IPW_Wrapup

May 25, 2018

Settings

Outcome model

The outcome Y_{ijl} is generated by:

$$\pi_{ijl} = expit(1 + 1.36 * i + x_{ijl} + \delta_{ij})$$

- 1. i is the treatment indicator. i = 1 treated; i = 0 control
- 2. x is the covariate. $x \sim N(0, 0.2)$ (The variance is 0.2. I choose a relatively small variance since I want to avoid non-convergence. However, this generated small differences between CRA and adjusted CRA.)
- 3. The variance of δ_{ij} changed based on different ICC (the ICC for the datasets):
- ICC=0.05, $\delta_{ij} \sim N(0, 0.173)$ (the variance is 0.173)
- ICC=0.1, $\delta_{ij} \sim N(0, 0.366)$ (the variance is 0.366)
- ICC=0.2, $\delta_{ij} \sim N(0, 0.823)$ (the variance is 0.823)
- 4. Number of clusters: 50 clusters in each intervention arm
- 5. Cluster size: the cluster size is from a Poisson distribution, which is not fixed. cluster size $\sim POI(50)$

Missingness generation model

$$logit(R_{iil} = 1|Y_{ii}, X_{ii}) = intercept + i + X_{iil} + \sigma_{ii}$$

- 1. The intercept is varied to make sure the missing percentage is around 30%
 - 2. i is the treatment indicator. i=1 treated; i=0 control
 - 3. x is the covariate. $x \sim N(0, 0.2)$ (The variance is 0.2)
 - 4. The variance of σ_{ij} represents the cluster effects in missingness. It changed based on different missingness ICC:
 - $\sigma_{ij} = 0$, the missing ICC=0, there is no cluster effects
 - ICC=0.1, $\sigma_{ij} \sim N(0, 0.366)$ (the variance is 0.366)
 - ICC=0.3, $\sigma_{ij} \sim N(0, 1.410)$ (the variance is 1.410)
 - ICC=0.8, $\sigma_{ij} \sim N(0, 13.163)$ (the variance is 13.163)
 - 5. 1000 replicates for each scenario

Missingness handling methods

- 1. Calculation of true value:
- Fit the GEE with the formula: Y ~ intervention arm (without covariates). Estimate the coefficient of intervention arm.
- With full datasets without missing values

- Repeat for 1000 times and calculate the mean value.
- 2. UCRA: unadjusted complete record analysis
- Fit the GEE with the formula: Y ∼ intervention arm (without covariates). Estimate the coefficient of intervention arm.
- Delete the records with missing values in Y
- Repeat for 1000 times.
- 3. CRA: adjusted complete record analysis
- Fit the GEE with formula: $Y \sim \text{intervention-arm} + X$ (with covariates). Estimate the coefficient of intervention arm.
- Delete the records with missing values in Y
- Repeat for 1000 times.
- 4. IPW: inverse probability weighting
- Calculate the weights by fitting GLM: $glm(y \sim arm + x)$
- Fit the GEE with the formula: Y ~ intervention arm (without covariates) with corresponding weights. Estimate the coefficient of intervention arm.
- Repeat for 1000 times.
- 5. IPWC: inverse probability weighting with cluster effects
- Calculate the weights by fitting generalized linear mixed effect model: glmer (y \sim arm + x + cluster effect)
- Fit the GEE with the formula: Y ~ intervention arm (without covariates) with corresponding weights. Estimate the coefficient of intervention arm.
- Repeat for 1000 times.
- 6. MMI: multilevel multiple imputation
- consider cluster effects in the imputation

The results:

The results were organized following Caille's paper. The bias, SD, MCSD, coverage, and non-convergence time were reported separately. Each kind of results was organized in a table, with different ICC, missingness ICC and missingness handling methods. Both independent working correlation matrix and exchangeable working correlation matrix were considered.

