Burden of Serious Harms from Diagnostic Error in the USA   *Newman-Toker et al., BMJQS 2023*

Supplemental File #2 for *Burden of Serious Harms from Diagnostic Error in the USA* by Newman-Toker, et al. BMJ Quality & Safety, 2023 (doi:10.1136/bmjqs-2021-014130)

Enclosed below are additional Supplementary Materials (Supplement 2) to the peer-reviewed, scientific journal publication entitled *Burden of Serious Harms from Diagnostic Error in the USA (2023).*

This is the full statistical code (R v4.2.2, Vienna, Austria) for the Monte Carlo analysis.

```
# load packages
rm(list = ls())
library(sn)
library(rootSolve)
library(gdata)
library(MASS)
library(DEoptim)


set.seed(37)
logit <- function(x) {
    out <- log(x/(1-x))
    return(out)
}


expit <- function(x) {
    out <- exp(x) / (1 + exp(x))
    return(out)
}


#### primary analysis  ####
dat <- read.csv(file = "big3_data_dx1.csv")


peh_general <- 374/1216 # general per-error-harm rate
```

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```
peh_general_se <- sqrt(1/374 + 1/(1216-374)) # standard error on logit scale

peh_general_lower <- expit(logit(peh_general) + qnorm(0.025) * peh_general_se)

peh_general_upper <- expit(logit(peh_general) + qnorm(0.975) * peh_general_se)


perror_big3 <- 717 / (717 + 509) # proportion of big 3 in errors

pharm_big3 <- 157 / 207 # proportion of big 3 in harms


vascular_index <- which(dat$category == "vascular" & dat$disease != "OTHER Vascular")

vascular_other_index <- which(dat$disease == "OTHER Vascular")

infection_index <- which(dat$category == "infection" & dat$disease != "OTHER Infection")

infection_other_index <- which(dat$disease == "OTHER Infection")

cancer_index <- which(dat$category == "cancer" & dat$disease != "OTHER Cancer")

cancer_other_index <- which(dat$disease == "OTHER Cancer")


dat$nerror <- dat$incidence_point * dat$misrate_point

shp <- dat$proportion_highharm # severity harm proportion


peh_fun <- function(peh_general, nerror) {

  # function to calculate disease-specific per-error-harm rates

    peh_rate <- rep(NA, nrow(dat))

    peh_rate[c(vascular_index, infection_index, cancer_index)] <- peh_general * pharm_big3 /
perror_big3 *

        (sum(nerror) * shp[c(vascular_index, infection_index, cancer_index)]) /

        (sum(nerror[vascular_index] * shp[vascular_index]) * 1684 / 1344 +

            sum(nerror[infection_index] * shp[infection_index]) * 992 / 600 +

            sum(nerror[cancer_index] * shp[cancer_index]) * 2793 / 1529)

    peh_rate[vascular_other_index] <- sum(nerror[vascular_index] * peh_rate[vascular_index] *
334/1334) /

        nerror[vascular_other_index]
```

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```
    peh_rate[infection_other_index] <- sum(nerror[infection_index] * peh_rate[infection_index] *
392/600) /

        nerror[infection_other_index]

    peh_rate[cancer_other_index] <- sum(nerror[cancer_index] * peh_rate[cancer_index] * 1264/1529)
/

        nerror[cancer_other_index]

    return(peh_rate)

}


# point estimate of per-error-serious harm rates

dat$peharmrate_point <- peh_fun(peh_general, dat$nerror)

dat$peharmrate_lb <- peh_fun(peh_general_lower, dat$nerror)

dat$peharmrate_ub <- peh_fun(peh_general_upper, dat$nerror)


# Monte Carlo simulation, to construct plausible intervals for harm rate and number of harm

snest <- function(u, lower, upper, lowerq = 0.025, upperq = 0.975) {

    solfun <- function(beta) {

        omega <- beta[1]

        alpha <- beta[2]

        out1 <- psn(lower, xi = u, omega = omega, alpha = alpha) - lowerq

        out2 <- psn(upper, xi = u, omega = omega, alpha = alpha) - upperq

        return((out1^2+out2^2))

    }

    start <- c(((upper-lower)/4)^2, 0) + mvrnorm(100, mu = rep(0, 2), Sigma = diag(1, 2))

    start[, 1] <- abs(start[, 1])

    tempfit <- t(apply(start, 1, function(x) {

        fit <- optim(fn = solfun, par = x,

                control = list(maxit = 500000))

        return(c(fit$par, fit$value))
```

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```
    }))

    tempfit <- tempfit[complete.cases(tempfit), ]

    return(tempfit[which(tempfit[, 3] == min(tempfit[, 3]))[1], 1:3])

}



totl <- 316283434

nmc <- 1*(10^7)

numerical_error <- NULL

dat$nerror_lb <- NA

dat$nerror_ub <- NA

dat$nharm_point <- dat$nerror * dat$peharmrate_point

dat$nharm_lb <- NA

dat$nharm_ub <- NA

dat$harmrate_point <- dat$misrate_point * dat$peharmrate_point

dat$harmrate_lb <- NA

dat$harmrate_ub <- NA



# Monte Carlo simulation based on skew-normal estimation

mc_result <- list()

for (i in 1:nrow(dat)) {

    mc_result[[i]] <- list()

    if (dat$incidence_lb[i] == dat$incidence_ub[i]) {

        mc_incidence <- rep(dat$incidence_point[i], nmc)

