observations in the validation study were then sampled from the main study.

We developed a user-friendly algorithm to assess the impact of measurement errors in dietary exposures on their associations with diseases outcome (simu_resul). Using this algorithm, readers can choose their own sets of parameters under different conditions.

In the current analysis, we mainly focused on changes of three parameters: the degree of measurement error (λ= 0.2, 0.4,0.6, and 0.8), the prevalence of diseases (CI=0.05, 0.1, 0.3, 0.5), and the strength of associations (true OR= 1.2, 1.5, 2, 2.5). According to **Figure 5** for the percentage of bias of the crude estimates under different scenarios, we found measurement errors embedded in the exposures tend to attenuate (bias towards the null) the ORs, and this bias would be exacerbated with less valid FFQ-derived exposures (smaller lambda) and stronger exposure-diseases associations (larger OR).

Figures 6-8 show the comparison results before and after measurement error correction. We observed the corrected beta estimates (blue) always have smaller (red) RMSE than the uncorrected ones (**Figure 6**). In addition, the coverage probability of true value is extremely low for uncorrected estimates, and much higher for the corrected estimates(**Figure 7**). This might be due to 1) more bias in the uncorrected estimates, and 2) larger variance and wider confidence interval for the corrected estimates. We also found the bias in ORs decreased after applying measurement error correction (**Figure 8**).

3 Conclusion

This study highlights that a 152-item, semi-quantitative FFQ is appropriate for ranking individuals to evaluate the dietary scores. Dietary scores derived from the FFQ showed moderate to high reproducibility when comparing estimates one year apart, and validity when compared with dietary scores derived from two weighed 7DDRs collected over 1 year. However, measurement error in FFQ estimates cannot be overlook. In the simulation analysis part, we demonstrated that the measurement error in FFQ-derived dietary exposures could distort the associations with health outcomes. Furthermore, we found applying appropriate measurement error correction methods could alleviate the bias. Therefore, in the future nutritional epidemiology studies, it is essential to validate the dietary exposures, as well as consider conducting measurement error correction analysis to justify their main findings.

Our current study also has some limitations which can be improved. First, we did find there are day-to-day random variation in dietary records (ICC<1), which would attenuate the validity estimates based on spearman correlation between dietary values derived from FFQ and dietary records. Hence, we can use Rosner. et al.'s method to account for the random variation in dietary records (12). Second, generalizability may be limited because our study population were all women due to the data availability issue. We can repeat the current analysis in Men's lifestyle validation study to further confirm our results. Third, we have only considered single dietary exposure in the simulation analysis. However, many dietary variables are correlated (e.g., energy intake is positively correlated with macronutrients and food intakes) and they could confound each other with diseases associations. Therefore, in the real-world analysis, we would usually include several dietary variables measured with error in the same model and need to use mthod that can correct measurement errors for multiple variables at the same time. Rosner. et al.'s have developed a multivariate correction method that can handle both the error with which each variable is measured and the correlation of errors (13).

4 Reference

1. Willett W. Nutritional epidemiology: Oxford University Press, 2012.
2. Satija A, Hu FB. Plant-based diets and cardiovascular health. Trends Cardiovasc Med 2018;28(7):437-41. doi: 10.1016/j.tcm.2018.02.004.
3. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. J Womens Health 1997;6(1):49-62. doi: 10.1089/jwh.1997.6.49.
4. Cho E, Chen WY, Hunter DJ, Stampfer MJ, Colditz GA, Hankinson SE, Willett WC. Red meat intake and risk of breast cancer among premenopausal women. Archives of internal medicine 2006;166(20):2253-9. doi: 10.1001/archinte.166.20.2253.
5. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016;15(2):155-63. doi: 10.1016/j.jcm.2016.02.012.
6. Rosner B, Glynn RJ. Interval estimation for rank correlation coefficients based on the probit transformation with extension to measurement error correction of correlated ranked data. Statistics in medicine 2007;26(3):633-46. doi: 10.1002/sim.2547.
7. Perisic I, Rosner B. Comparisons of measures of interclass correlations: the general case of unequal group size. Statistics in medicine 1999;18(12):1451-66. doi: 10.1002/(sici)1097-0258(19990630)18:12<1451::aid-sim142>3.0.co;2-k.
8. Bingham SA, Gill C, Welch A, Cassidy A, Runswick SA, Oakes S, Lubin R, Thurnham DI, Key T, Roe L. Validation of dietary assessment methods in the UK arm of EPIC using weighed records, and 24-hour urinary nitrogen and potassium and serum vitamin C and carotenoids as biomarkers. International journal of epidemiology 1997;26(suppl_1):S137.
9. Rosner B, Spiegelman D, Willett W. Correction of logistic regression relative risk estimates and confidence intervals for measurement error: the case of multiple covariates measured with error. American journal of epidemiology 1990;132(4):734-45.
10. Kaaks R, Riboli E, Van Staveren W. Calibration of dietary intake measurements in prospective cohort studies. American journal of epidemiology 1995;142(5):548-56.

11. Rosner B, Willett WC, Spiegelman D. Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. Stat Med 1989;8(9):1051-69; discussion 71-3. doi: 10.1002/sim.4780080905.
12. Rosner B, Willett WC. Interval estimates for correlation coefficients corrected for within-person variation: implications for study design and hypothesis testing. Am J Epidemiol 1988;127(2):377-86. doi: 10.1093/oxfordjournals.aje.a114811.
13. Spiegelman D, McDermott A, Rosner B. Regression calibration method for correcting measurement-error bias in nutritional epidemiology. The American journal of clinical nutrition 1997;65(4 Suppl):1179S-86S. doi: 10.1093/ajcn/65.4.1179S.

