Chapter 11: Online Appendices

Online Supplementary Material

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11.10: Details of the sample size estimation process

In the examples shown above, the details of the sample size estimation procedure were "cloaked" in an **`RJafroc`** function. This function can also be used to perform ORH analysis. The online distribution has a file **`mainSsOrhDetails.R`**, for "*sample size ORH method details*". This file explicitly shows the steps of the sample size estimation procedure using the ORH method. **Error! Reference source not found.** summarizes the results of running **`mainSsOrhDetails.R`** for the two datasets. The first three columns list the dataset name, the parameters of the sample size estimation method and their values. The body of the table lists the numbers of readers and cases, the critical value $F_{1-\alpha;ndf,ddf}$, ddf, Δ, and Power: in each case three values are listed, separated by slashes, corresponding to the three generalizations.

This table clearly shows that not only is the effect-size much smaller for the Franken dataset, it is also characterized by larger variability components.

Table 11.A.1: Summary of ORH parameters and intermediate quantities involved in random-reader random-case (RRRC), fixed-reader random-case (FRRC) and random-reader fixed-case (RRFC) power analyses for two datasets. VD = Van Dyke and FR = Franken. J / K denote numbers of readers and numbers of cases considered. In all cases ndf = 1 and α = 0.05. Where three values are listed, separated by slashes, they correspond to RRRC/FRRC/RRFC. Note the much larger non-centrality parameter and smaller variances in ORH model for the VD dataset, leading to higher power values.

Dataset	Parameter	Value	Sample size parameters for RRRC/FRRC/RRFC				
			J / K	$F_{1-\alpha;ndf,ddf}$	ddf	Δ	Power
VD	$d = d_{obs}$ = -0.0438 (-0.088, 0.000)						
	Var	0.0008	5 / 114	4.53 / 3.93 / 7.71	15.3 / 113 / 4	4.46 / 5.48 / 8.70	0.507 / 0.641 / 0.606
	Cov_1	0.00035	5 / 228	4.79 / 3.88 / 7.71	11.5 / 227 / 4	7.51 / 11.0 / 12.8	0.708 / 0.909 / 0.761
	Cov_2	0.00034	10 / 114	3.97 / 3.93 / 5.12	76.0 / 113 / 9	5.99 / 6.85 / 17.4	0.676 / 0.737 / 0.959
	Cov_3	0.00024	10 / 228	4.03 / 3.88 / 5.12	51.8 / 227 / 9	10.6 / 13.7 / 25.5	0.893 / 0.958 / 0.994
	$\sigma^2_{\tau R}$	0.00020					
FR	$d = d_{obs}$ = 0.011 (-0.005, 0.027)						
	Var	0.0015	4 / 100	10.1 / 3.94/ 10.1	3 / 99 /3	0.321 / 0.321 /0.321	0.070 / 0.087 /0.087
	Cov_1	0.00079	4 / 200	10.1 / 3.89 / 10.1	3 / 199 / 3	0.642 / 0.642 /0.642	0.089 / 0.125 / 0.089
	Cov_2	0.00048	8 / 100	5.59 / 3.94 / 5.59	7 / 99 / 7	0.642 /0.642 / 0.642	0.107 / 0.125 / 0.107
	Cov_3	0.00051	8 / 200	5.59 / 3.89 / 5.59	7 / 199 / 7	1.28 / 1.28 / 1.28	0.166 / 0.204 / 0.166
	$\sigma^2_{\tau R}$	0					

