

# Evaluation of Energy Intake from BXD Datasets

Dave Bridges

January 19, 2022

## Contents

<b>Analysis</b>	<b>2</b>
Comparason of Datasets . . . . .	2
Adjusting for Lean Mass . . . . .	3
Adaptive Thermogenesis . . . . .	8
<b>Session Information</b>	<b>11</b>

The goal is to identify genetic determinants of energy expenditure and of adaptive thermogenesis from BXD mice. To start we searched gene network for energy expenditure data, ignoring those involved in exercise physiology.

- **BXD\_17621** Oxygen intake over 24h on NCD at 16 w age. Also included light/dark. Not adjusted for lean mass. Has mean +/- SE in mL/kg/h. From Prinen 2014 (<https://doi.org/10.1016/j.cmet.2014.04.002>)
- **BXD\_17618** Oxygen intake over 24h at 16 w age on HFD?, males. Not adjusted for lean mass. Has mean +/- SE in mL/kg/h. From Williams (2016). Body weight in BXD\_17559, lean mass in BXD\_17573
- **BXD\_17622** Oxygen intake over 24h at 16 w age on HFD?, males. Not adjusted for lean mass. Has mean +/- SE in mL/kg/h. From Williams (2016). Body weight in BXD\_17560, lean mass in BXD\_17574

```
library(readr)
ncd.pirinen <- read_csv("BXD_17621.csv", skip=9) %>%
  mutate(Diet="NCD",Age=16,Dataset="Prinen")

williams.ncd.ee <- read_csv("BXD_17622.csv", skip=9)%>% #may be mislabelled on genenetwork, assigned ba
  mutate(Diet="NCD",Age=16,Dataset="Williams")
williams.ncd.bw <- read_csv("BXD_17559.csv" , skip=9)%>%
  mutate(Diet="NCD",Age=16,Dataset="Williams")
williams.ncd.lm <- read_csv("BXD_17573.csv" , skip=9)%>%
  mutate(Diet="NCD",Age=16,Dataset="Williams")

williams.ncd <- full_join(williams.ncd.ee,williams.ncd.bw, suffix=c('_ee','_bw'), by=c("Name","Dataset")
  full_join(williams.ncd.lm) %>%
  mutate(Value_lm = Value,
         SE_lm = SE)

williams.hfd.ee <- read_csv("BXD_17618.csv" , skip=9)%>% #may be mislabelled on genenetwork
  mutate(Diet="HFD",Age=16,Dataset="Williams")
williams.hfd.bw <- read_csv("BXD_17560.csv", skip=9)%>%
  mutate(Diet="HFD",Age=16,Dataset="Williams")
```

```

williams.hfd.lm <- read_csv("BXD_17574.csv", skip=9)%>%
  mutate(Diet="HFD",Age=16,Dataset="Williams")

williams.hfd <- full_join(williams.hfd.ee,williams.hfd.bw, suffix=c('_ee','_bw'), by=c("Name","Dataset"))
  full_join(williams.hfd.lm) %>%
  mutate(Value_lm = Value,
         SE_lm = SE)

data <- bind_rows(#ncd.pirinen,
                  williams.ncd,
                  williams.hfd) %>% # in mL/kg/h
  mutate(VO2_g_min = Value_ee/1000) %>% #in mL/g/h
  mutate(VO2_min = VO2_g_min*Value_bw/60) %>% # in mL/min #this seems reasonable
  mutate(MR_KJ_d = VO2_min * 60 * 24 / 1000 * 4.84 * 4.184,
         MR_KJ_d_SE = SE_ee/1000*Value_bw/60* 60 * 24 / 1000 * 4.84 * 4.184) %>% # 60min/h x 24h/day /
  mutate(MR_W = MR_KJ_d * 0.0115740741,
         MR_W_SE = MR_KJ_d_SE* 0.0115740741) %>% # in Watts
  mutate(Diet = relevel(factor(Diet), ref="NCD"))

```

These data can be found in /Users/davebrid/Documents/GitHub/TissueSpecificTscKnockouts/Other Published Data/Systems Biology. This script was most recently updated on Wed Jan 19 13:30:30 2022.