5 Appendix

5.1 Tables and Figures

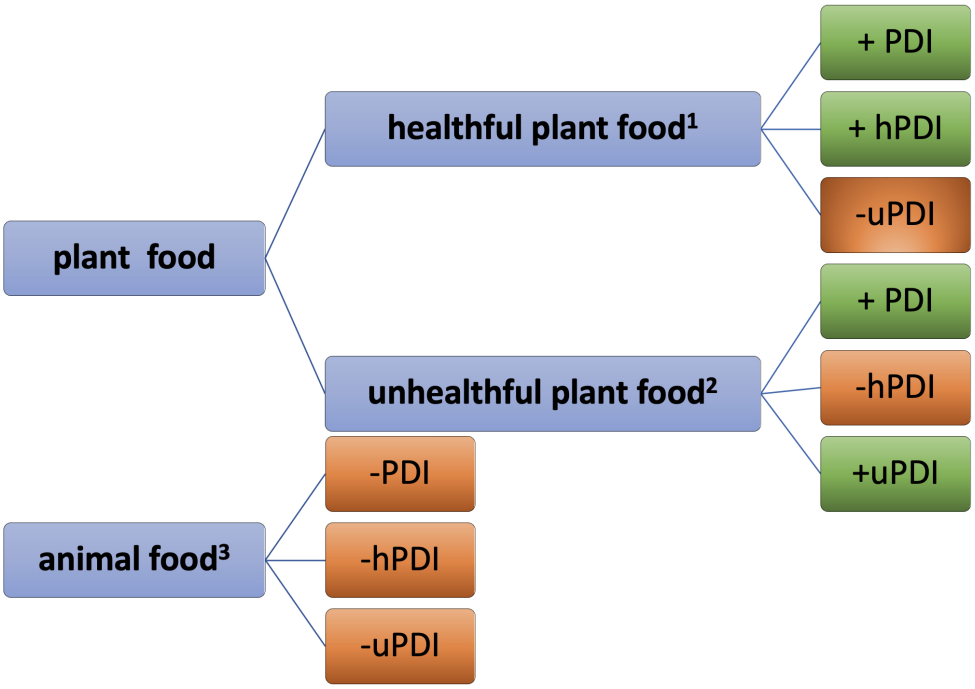


Figure 1: Scoring methods for plant-based diet indices

+means higher intakes receive higher scores; - means higher intakes receive lower scores
1. Healthful plant food group (n=7): whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea & coffee
2. Unhealthful plant food group (n=5): fruit juices , refined grains, potatoes, sugar-sweetened beverage, sweets and desserts
3. Animal Food Group (n=6): animal fat, dairy, egg, fish or seafood, meat (red, processed meat, poultry), miscellaneous animal-based foods

Table 1: Summary statistics of the dietary exposures derived from FFQs and dietary records

X.	pdi	hpdi	updi	hplant	uplant	tplant	animal
	(N=742)	(N=742)	(N=742)	(N=742)	(N=742)	(N=742)	(N=742)
FFQ1	53.0 [6.46]	54.5 [7.58]	53.9 [8.04]	20.5 [5.27]	14.2 [4.41]	34.8 [7.13]	17.8 [4.16]
Missing	17 (2.3%)	17 (2.3%)	17 (2.3%)	17 (2.3%)	17 (2.3%)	17 (2.3%)	17 (2.3%)
FFQ2	52.8 [6.52]	54.5 [7.95]	53.9 [7.97]	20.5 [5.34]	14.2 [4.52]	34.6 [7.34]	18.2 [4.06]
DR_wk1	53.5 [6.57]	55.3 [7.53]	53.5 [7.95]	21.0 [5.12]	14.1 [3.71]	35.0 [5.92]	17.6 [3.88]
Missing	4 (0.5%)	4 (0.5%)	4 (0.5%)	4 (0.5%)	4 (0.5%)	4 (0.5%)	4 (0.5%)
DR_wk2	53.6 [6.40]	54.4 [7.36]	53.8 [7.57]	20.9 [5.00]	14.6 [3.65]	35.5 [5.85]	17.9 [3.63]
Missing	7 (0.9%)	7 (0.9%)	7 (0.9%)	7 (0.9%)	7 (0.9%)	7 (0.9%)	7 (0.9%)

