

Evaluation of Energy Expenditure from BXD Datasets

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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_17618.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_17622.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 Sun Mar 27 10:21:25 2022.

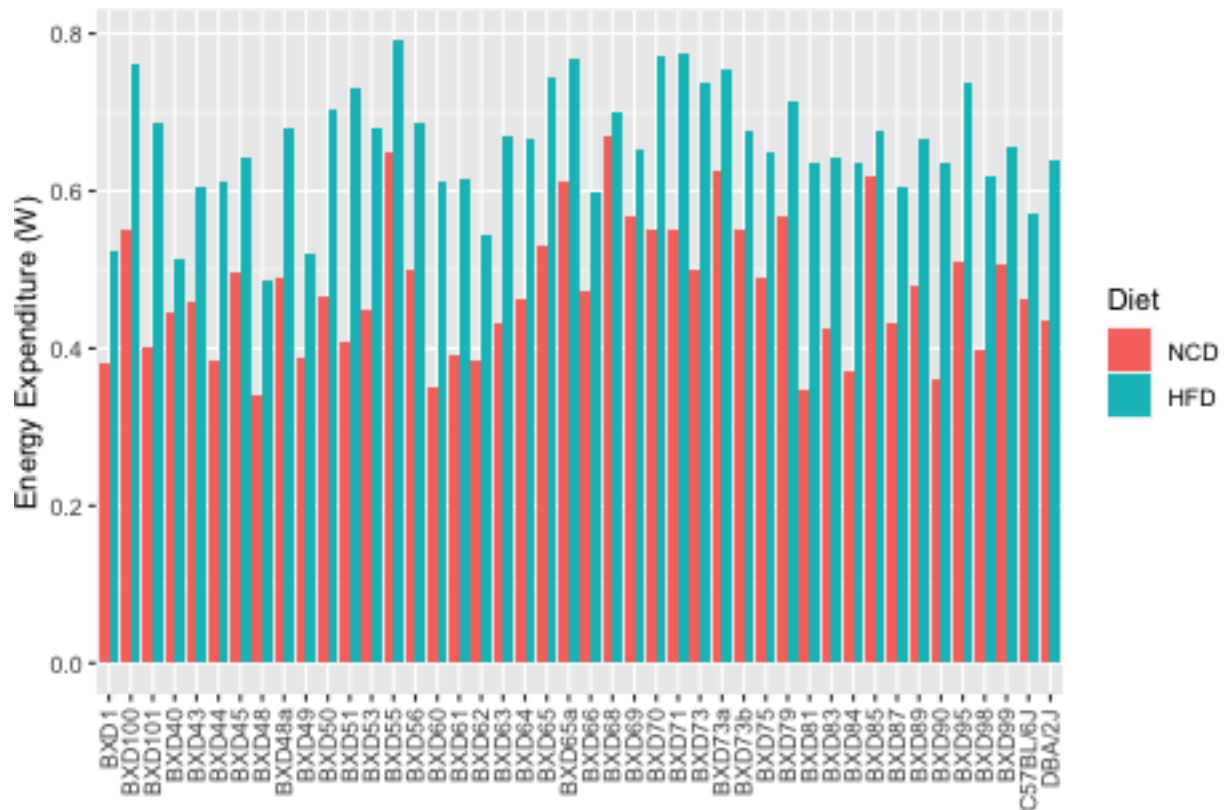
Analysis

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
```

```
mr.order <-
```

```
data %>%
```

```
filter(Diet == "NCD") %>%
```

```
arrange(desc(MR_W)) %>%
```

```
mutate(Name = factor(Name))
```

```
data %>%
```

```
filter(!is.na(MR_W)) %>% # complete cases only
```

```
mutate(Name = factor(Name, levels = mr.order$Name, ordered = TRUE)) %>%
```

```
ggplot(aes(y=MR_W,
```

```
  x=Name,
```

```
  ymin=MR_W-MR_W_SE,
```

```
  ymax=MR_W+MR_W_SE,
```

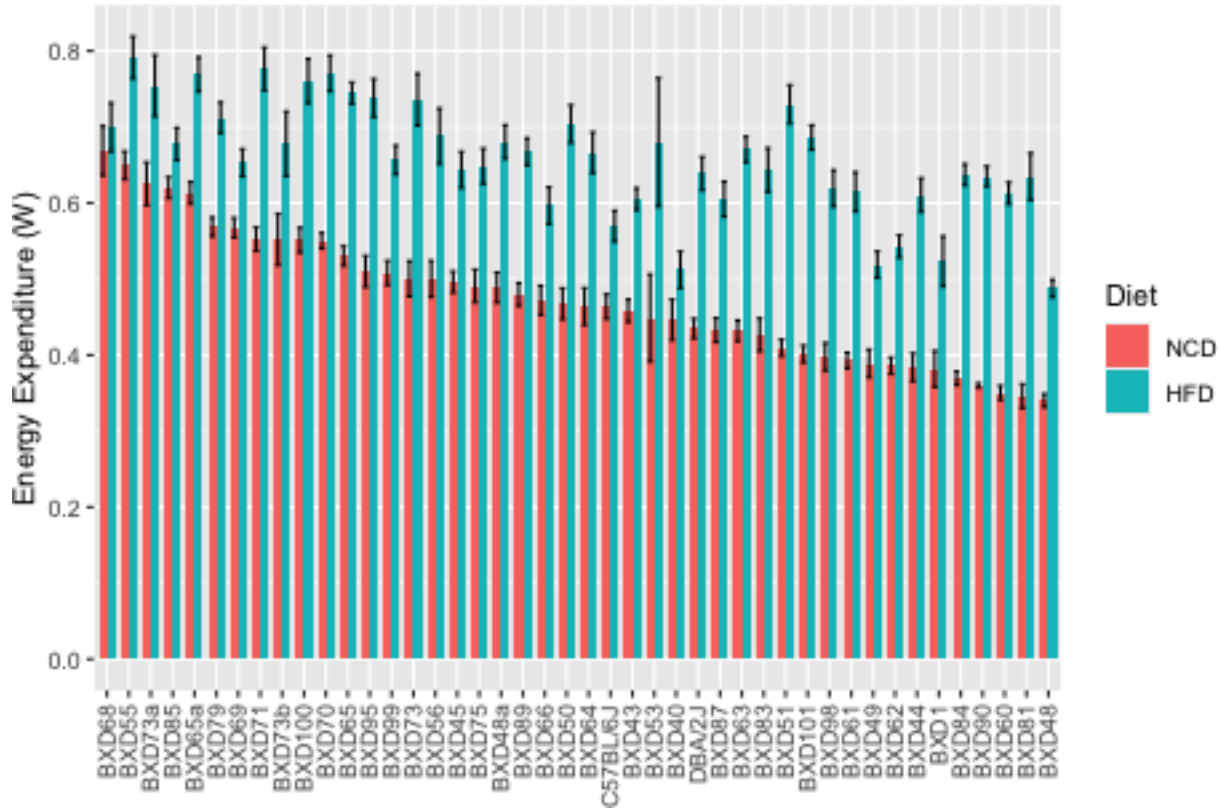
```
  fill=Diet)) +
```

```
geom_bar(stat='identity',position='dodge', width=0.75) +
```

```
geom_errorbar(position=position_dodge(width=0.75), width=0.5) +
```

```
labs(y="Energy Expenditure (W)",x="") +
```

```
theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))
```



Estimating Effect Sizes

```
data %>%
  group_by(Diet) %>%
  summarize(Max = max(MR_W, na.rm=T),
            Min = min(MR_W, na.rm=T),
            Mean = mean(MR_W, na.rm=T),
            SE = mean(MR_W_SE, na.rm=T),
            N = mean(N, na.rm=T)) %>%
  mutate(SD = SE*sqrt(mean(N, na.rm=T))) %>%
  mutate(Rel.SD = SD/Mean*100) %>%
  kable(caption="Summary statistics for thermogenesis from BXD mice")
```

Table 1: Summary statistics for thermogenesis from BXD mice

Diet	Max	Min	Mean	SE	N	SD	Rel.SD
NCD	0.669	0.340	0.475	0.018	4.44	0.038	7.95
HFD	0.791	0.488	0.659	0.025	4.47	0.052	7.96