    } else {

        fit_incidence <- snest(logit(dat$incidence_point[i] / totl),

                    lower = logit(dat$incidence_lb[i] / totl),

                    upper = logit(dat$incidence_ub[i] / totl))

        while(fit_incidence[3] > 10^(-10)) {
```

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```
        fit_incidence <- snest(logit(dat$incidence_point[i] / totl),

                        lower = logit(dat$incidence_lb[i] / totl),

                        upper = logit(dat$incidence_ub[i] / totl))

    }

    mc_incidence <- expit(rsn(n = nmc, xi = logit(dat$incidence_point[i] / totl),

                    omega = fit_incidence[1], alpha = fit_incidence[2])) * totl

}

temp <- (c(quantile(mc_incidence, c(0.025, 0.975)) - c(dat$incidence_lb[i], dat$incidence_ub[i]))) /
totl


if (i %in% c(vascular_index, infection_index, cancer_index)) {

    fit_misrate <- snest(logit(dat$misrate_point[i]),

                    lower = logit(dat$misrate_lb[i]),

                    upper = logit(dat$misrate_ub[i]))

    while(fit_misrate[3] > 10^(-10)) {

        fit_misrate <- snest(logit(dat$misrate_point[i]),

                        lower = logit(dat$misrate_lb[i]),

                        upper = logit(dat$misrate_ub[i]))

    }


    mc_misrate <- expit(rsn(n = nmc, xi = logit(dat$misrate_point[i]),

                    omega = fit_misrate[1], alpha = fit_misrate[2]))

    temp <- c(temp, quantile(mc_misrate, c(0.025, 0.975)) - c(dat$misrate_lb[i], dat$misrate_ub[i]))


    mc_result[[i]]$fit_misrate <- fit_misrate

    mc_result[[i]]$mc_misrate <- mc_misrate

} else {

    temp <- c(temp, rep(NA, 2))

}
```

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```r
    fit_peh <- snest(logit(dat$peharmrate_point[i]),

                lower = logit(dat$peharmrate_lb[i]),

                upper = logit(dat$peharmrate_ub[i]))

    while(fit_peh[3] > 10^(-10)) {

        fit_peh <- snest(logit(dat$peharmrate_point[i]),

                    lower = logit(dat$peharmrate_lb[i]),

                    upper = logit(dat$peharmrate_ub[i]))

    }

    mc_peh <- expit(rsn(n = nmc, xi = logit(dat$peharmrate_point[i]),

                omega = fit_peh[1], alpha = fit_peh[2]))

    temp <- c(temp, quantile(mc_peh, c(0.025, 0.975)) - c(dat$peharmrate_lb[i], dat$peharmrate_ub[i]))


    numerical_error <- rbind(numerical_error, temp)


    mc_result[[i]]$fit_incidence <- fit_incidence

    mc_result[[i]]$mc_incidence <- mc_incidence


    mc_result[[i]]$fit_peh <- fit_peh

    mc_result[[i]]$mc_peh <- mc_peh

    mc_result[[i]]$numerical_error <- numerical_error

}


summary(numerical_error)


# calculate plausible intervals for "OTHER" vascular/infection/censor harm rate (misrate)

# because point estimate is calculated as weighted sum and plausible intervals should be calcualted accordingly

temp1 <- 0
```

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```r
temp2 <- 0

for (i in vascular_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

mc_result[[vascular_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[vascular_other_index] <- quantile(mc_result[[vascular_other_index]]$mc_misrate,
0.025)

dat$misrate_ub[vascular_other_index] <- quantile(mc_result[[vascular_other_index]]$mc_misrate,
0.975)



temp1 <- 0

temp2 <- 0

for (i in infection_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

mc_result[[infection_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[infection_other_index] <- quantile(mc_result[[infection_other_index]]$mc_misrate,
0.025)

dat$misrate_ub[infection_other_index] <- quantile(mc_result[[infection_other_index]]$mc_misrate,
0.975)



temp1 <- 0

temp2 <- 0

for (i in cancer_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}
```

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```
mc_result[[cancer_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[cancer_other_index] <- quantile(mc_result[[cancer_other_index]]$mc_misrate, 0.025)

dat$misrate_ub[cancer_other_index] <- quantile(mc_result[[cancer_other_index]]$mc_misrate, 0.975)




# calculate plausible intervals for number of errors, number of harms and harm rate

# based on Monte Carlo generated data

for (i in 1:nrow(dat)) {

    mc_incidence <- mc_result[[i]]$mc_incidence

    mc_misrate <- mc_result[[i]]$mc_misrate

    mc_peh <- mc_result[[i]]$mc_peh

    dat$nerror_lb[i] <- quantile(mc_incidence * mc_misrate, 0.025)

    dat$nerror_ub[i] <- quantile(mc_incidence * mc_misrate, 0.975)


    dat$nharm_lb[i] <- quantile(mc_incidence * mc_misrate * mc_peh, 0.025)

    dat$nharm_ub[i] <- quantile(mc_incidence * mc_misrate * mc_peh, 0.975)


    dat$harmrate_lb[i] <- quantile(mc_misrate * mc_peh, 0.025)

    dat$harmrate_ub[i] <- quantile(mc_misrate * mc_peh, 0.975)