Table 1: The Bias of each method with different ICCs and missingness ICCs, an independent working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.033 | 0.036 | 0.006 | 0.006 | 0.008 |
| | 0.1 | 0.030 | 0.035 | 0.004 | 0.003 | 0.005 |
| | 0.3 | 0.020 | 0.037 | 0.001 | 0.004 | 0.006 |
| | 0.8 | 0.004 | 0.038 | 0.001 | 0.093 | 0.002 |
| | | | | | | |
| 0.10 | 0.0 | 0.033 | 0.033 | 0.009 | 0.009 | 0.007 |

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| | 0.1 | 0.030 | 0.032 | 0.006 | 0.005 | 0.004 |
| | 0.3 | 0.020 | 0.034 | 0.003 | 0.005 | 0.005 |
| | 0.8 | 0.004 | 0.036 | 0.000 | 0.105 | 0.002 |
| 0.20 | 0.0 | 0.033 | 0.027 | 0.011 | 0.011 | 0.005 |
| | 0.1 | 0.028 | 0.028 | 0.008 | 0.007 | 0.004 |
| | 0.3 | 0.020 | 0.028 | 0.005 | 0.007 | 0.004 |
| | 0.8 | 0.005 | 0.030 | 0.002 | 0.123 | 0.002 |

• ICC: dataset ICC

• ICCM: missingness ICC

• UCRA: unadjusted complete record analysis

• CRA: adjusted record analysis

• IPW: inverse probability weighting

• IPWC: inverse probability weighting with cluster effect

• MMI: multilevle multiple imputation

• BIAS = Absolute value of (estimate-true value)

IPW, IPWC, and MMI have better effects than CRA and UCRA. UCRA is more close to 0 than CRA, although the differences are not big. The differences may become obvious with a larger variance of x. I chose a small value since I want to avoid non-convergence.

Table 2: The Bias of each method with different ICCs and missingness ICCs, an exchangeable working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.033 | 0.036 | 0.027 | 0.027 | 0.008 |
| | 0.1 | 0.031 | 0.034 | 0.023 | 0.025 | 0.005 |
| | 0.3 | 0.023 | 0.035 | 0.016 | 0.020 | 0.006 |
| | 0.8 | 0.006 | 0.036 | 0.003 | 0.105 | 0.002 |
| 0.10 | 0.0 | 0.033 | 0.030 | 0.055 | 0.055 | 0.007 |
| | 0.1 | 0.032 | 0.029 | 0.047 | 0.050 | 0.004 |
| | 0.3 | 0.025 | 0.030 | 0.033 | 0.038 | 0.005 |
| | 0.8 | 0.007 | 0.031 | 0.005 | 0.129 | 0.002 |
| 0.20 | 0.0 | 0.032 | 0.019 | 0.106 | 0.106 | 0.005 |
| | 0.1 | 0.030 | 0.020 | 0.095 | 0.090 | 0.004 |
| | 0.3 | 0.025 | 0.021 | 0.069 | 0.073 | 0.004 |
| | 0.8 | 0.009 | 0.019 | 0.011 | 0.165 | 0.001 |

The results are very similar to the independent working correlation matrix

Table 3: The Standard Deviation of each method with different ICCs and missingness ICCs, the independent working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.125 | 0.128 | 0.129 | 0.129 | 0.176 |
| | 0.1 | 0.126 | 0.129 | 0.129 | 0.141 | 0.176 |
| | 0.3 | 0.127 | 0.130 | 0.129 | 0.171 | 0.180 |
| | 0.8 | 0.131 | 0.133 | 0.131 | 0.217 | 0.192 |
| 0.10 | 0.0 | 0.148 | 0.151 | 0.151 | 0.151 | 0.197 |
| | 0.1 | 0.149 | 0.152 | 0.151 | 0.165 | 0.199 |
| | 0.3 | 0.151 | 0.154 | 0.152 | 0.202 | 0.202 |
| | 0.8 | 0.157 | 0.161 | 0.157 | 0.255 | 0.219 |
| 0.20 | 0.0 | 0.186 | 0.190 | 0.187 | 0.187 | 0.233 |
| | 0.1 | 0.188 | 0.192 | 0.189 | 0.207 | 0.236 |
| | 0.3 | 0.192 | 0.196 | 0.192 | 0.254 | 0.241 |
| | 0.8 | 0.203 | 0.207 | 0.202 | 0.318 | 0.265 |

As ICC and ICCM get larger, the SD also get larger. The IPWC and MMI have larger SD than other methods. MMI has the biggest SD in each scenario except for the one when ICCM=0.8. In this scenario, IPWC has the biggest SD.