In the Van Dyke dataset the constraint applied by Hillis to maintain the correct ordering of Cov_2 and Cov_3 is unnecessary, as they already have the correct ordering. In the Franken dataset, these covariances are incorrectly ordered. Therefore, according to the defining equation, *ddf* is *J-1*, see *ddf* column of Table 11.A.1. *Anticipating a positive value for* $\sigma^2_{\tau R}$ *would further decrease power for this dataset.* Given the small observed effect-size, a pivotal study would probably not be warranted for the Franken dataset, even though the effect-size is in the "right direction", i.e., digital > plain film (modality 1 is digital). Even taking the upper limit of the 95% CI as the anticipated effect-size, one needs 10 readers and 203 cases for RRRC generalization, **Error! Reference source not found.**. Any larger anticipated effect-size would be so overly optimistic, given the technology at that time, as to be clinically meaningless. A pivotal study was *not* in fact conducted. It is interesting that in the early days of reporting the results of ROC studies, failure to reject the NH was sometimes taken as evidence that the NH is correct, i.e., the modalities are "equivalent" or "comparable", which is a fallacy. This is a very common mistake, even nowadays. The conclusion of the Franken paper[9] states: "*The study suggest that for pediatric plain film images, video images offer diagnostic information comparable with that of conventional radiographs for neonatal examinations*". There is a human tendency to put the best face on new technology. This example also shows that it is more informative to quote a CI in addition to a quoting p-value. The late Prof. Metz has an interesting paper on this[10] appropriately titled "*Quantification of Failure to Demonstrate Statistical Significance: The Usefulness of Confidence Intervals*". *A study that fails to reject the NH is nevertheless useful in the archival literature if it reports a CI, because others can use it to select a realistic effect-size.*

Online Appendix 11.A: Sample size formulae using the ORH approach

This section gives the sample-size formulae for the DBMH method of analysis and shows, via an example, that the two methods give identical results. According to Eqn. 6 in Hillis and Berbaum[2], the non-centrality parameter Δ is (*J* = number of readers and *K* = number of cases in the pivotal study and the *Y* subscript is used to denote pseudovalue derived variances):

$$\Delta = JK\,d^2 / 2 \Big/ \left(K\sigma^2_{Y;\tau R} + J\sigma^2_{Y;\tau C} + \sigma^2_{Y;\tau RC} + \sigma^2_{Y;\varepsilon} \right) \quad \textbf{(0.1.1)}$$

.

$$\Delta = \frac{J\sum_{i=1}^{I}\left(\theta_{i\bullet} - \theta_{\bullet\bullet}\right)^2}{\sigma^2_{TR} + \frac{K^*}{K}\left[Var - Cov_1 + \left(J-1\right)\max\left(Cov_2 - Cov_3, 0\right)\right]} \quad . \quad \textbf{(0.1.2)}$$

For two modalities, $I = 2$, it is easily shown that the numerator of the expression for Δ becomes $Jd^2/2$, where *d* is the difference of the two FOMs (the sign of the difference does not affect the sample size estimate, but is crucial to the decision whether to conduct a pivotal study at all, see below), i.e.,

$$d = \theta_{1\bullet} - \theta_{2\bullet} \quad . \quad \textbf{(0.1.3)}$$

$$\Delta = \frac{J\sum_{i=1}^{I}\left(\theta_{i\bullet} - \theta_{\bullet\bullet}\right)^2}{\sigma^2_{TR} + \frac{K^*}{K}\left[Var - Cov_1 + \left(J-1\right)\max\left(Cov_2 - Cov_3, 0\right)\right]} \quad . \quad \textbf{(0.1.4)}$$

For two modalities, $I = 2$, it is easily shown that the numerator of the expression for Δ becomes $Jd^2/2$, where *d* is the difference of the two FOMs (the sign of the difference does not affect the sample size estimate, but is crucial to the decision whether to conduct a pivotal study at all, see below), i.e.,

$$d = \theta_{1\bullet} - \theta_{2\bullet} \quad . \quad \textbf{(0.1.5)}$$

$$\Delta = \frac{Jd^2/2}{\sigma_{TR}^2 + \frac{K^*}{K}\left[Var - Cov_1 + (J-1)\max(Cov_2 - Cov_3, 0)\right]} \quad . \quad \textbf{(0.1.6)}$$

The denominator degrees of freedom ddf of the non-central F-distribution is defined by:

$$ddf = (J-1)\frac{\left\{\sigma_{TR}^2 + \frac{K^*}{K}\left[Var - Cov_1 + (J-1)\max(Cov_2 - Cov_3, 0)\right]\right\}^2}{\left\{\sigma_{TR}^2 + \frac{K^*}{K}\left[Var - Cov_1 - \max(Cov_2 - Cov_3, 0)\right]\right\}^2} \quad . \quad \textbf{(0.1.7)}$$

Statistical power follows from:

$$\text{Power} = P\left(F > F_{1-\alpha;ndf,ddf} \middle| F \sim F_{ndf,ddf;\Delta}\right) \quad . \quad \textbf{(0.1.8)}$$