}


# calculate subtotals and plausible intervals

# create structure for subtotals

temp <- c("Top 5 Vascular Subtotal",

    "Top 5 Infection Subtotal",

    "Top 5 Cancer Subtotal",

    "Top 15 Subtotal",

    "Total Vascular",
```

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```
      "Total Infection",

      "Total Cancer",

      "Big 3 Subtotal",

      "All Other Dx Errors",

      "Grand Total")

temp2 <- data.frame(matrix(NA, nrow = length(temp), ncol = ncol(dat)))

colnames(temp2) <- colnames(dat)

temp2[, 2] <- temp

temp2[, 1] <- rep("Subtotals", length(temp))

dat <- rbind(dat, temp2)


dat[, -c(1:2)] <- apply(dat[, -c(1:2)], c(1, 2), as.numeric)


# calculate subtotal incidence

dat$incidence_point[19] <- sum(dat$incidence_point[1:5])

dat$incidence_point[20] <- sum(dat$incidence_point[7:11])

dat$incidence_point[21] <- sum(dat$incidence_point[13:17])

dat$incidence_point[22] <- sum(dat$incidence_point[19:21])


dat$incidence_point[23] <- sum(dat$incidence_point[1:6])

dat$incidence_point[24] <- sum(dat$incidence_point[7:12])

dat$incidence_point[25] <- sum(dat$incidence_point[13:18])

dat$incidence_point[26] <- sum(dat$incidence_point[1:18])


temp <-lapply(1:18, function(i) return(mc_result[[i]]$mc_incidence))


temp1 <- rep(0, nmc)

for (i in 1:5) {
```

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```
    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[19] <- quantile(temp1, 0.025)

dat$incidence_ub[19] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[20] <- quantile(temp1, 0.025)

dat$incidence_ub[20] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)

for (i in 13:17) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[21] <- quantile(temp1, 0.025)

dat$incidence_ub[21] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[22] <- quantile(temp1, 0.025)

dat$incidence_ub[22] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)
```

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```
for (i in 1:6) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[23] <- quantile(temp1, 0.025)

dat$incidence_ub[23] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[24] <- quantile(temp1, 0.025)

dat$incidence_ub[24] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[25] <- quantile(temp1, 0.025)

dat$incidence_ub[25] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[26] <- quantile(temp1, 0.025)

dat$incidence_ub[26] <- quantile(temp1, 0.975)
```

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```
dat[27:28, 3:5] <- NA


# calculate subtotal number of errors

dat$nerror[19] <- sum(dat$nerror[1:5])

dat$nerror[20] <- sum(dat$nerror[7:11])

dat$nerror[21] <- sum(dat$nerror[13:17])

dat$nerror[22] <- sum(dat$nerror[19:21])


dat$nerror[23] <- sum(dat$nerror[1:6])

dat$nerror[24] <- sum(dat$nerror[7:12])

dat$nerror[25] <- sum(dat$nerror[13:18])

dat$nerror[26] <- sum(dat$nerror[1:18])


dat$nerror[27] <- dat$nerror[26] / perror_big3 * (1 - perror_big3)

dat$nerror[28] <- dat$nerror[26] / perror_big3




temp1 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[19] <- quantile(temp1, 0.025)

dat$nerror_ub[19] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
```

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```
}
dat$nerror_lb[20] <- quantile(temp1, 0.025)
dat$nerror_ub[20] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)
for (i in 13:17) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
}
dat$nerror_lb[21] <- quantile(temp1, 0.025)
dat$nerror_ub[21] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)
for (i in c(1:5, 7:11, 13:17)) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
}
dat$nerror_lb[22] <- quantile(temp1, 0.025)
dat$nerror_ub[22] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)
for (i in 1:6) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
}
dat$nerror_lb[23] <- quantile(temp1, 0.025)
dat$nerror_ub[23] <- quantile(temp1, 0.975)



temp1 <- rep(0, nmc)
```

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```
for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[24] <- quantile(temp1, 0.025)

dat$nerror_ub[24] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[25] <- quantile(temp1, 0.025)

dat$nerror_ub[25] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[26] <- quantile(temp1, 0.025)

dat$nerror_ub[26] <- quantile(temp1, 0.975)


dat$nerror_lb[27] <- quantile(temp1 / perror_big3 * (1 - perror_big3), 0.025)

dat$nerror_ub[27] <- quantile(temp1 / perror_big3 * (1 - perror_big3), 0.975)


dat$nerror_lb[28] <- quantile(temp1 / perror_big3, 0.025)

dat$nerror_ub[28] <- quantile(temp1 / perror_big3, 0.975)
```

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```
# calculate subtotal misrate

dat$misrate_point[19:28] <- dat$nerror[19:28] / dat$incidence_point[19:28]


temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[19] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[19] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[20] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[20] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 13:17) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}
```

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```
dat$misrate_lb[21] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[21] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[22] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[22] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[23] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[23] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence
```

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```r
}
dat$misrate_lb[24] <- quantile(temp1 / temp2, 0.025)
dat$misrate_ub[24] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)
temp2 <- rep(0, nmc)
for (i in 13:18) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
    temp2 <- temp2 + mc_result[[i]]$mc_incidence
}
dat$misrate_lb[25] <- quantile(temp1 / temp2, 0.025)
dat$misrate_ub[25] <- quantile(temp1 / temp2, 0.975)



temp1 <- rep(0, nmc)
temp2 <- rep(0, nmc)
for (i in 1:18) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
    temp2 <- temp2 + mc_result[[i]]$mc_incidence
}
dat$misrate_lb[26] <- quantile(temp1 / temp2, 0.025)
dat$misrate_ub[26] <- quantile(temp1 / temp2, 0.975)



# calculate subtotal nharm, peh, and harm rate
dat$nharm_point[19] <- sum(dat$nharm_point[1:5])
dat$nharm_point[20] <- sum(dat$nharm_point[7:11])
```