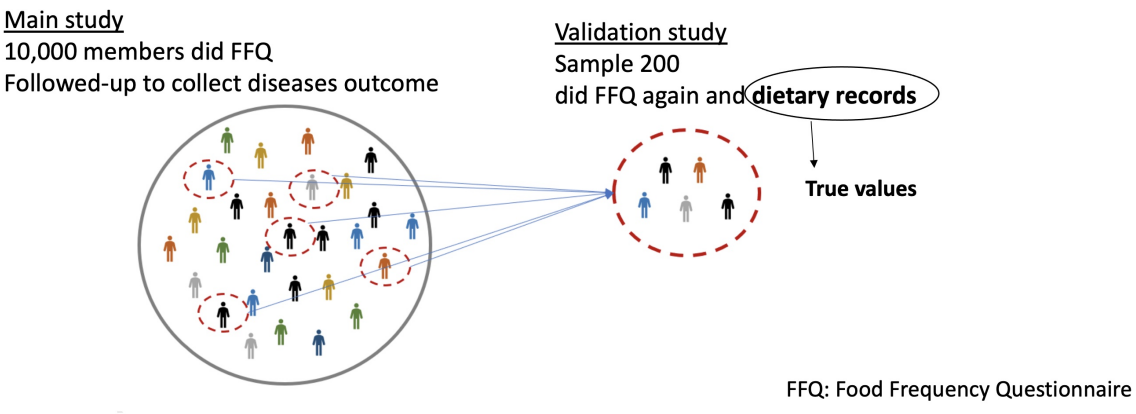


Figure 2: Illustration of simulated main and validation study

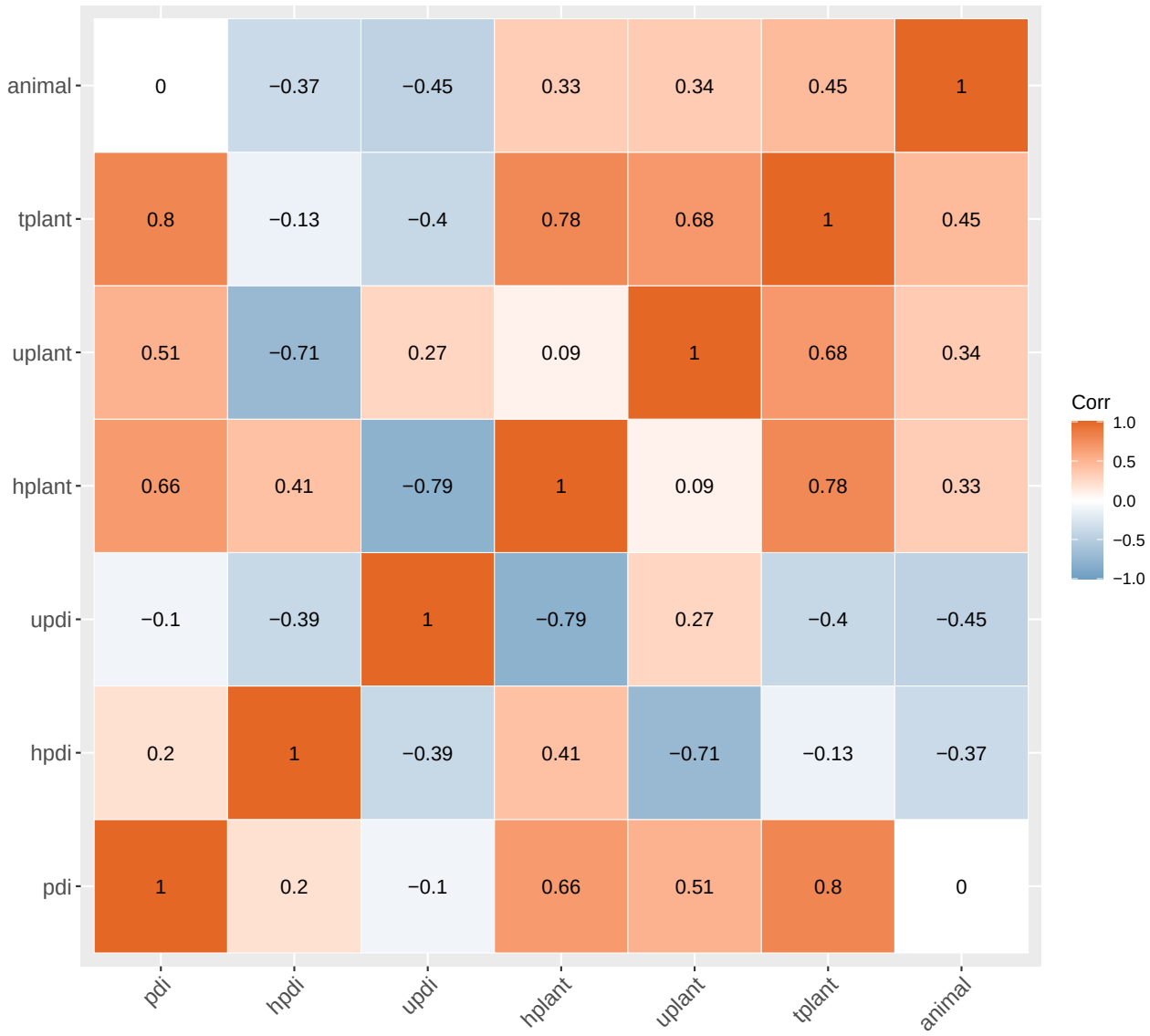


Figure 3: Spearman correlation matrix between plant-based diet indices and their scoring components, using the FFQ2

Table 2: Reproducibility and validity results

vararible	ICC_FFQs	ICC_DRs	validity_FFQ2
pdi	0.69	0.57	0.47
hpdi	0.77	0.56	0.63
updi	0.73	0.62	0.61
hplant	0.76	0.68	0.55
uplant	0.77	0.50	0.48
tplant	0.76	0.61	0.40
animal	0.54	0.50	0.30