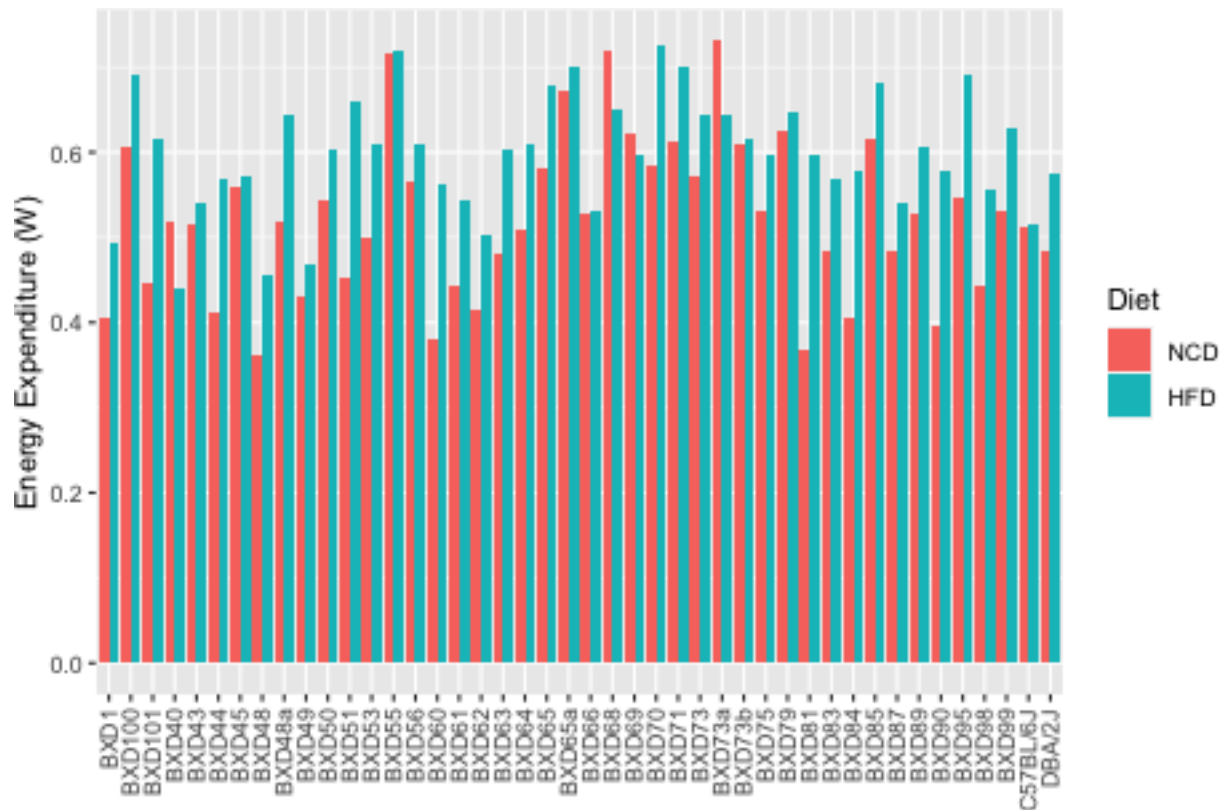
## Analysis

### Comparason of Datasets

```

library(ggplot2)
data %>%
  filter(!(is.na(MR_W))) %>% # complete cases only
  ggplot(aes(y=MR_W,
            x=Name,
            ymin=MR_W-MR_W_SE,
            ymax=MR_W+MR_W_SE,
            fill=Diet)) +
  geom_bar(stat='identity',position='dodge') +
  labs(y="Energy Expenditure (W)",
       x="") +
  theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))

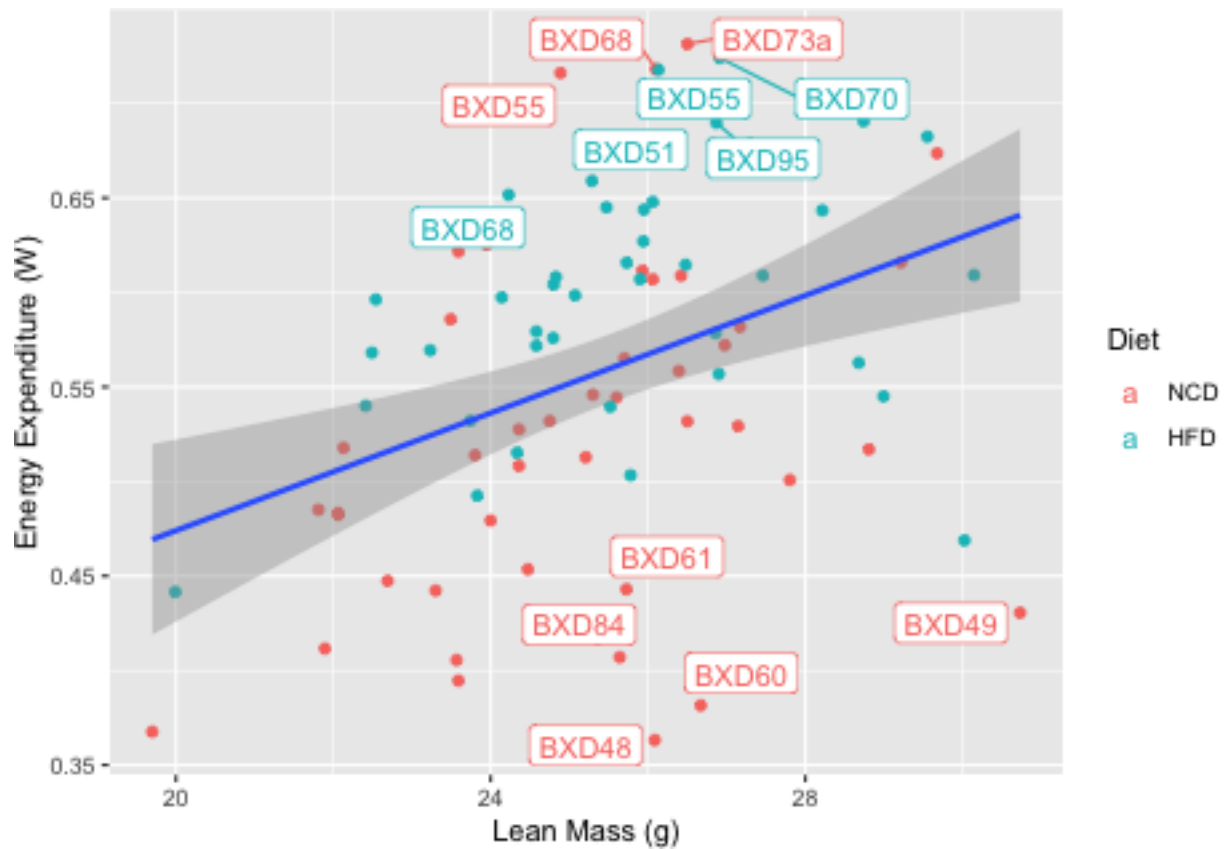
```