For two modalities the numerator degrees of freedom (*ndf*) of the F-distribution is unity. The Hillis-denominator degrees of freedom (*ddf*) is:

$$ddf = (J-1)\left(K\sigma_{Y;\tau R}^2 + \max\left(J\sigma_{Y;\tau C}^2, 0\right) + \sigma_{Y;\tau RC}^2 + \sigma_{Y;\varepsilon}^2\right)^2 \Big/ \left(K\sigma_{Y;\tau R}^2 + \sigma_{Y;\tau RC}^2 + \sigma_{Y;\varepsilon}^2\right)^2 \quad . \quad \textbf{(0.1.9)}$$

The critical value of the F-distribution is $F_{1-\alpha;1,ddf}$ and a significant result is obtained when the observed value of the F-statistic exceeds the critical value. The statistical power is:

$$power \approx \text{Prob}\left(F_{1,ddf;\Delta} > F_{1-\alpha;1,ddf}\right) \quad . \quad \textbf{(0.1.10)}$$

Here $F_{1,ddf;\Delta}$ is a sample from the non-central F-distribution with non-centrality parameter Δ and numerator and denominator degrees of freedom equal to 1 and *ddf*, respectively.

For FRRC and RRFC analyses, for the non-centrality parameter in Eqn. 11.B.1, one sets $\sigma_{Y;\tau R}^2 = 0$ and $\sigma_{Y;\tau C}^2 = 0$, respectively, and for the denominator degrees of freedom one sets $ddf = (K-1)$ and $ddf = (J-1)$, respectively.

The following code listing, in file **`mainSsDbmh.R`**, is identical to **`mainSsOrh.R`** except that a few lines have been addedto implement the above formulae. Line 8 extracts the pseudovalue variance components contained in **`retDbm`**. Since the previous calculation predicted that ten readers and 163 cases yields 80% power, the variables **`J`** and **`K`** are set to these values, respectively. The remaining lines implement the formulae.

Online Appendix 11.A.1: Code Listing

```
rm(list = ls()) #mainSsDbmh.R
library(RJafroc)
fileName <- "VanDyke.lrc"
#fileName <- "Franken1.lrc"
alpha <- 0.05
rocData <- ReadDataFile(fileName, format = "MRMC")
retDbm <- DBMHAnalysis(dataset = rocData, fom = "Wilcoxon")
varTr <- retDbm$varComp$varComp[3];varTc <- retDbm$varComp$varComp[4];varEps <-
retDbm$varComp$varComp[6]
effectSize <- retDbm$ciDiffTrtRRRC$Estimate
powTab <- SsPowerTable(alpha = alpha, effectSize = effectSize, desiredPower = 0.8,
                       method = "DBMH", option = "ALL", varTr, varTc, varEps)
print(powTab)

J <- 5; K <- 114
#RRRC
ncp <- (0.5*J*K*(effectSize)^2)/(K*varTr+max(J*varTc,0)+varEps)
ddf <- (J-1)*(K*varTr+max(J*varTc,0)+varEps)^2/(K*varTr+varEps)^2
FCrit <- qf(1 - alpha, 1, ddf)
Power <- 1-pf(FCrit, 1, ddf, ncp = ncp)
cat("FCrit = ", FCrit, "ddf = ", ddf, ", ncp = ", ncp, ", RRRC power = ", Power, "\n")

#FRRC
#varTr <- 0
ncp <- (0.5*J*K*(effectSize)^2)/(K*0+max(J*varTc,0)+varEps) # set to zero here
ddf <- (K-1)
FCrit <- qf(1 - alpha, 1, ddf)
Power <- 1-pf(FCrit, 1, ddf, ncp = ncp)
cat("FCrit = ", FCrit, "ddf = ", ddf, ", ncp = ", ncp, ", FRRC power = ", Power, "\n")

#RRFC
#varTc <- 0
ncp <- (0.5*J*K*(effectSize)^2)/(K*varTr+max(J*0,0)+varEps)  # set to zero here
ddf <- (J-1)
FCrit <- qf(1 - alpha, 1, ddf)
Power <- 1-pf(FCrit, 1, ddf, ncp = ncp)
cat("FCrit = ", FCrit, "ddf = ", ddf, ", ncp = ", ncp, ", RRFC power = ", Power, "\n")
```