```
data %>%
  group_by(Diet) %>%
  summarize(Max = max(Value_lm, na.rm=T),
            Min = min(Value_lm, na.rm=T),
            Mean = mean(Value_lm, na.rm=T),
            SE = mean(SE_lm, na.rm=T),
```

```

N = mean(N,na.rm=T)) %>%
mutate(SD = SE*sqrt(mean(N,na.rm=T))) %>%
mutate(Rel.SD = SD/Mean*100) %>%
kable(caption="Summary statistics for lean mass from BXD mice")

```

Table 2: Summary statistics for lean mass from BXD mice

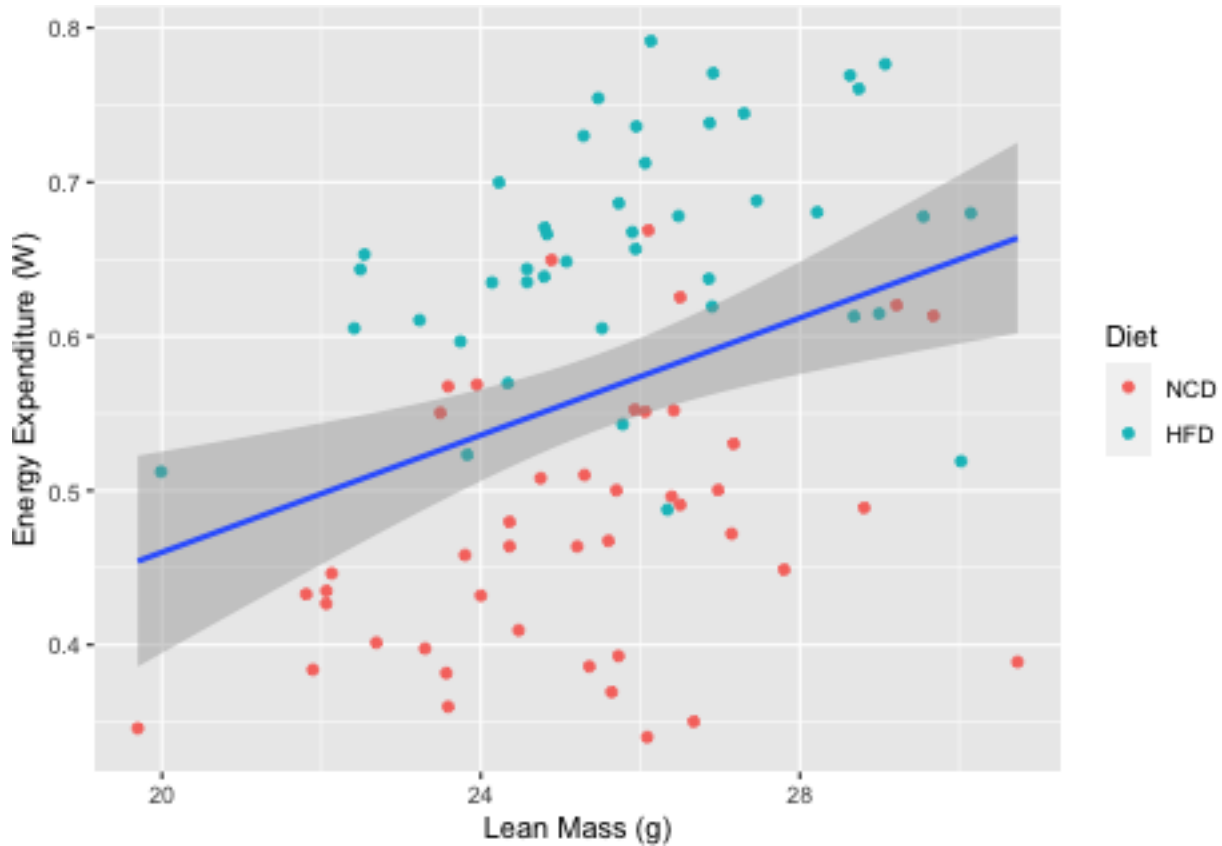
Diet	Max	Min	Mean	SE	N	SD	Rel.SD
NCD	30.7	19.7	25.4	0.623	4.44	1.31	5.19
HFD	30.2	20.0	26.0	0.612	4.47	1.29	4.97

Adjusting for Lean Mass

```

library(ggrepel)
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=N))
  labs(y="Energy Expenditure (W)",
       x="Lean Mass (g)")

```



```

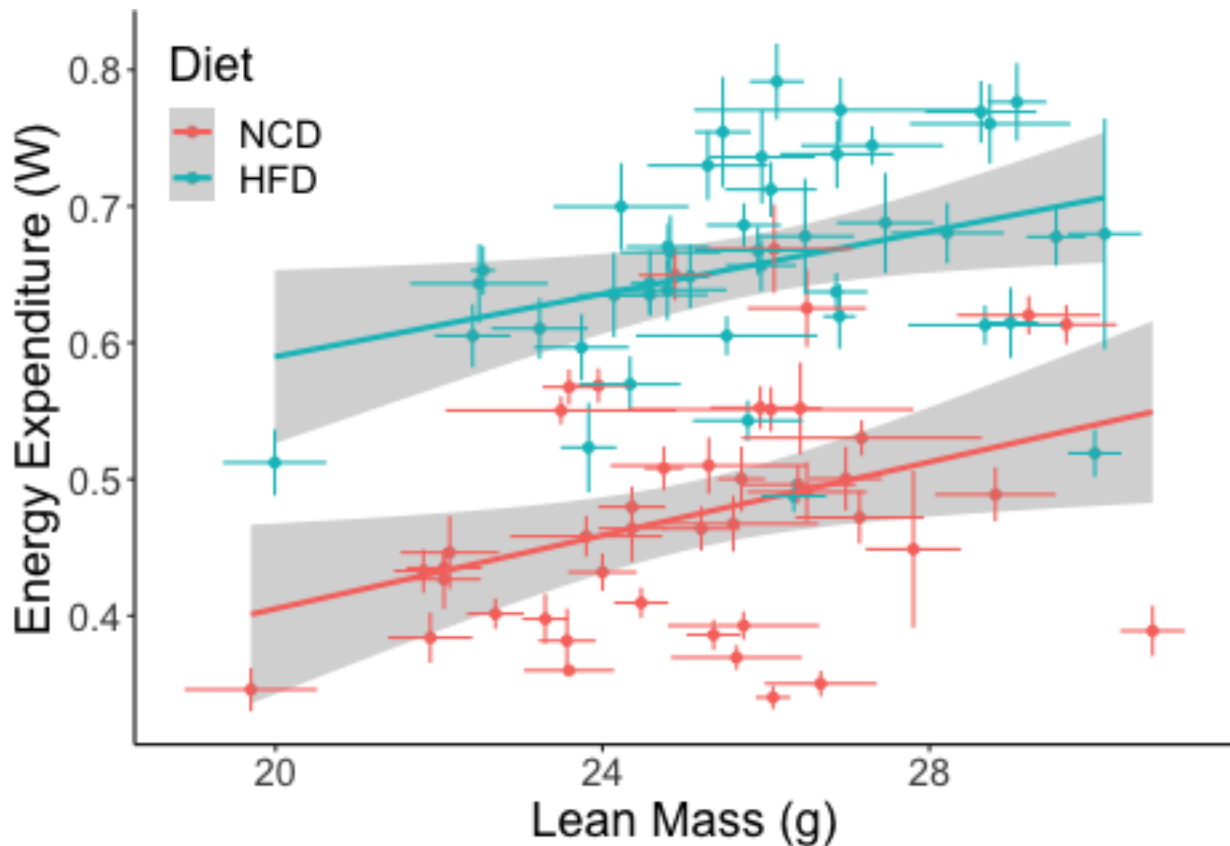
ggplot(data, aes(y=MR_W,
                  x=Value_lm,

```