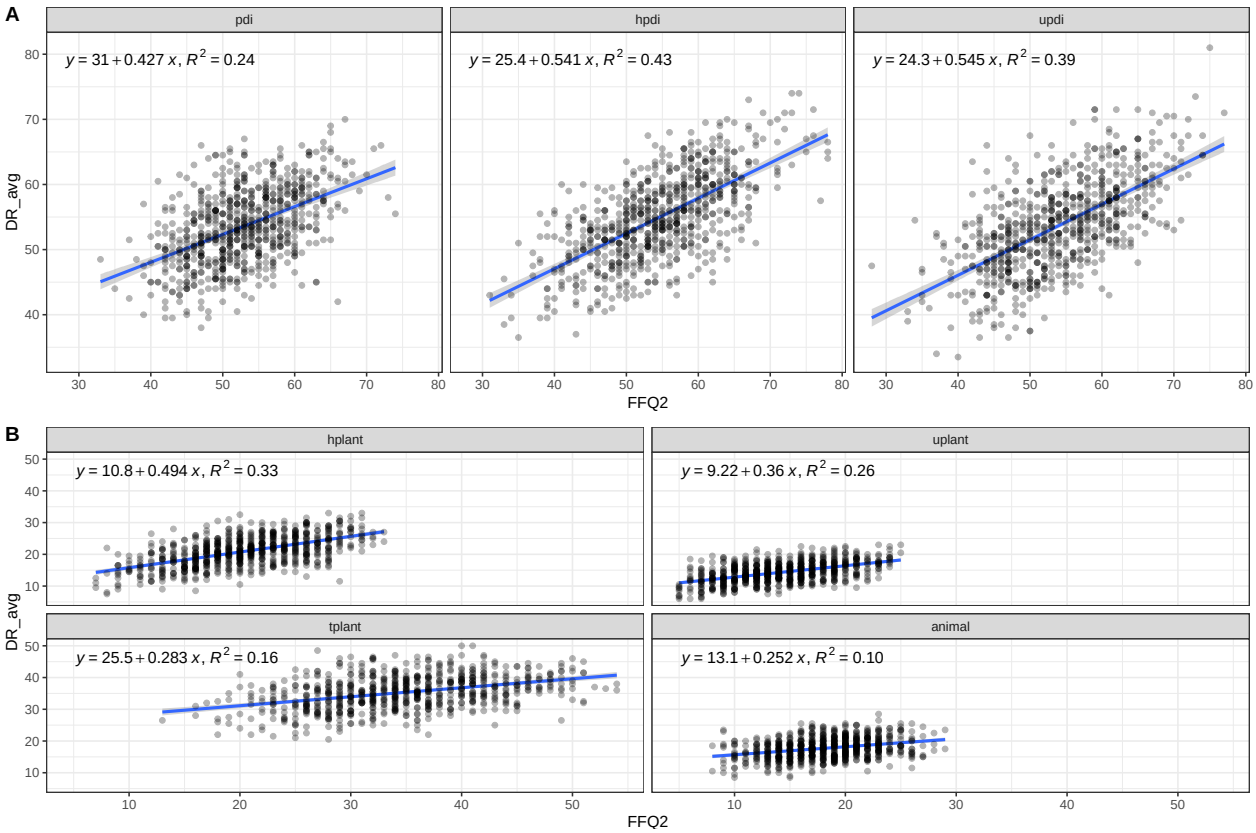


Figure 4: Scatter plots with calibration coeffients of estimates from the average of the two dietary records against FFQ 2 estimates

A: Plots for three plant-based diet indices
B: Plots for scoring components of plant-based diet

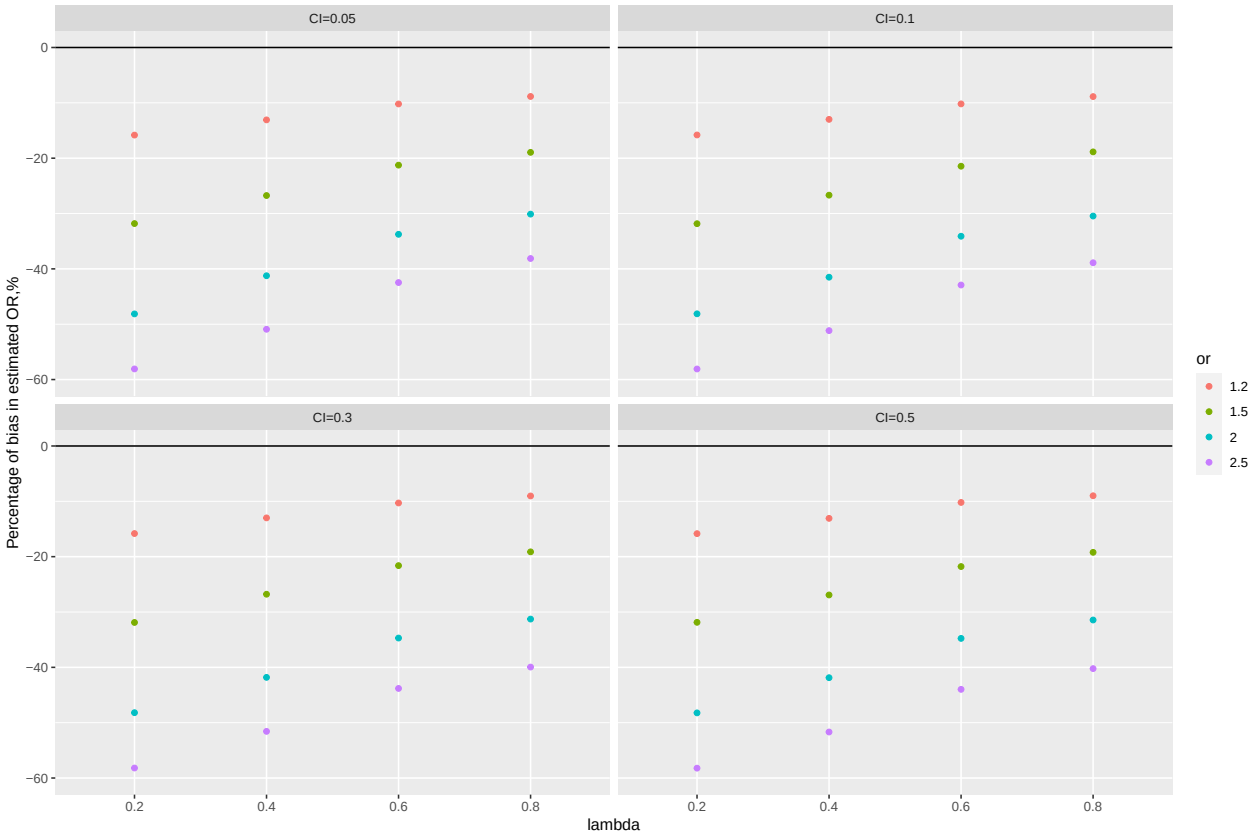


Figure 5: Percentage of bias in estimated OR before correcting for measurement error