Table 4: The Standard Deviation of each method with different ICCs and missingness ICCs, an exchangeable working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.125 | 0.128 | 0.134 | 0.134 | 0.175 |
| | 0.1 | 0.126 | 0.129 | 0.133 | 0.145 | 0.176 |
| | 0.3 | 0.127 | 0.129 | 0.132 | 0.177 | 0.180 |
| | 0.8 | 0.130 | 0.133 | 0.131 | 0.232 | 0.191 |
| 0.10 | 0.0 | 0.147 | 0.151 | 0.160 | 0.160 | 0.196 |
| | 0.1 | 0.148 | 0.152 | 0.158 | 0.174 | 0.198 |
| | 0.3 | 0.149 | 0.153 | 0.156 | 0.217 | 0.202 |
| | 0.8 | 0.155 | 0.159 | 0.156 | 0.283 | 0.218 |
| 0.20 | 0.0 | 0.185 | 0.190 | 0.207 | 0.207 | 0.232 |
| 0.20 | 0.1 | 0.186 | 0.191 | 0.204 | 0.230 | 0.235 |
| | 0.3 | 0.188 | 0.193 | 0.200 | 0.292 | 0.241 |
| | 0.8 | 0.196 | 0.202 | 0.198 | 0.373 | 0.264 |

It has similar results as the independent working correlation matrix. As ICC and ICCM get larger, the SD also get larger. The IPWC and MMI have larger SD than other methods. MMI has the biggest SD in each scenario except for the one when ICCM=0.8. In this scenario, IPWC has the biggest SD.

Table 5: The MCSD of each method with different ICCs and missingness ICCs, an independent working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.125 | 0.127 | 0.128 | 0.128 | 0.126 |

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| | 0.1 | 0.131 | 0.134 | 0.135 | 0.150 | 0.131 |
| | 0.3 | 0.135 | 0.137 | 0.137 | 0.190 | 0.135 |
| | 0.8 | 0.139 | 0.142 | 0.140 | 0.237 | 0.138 |
| 0.10 | 0.0 | 0.147 | 0.150 | 0.149 | 0.149 | 0.148 |
| | 0.1 | 0.153 | 0.156 | 0.156 | 0.173 | 0.152 |
| | 0.3 | 0.157 | 0.161 | 0.159 | 0.221 | 0.156 |
| | 0.8 | 0.164 | 0.168 | 0.164 | 0.280 | 0.161 |
| 0.20 | 0.0 | 0.184 | 0.187 | 0.183 | 0.183 | 0.185 |
| | 0.1 | 0.193 | 0.197 | 0.193 | 0.216 | 0.191 |
| | 0.3 | 0.198 | 0.203 | 0.198 | 0.281 | 0.194 |
| | 0.8 | 0.210 | 0.215 | 0.209 | 0.352 | 0.201 |

Do not have big differences with the SD results.

Table 6: The MCSD of each method with different ICCs and missingness ICCs, an exchangeable working correlation matrix

| $\overline{\mathrm{ICC}}$ | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|---------------------------|------|-------|-------|-------|-------|-------|
| ${0.05}$ | 0.0 | 0.124 | 0.126 | 0.133 | 0.133 | 0.126 |
| | 0.1 | 0.130 | 0.132 | 0.138 | 0.154 | 0.130 |
| | 0.3 | 0.133 | 0.136 | 0.140 | 0.197 | 0.134 |
| | 0.8 | 0.138 | 0.141 | 0.139 | 0.254 | 0.137 |
| 0.10 | 0.0 | 0.145 | 0.148 | 0.159 | 0.159 | 0.146 |
| | 0.1 | 0.150 | 0.154 | 0.163 | 0.183 | 0.151 |
| | 0.3 | 0.154 | 0.158 | 0.163 | 0.239 | 0.154 |
| | 0.8 | 0.160 | 0.164 | 0.162 | 0.309 | 0.160 |
| 0.20 | 0.0 | 0.181 | 0.186 | 0.207 | 0.207 | 0.183 |
| | 0.1 | 0.187 | 0.193 | 0.212 | 0.241 | 0.189 |
| | 0.3 | 0.191 | 0.197 | 0.209 | 0.323 | 0.192 |
| | 0.8 | 0.199 | 0.206 | 0.203 | 0.409 | 0.199 |

Do not have big differences with the SD results.