```

    col=Diet)) +
  geom_point() +
  geom_smooth(method="lm") +
  geom_errorbar(aes(ymin=MR_W-MR_W_SE,
                    ymax=MR_W+MR_W_SE)) +
  geom_errorbarh(aes(xmin=Value_lm-SE_lm,
                     xmax=Value_lm+SE_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)") +
  theme_classic() +
  theme(legend.position = c(0.1,0.85),
        text=element_text(size=18))

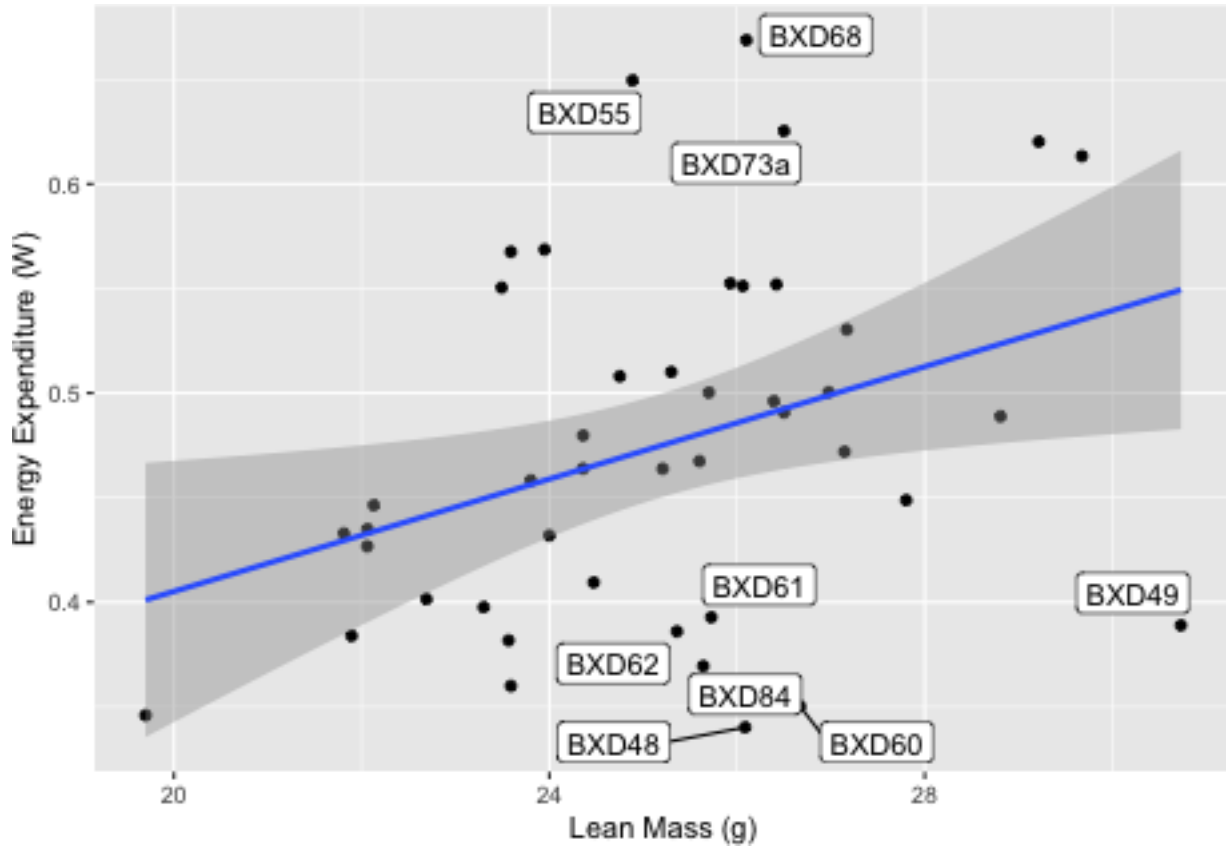
```



```

#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 < 0.43&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 3: Model 1 summary for adjusting for lean mass

term	df	sumsq	meansq	statistic	p.value
Value_lm	1	0.040	0.040	5.96	0.019
Residuals	42	0.279	0.007	NA	NA

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

Table 4: Model 1 coefficients for adjusting for lean mass

term	estimate	std.error	statistic	p.value
(Intercept)	0.136	0.139	0.981	0.332
Value_lm	0.013	0.006	2.442	0.019

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

Table 5: Model 2 summary for adjusting for lean mass

term	df	sumsq	meansq	statistic	p.value
Value_lm	1	0.159	0.159	27.2	0
Diet	1	0.639	0.639	109.5	0
Residuals	84	0.490	0.006	NA	NA

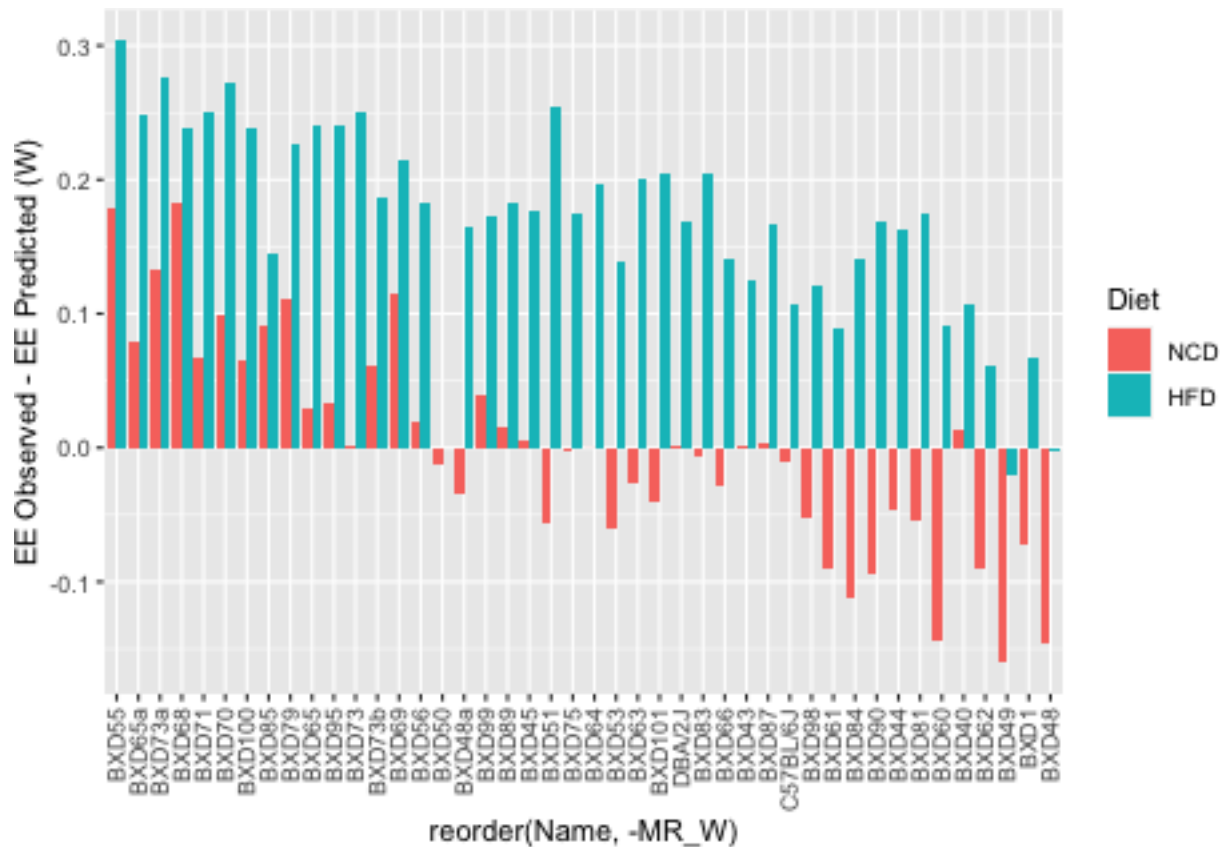
```
summary(lm.model.2) %>% tidy %>% kable(caption="Model 2 coefficients for adjusting for lean mass")
```