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```r
dat$nharm_point[21] <- sum(dat$nharm_point[13:17])

dat$nharm_point[22] <- sum(dat$nharm_point[19:21])


dat$nharm_point[23] <- sum(dat$nharm_point[1:6])

dat$nharm_point[24] <- sum(dat$nharm_point[7:12])

dat$nharm_point[25] <- sum(dat$nharm_point[13:18])

dat$nharm_point[26] <- sum(dat$nharm_point[1:18])


dat$nharm_point[27] <- dat$nharm_point[26] / pharm_big3 * (1 - pharm_big3)

dat$nharm_point[28] <- dat$nharm_point[26] / pharm_big3



dat$harmrate_point[19:28] <- dat$nharm_point[19:28] / dat$incidence_point[19:28]

dat$peharmrate_point[19:28] <- dat$nharm_point[19:28] / dat$nerror[19:28]



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[19] <- quantile(temp3, 0.025)

dat$nharm_ub[19] <- quantile(temp3, 0.975)


dat$harmrate_lb[19] <- quantile(temp3 / temp1, 0.025)
```

Supplementary Materials (Supplemental File #2)   *Page **18** of **48***

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```
dat$harmrate_ub[19] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[19] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[19] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[20] <- quantile(temp3, 0.025)

dat$nharm_ub[20] <- quantile(temp3, 0.975)


dat$harmrate_lb[20] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[20] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[20] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[20] <- quantile(temp3 / temp2, 0.975)
```

Supplementary Materials (Supplemental File #2)

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```
temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 13:17) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[21] <- quantile(temp3, 0.025)

dat$nharm_ub[21] <- quantile(temp3, 0.975)


dat$harmrate_lb[21] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[21] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[21] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[21] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh
```

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```
}


dat$nharm_lb[22] <- quantile(temp3, 0.025)

dat$nharm_ub[22] <- quantile(temp3, 0.975)


dat$harmrate_lb[22] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[22] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[22] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[22] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[23] <- quantile(temp3, 0.025)

dat$nharm_ub[23] <- quantile(temp3, 0.975)


dat$harmrate_lb[23] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[23] <- quantile(temp3 / temp1, 0.975)
```

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```
dat$peharmrate_lb[23] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[23] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[24] <- quantile(temp3, 0.025)

dat$nharm_ub[24] <- quantile(temp3, 0.975)


dat$harmrate_lb[24] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[24] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[24] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[24] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)
```

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```
temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[25] <- quantile(temp3, 0.025)

dat$nharm_ub[25] <- quantile(temp3, 0.975)


dat$harmrate_lb[25] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[25] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[25] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[25] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}
```

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```
dat$nharm_lb[26] <- quantile(temp3, 0.025)

dat$nharm_ub[26] <- quantile(temp3, 0.975)


dat$harmrate_lb[26] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[26] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[26] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[26] <- quantile(temp3 / temp2, 0.975)



dat$nharm_lb[27] <- quantile(temp3 / pharm_big3 * (1 - pharm_big3), 0.025)

dat$nharm_ub[27] <- quantile(temp3 / pharm_big3 * (1 - pharm_big3), 0.975)


dat$nharm_lb[28] <- quantile(temp3 / pharm_big3, 0.025)

dat$nharm_ub[28] <- quantile(temp3 / pharm_big3, 0.975)



dat$peharmrate_lb[27] <- quantile((temp3 / pharm_big3 * (1 - pharm_big3)) /

                    (temp2 / perror_big3 * (1 - perror_big3)), 0.025)

dat$peharmrate_ub[27] <- quantile((temp3 / pharm_big3 * (1 - pharm_big3)) /

                    (temp2 / perror_big3 * (1 - perror_big3)), 0.975)


dat$peharmrate_lb[28] <- quantile((temp3 / pharm_big3) / (temp2 / perror_big3), 0.025)

dat$peharmrate_ub[28] <- quantile((temp3 / pharm_big3) / (temp2 / perror_big3), 0.975)


dat$weight <- dat$peharmrate_point / peh_general

dat <- dat[, c(1:2, 9:10, 23, 3:5,

        6:8, 12:14, 20:22,

        11, 15, 16, 17:19)]
```

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```
all(dat$misrate_lb < dat$misrate_point, na.rm = T)

all(dat$misrate_ub > dat$misrate_point, na.rm = T)

all(dat$harmrate_lb < dat$harmrate_point, na.rm = T)

all(dat$harmrate_ub > dat$harmrate_point, na.rm = T)

all(dat$nharm_lb < dat$nharm_point, na.rm = T)

all(dat$nharm_ub > dat$nharm_point, na.rm = T)

all(dat$nerror_lb < dat$nerror, na.rm = T)

all(dat$nerror_ub > dat$nerror, na.rm = T)


write.csv(dat, file = "big3_results_dx1_updated.csv")




#### secondary analysis  ####

dat <- read.csv(file = "big3_data_combo.csv")

set.seed(37)

peh_general <- 374/1216 # general per-error-harm rate

peh_general_se <- sqrt(1/374 + 1/(1216-374)) # standard error on logit scale

peh_general_lower <- expit(logit(peh_general) + qnorm(0.025) * peh_general_se)

peh_general_upper <- expit(logit(peh_general) + qnorm(0.975) * peh_general_se)


perror_big3 <- 717 / (717 + 509) # big 3 error rate

pharm_big3 <- 157 / 207 # harm rate


vascular_index <- which(dat$category == "vascular" & dat$disease != "OTHER Vascular")

vascular_other_index <- which(dat$disease == "OTHER Vascular")

infection_index <- which(dat$category == "infection" & dat$disease != "OTHER Infection")
```