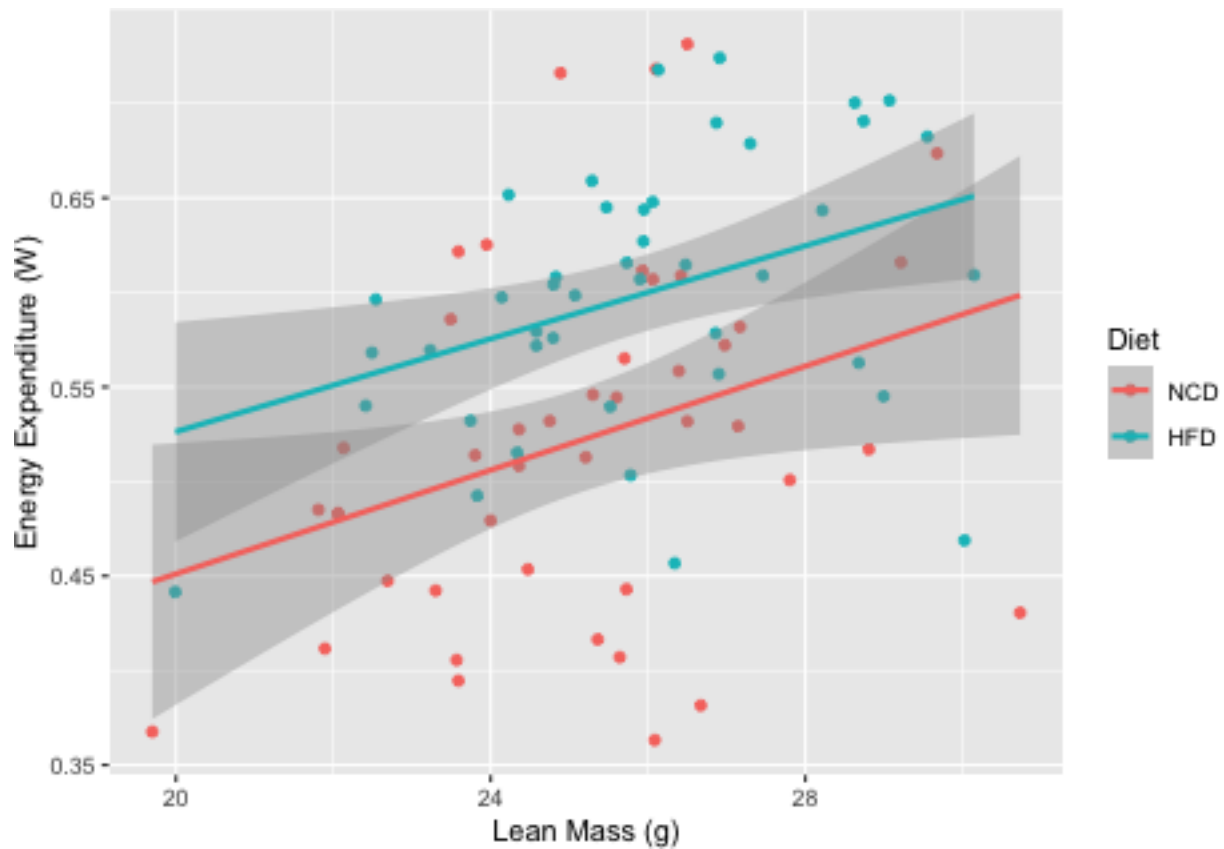
```
#lm(Value~Name+Diet,data=data) %>% summary
```