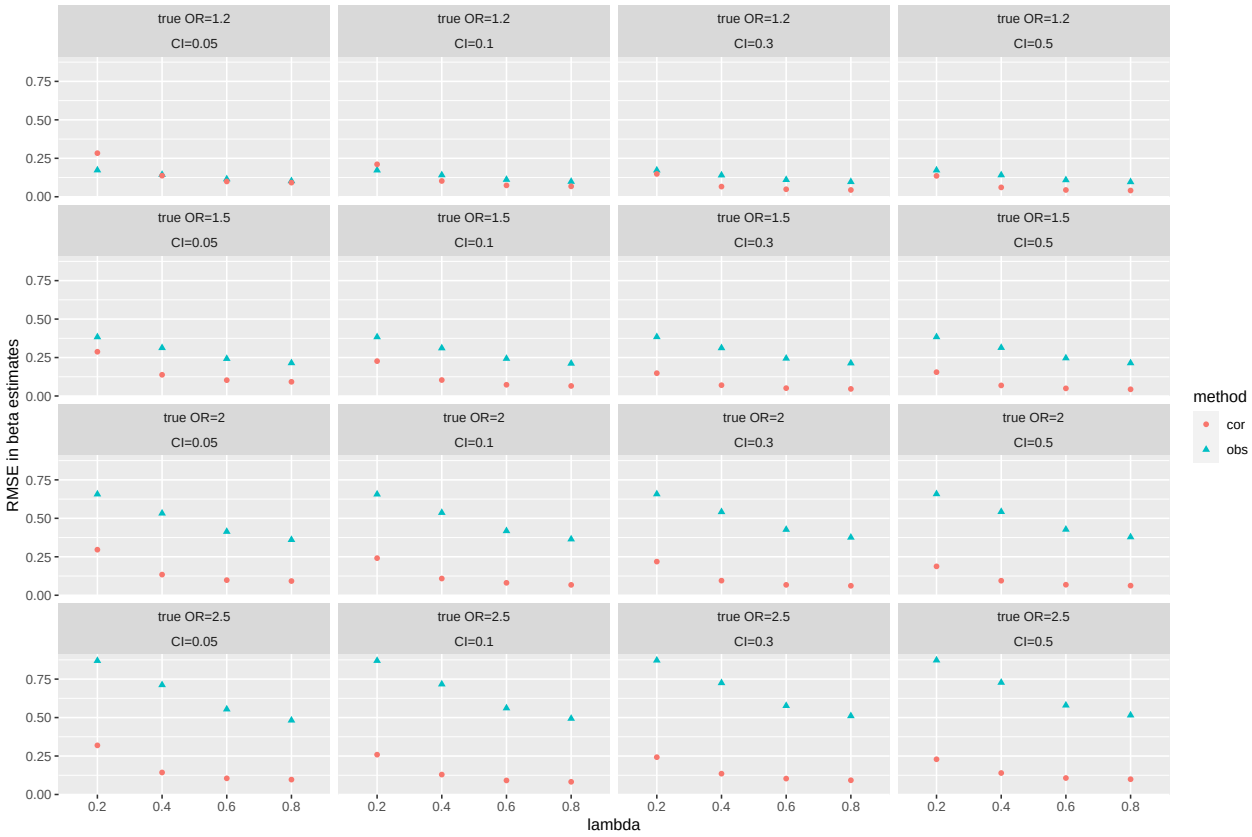


Figure 6: RMSE in beta estimates before and after correcting for measurement error