Table 7: The Coverage of each method with different ICCs and missingness ICCs, an independent working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.934 | 0.936 | 0.949 | 0.949 | 0.992 |
| | 0.1 | 0.935 | 0.933 | 0.944 | 0.930 | 0.988 |
| | 0.3 | 0.930 | 0.938 | 0.944 | 0.915 | 0.989 |
| | 0.8 | 0.925 | 0.927 | 0.931 | 0.235 | 0.992 |
| | | | | | | |
| 0.10 | 0.0 | 0.938 | 0.944 | 0.944 | 0.945 | 0.988 |

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| | 0.1 | 0.935 | 0.939 | 0.937 | 0.942 | 0.986 |
| | 0.3 | 0.932 | 0.943 | 0.950 | 0.917 | 0.992 |
| | 0.8 | 0.933 | 0.926 | 0.930 | 0.241 | 0.992 |
| 0.20 | 0.0 | 0.943 | 0.953 | 0.947 | 0.947 | 0.984 |
| | 0.1 | 0.934 | 0.952 | 0.944 | 0.936 | 0.979 |
| | 0.3 | 0.942 | 0.940 | 0.948 | 0.922 | 0.989 |
| | 0.8 | 0.940 | 0.938 | 0.940 | 0.267 | 0.990 |

- with small ICCM, the IPW and IPWC have good coverage rates.
- MMI gets over-coverage. (since it has a larger SD?)
- When ICCM is big (ICCM=0.8) the IPW meets the non-convergence problem and gets bad coverage.

Table 8: The Coverage of each method with different ICCs and missingness ICCs, an exchangeable working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|-------|-------|-------|-------|-------|
| 0.05 | 0.0 | 0.937 | 0.940 | 0.951 | 0.949 | 0.992 |
| | 0.1 | 0.935 | 0.934 | 0.938 | 0.927 | 0.989 |
| | 0.3 | 0.930 | 0.942 | 0.939 | 0.909 | 0.988 |
| | 0.8 | 0.935 | 0.927 | 0.937 | 0.234 | 0.992 |
| 0.10 | 0.0 | 0.939 | 0.952 | 0.943 | 0.943 | 0.988 |
| | 0.1 | 0.939 | 0.945 | 0.945 | 0.935 | 0.989 |
| | 0.3 | 0.939 | 0.947 | 0.939 | 0.905 | 0.992 |
| | 0.8 | 0.940 | 0.935 | 0.944 | 0.235 | 0.994 |
| 0.20 | 0.0 | 0.946 | 0.953 | 0.924 | 0.923 | 0.983 |
| | 0.1 | 0.942 | 0.951 | 0.930 | 0.914 | 0.982 |
| | 0.3 | 0.946 | 0.948 | 0.928 | 0.891 | 0.988 |
| | 0.8 | 0.937 | 0.945 | 0.940 | 0.260 | 0.990 |

The results are similar to independent working correlation matrix

Table 9: The non-convergence of each method with different ICCs and missingness ICCs, an independent working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|------|-----|-----|------|-----|
| 0.05 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | 0.1 | 0 | 0 | 0 | 0 | 0 |
| | 0.3 | 0 | 0 | 0 | 0 | 0 |
| | 0.8 | 0 | 0 | 0 | 731 | 0 |
| 0.10 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | 0.1 | 0 | 0 | 0 | 0 | 0 |
| | 0.3 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | |

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|--------------|------|-----|-----|------|-----|
| | 0.8 | 0 | 0 | 0 | 730 | 0 |
| 0.20 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | $0.1 \\ 0.3$ | 0 | 0 | 0 | 0 | 0 |
| | 0.8 | 0 | 0 | 0 | 697 | 0 |

When ICCM=0.8, IPWC has a lot of non-covergence. Since when ICCM=0.8, the $\sigma_{ij} = 13.162$, which is very big and brings large weights.

Table 10: The non-convergence of each method with different ICCs and missingness ICCs, an exchangeable working correlation matrix

| ICC | ICCM | UCRA | CRA | IPW | IPWC | MMI |
|------|------|------|-----|-----|------|-----|
| 0.05 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | 0.1 | 0 | 0 | 0 | 0 | 0 |
| | 0.3 | 0 | 0 | 0 | 0 | 0 |
| | 0.8 | 0 | 0 | 0 | 731 | 0 |
| 0.10 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | 0.1 | 0 | 0 | 0 | 0 | 0 |
| | 0.3 | 0 | 0 | 0 | 0 | 0 |
| | 0.8 | 0 | 0 | 0 | 730 | 0 |
| 0.20 | 0.0 | 0 | 0 | 0 | 0 | 0 |
| | 0.1 | 0 | 0 | 0 | 0 | 0 |
| | 0.3 | 0 | 0 | 0 | 0 | 0 |
| | 0.8 | 0 | 0 | 0 | 697 | 0 |

Similar results with an independent working correlation matrix.