## Adjusting for Lean Mass

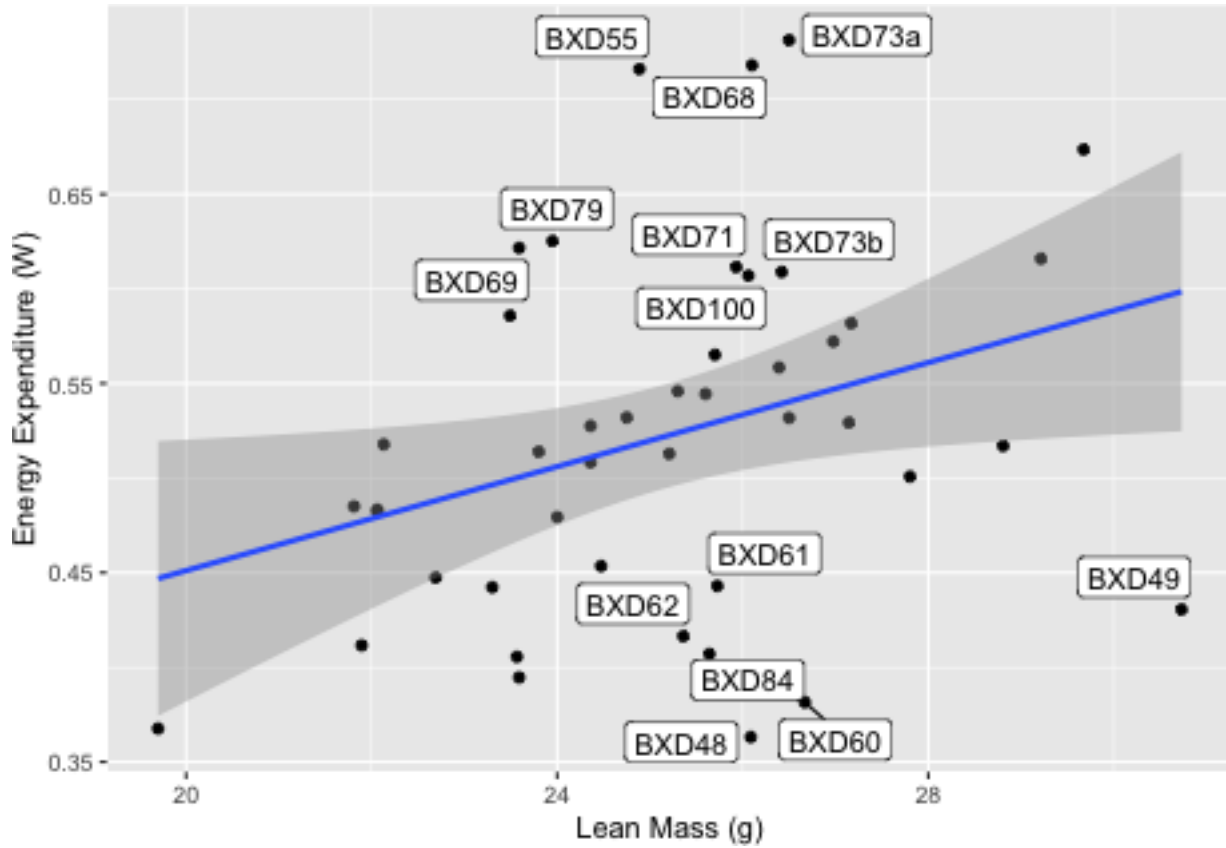
```
library(ggplot2)
ggplot(data, aes(y=MR_W,
                  x=Value_lm)) +
  geom_point(aes(col=Diet)) +
  geom_smooth(method="lm") +
  geom_label_repel(data = subset(data, (MR_W < 0.45&Value_lm>25.5)|MR_W>0.65&Value_lm<27),
                  aes(label=Name,
                      col=Diet)) +
  labs(y="Energy Expenditure (W)",
       x="Lean Mass (g)")
```



```
ggplot(data, aes(y=MR_W,
  x=Value_lm,
  col=Diet)) +
  geom_point() +
  geom_smooth(method="lm") +
  #geom_label_repel(data = subset(data, (MR_W < 0.45&Value_lm>25.5)|MR_W>0.65&Value_lm<27), aes(label=Name))
  labs(y="Energy Expenditure (W)",
    x="Lean Mass (g)")
```



```
#chow only
ggplot(data %>% filter(Diet=="NCD"), aes(y=MR_W,
  x=Value_lm)) +
  geom_point() +
  geom_smooth(method="lm") +
  geom_label_repel(data = subset(data %>% filter(Diet=="NCD"),
    (MR_W < 0.48&Value_lm>24.5) | MR_W>0.60&Value_lm<27),
    aes(label=Name)) +
  guides(fill = guide_legend(override.aes = aes(color = NA))) +
  labs(y="Energy Expenditure (W)",
    x="Lean Mass (g)")
```



```
lm.model.1 <- lm(MR_W~Value_lm,data=data %>% filter(Diet=="NCD")) #model built on only NCD
lm.model.2 <- lm(MR_W~Value_lm+Diet,data=data) #model built on NCD and AT
library(broom)
aov(lm.model.1) %>% tidy %>% kable(caption="Model 1 summary for adjusting for lean mass")
```