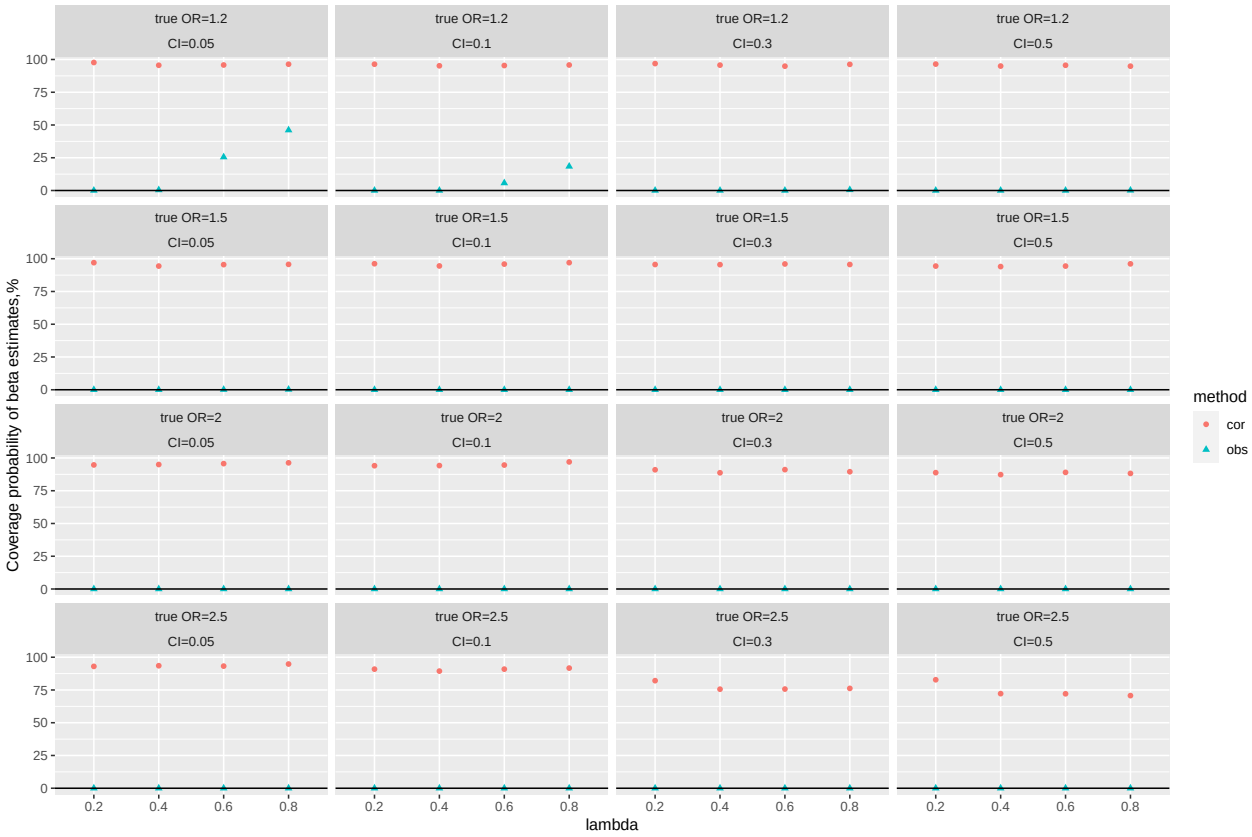
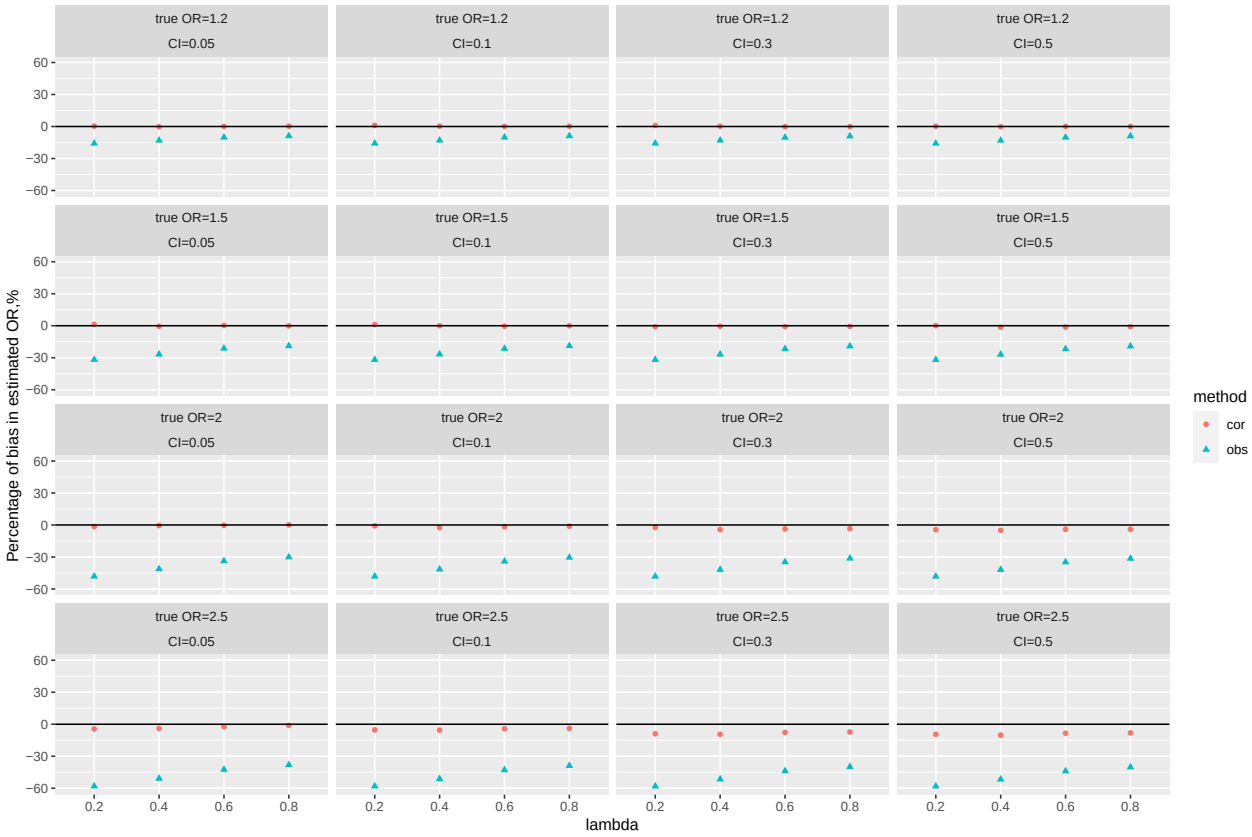


Figure 7: Coverage probability of beta estimates before and after correcting for measurement error


true OR=1.2
CI=0.05
true OR=1.2
CI=0.1
true OR=1.2
CI=0.3
true OR=1.2
CI=0.5
true OR=1.5
CI=0.05
true OR=1.5
CI=0.1
true OR=1.5
CI=0.3
true OR=1.5
CI=0.5
true OR=2
CI=0.05
true OR=2
CI=0.1
true OR=2
CI=0.3
true OR=2
CI=0.5
true OR=2.5
CI=0.05
true OR=2.5
CI=0.1
true OR=2.5
CI=0.3
true OR=2.5
CI=0.5
Percentage of bias in estimated OR,%
60
30
0
−30
−60
0.2
0.4
0.6
0.8
lambda
method
cor
obs