Table 6: Model 2 coefficients for adjusting for lean mass

term	estimate	std.error	statistic	p.value
(Intercept)	0.160	0.094	1.71	0.091
Value_lm	0.012	0.004	3.38	0.001
DietHFD	0.174	0.017	10.47	0.000

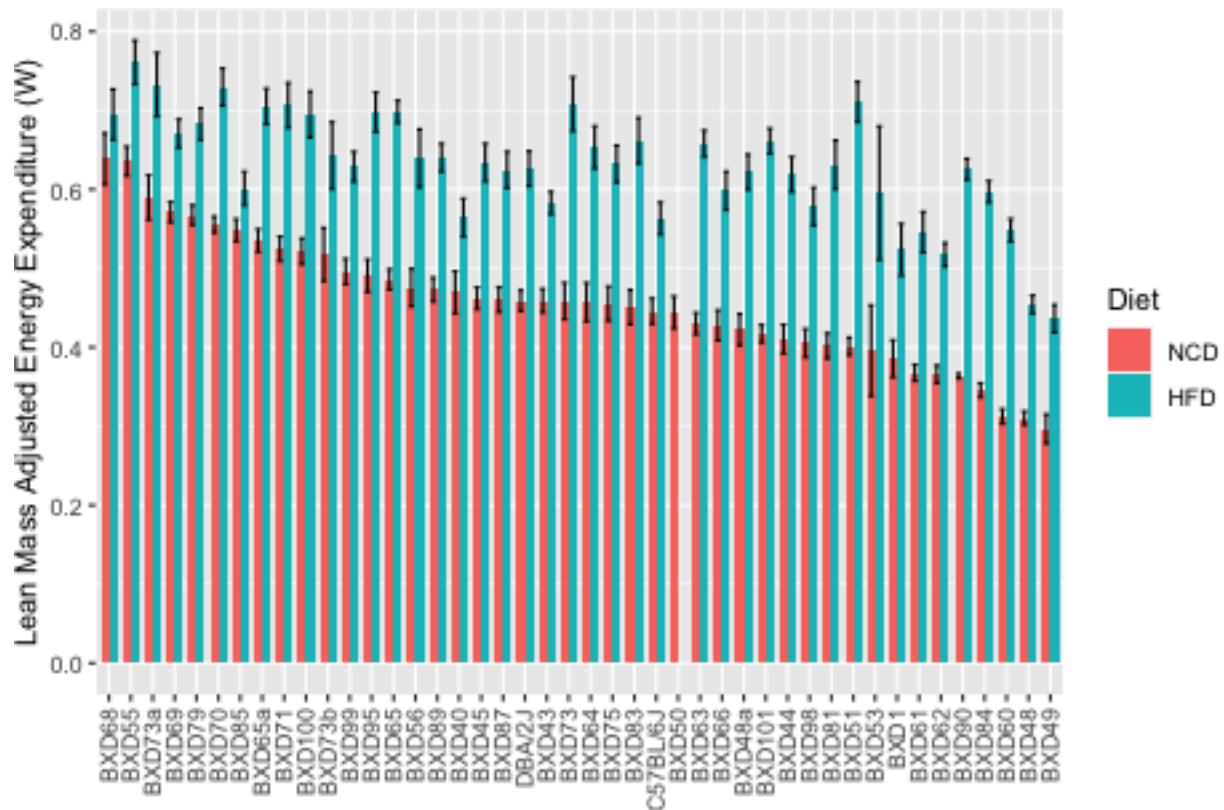
```
data <- data %>%
  mutate(MR_predicted = predict(lm.model.1, newdata = list(Value_lm=Value_lm))) %>%
  mutate(MR_resid = MR_W-MR_predicted) %>%
  mutate(MR_adj = MR_resid + coef(lm.model.1)['(Intercept)'] + coef(lm.model.2)['Value_lm']*mean(data$V

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))
```

```
mr.adj.order <-
  data %>%
    filter(Diet == "NCD") %>%
    arrange(desc(MR_adj)) %>%
    mutate(Name = factor(Name))

data %>%
  filter(!is.na(MR_W)) %>% # complete cases only
  mutate(Name = factor(Name, levels = mr.adj.order$Name, ordered = TRUE)) %>%
  ggplot(aes(y=MR_adj,
    x=Name,
    ymin=MR_adj-MR_W_SE,
    ymax=MR_adj+MR_W_SE,
    fill=Diet)) +
  geom_bar(stat='identity',position='dodge', width=0.75) +
  geom_errorbar(position=position_dodge(width=0.75), width=0.5) +
  labs(y="Lean Mass Adjusted Energy Expenditure (W)",x="") +
  theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1))
```



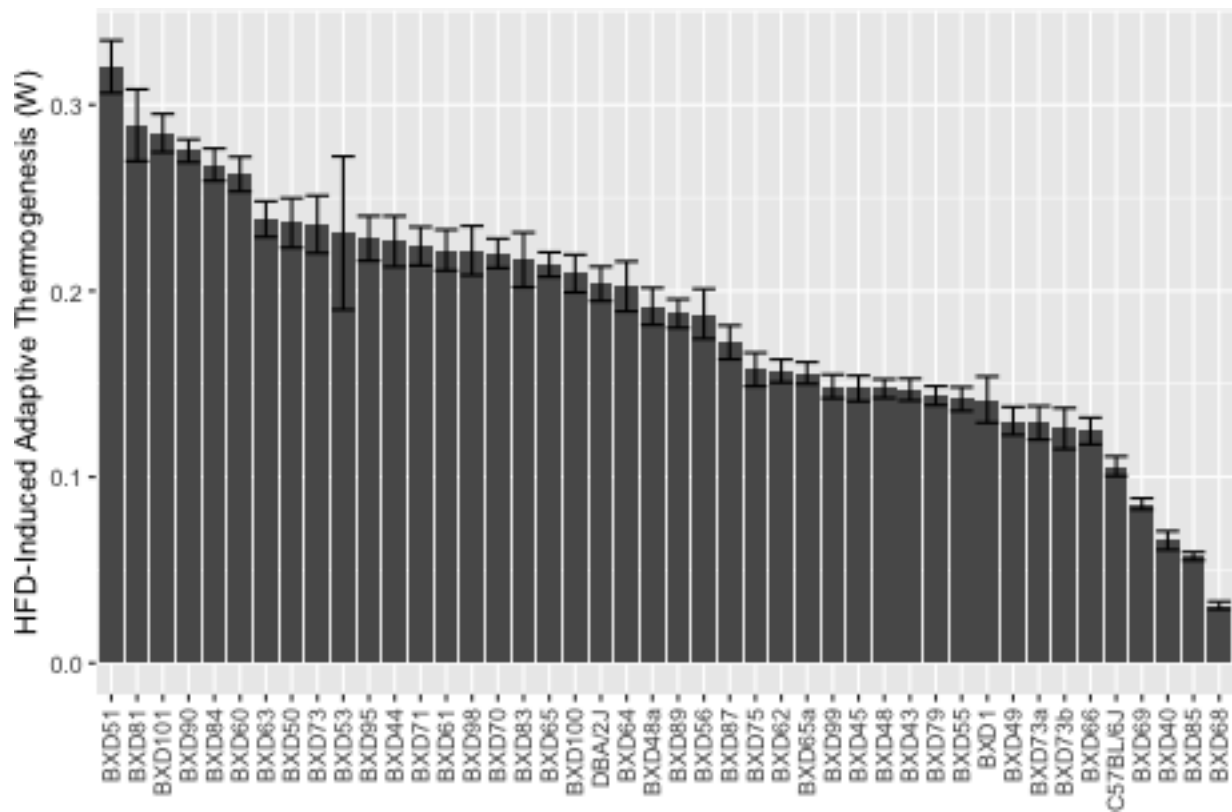
based on this modelling after adjusting for lean mass, HFD increases thermogenesis by $(\text{coef}(\text{lm.model.2})["(\text{Intercept})"] - c$