If one **`sources`** the code, one sees:

Online Appendix 11.A.2: Code Output

```
> source('~/book2/03 B Statistics of ROC analysis/B11 Sample Size/software/mainSsDbmh.R')
$powerTableRRRC
  numReaders numCases power
1          2    >2000  <NA>
2          3    >2000  <NA>
3          4     1089   0.8
4          5      344 0.801
5          6      251 0.801
6          7      211 0.801
7          8      188 0.801
8          9      173 0.801
9         10      163 0.802

$powerTableFRRF
  numReaders numCases power
1          2      264 0.801
2          3      209 0.800
3          4      182 0.801
4          5      166 0.802
5          6      155 0.801
6          7      147 0.801
7          8      141 0.801
8          9      137 0.802
9         10      133 0.801

$powerTableRRFC
  numReaders numCases power
1          2    >2000  <NA>
2          3    >2000  <NA>
3          4    >2000  <NA>
4          5      289   0.8
5          6      151 0.801
6          7      102   0.8
7          8       78 0.803
```

```
8          9        63 0.804
9         10        53 0.805

FCrit =  4.529639 ddf =  15.25967 , ncp =  4.456319 , RRRC power =  0.507043
FCrit =  3.925076 ddf =  113 , ncp =  5.475953 , FRRC power =  0.6406559
FCrit =  7.708647 ddf =  4 , ncp =  13.6788 , RRFC power =  0.605623
```

The reader can confirm that these results are identical to those in §**Error! Reference source not found.** obtained by ORH analysis. The last three lines correspond to the results in the first row of the results in **Error! Reference source not found.**. In setting variance components equal to zero, one has to be careful to not affect subsequent calculations, see line 24 and line 32.

Online Appendix 11.B: ORH fixed-readers random-case (FRRC)

The formulae for fixed reader and fixed case analysis are, to the best of the author's knowledge, unpublished. It is possible these extensions are obvious to statisticians. The author has a pdf document titled "MRMC Sample Size Program User Guide" by Hillis and Berbaum, downloaded by the author around Feb 2011 from the Iowa website. This document is no longer available on the cited website and is included with this distribution. It describes usage of the DBM method for sample size estimation including the special cases of FRRC and RRFC generalizations. From this, using published formulae, one can extrapolate to the ORH formulae as shown next.

From the cited document the non-centrality parameter for the DBM method for FRRC generalization is (the Y-subscripts emphasize that one is dealing here with pseudovalue derived quantities):

$$\Delta = \frac{JKd^2/2}{J\sigma^2_{Y;\tau C} + \sigma^2_{Y;\tau RC} + \sigma^2_{Y;\varepsilon}} \quad . \quad \textbf{(0.91.1)}$$

This expression can be derived from the general RRRC formula, Eqn. (0.1.1), by simply setting $\sigma^2_{Y;\tau R} = 0$. According to Table III of Hillis et al 2005 paper[1] the relationship between DBM and OR components is:

$$\begin{aligned} \sigma^2_{Y;\tau C} &= K^* \max\left(Cov_2 - Cov_3, 0\right) \\ \sigma^2_{Y;\tau RC} + \sigma^2_{Y;\varepsilon} &= K^*\left(Var - Cov_1 - Cov_2 + Cov_3\right) \end{aligned} \quad . \quad \textbf{(0.91.2)}$$

Hence, the non-centrality parameter can be written in terms of ORH parameters as follows:

$$\Delta = \frac{Jd^2/2}{\frac{1}{K}\left(JK^*\left(Cov_2 - Cov_3\right) + K^*\left(Var - Cov_1 - Cov_2 + Cov_3\right)\right)} \quad . \quad \textbf{(0.91.3)}$$

Imposing the ordering constraint:

$$\Delta = \frac{Jd^2/2}{\frac{K^*}{K}\left(Var - Cov_1 + \left(J-1\right)\max\left(Cov_2 - Cov_3, 0\right)\right)} \quad . \quad \textbf{(0.91.4)}$$