The observed problem:

- mmi always over-coverage.
- package CRTgeeDR, not work well when the data has a large ICC
- package geepack does not work well when the data has a large missing ICC

I found that previously we only controlled one ICC, which was missing ICC. And for the datasets' ICC, we just followed Hossain's settings. In this setting the results from CRTgeeDR are reasonable. On April 2 setting, we set there were no cluster effects in missingness (ICCM=0) and varied the dataset ICC, however, there was low coverage rate when ICC got large.

I think, if we want to use geepack, we may recommend that people can apply IPW since it works well and much faster than MMI. The cluster effects are not necessary to be considered in IPW since IPWC does not have a big difference with IPW and IPWC is easy to get non-convergence and brings some problem. If we want to use CRTgeeDR, we may restrict to scenarios with low ICCs.

| | Bias | | | MCSD | | | | SD | | | | | |
|-----|------|-------|--------|-------|-------|--------|-------|-------|--------|------|-------|--------|-----|
| ICC | True | IPW | IPWclu | True | IPW | IPWclu | True | IPW | IPWclu | True | IPW | IPWclu | non |
| 0.1 | 0 | 0.008 | 0.005 | 0.065 | 0.114 | 0.130 | 0.079 | 0.107 | 0.115 | 0.99 | 0.920 | 0.915 | 0 |
| 0.2 | 0 | 0.002 | 0.001 | 0.065 | 0.110 | 0.144 | 0.079 | 0.106 | 0.128 | 0.99 | 0.945 | 0.925 | 0 |
| 0.3 | 0 | 0.000 | 0.000 | 0.065 | 0.109 | 0.152 | 0.079 | 0.104 | 0.141 | 0.99 | 0.940 | 0.925 | 0 |
| 0.4 | 0 | 0.001 | 0.004 | 0.065 | 0.104 | 0.164 | 0.079 | 0.103 | 0.154 | 0.99 | 0.955 | 0.930 | 0 |
| 0.5 | 0 | 0.003 | 0.001 | 0.065 | 0.102 | 0.179 | 0.079 | 0.102 | 0.165 | 0.99 | 0.930 | 0.930 | 0 |
| 0.6 | 0 | 0.002 | 0.001 | 0.065 | 0.098 | 0.190 | 0.079 | 0.101 | 0.170 | 0.99 | 0.970 | 0.900 | 0 |
| 0.7 | 0 | 0.002 | 0.010 | 0.065 | 0.095 | 0.179 | 0.079 | 0.099 | 0.167 | 0.99 | 0.955 | 0.935 | 0 |
| 0.8 | 0 | 0.001 | 0.007 | 0.065 | 0.090 | 0.171 | 0.079 | 0.097 | 0.155 | 0.99 | 0.965 | 0.930 | 0 |
| 0.9 | 0 | 0.002 | 0.007 | 0.065 | 0.083 | 0.140 | 0.079 | 0.094 | 0.136 | 0.99 | 0.975 | 0.930 | 0 |

Figure 1: CRTgeeDR results with different missing ICC $\,$

| ICC | BIAS | | | | | | | MCSD | | | Coverage | | | | |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|-------|-----|
| ICC | CRA | CRAad | IPW | IPWC | MMI | CRA | CRAad | IPW | IPWC | MMI | CRA | CRAad | IPW | IPWC | MMI |
| 0.01 | 0.315 | 0 | 0.008 | 0.008 | 0.019 | 0.076 | 0.091 | 0.166 | 0.166 | 0.103 | 0.020 | 0.941 | 0.930 | 0.929 | 1 |
| 0.05 | 0.298 | 0 | 0.010 | 0.010 | 0.008 | 0.093 | 0.116 | 0.174 | 0.174 | 0.123 | 0.111 | 0.954 | 0.873 | 0.873 | 1 |
| 0.10 | 0.273 | 0 | 0.009 | 0.009 | 0.004 | 0.114 | 0.145 | 0.189 | 0.189 | 0.149 | 0.315 | 0.941 | 0.766 | 0.764 | 1 |

Figure 2: CRTgeeDR results with different data ICC, no cluster effects in missingness