Adaptive Thermogenesis

Defined as lean mass adjusted VO2 from HFD - NCD

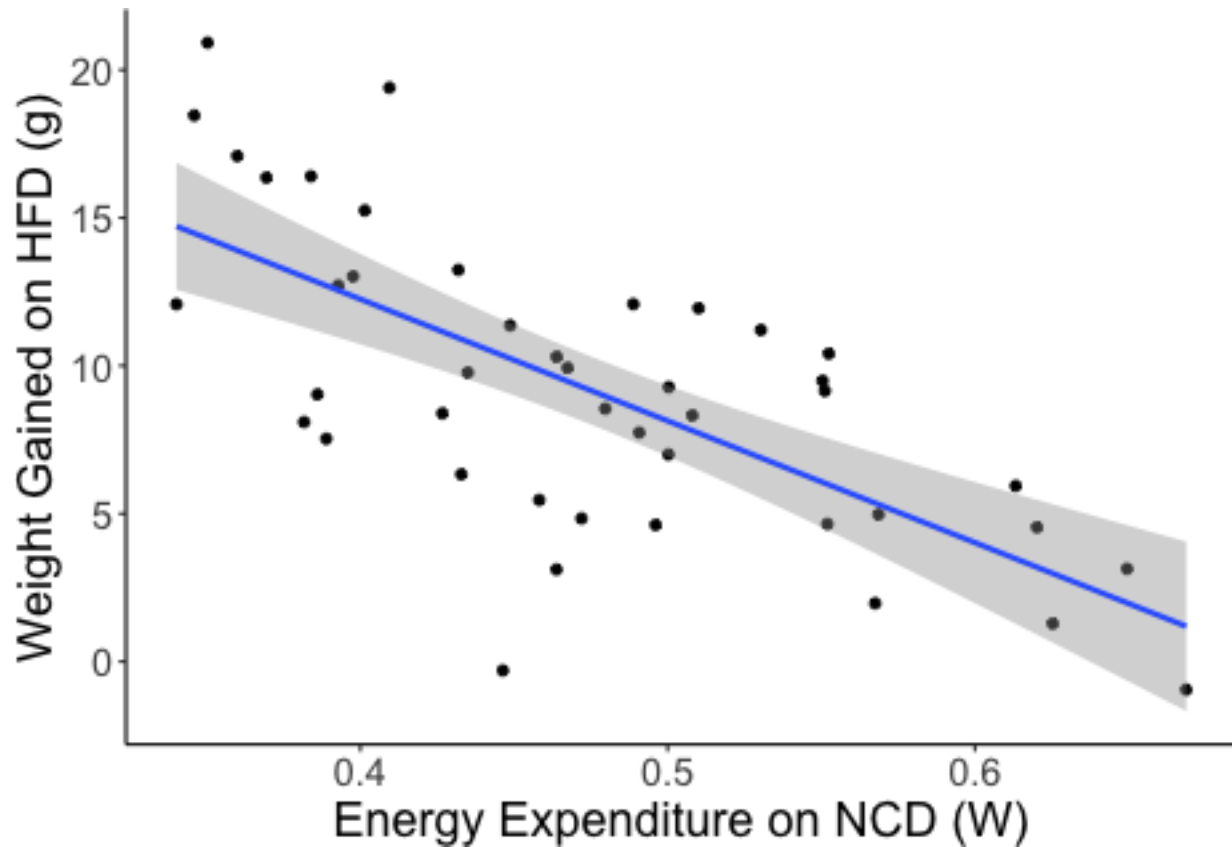
```
data.wide <-
  data %>%
  select(Value_lm, SE, Value_bw, MR_W, MR_W_SE, MR_adj, Name, Diet) %>%
  pivot_wider(names_from=Diet, id_cols=Name, values_from=c(Value_lm, Value_bw, MR_W, MR_W_SE, MR_adj, SE)) %>%
  mutate(AT = MR_W_HFD - MR_W_NCD,
         AT_SE = sqrt((MR_W_SE_NCD/MR_W_NCD)^2 + (MR_W_SE_HFD/MR_W_HFD)^2) * AT,
         Wt_SE = sqrt((SE_NCD/Value_bw_NCD)^2 + (SE_HFD/Value_bw_NCD)^2) * Value_bw_NCD,
         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 (g)",
       x="Energy Expenditure on NCD (W)") +
  geom_point() +
  geom_smooth(method="lm") +
  theme_classic() +
  theme(text=element_text(size=18))
```

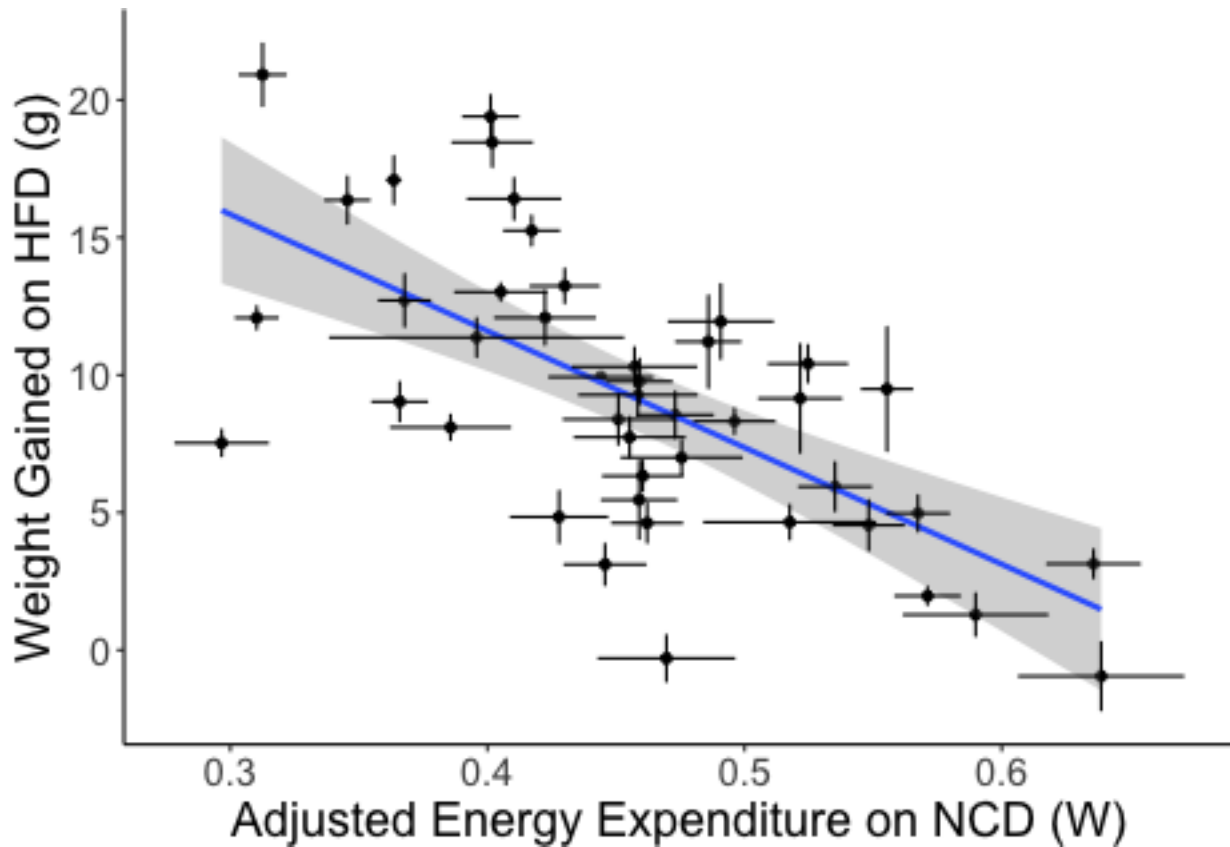


```
lm(Wt.Gain~MR_W_NCD, data=data.wide) %>% glance %>% kable(caption="Summary of relationship between energy
```

Table 7: 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
0.474	0.462	3.77	37.9	2.4e-07	1	-120	246	251	598	42	44

```
data.wide %>%
  ggplot(aes(y=Wt.Gain,
             x=MR_adj_NCD)) +
  labs(y="Weight Gained on HFD (g)",
       x="Adjusted Energy Expenditure on NCD (W)") +
  geom_point() +
  geom_smooth(method="lm") +
  geom_errorbarh(aes(xmin=MR_adj_NCD-MR_W_SE_NCD,
                    xmax=MR_adj_NCD+MR_W_SE_NCD))+
  geom_errorbar(aes(ymin=Wt.Gain-Wt_SE,
                    ymax=Wt.Gain+Wt_SE)) +
  theme_classic() +
  theme(text=element_text(size=18))
```