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```
infection_other_index <- which(dat$disease == "OTHER Infection")

cancer_index <- which(dat$category == "cancer" & dat$disease != "OTHER Cancer")

cancer_other_index <- which(dat$disease == "OTHER Cancer")


dat$nerror <- dat$incidence_point * dat$misrate_point

shp <- dat$proportion_highharm # severity harm proportion


peh_fun <- function(peh_general, nerror) {
 # function to calculate disease-specific per-error-harm rates
    peh_rate <- rep(NA, nrow(dat))
    peh_rate[c(vascular_index, infection_index, cancer_index)] <- peh_general * pharm_big3 /
perror_big3 *
        (sum(nerror) * shp[c(vascular_index, infection_index, cancer_index)]) /
        (sum(nerror[vascular_index] * shp[vascular_index]) * 1684 / 1344 +
            sum(nerror[infection_index] * shp[infection_index]) * 992 / 600 +
            sum(nerror[cancer_index] * shp[cancer_index]) * 2793 / 1529)
    peh_rate[vascular_other_index] <- sum(nerror[vascular_index] * peh_rate[vascular_index] *
334/1334) /
        nerror[vascular_other_index]
    peh_rate[infection_other_index] <- sum(nerror[infection_index] * peh_rate[infection_index] *
392/600) /
        nerror[infection_other_index]
    peh_rate[cancer_other_index] <- sum(nerror[cancer_index] * peh_rate[cancer_index] * 1264/1529)
/
        nerror[cancer_other_index]
    return(peh_rate)
}


# point estimate of per-error-serious harm rates

dat$peharmrate_point <- peh_fun(peh_general, dat$nerror)
```

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```
dat$peharmrate_lb <- peh_fun(peh_general_lower, dat$nerror)

dat$peharmrate_ub <- peh_fun(peh_general_upper, dat$nerror)


# Monte Carlo simulation, to construct plausible intervals for harm rate and number of harm

snest <- function(u, lower, upper, lowerq = 0.025, upperq = 0.975) {

    solfun <- function(beta) {

        omega <- beta[1]

        alpha <- beta[2]

        out1 <- psn(lower, xi = u, omega = omega, alpha = alpha) - lowerq

        out2 <- psn(upper, xi = u, omega = omega, alpha = alpha) - upperq

        return((out1^2+out2^2))

    }

    start <- c(((upper-lower)/4)^2, 0) + mvrnorm(100, mu = rep(0, 2), Sigma = diag(1, 2))

    start[, 1] <- abs(start[, 1])

    tempfit <- t(apply(start, 1, function(x) {

        fit <- optim(fn = solfun, par = x,

                control = list(maxit = 500000))

        return(c(fit$par, fit$value))

    }))

    tempfit <- tempfit[complete.cases(tempfit), ]

    return(tempfit[which(tempfit[, 3] == min(tempfit[, 3]))[1], 1:3])

}


totl <- 316283434

nmc <- 1*(10^7)

numerical_error <- NULL

dat$nerror_lb <- NA

dat$nerror_ub <- NA

dat$nharm_point <- dat$nerror * dat$peharmrate_point
```

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```
dat$nharm_lb <- NA

dat$nharm_ub <- NA

dat$harmrate_point <- dat$misrate_point * dat$peharmrate_point

dat$harmrate_lb <- NA

dat$harmrate_ub <- NA


# Monte Carlo simulation based on skew-normal estimation

mc_result <- list()

for (i in 1:nrow(dat)) {

    mc_result[[i]] <- list()

    if (dat$incidence_lb[i] == dat$incidence_ub[i]) {

        mc_incidence <- rep(dat$incidence_point[i], nmc)

    } else {

        fit_incidence <- snest(logit(dat$incidence_point[i] / totl),

                        lower = logit(dat$incidence_lb[i] / totl),

                        upper = logit(dat$incidence_ub[i] / totl))

        while(fit_incidence[3] > 10^(-10)) {

            fit_incidence <- snest(logit(dat$incidence_point[i] / totl),

                            lower = logit(dat$incidence_lb[i] / totl),

                            upper = logit(dat$incidence_ub[i] / totl))