Table 1: Model 1 summary for adjusting for lean mass

term	df	sumsq	meansq	statistic	p.value
Value_lm	1	0.041	0.041	5.08	0.029
Residuals	42	0.342	0.008	NA	NA

```
summary(lm.model.1) %>% tidy %>% kable(caption="Model 1 coefficients for adjusting for lean mass")
```

Table 2: Model 1 coefficients for adjusting for lean mass

term	estimate	std.error	statistic	p.value
(Intercept)	0.176	0.154	1.15	0.258
Value_lm	0.014	0.006	2.25	0.029

```
aov(lm.model.2) %>% tidy %>% kable(caption="Model 2 summary for adjusting for lean mass")
```

Table 3: Model 2 summary for adjusting for lean mass

term	df	sumsq	meansq	statistic	p.value
Value_lm	1	0.106	0.106	17.2	0
Diet	1	0.095	0.095	15.5	0
Residuals	84	0.519	0.006	NA	NA

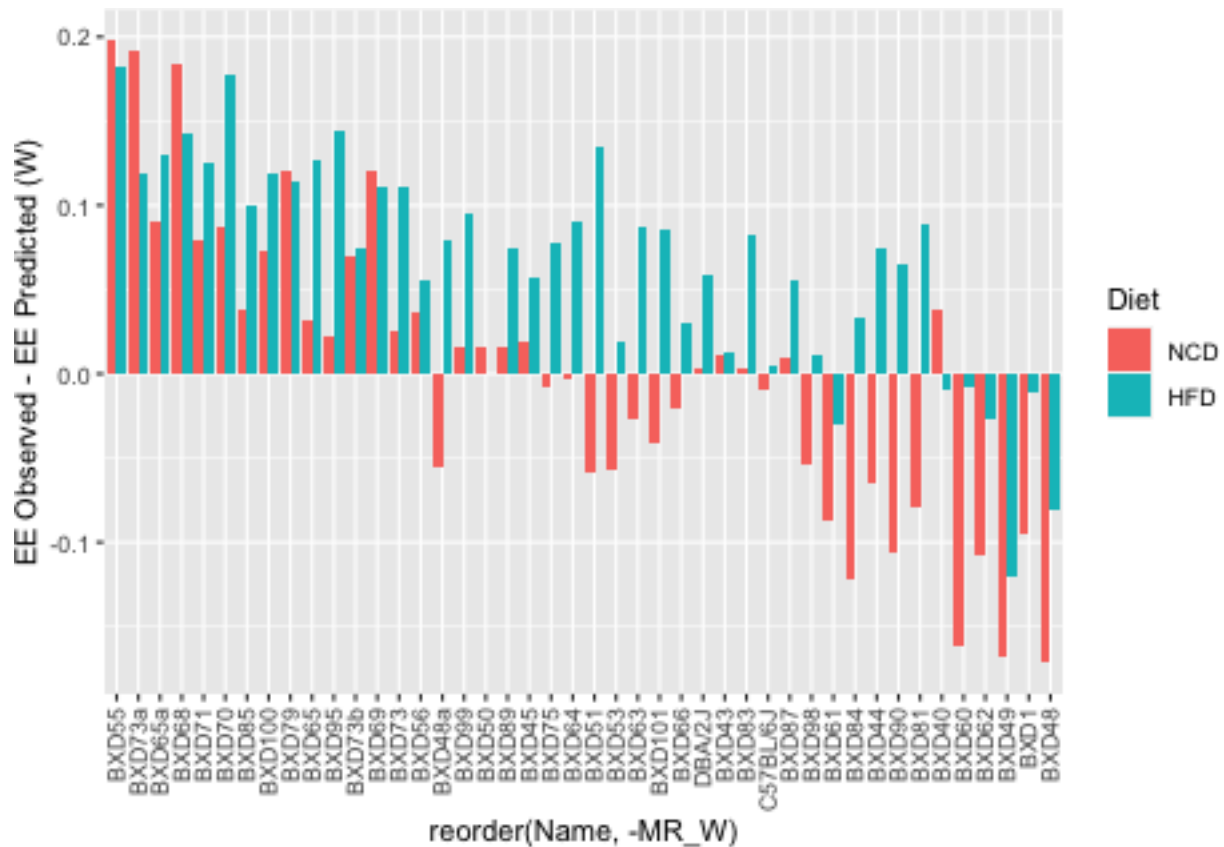
```
summary(lm.model.2) %>% tidy %>% kable(caption="Model 2 coefficients for adjusting for lean mass")
```

Table 4: Model 2 coefficients for adjusting for lean mass

term	estimate	std.error	statistic	p.value
(Intercept)	0.194	0.096	2.02	0.047
Value_lm	0.013	0.004	3.43	0.001
DietHFD	0.067	0.017	3.93	0.000

```
data <- data %>%
  mutate(MR_predicted = predict(lm.model.1, newdata = list(Value_lm=Value_lm))) %>%
  mutate(MR_resid = MR_W-MR_predicted)

data %>%
  filter(!is.na(MR_W)) %>% # complete cases only
  ggplot(aes(y=MR_resid,
             x=reorder(Name,-MR_W),
             ymin=MR_resid-MR_W_SE,
             ymax=MR_resid+MR_W_SE,
             fill=Diet)) +
  #geom_label_repel(label=Name) +
  geom_bar(stat='identity',position='dodge') +
  labs(y="EE Observed - EE Predicted (W)") +
  theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))
```



based on this modelling after adjusting for lean mass, HFD increases thermogenesis by  $(\text{coef}(\text{lm.model.2})["(\text{Intercept})"] - c$