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

Table 8: Summary of relationship between lean mass adjusted energy expenditure and diet-induced weight gain

r.squared	adj.r.squared	sigma	statistic	p.value	df	logLik	AIC	BIC	deviance	df.residual	nobs
0.441	0.427	3.89	33.1	9e-07	1	-121	248	254	636	42	44

```
gemma.phenotype.export <- 'Strain Level Energy Expenditure Data.csv'
data %>%
  filter(Diet=="NCD") %>%
  select(Name, MR_W, MR_adj) %>%
  write_csv(gemma.phenotype.export)
```

The data on lean mass adjusted thermogenesis was exported to Strain Level Energy Expenditure Data.csv

Heritability of NCD Thermogenesis

Since we dont have individual mouse data we will make fake data based on the mean and se of MR

```
new.sim.data <- data.frame(Name=NA, Diet=NA,EE=NA)
```

```
for (row in 1:dim(data)[1]) {
  strain.data <- data[row,]
  if(!is.na(strain.data$MR_W)){
    sim.data <- with(strain.data,
```

```

        rnorm(mean=MR_W,
              sd=MR_W_SE * sqrt(N),
              n=N_ee
        ))
sim.lean.data <- with(strain.data,
  rnorm(mean=Value_lm,
        sd=SE_lm * sqrt(N),
        n=N_ee
  ))
sim.dataset <- data.frame(Name=strain.data$Name,
  Diet=strain.data$Diet,
  EE=sim.data,
  Lean=sim.lean.data)
new.sim.data <- bind_rows(new.sim.data,sim.dataset)
}
else{
  sim.dataset <- data.frame(Name=strain.data$Name,
    Diet=strain.data$Diet,
    EE=NA,
    Lean=NA)
  new.sim.data <- bind_rows(new.sim.data,sim.dataset)
}
}

aov(Ee ~ Name, data=new.sim.data %>% filter(Diet=='NCD')) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq),
    Pct.Var = meansq/Total.Var*100) %>%
  kable(caption="Overall heritability of energy expenditure on NCD mice")

```

Table 9: Overall heritability of energy expenditure on NCD mice

term	df	sumsq	meansq	statistic	p.value	Total.Var	Pct.Var
Name	43	1.600	0.037	20	0	0.039	95.24
Residuals	148	0.275	0.002	NA	NA	0.039	4.76

```

aov(Ee ~ Lean + Name, data=new.sim.data %>% filter(Diet=='NCD')) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq),
    Pct.Var = meansq/Total.Var*100) %>%
  kable(caption="Overall heritability of energy expenditure on NCD including lean mass")

```

Table 10: Overall heritability of energy expenditure on NCD including lean mass

term	df	sumsq	meansq	statistic	p.value	Total.Var	Pct.Var
Lean	1	0.090	0.090	48.9	0	0.127	70.95
Name	43	1.513	0.035	19.0	0	0.127	27.60
Residuals	147	0.272	0.002	NA	NA	0.127	1.45

```

aov(Ee ~ Lean + Name, data=new.sim.data %>% filter(Diet=='NCD')) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq[2:3]),
         Pct.Var = meansq/Total.Var*100) -> lean.adj.ee.lean

aov(Ee ~ Lean + Name, data=new.sim.data %>% filter(Diet=='NCD')) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq),
         Pct.Var = meansq/Total.Var*100) -> lean.adj.ee.all

lean.adj.ee.lean %>% kable(caption="Overall heritability of energy expenditure on NCD adjusting for lean

```

Table 11: Overall heritability of energy expenditure on NCD adjusting for lean mass

term	df	sumsq	meansq	statistic	p.value	Total.Var	Pct.Var
Lean	1	0.090	0.090	48.9	0	0.037	244.20
Name	43	1.513	0.035	19.0	0	0.037	95.01
Residuals	147	0.272	0.002	NA	NA	0.037	4.99

```

aov(Ee ~ Lean + Name + Diet + Name:Diet, data=new.sim.data) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq),
         Pct.Var = meansq/Total.Var*100) -> hfd.incl.ee

hfd.incl.ee %>% kable(caption="Overall heritability of energy expenditure including diet and lean mass

```

Table 12: Overall heritability of energy expenditure including diet and lean mass

term	df	sumsq	meansq	statistic	p.value	Total.Var	Pct.Var
Lean	1	0.361	0.361	149.97	0	3.26	11.059
Name	43	2.063	0.048	19.95	0	3.26	1.471
Diet	1	2.837	2.837	1179.99	0	3.26	87.009
Name:Diet	42	0.530	0.013	5.25	0	3.26	0.387
Residuals	291	0.700	0.002	NA	NA	3.26	0.074

```

aov(Ee ~ Lean + Name + Diet + Name:Diet, data=new.sim.data) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq[c(2,4,5)]),
         Pct.Var = meansq/Total.Var*100) -> hfd.adj.ee.adj

aov(Ee ~ Lean + Name + Diet + Name:Diet, data=new.sim.data) %>%
  tidy %>%
  mutate(Total.Var=sum(meansq[c(2,3,4,5)]),
         Pct.Var = meansq/Total.Var*100) -> hfd.adj.ee.all

hfd.adj.ee.adj %>% kable(caption="Overall heritability of energy expenditure adjusted for diet and lean

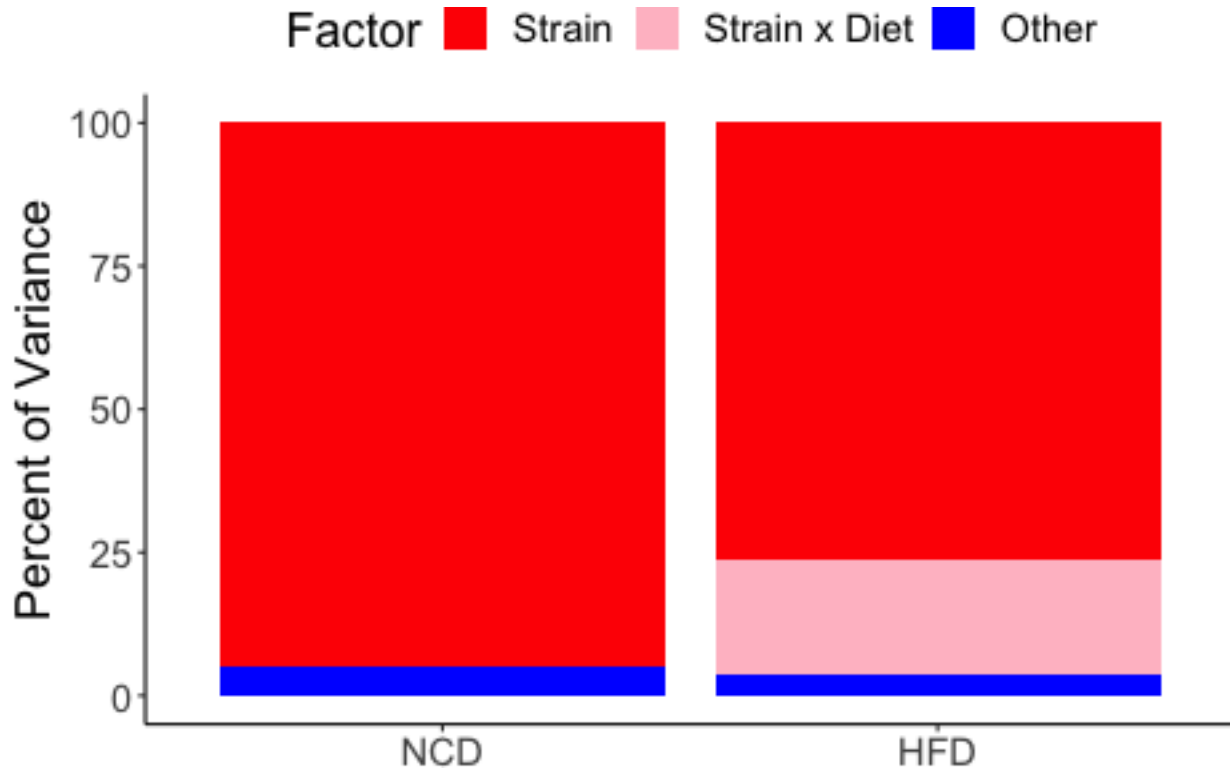
```