        }

        mc_incidence <- expit(rsn(n = nmc, xi = logit(dat$incidence_point[i] / totl),

                            omega = fit_incidence[1], alpha = fit_incidence[2])) * totl

    }

    temp <- (c(quantile(mc_incidence, c(0.025, 0.975)) - c(dat$incidence_lb[i], dat$incidence_ub[i]))) /
totl


    if (i %in% c(vascular_index, infection_index, cancer_index)) {

        fit_misrate <- snest(logit(dat$misrate_point[i]),
```

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```
                    lower = logit(dat$misrate_lb[i]),

                    upper = logit(dat$misrate_ub[i]))

     while(fit_misrate[3] > 10^(-10)) {

         fit_misrate <- snest(logit(dat$misrate_point[i]),

                     lower = logit(dat$misrate_lb[i]),

                     upper = logit(dat$misrate_ub[i]))

     }


     mc_misrate <- expit(rsn(n = nmc, xi = logit(dat$misrate_point[i]),

                     omega = fit_misrate[1], alpha = fit_misrate[2]))

     temp <- c(temp, quantile(mc_misrate, c(0.025, 0.975)) - c(dat$misrate_lb[i], dat$misrate_ub[i]))


     mc_result[[i]]$fit_misrate <- fit_misrate

     mc_result[[i]]$mc_misrate <- mc_misrate

  } else {

     temp <- c(temp, rep(NA, 2))

  }


  fit_peh <- snest(logit(dat$peharmrate_point[i]),

         lower = logit(dat$peharmrate_lb[i]),

         upper = logit(dat$peharmrate_ub[i]))

  while(fit_peh[3] > 10^(-10)) {

     fit_peh <- snest(logit(dat$peharmrate_point[i]),

            lower = logit(dat$peharmrate_lb[i]),

            upper = logit(dat$peharmrate_ub[i]))

  }

  mc_peh <- expit(rsn(n = nmc, xi = logit(dat$peharmrate_point[i]),

         omega = fit_peh[1], alpha = fit_peh[2]))

  temp <- c(temp, quantile(mc_peh, c(0.025, 0.975)) - c(dat$peharmrate_lb[i], dat$peharmrate_ub[i]))
```

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```
    numerical_error <- rbind(numerical_error, temp)


    mc_result[[i]]$fit_incidence <- fit_incidence

    mc_result[[i]]$mc_incidence <- mc_incidence


    mc_result[[i]]$fit_peh <- fit_peh

    mc_result[[i]]$mc_peh <- mc_peh

    mc_result[[i]]$numerical_error <- numerical_error

}

summary(numerical_error) # 10e-5



# calculate plausible intervals for "OTHER" vascular/infection/censor harm rate (misrate)

# because point estimate is calculated as weighted sum and plausible intervals should be calcualted
accordingly

temp1 <- 0

temp2 <- 0

for (i in vascular_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

mc_result[[vascular_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[vascular_other_index] <- quantile(mc_result[[vascular_other_index]]$mc_misrate,
0.025)

dat$misrate_ub[vascular_other_index] <- quantile(mc_result[[vascular_other_index]]$mc_misrate,
0.975)



temp1 <- 0

temp2 <- 0
```

Burden of Serious Harms from Diagnostic Error in the USA   *Newman-Toker et al., BMJQS 2023*

```
for (i in infection_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

mc_result[[infection_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[infection_other_index] <- quantile(mc_result[[infection_other_index]]$mc_misrate,
0.025)

dat$misrate_ub[infection_other_index] <- quantile(mc_result[[infection_other_index]]$mc_misrate,
0.975)


temp1 <- 0

temp2 <- 0

for (i in cancer_index) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

mc_result[[cancer_other_index]]$mc_misrate <- temp1 / temp2

dat$misrate_lb[cancer_other_index] <- quantile(mc_result[[cancer_other_index]]$mc_misrate, 0.025)

dat$misrate_ub[cancer_other_index] <- quantile(mc_result[[cancer_other_index]]$mc_misrate, 0.975)




# calculate plausible intervals for number of errors, number of harms and harm rate

# based on Monte Carlo generated data

for (i in 1:nrow(dat)) {

    mc_incidence <- mc_result[[i]]$mc_incidence

    mc_misrate <- mc_result[[i]]$mc_misrate

    mc_peh <- mc_result[[i]]$mc_peh

    dat$nerror_lb[i] <- quantile(mc_incidence * mc_misrate, 0.025)
```

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```r
    dat$nerror_ub[i] <- quantile(mc_incidence * mc_misrate, 0.975)


    dat$nharm_lb[i] <- quantile(mc_incidence * mc_misrate * mc_peh, 0.025)

    dat$nharm_ub[i] <- quantile(mc_incidence * mc_misrate * mc_peh, 0.975)


    dat$harmrate_lb[i] <- quantile(mc_misrate * mc_peh, 0.025)

    dat$harmrate_ub[i] <- quantile(mc_misrate * mc_peh, 0.975)

}


# calculate subtotals and plausible intervals
# create structure for subtotals
temp <- c("Top 5 Vascular Subtotal",

      "Top 5 Infection Subtotal",

      "Top 5 Cancer Subtotal",

      "Top 15 Subtotal",

      "Total Vascular",

      "Total Infection",

      "Total Cancer",

      "Big 3 Subtotal",

      "All Other Dx Errors",

      "Grand Total")

temp2 <- data.frame(matrix(NA, nrow = length(temp), ncol = ncol(dat)))

colnames(temp2) <- colnames(dat)

temp2[, 2] <- temp

temp2[, 1] <- rep("Subtotals", length(temp))

dat <- rbind(dat, temp2)


dat[, -c(1:2)] <- apply(dat[, -c(1:2)], c(1, 2), as.numeric)
```