5.2 Analysis Code

```
library(visdat)
library(heatmaply)
library(data.table)
library(data.table)
library(tidyverse)
library(haven)
library(stats)
library(ggplot2)
library(ggpmisc)
library(irr)
library(table1)
library(ggplot2)
library(ggcorrplot)
library(kableExtra)
library(gridExtra)
library(cowplot)
img_path <- "img"
data_path<-"data"
wlvs<-read_sas("data/wlvs.sas7bdat")
var_na<-c("id","pdi","updi","hpdi","hplant","uplant","animal","tplant")
wlvs_clean<-
  wlvs%>%select(starts_with(var_na))


#reshaping data
var_names <- c("vararible","method")
wlvs_reshape<-
  wlvs_clean%>%pivot_longer(-id)%>%
  separate(name, var_names, fill = "right") %>%
  pivot_wider(names_from=method)%>%
  rowwise()%>%
  transmute(
    id,
    vararible,
    FFQ1=ffq1,
    FFQ2=ffq2,
    DR_wk1=week1,
    DR_wk2=week2,
    DR_avg=mean(c(week1,week2)),
         vararible=factor(vararible,
                          levels=list("pdi","hpdi","updi","hplant","uplant","tplant","animal")))

var<-c("FFQ1","FFQ2","DR_wk1","DR_wk2","DR_wk2")
form<-paste("~",paste(var,collapse = "+"),"|vararible")
tab1<-as_tibble(table1(as.formula(form),wlvs_reshape, render.continuous="Mean [SD]")%>%
  data.frame()%>%
  #filter(!grepl("missing",X.,ignore.case = T))%>%
  select(-Overall))


#correlation matrix
```

```r
corr_data=
  wlvs_reshape%>%
  select(id,vararible,FFQ2)%>%
  arrange(vararible)%>%
  pivot_wider(names_from=vararible,values_from = FFQ2)%>%
  select(-1)
 corr <-  round(cor(corr_data,method="spearman"), 2)
 fig3<-ggcorrplot(corr,
  outline.color = "white",
  ggtheme = ggplot2::theme_gray,
  colors = c("#6D9EC1", "white", "#E46726"),
   lab = TRUE)

#calculate the ICC
icc_yy<-function(varn){
  icc_ffq<-wlvs_reshape%>%
  filter(vararible==varn)%>%
  select(FFQ1,FFQ2)%>%
  drop_na()%>%
  icc(., model = "oneway",
    type = "agreement",
    unit = "single")

  icc_week<-wlvs_reshape%>%
  filter(vararible==varn)%>%
  select(DR_wk1,DR_wk2)%>%
  drop_na()%>%
  icc(., model = "oneway",
    type = "agreement",
    unit = "single")
data.frame(
vararible=varn,
ICC_FFQs=round(icc_ffq$value,2),
ICC_DRs=round(icc_week$value,2))
}
vars<-c("pdi","hpdi","updi","hplant","uplant","tplant","animal")
ICC_final<-NULL
for (varn in vars){
ICC_final=rbind(ICC_final,icc_yy(varn))
}


#calculate the validity
validaity_final<-wlvs_reshape%>%
  group_by(vararible)%>%
  #drop_na()%>%
    summarize(validity_FFQ2=cor(FFQ2, DR_avg,method = "spearman",use="complete.obs"))
tab2<-ICC_final%>%
  left_join(validaity_final,by="vararible")
##visualize the scatterplot and calibration coeffients
p1=
  wlvs_reshape%>%
  filter(vararible%in%c("pdi","hpdi","updi"))%>%
```

```
  ggplot( aes(x =FFQ2 , y = DR_avg)) +
  stat_poly_line() +
  stat_poly_eq(aes(label = paste(after_stat(eq.label),
                                 after_stat(rr.label), sep = "*\", \"*"))) +
  geom_point(alpha=0.3)+facet_wrap(~vararible, ncol = 3)+ theme_bw()

p2= wlvs_reshape%>%
  filter(vararible%in%c("hplant","uplant","tplant","animal"))%>%
  ggplot( aes(x =FFQ2 , y = DR_avg)) +
  stat_poly_line() +
  stat_poly_eq(aes(label = paste(after_stat(eq.label),
                                 after_stat(rr.label), sep = "*\", \"*"))) +
  geom_point(alpha=0.3)+facet_wrap(~vararible, ncol = 2)+ theme_bw()

fig4<-plot_grid(p1, p2, labels=c("A", "B"), ncol = 1, nrow = 2)

# simulation analysis
simu_result<-function(N_main,N_val,eps,lambda,ci,or){
B=1000
a = log(ci/(1-ci))
b = log(or)
simu_resul=replicate(B,
       {  #main study
  x = rnorm(N_main, 0, 1)
  e = c(rnorm(N_main/2, 1, (1-lambda)/(lambda)),rnorm(N_main/2, -1, (1-lambda)/(lambda)))
  #var=(1-lambda)/lambda
  z = x + e+rnorm(1,0,eps)
  d = rep(0, N_main)

  for (i in 1:N_main){
  d[i] = rbinom(n=1, size=1, prob=exp(a+b*x[i])/(1+exp(a+b*x[i])))
  }
  main <- as.data.frame(cbind(x, e, z, d))

  #validation study
  xv = sample(x,N_val,replace = F)
  ev = c(rnorm(N_val/2, 1,(1-lambda)/(lambda)),rnorm(N_val/2, -1, (1-lambda)/(lambda)))
  zv = xv + ev+rnorm(1,0,eps)