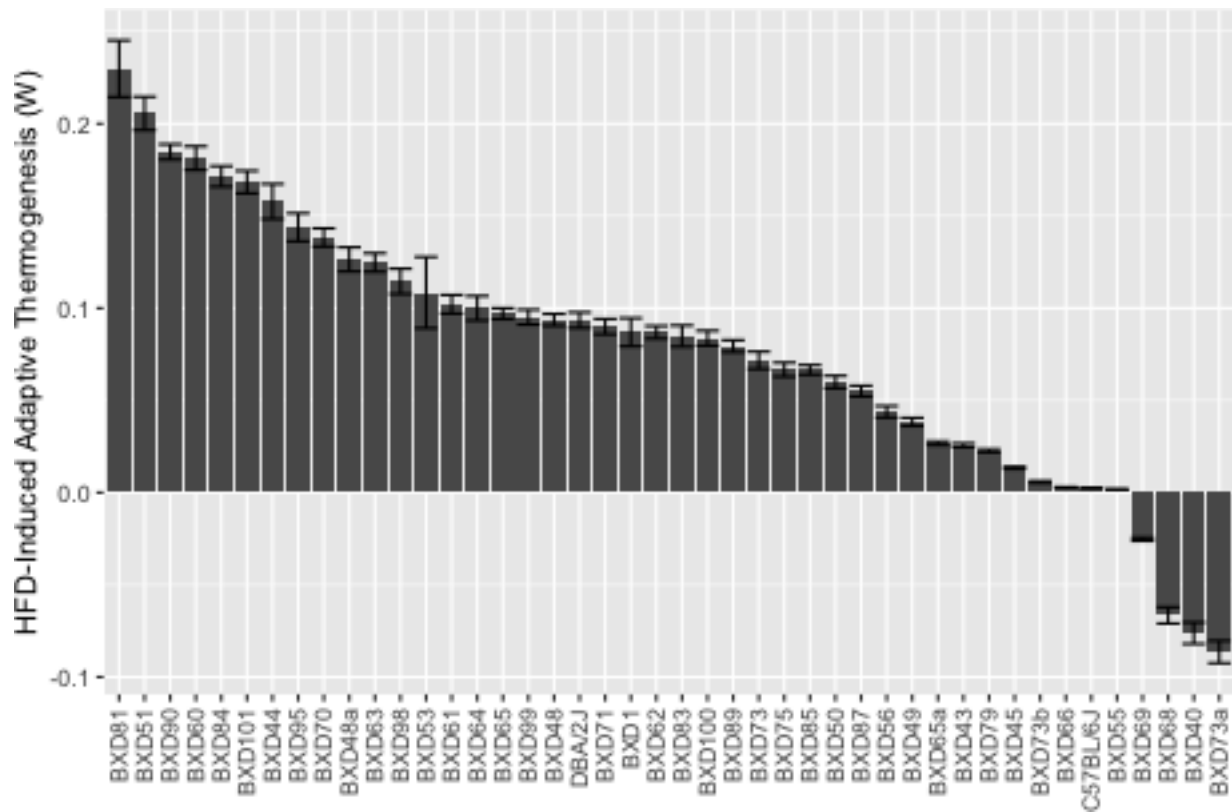
## Adaptive Thermogenesis

Defined as lean mass adjusted VO2 from HFD - NCD

```
data.wide <-
  data %>%
  select(Value_lm, Value_bw, MR_W, MR_W_SE, Name, Diet) %>%
  pivot_wider(names_from=Diet, id_cols=Name, values_from=c(Value_lm, Value_bw, MR_W, MR_W_SE)) %>%
  mutate(AT = MR_W_HFD - MR_W_NCD,
         AT_SE = sqrt((MR_W_SE_NCD/MR_W_NCD)^2 + (MR_W_SE_HFD/MR_W_HFD)^2) * AT,
         Wt.Gain = Value_bw_HFD - Value_bw_NCD)

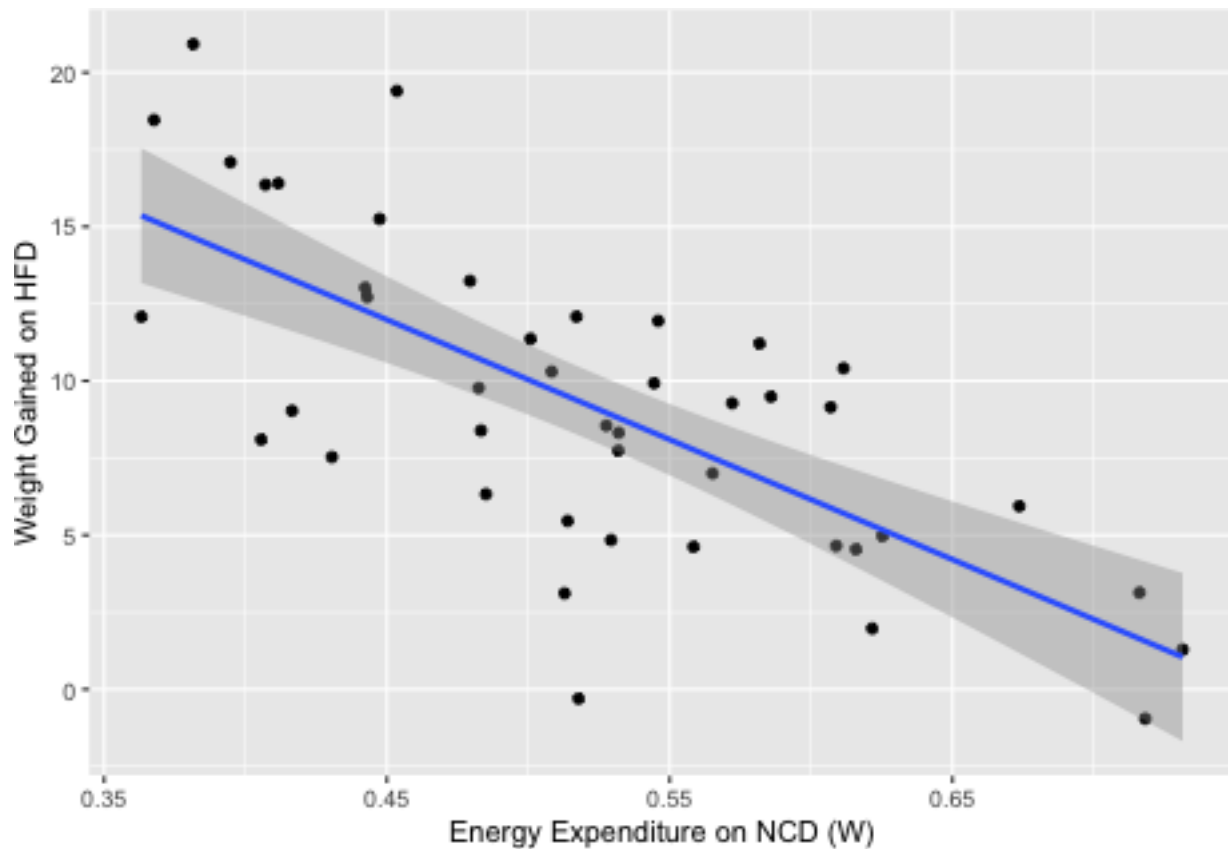
data.wide %>%
  filter(!is.na(AT)) %>% # complete cases only
  ggplot(aes(y=AT,
             x=reorder(Name, -AT),
             ymin=AT-AT_SE,
             ymax=AT+AT_SE)) +
  geom_bar(stat='identity', position='dodge') +
  geom_errorbar() +
  labs(y="HFD-Induced Adaptive Thermogenesis (W)",
       x="") +
  theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))
```





### Thermogenesis on NCD as a Predictor of Weight Gain

```
data.wide %>%
  ggplot(aes(y=Wt.Gain,
             x=MR_W_NCD)) +
  labs(y="Weight Gained on HFD",
       x="Energy Expenditure on NCD (W)") +
  geom_point() +
  geom_smooth(method="lm")
```