Table 13: Overall heritability of energy expenditure adjusted for diet and lean mass

term	df	sumsq	meansq	statistic	p.value	Total.Var	Pct.Var
Lean	1	0.361	0.361	149.97	0	0.063	572.34
Name	43	2.063	0.048	19.95	0	0.063	76.15
Diet	1	2.837	2.837	1179.99	0	0.063	4503.12
Name:Diet	42	0.530	0.013	5.25	0	0.063	20.03
Residuals	291	0.700	0.002	NA	NA	0.063	3.82

```
ee.var.data <- bind_rows(lean.adj.ee.lean %>% mutate(Diet="NCD"), hfd.adj.ee.adj %>% mutate(Diet="HFD"))

ggplot(ee.var.data %>% filter(term %in% c('Name', 'Name:Diet', 'Residuals'))),
  aes(x=reorder(Diet, -Pct.Var),
    y=Pct.Var,
    fill=term)) +
  geom_bar(position="stack", stat='identity') +
  scale_fill_manual(labels = c("Strain", "Strain x Diet", "Other"), values = c("red", "pink", "blue"),
    name="Factor") +
  labs(y="Percent of Variance",
    x="") +
  theme_classic() +
  theme(legend.position="top")+
  theme(text=element_text(size=18))
```



```
ee.var.all.data <- bind_rows(lean.adj.ee.all %>% mutate(Diet="NCD", Corr="None"),
  lean.adj.ee.lean %>% mutate(Diet="NCD", Corr="Lean Mass"),
  hfd.adj.ee.all %>% mutate(Diet="HFD", Corr="Lean Mass"),
  hfd.adj.ee.adj %>% mutate(Diet="HFD", Corr="Lean Mass,Diet")) %>%
```

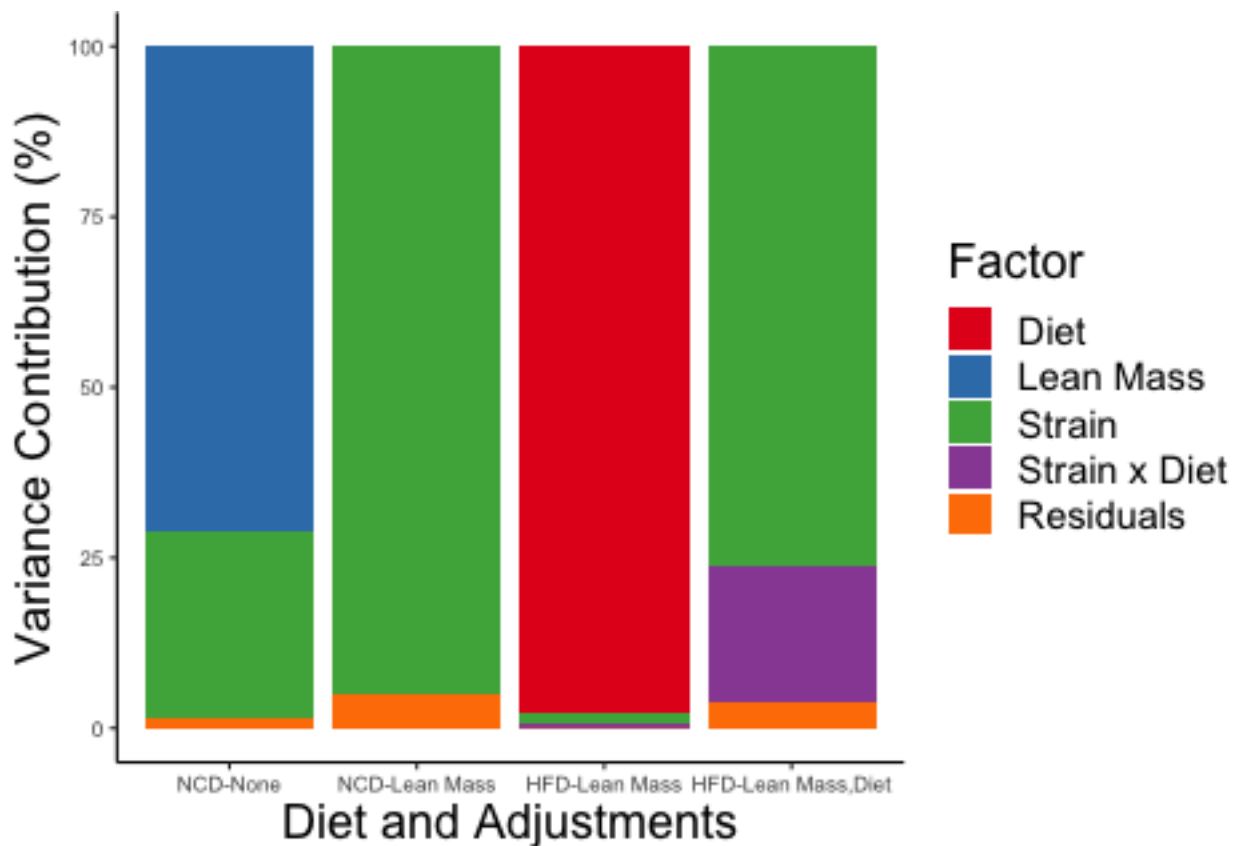


```

mutate(Group=paste(Diet,Corr,sep="-"))

library(RColorBrewer)
ee.var.all.data %>%
  filter(term %in% c('Lean','Name','Name:Diet','Diet','Residuals')) %>%
  filter(!(term=='Lean'&Corr=='Lean Mass')) %>%
  filter(!(term=='Lean'&Corr=="Lean Mass,Diet")) %>%
  filter(!(term=='Diet'&Corr=="Lean Mass,Diet")) %>%
ggplot(aes(x=ordered(Group, levels=c("NCD-None", "NCD-Lean Mass", "HFD-Lean Mass", "HFD-Lean Mass,Diet")),
  y=Pct.Var,
  fill=term)) +
  geom_bar(position="stack",stat='identity') +
  scale_fill_manual(name="Factor",
    labels = c("Diet", "Lean Mass", "Strain", "Strain x Diet", "Residuals"),
    values=brewer.pal(5, "Set1")) +
  labs(y="Variance Contribution (%)",
    x="Diet and Adjustments") +
  theme_classic() +
  theme(text=element_text(size=18),
    axis.text=element_text(size=8))