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```
# calculate subtotal incidence

dat$incidence_point[19] <- sum(dat$incidence_point[1:5])

dat$incidence_point[20] <- sum(dat$incidence_point[7:11])

dat$incidence_point[21] <- sum(dat$incidence_point[13:17])

dat$incidence_point[22] <- sum(dat$incidence_point[19:21])


dat$incidence_point[23] <- sum(dat$incidence_point[1:6])

dat$incidence_point[24] <- sum(dat$incidence_point[7:12])

dat$incidence_point[25] <- sum(dat$incidence_point[13:18])

dat$incidence_point[26] <- sum(dat$incidence_point[1:18])



temp <-lapply(1:18, function(i) return(mc_result[[i]]$mc_incidence))


temp1 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[19] <- quantile(temp1, 0.025)

dat$incidence_ub[19] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[20] <- quantile(temp1, 0.025)

dat$incidence_ub[20] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)
```

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```
for (i in 13:17) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[21] <- quantile(temp1, 0.025)

dat$incidence_ub[21] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[22] <- quantile(temp1, 0.025)

dat$incidence_ub[22] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[23] <- quantile(temp1, 0.025)

dat$incidence_ub[23] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[24] <- quantile(temp1, 0.025)

dat$incidence_ub[24] <- quantile(temp1, 0.975)
```

Burden of Serious Harms from Diagnostic Error in the USA   *Newman-Toker et al., BMJQS 2023*

```
temp1 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[25] <- quantile(temp1, 0.025)

dat$incidence_ub[25] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + temp[[i]]

}

dat$incidence_lb[26] <- quantile(temp1, 0.025)

dat$incidence_ub[26] <- quantile(temp1, 0.975)


dat[27:28, 3:5] <- NA


# calculate subtotal number of errors

dat$nerror[19] <- sum(dat$nerror[1:5])

dat$nerror[20] <- sum(dat$nerror[7:11])

dat$nerror[21] <- sum(dat$nerror[13:17])

dat$nerror[22] <- sum(dat$nerror[19:21])


dat$nerror[23] <- sum(dat$nerror[1:6])

dat$nerror[24] <- sum(dat$nerror[7:12])

dat$nerror[25] <- sum(dat$nerror[13:18])

dat$nerror[26] <- sum(dat$nerror[1:18])
```

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```
dat$nerror[27] <- dat$nerror[26] / perror_big3 * (1 - perror_big3)

dat$nerror[28] <- dat$nerror[26] / perror_big3




temp1 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[19] <- quantile(temp1, 0.025)

dat$nerror_ub[19] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[20] <- quantile(temp1, 0.025)

dat$nerror_ub[20] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 13:17) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[21] <- quantile(temp1, 0.025)

dat$nerror_ub[21] <- quantile(temp1, 0.975)


temp1 <- rep(0, nmc)
```

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```
for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[22] <- quantile(temp1, 0.025)

dat$nerror_ub[22] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[23] <- quantile(temp1, 0.025)

dat$nerror_ub[23] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[24] <- quantile(temp1, 0.025)

dat$nerror_ub[24] <- quantile(temp1, 0.975)




temp1 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[25] <- quantile(temp1, 0.025)

dat$nerror_ub[25] <- quantile(temp1, 0.975)
```

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```r
temp1 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

}

dat$nerror_lb[26] <- quantile(temp1, 0.025)

dat$nerror_ub[26] <- quantile(temp1, 0.975)


dat$nerror_lb[27] <- quantile(temp1 / perror_big3 * (1 - perror_big3), 0.025)

dat$nerror_ub[27] <- quantile(temp1 / perror_big3 * (1 - perror_big3), 0.975)


dat$nerror_lb[28] <- quantile(temp1 / perror_big3, 0.025)

dat$nerror_ub[28] <- quantile(temp1 / perror_big3, 0.975)




# calculate subtotal misrate

dat$misrate_point[19:28] <- dat$nerror[19:28] / dat$incidence_point[19:28]


temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[19] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[19] <- quantile(temp1 / temp2, 0.975)
```

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```
temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[20] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[20] <- quantile(temp1 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 13:17) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[21] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[21] <- quantile(temp1 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[22] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[22] <- quantile(temp1 / temp2, 0.975)
```

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```
temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[23] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[23] <- quantile(temp1 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[24] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[24] <- quantile(temp1 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[25] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[25] <- quantile(temp1 / temp2, 0.975)
```

```
temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

for (i in 1:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp2 <- temp2 + mc_result[[i]]$mc_incidence

}

dat$misrate_lb[26] <- quantile(temp1 / temp2, 0.025)

dat$misrate_ub[26] <- quantile(temp1 / temp2, 0.975)



# calculate subtotal nharm, peh, and harm rate

dat$nharm_point[19] <- sum(dat$nharm_point[1:5])

dat$nharm_point[20] <- sum(dat$nharm_point[7:11])

dat$nharm_point[21] <- sum(dat$nharm_point[13:17])

dat$nharm_point[22] <- sum(dat$nharm_point[19:21])


dat$nharm_point[23] <- sum(dat$nharm_point[1:6])

dat$nharm_point[24] <- sum(dat$nharm_point[7:12])

dat$nharm_point[25] <- sum(dat$nharm_point[13:18])

dat$nharm_point[26] <- sum(dat$nharm_point[1:18])


dat$nharm_point[27] <- dat$nharm_point[26] / pharm_big3 * (1 - pharm_big3)

dat$nharm_point[28] <- dat$nharm_point[26] / pharm_big3



dat$harmrate_point[19:28] <- dat$nharm_point[19:28] / dat$incidence_point[19:28]
```

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```
dat$peharmrate_point[19:28] <- dat$nharm_point[19:28] / dat$nerror[19:28]



temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 1:5) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}



dat$nharm_lb[19] <- quantile(temp3, 0.025)

dat$nharm_ub[19] <- quantile(temp3, 0.975)



dat$harmrate_lb[19] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[19] <- quantile(temp3 / temp1, 0.975)



dat$peharmrate_lb[19] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[19] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 7:11) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence
```