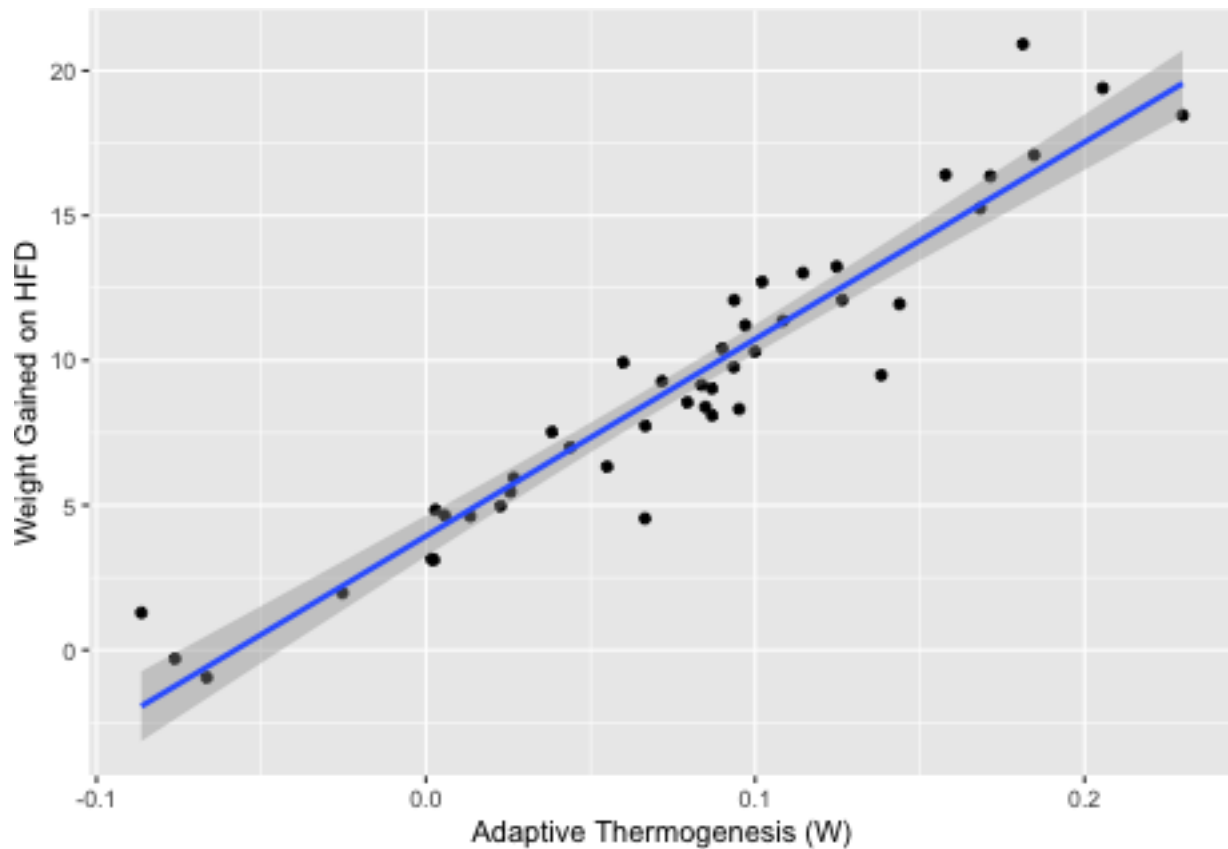
```
lm(Wt.Gain~MR_W_NCD, data=data.wide) %>% glance %>% kable(caption="Summary of relationship between energy expenditure and diet-induced weight gain")
```

Table 5: Summary of relationship between energy expenditure and diet-induced weight gain

r.squared	adj.r.squared	sigma	statistic	p.value	df	logLik	AIC	BIC	deviance	df.residual	nobs
0.509	0.498	3.65	43.6	0	1	-118	243	248	558	42	44

### Adaptive Thermogenesis vs Weight Gain

```
data.wide %>%
  ggplot(aes(y=Wt.Gain,
             x=AT)) +
  labs(y="Weight Gained on HFD",
       x="Adaptive Thermogenesis (W)") +
  geom_point() +
  geom_smooth(method="lm")
```



```
lm(Wt.Gain~AT, data=data.wide) %>% glance %>% kable(caption="Summary of relationship between energy exp
```

Table 6: Summary of relationship between energy expenditure and diet-induced weight gain

r.squared	adj.r.squared	sigma	statistic	p.value	df	logLik	AIC	BIC	deviance	df.residual	nobs
0.908	0.906	1.58	414	0	1	-81.5	169	174	105	42	44

## Session Information

```
sessionInfo()
```

```
## R version 4.0.2 (2020-06-22)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS 10.16
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRblas.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
```

```
## [1] stats      graphics  grDevices utils      datasets  methods  base
##
## other attached packages:
## [1] broom_0.7.11  ggrepel_0.9.1 ggplot2_3.3.5 readr_2.1.1  dplyr_1.0.7
## [6] tidyr_1.1.4   knitr_1.37
##
## loaded via a namespace (and not attached):
## [1] tidyselect_1.1.1 xfun_0.29      purrr_0.3.4    splines_4.0.2
## [5] lattice_0.20-45  colorspace_2.0-2 vctrs_0.3.8    generics_0.1.1
## [9] htmltools_0.5.2 yaml_2.2.1     mgcv_1.8-38    utf8_1.2.2
## [13] rlang_0.4.12     pillar_1.6.4   glue_1.6.0     withr_2.4.3
## [17] DBI_1.1.2        bit64_4.0.5    lifecycle_1.0.1 stringr_1.4.0
## [21] munsell_0.5.0    gtable_0.3.0   evaluate_0.14   labeling_0.4.2
## [25] tzdb_0.2.0       fastmap_1.1.0  parallel_4.0.2 fansi_1.0.0
## [29] highr_0.9        Rcpp_1.0.7     backports_1.4.1 scales_1.1.1
## [33] vroom_1.5.7      magick_2.7.3   farver_2.1.0    bit_4.0.4
## [37] hms_1.1.1        digest_0.6.29  stringi_1.7.6   grid_4.0.2
## [41] cli_3.1.0        tools_4.0.2    magrittr_2.0.1  tibble_3.1.6
## [45] crayon_1.4.2     pkgconfig_2.0.3 ellipsis_0.3.2  Matrix_1.4-0
## [49] assertthat_0.2.1 rmarkdown_2.11 rstudioapi_0.13 R6_2.5.1
## [53] nlme_3.1-153     compiler_4.0.2
```