```



Adaptive Thermogenesis vs Weight Gain

```

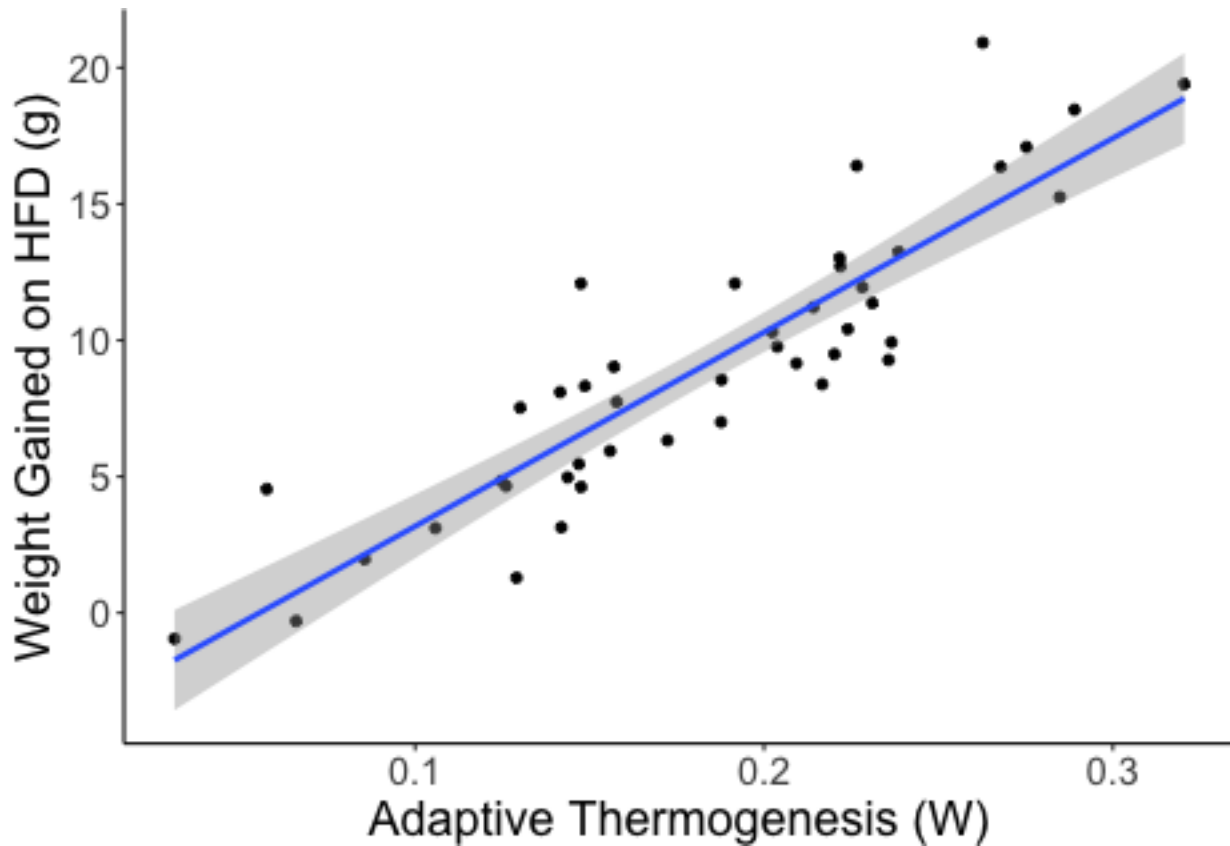
data.wide %>%
  ggplot(aes(y=Wt.Gain,

```

```

x=AT)) +
labs(y="Weight Gained on HFD (g)",
     x="Adaptive Thermogenesis (W)") +
geom_point() +
geom_smooth(method="lm") + theme_classic() +
theme(text=element_text(size=18))

```



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

Table 14: 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
0.801	0.796	2.32	169	0	1	-98.5	203	208	226	42	44

Integration with Lifespan

To ask whether BMR is related to experimental lifespan we used the data from Roy et al 2021. This determined lifespan of **female** mice in days

```

aging.datafile <- 'BXD_18441.csv'

aging.data <- read_csv(aging.datafile, skip=8) %>%
  rename(Age = Value,
         Age.SE = SE,

```

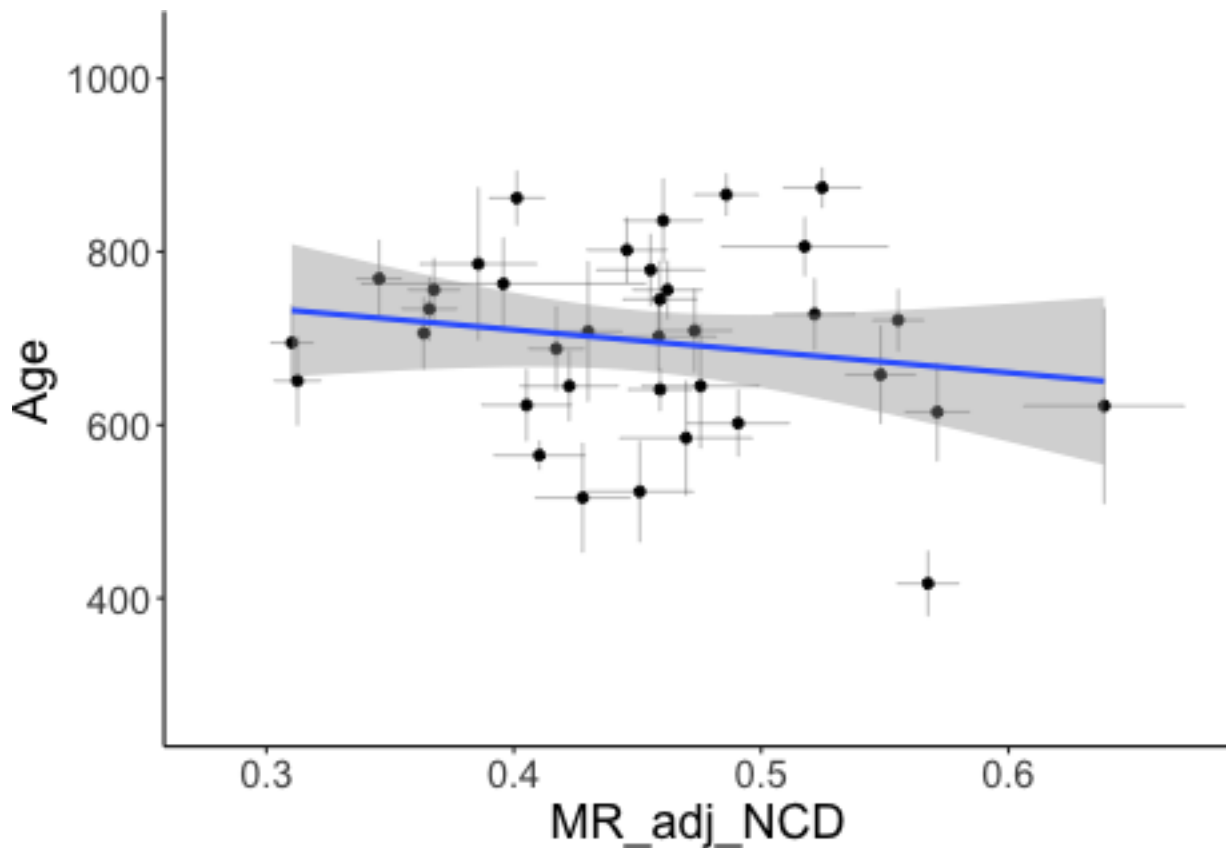
```

Age.N = N)

combined.age.mr.data <-
  full_join(aging.data, data.wide)

combined.age.mr.data %>%
  ggplot(aes(y=Age,
             x=MR_adj_NCD)) +
  geom_point() +
  geom_errorbar(aes(ymin=Age-Age.SE,
                   ymax=Age+Age.SE),
               alpha=0.25) +
  geom_errorbarh(aes(xmin=MR_adj_NCD-MR_W_SE_NCD,
                    xmax=MR_adj_NCD+MR_W_SE_NCD),
                alpha=0.25) +
  geom_smooth(method="lm") +
  theme_classic() +
  theme(text=element_text(size=18))

```



```

combined.age.mr.data %>%
  mutate_at(vars(Age, MR_adj_NCD), .funs=as.numeric) %>%
  summarize_at(vars(Age, MR_adj_NCD), .funs=function(x) shapiro.test(x)$p.value) %>%
  kable(caption="Shapiro-Wilk tests for normality")

```

Table 15: Shapiro-Wilk tests for normality

Age	MR_adj_NCD
0.98	0.725

```
with(combined.age.mr.data, cor.test(Age, MR_adj_NCD)) %>%
  tidy %>%
  kable(caption="Relationship between age (of female BXD mice) and adjusted metabolic rate")
```

Table 16: Relationship between age (of female BXD mice) and adjusted metabolic rate

estimate	statistic	p.value	parameter	conf.low	conf.high	method	alternative
-0.177	-1.05	0.302	34	-0.478	0.161	Pearson's product-moment correlation	two.sided

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] RColorBrewer_1.1-2 broom_0.7.11      ggrepel_0.9.1      ggplot2_3.3.5
## [5] readr_2.1.1        dplyr_1.0.7      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
```