The corresponding *ddf* for two treatments ($I = 2$) is defined by:

$$ddf = K - 1 \quad . \quad \textbf{(0.92.1)}$$

From the cited document the equation for the non-centrality parameter for the DBM method for RRFC generalization is:

$$\Delta = \frac{JKd^2/2}{K\sigma^2_{Y;\tau R} + \sigma^2_{Y;\tau RC} + \sigma^2_{Y;\varepsilon}} \quad . \quad \textbf{(0.93.1)}$$

This expression can be derived from the general RRRC formula, Eqn. (0.1.1), by setting $\sigma^2_{Y;\tau C} = 0$. According to Table III of Hillis et al 2005 paper[1],

$$\sigma^2_{Y;\tau R} = \sigma^2_{\tau R} \quad . \quad \textbf{(0.93.2)}$$

Hence, the non-centrality parameter can be written as:

$$\Delta = \frac{Jd^2/2}{\sigma^2_{TR} + \frac{K^*}{K}\left(Var - Cov_1 - \max\left(Cov_2 - Cov_3, 0\right)\right)} \quad . \quad \textbf{(0.93.3)}$$

The corresponding *ddf* is given by:

$$ddf = J - 1 \quad . \quad \textbf{(0.93.4)}$$

Table II. Relationship between DBM pseudovalue mean squares and estimates of the OR model parameters σ^2_ε, Cov1, Cov2, and Cov3 based on jackknife variance and covariance estimates.

$$\hat{\sigma}^2_{\varepsilon;\text{jack}} = \frac{1}{trc}\{\text{MS}(C)_{\text{pseudo}} + (t-1)\text{MS}(T^*C)_{\text{pseudo}} + (r-1)\text{MS}(R^*C)_{\text{pseudo}} + (t-1)(r-1)\text{MS}(T^*R^*C)_{\text{pseudo}}\}$$

$$\widehat{\text{Cov}1}_{\text{jack}} = \frac{1}{trc}\{\text{MS}(C)_{\text{pseudo}} - \text{MS}(T^*C)_{\text{pseudo}} + (r-1)[\text{MS}(R^*C)_{\text{pseudo}} - \text{MS}(T^*R^*C)_{\text{pseudo}}]\}$$

$$\widehat{\text{Cov}2}_{\text{jack}} = \frac{1}{trc}\{\text{MS}(C)_{\text{pseudo}} - \text{MS}(R^*C)_{\text{pseudo}} + (t-1)[\text{MS}(T^*C)_{\text{pseudo}} - \text{MS}(T^*R^*C)_{\text{pseudo}}]\}$$

$$\widehat{\text{Cov}3}_{\text{jack}} = \frac{1}{trc}\{\text{MS}(C)_{\text{pseudo}} - \text{MS}(T^*C)_{\text{pseudo}} - \text{MS}(R^*C)_{\text{pseudo}} + \text{MS}(T^*R^*C)_{\text{pseudo}}\}$$

Table III. Relationship between DBM and OR model parameters when both models are based on the same accuracy measure.

OR model parameter	Equivalent function of DBM model parameters
μ	$= \mu$
τ_i	$= \tau_i$
σ^2_R	$= \sigma^2_R$
$\sigma^2_{\tau R}$	$= \sigma^2_{\tau R}$
σ^2_ε	$= \frac{1}{c}(\sigma^2_C + \sigma^2_{\tau C} + \sigma^2_{RC} + \sigma^2_{\tau RC} + \sigma^2_\varepsilon)$
Cov1	$= \frac{1}{c}(\sigma^2_C + \sigma^2_{RC})$
Cov2	$= \frac{1}{c}(\sigma^2_C + \sigma^2_{\tau C})$
Cov3	$= \frac{1}{c}\sigma^2_C$
DBM model parameter	**Equivalent function of OR model parameters**
σ^2_C	$= c\text{Cov3}$
$\sigma^2_{\tau C}$	$= c(\text{Cov2} - \text{Cov3})$
σ^2_{RC}	$= c(\text{Cov1} - \text{Cov3})$
$\sigma^2_{\tau RC} + \sigma^2_\varepsilon$	$= c(\sigma^2_\varepsilon - \text{Cov1} - \text{Cov2} + \text{Cov3})$

They also assume the same linear constraint for the τ_i (e.g., $\sum \tau_i = 0$) for both models.