  # dv = rep(0, 100)
  # for (i in 1:100){
  # dv[i] = rbinom(n=1, size=1, prob=exp(a+b*xv[i])/(1+exp(a+b*xv[i])))
  # }
  val <- as.data.frame(cbind(xv, ev, zv))

  #logistic regression of D on Z
  mod <- glm(d ~ z, family=binomial(link="logit"), data = main)
  bobs= summary(mod)$coef[2]
  vbobs = summary(mod)$coef[2,2]^2
  llo= summary(mod)$coef[2]-1.96*summary(mod)$coef[2,2]
  ulo = summary(mod)$coef[2]+1.96*summary(mod)$coef[2,2]

  #linear regression of X on Z
  modv <- glm(xv ~ zv, family=gaussian(link="identity"), data = val)
```

```
  lambdahat = summary(modv)$coef[2]
  vlambdahat = summary(modv)$coef[2,2]^2

  #point estimate, variance and CI for corrected beta
  bcor = bobs/lambdahat
  vbcor = (1/lambdahat^2)*vbobs + (bobs^2/lambdahat^4)*vlambdahat
  sebcor = sqrt(vbcor)
  llc = bcor-1.96*sebcor
  ulc = bcor +1.96*sebcor
  data.frame(bobs=bobs,
             vbobs=vbobs,
             llo=llo,
             ulo=ulo,
            bcor=bcor,
            vbcor=vbcor,
            llc=llc,
          ulc=ulc )},simplify = T)

#aveagre varaince of beta
mvar_obs=mean(as.numeric(simu_resul["vbobs",]))
mvar_cor=mean(as.numeric(simu_resul["vbcor",]))
#RMSE
#uncorr
rmse_obs = sqrt(sum((as.numeric(simu_resul["bobs",])-b)^2)/B)
rmse_cor=sqrt( sum((as.numeric(simu_resul["bcor",])-b)^2)/B)

#Percentage bias
#uncorr
bobsm = mean(as.numeric(simu_resul["bobs",]))
pbias_obs = (exp(bobsm)/exp(b)-1)*100
#corr
bcorm = mean(as.numeric(simu_resul["bcor",]))
pbias_cor = (exp(bcorm)/exp(b)-1)*100
#convergency pro
coverage_obs=(sum(as.numeric(simu_resul["llo",])<b &as.numeric(simu_resul["ulo",])>b)/B)*100
coverage_cor=(sum(as.numeric(simu_resul["llc",])<b &as.numeric(simu_resul["ulc",])>b)/B)*100

data.frame(
          mvar_obs=mvar_obs,
          mvar_cor=mvar_cor,
          rmse_obs=rmse_obs,
           rmse_cor=rmse_cor,
           pbias_obs=pbias_obs,
           pbias_cor=pbias_cor,
           coverage_obs=coverage_obs,
           coverage_cor=coverage_cor

           )

}
grid<-expand.grid(N_main=5000,N_val=500,
                  lambda=seq(0.2,0.8,0.2),eps=0.001,
                  ci=c(0.05, 0.1, 0.3, 0.5),or=c(1.2,1.5, 2,2.5))
```

```r
re<-pmap(grid,simu_result)
results<-bind_rows(re, .id = "label")
final_out<-grid%>%
  mutate(label=as.character(row_number()))%>%
  left_join(results,by="label")

final_reshape<-
  final_out%>%
  pivot_longer(rmse_obs:coverage_cor)%>%
  separate(name, var_names, fill = "right") %>%
  pivot_wider(names_from=vararible)%>%
  mutate(ci=factor(ci,levels=list(0.05,0.1, 0.3, 0.5),
                   labels=list("CI=0.05","CI=0.1","CI=0.3","CI=0.5")),
         method=factor(method),
         or=factor(or),
         lambda=factor(lambda)
         )

fig5<-
  final_reshape%>%
  filter(method=="obs")%>%
  ggplot(aes(x=lambda,y=pbias,color=or))+
  geom_point()+
  geom_hline(yintercept=0,color="black")+
  scale_y_continuous(name="Percentage of bias in estimated OR,%",limits=c(-60,0))+
  facet_wrap(~ci)



fig6<-
  final_reshape%>%
  mutate( or=ordered(or,levels = c(1.2,1.5, 2,2.5),
                     labels=c("true OR=1.2","true OR=1.5","true OR=2","true OR=2.5")),
         )%>%
  ggplot(aes(x=lambda,y=rmse,color=method,shape=method))+
  geom_point()+
  scale_y_continuous(name="RMSE in beta estimates")+
  facet_wrap(or~ci)


fig7<-final_reshape%>%
    mutate( or=ordered(or,levels = c(1.2,1.5, 2,2.5),
                       labels=c("true OR=1.2","true OR=1.5","true OR=2","true OR=2.5")),
         )%>%
  ggplot(aes(x=lambda,y=coverage))+
  geom_point(aes(color=method,shape=method))+
  geom_hline(yintercept=0,color="black")+
  scale_y_continuous(name="Coverage probability of beta estimates,%")+
  facet_wrap(or~ci)

fig8<-final_reshape%>%
  mutate( or=ordered(or,levels = c(1.2,1.5, 2,2.5),
                     labels=c("true OR=1.2","true OR=1.5","true OR=2","true OR=2.5")),
```

```
        )%>%
  ggplot(aes(x=lambda,y=pbias))+
  geom_point(aes(color=method,shape=method))+
  geom_hline(yintercept=0,color="black")+
  scale_y_continuous(name="Percentage of bias in estimated OR,%",limits=c(-60,60))+
  facet_wrap(or~ci)
```