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```
        temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

        temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[20] <- quantile(temp3, 0.025)

dat$nharm_ub[20] <- quantile(temp3, 0.975)


dat$harmrate_lb[20] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[20] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[20] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[20] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 13:17) {

        temp1 <- temp1 + mc_result[[i]]$mc_incidence

        temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

        temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[21] <- quantile(temp3, 0.025)

dat$nharm_ub[21] <- quantile(temp3, 0.975)


dat$harmrate_lb[21] <- quantile(temp3 / temp1, 0.025)
```

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```r
dat$harmrate_ub[21] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[21] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[21] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in c(1:5, 7:11, 13:17)) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[22] <- quantile(temp3, 0.025)

dat$nharm_ub[22] <- quantile(temp3, 0.975)


dat$harmrate_lb[22] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[22] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[22] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[22] <- quantile(temp3 / temp2, 0.975)
```

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```r
temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 1:6) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[23] <- quantile(temp3, 0.025)

dat$nharm_ub[23] <- quantile(temp3, 0.975)


dat$harmrate_lb[23] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[23] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[23] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[23] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 7:12) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh
```

Burden of Serious Harms from Diagnostic Error in the USA   *Newman-Toker et al., BMJQS 2023*

```
}


dat$nharm_lb[24] <- quantile(temp3, 0.025)

dat$nharm_ub[24] <- quantile(temp3, 0.975)


dat$harmrate_lb[24] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[24] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[24] <- quantile(temp3 / temp2, 0.025)

dat$peharmrate_ub[24] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)

temp2 <- rep(0, nmc)

temp3 <- rep(0, nmc)

for (i in 13:18) {

    temp1 <- temp1 + mc_result[[i]]$mc_incidence

    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate

    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh

}


dat$nharm_lb[25] <- quantile(temp3, 0.025)

dat$nharm_ub[25] <- quantile(temp3, 0.975)


dat$harmrate_lb[25] <- quantile(temp3 / temp1, 0.025)

dat$harmrate_ub[25] <- quantile(temp3 / temp1, 0.975)
```

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```
dat$peharmrate_lb[25] <- quantile(temp3 / temp2, 0.025)
dat$peharmrate_ub[25] <- quantile(temp3 / temp2, 0.975)




temp1 <- rep(0, nmc)
temp2 <- rep(0, nmc)
temp3 <- rep(0, nmc)
for (i in 1:18) {
    temp1 <- temp1 + mc_result[[i]]$mc_incidence
    temp2 <- temp2 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate
    temp3 <- temp3 + mc_result[[i]]$mc_incidence * mc_result[[i]]$mc_misrate * mc_result[[i]]$mc_peh
}


dat$nharm_lb[26] <- quantile(temp3, 0.025)
dat$nharm_ub[26] <- quantile(temp3, 0.975)


dat$harmrate_lb[26] <- quantile(temp3 / temp1, 0.025)
dat$harmrate_ub[26] <- quantile(temp3 / temp1, 0.975)


dat$peharmrate_lb[26] <- quantile(temp3 / temp2, 0.025)
dat$peharmrate_ub[26] <- quantile(temp3 / temp2, 0.975)



dat$nharm_lb[27] <- quantile(temp3 / pharm_big3 * (1 - pharm_big3), 0.025)
dat$nharm_ub[27] <- quantile(temp3 / pharm_big3 * (1 - pharm_big3), 0.975)
```

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```
dat$nharm_lb[28] <- quantile(temp3 / pharm_big3, 0.025)

dat$nharm_ub[28] <- quantile(temp3 / pharm_big3, 0.975)



dat$peharmrate_lb[27] <- quantile((temp3 / pharm_big3 * (1 - pharm_big3)) /

                (temp2 / perror_big3 * (1 - perror_big3)), 0.025)

dat$peharmrate_ub[27] <- quantile((temp3 / pharm_big3 * (1 - pharm_big3)) /

                (temp2 / perror_big3 * (1 - perror_big3)), 0.975)



dat$peharmrate_lb[28] <- quantile((temp3 / pharm_big3) / (temp2 / perror_big3), 0.025)

dat$peharmrate_ub[28] <- quantile((temp3 / pharm_big3) / (temp2 / perror_big3), 0.975)



dat$weight <- dat$peharmrate_point / peh_general

dat <- dat[, c(1:2, 9:10, 23, 3:5,

        6:8, 12:14, 20:22,

        11, 15, 16, 17:19)]



all(dat$misrate_lb < dat$misrate_point, na.rm = T)

all(dat$misrate_ub > dat$misrate_point, na.rm = T)

all(dat$harmrate_lb < dat$harmrate_point, na.rm = T)

all(dat$harmrate_ub > dat$harmrate_point, na.rm = T)

all(dat$nharm_lb < dat$nharm_point, na.rm = T)

all(dat$nharm_ub > dat$nharm_point, na.rm = T)

all(dat$nerror_lb < dat$nerror, na.rm = T)

all(dat$nerror_ub > dat$nerror, na.rm = T)



write.csv(dat, file = "big3_results_combo_updated.csv")
```