These relationships assume that the constraints for the OR model parameters are those implied by the DBM model: $\sigma^2_\varepsilon \geqslant (\text{Cov1} + \text{Cov2} - \text{Cov3})$, $\text{Cov1} \geqslant \text{Cov3}, \text{Cov2} \geqslant \text{Cov3}$, and $\text{Cov3} \geqslant 0$.

Online Appendix 11.D: Details on effect-size specification

Listed below is the code to demonstrate the consequence of specifying a fixed effect-size in AUC units, 0.05 in the code, on the implied increase in the separation parameter necessary to achieve that effect-size.

Online Appendix 11.D.1: Code Listing

```
rm(list = ls()) #mainEffectSizeFixedAucEs.R
source("AzDeePrimeTransformations.R")
require(ggplot2)

esAuc = 0.05
nBins <- 100
AzNh  <-  seq(0.55,1,length.out = nBins)
esDp <-  effectSizeDeePrime(esAuc, AzNh)
AzNh <-  AzNh[1:length(esDp)]
esDpRatio  <-  esDp / azToDeePrime(AzNh)
ConstAucPlot  <-  rep(esAuc, length.out = length(esDpRatio))
df <- data.frame(Az = c(AzNh, AzNh),DpMultipler = c(esDpRatio, ConstAucPlot),
                 truth = c(rep('ES: dp multiple', length(AzNh)), rep('Const. Az ES',
length(AzNh))))

myPlot <- ggplot(df, aes(x = Az, y = DpMultipler, color = truth)) +
  geom_line() +
  scale_colour_manual(values=c("red","green")) +
  theme(legend.title = element_blank(), legend.position = c(0.52, 0.85))

print(myPlot)
```

Line 5 specifies the effect-size in AUC units. Line 7 defines **`AzNh`** , an equally spaced array of length 100 ranging from 0.55 to 1. Line 8 calls function **`effectSizeDeePrime()`** to convert the specified AUC effect-

sizes to d' effect-sizes **esDp**. The reader should examine this code to be convinced that this is indeed what it does. As stated several times before, the debugging capability is quite useful to enter into a function and see what is going on. The array is of shorter length than 100, since some of the AUC values would cause the AH AUC to exceed unity; line 9 discards those values of AUC. Line 10 divides the effect-sizes in d' units by the baseline d' values, and the ratio **esAucFixed** is the quantity plotted as the red line. For comparison, the green line shows the constant AUC effect-size that was used in this code.

Online Appendix 11.A.2: Code Listing

```
rm(list = ls()) ##mainEffectSizeFixedDpMultiple.R
source("AzDeePrimeTransformations.R")
require(ggplot2)

nBins <- 100
dpMultiple = 0.6
azNh  <-  seq(0.55,0.99,length.out = nBins)
dpAH <- azToDeePrime(azNh) * (1 + dpMultiple)
azAh <-  deePrimeToAz(dpAH)
esAz <- azAh - azNh
ConstDpPlot  <-  rep(dpMultiple, length.out = nBins)
df <- data.frame(Az = c(azNh, azNh),esAuc = c(esAz, ConstDpPlot),  length(azNh))))

myPlot <- ggplot(df, aes(x = Az, y = esAuc, color = truth)) +
  geom_line() +
  scale_colour_manual(values=c("red","green")) +
  theme(legend.title = element_blank(), legend.position = c(0.52, 0.7))

print(myPlot)
```

Line 6 specifies a fixed effect-size as a multiple of d'. Three values are used, 0.02, 0.04 and 0.06. Line 8 uses the function **azToDeePrime()** to convert the specified NH AUC effect-sizes to d' effect-sizes and multiplies the results by $1+d'$ to get **dpAH**. Line 9 and 10 converts this array to an array of effect-sizes in AUC units, **esAz**, which is plotted as the red line in **Error! Reference source not found.**. For comparison, the green line shows the constant d' effect-size that was used in this code.

11.13: References

1. Hillis SL, Obuchowski NA, Schartz KM, Berbaum KS. A comparison of the Dorfman-Berbaum-Metz and Obuchowski-Rockette methods for receiver operating characteristic (ROC) data. *Statistics in Medicine.* 2005;24(10):1579-1607.
2. Hillis SL, Berbaum KS. Power Estimation for the Dorfman-Berbaum-Metz Method. *Acad Radiol.* 2004;11(11):1260-1273.