

Absolute treatment effect by Pointwise meta-analysis - severe stunting

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2024-12-16

```
source(here::here("R", "0-config.R"))
```

```
##
##           0      1
## DOSE      811  126
## DYADG     1024   13
## DYADM      589   67
## GHANA      158    1
## HAITI      287   10
## JiVitA    3651  483
## MAHAY     2588  796
## PROMISBF   1695   82
## PROMISBF_CS 828   39
## PROMISM     926   86
## PROMISM_CS 1726  163
## RDNS      2269  209
## SHINE_HIV- 3372  302
## WASHB      4069  492
## WASHK      6013  581
## ZINC       2383  224
```

Note: DYADG and DYADM have empty rows for arm_primary – why? These are the studies that had maternal interventions. Removing them from the analysis. Also removed HAITI and GHANA because of very small sample sizes for severe stunting

```
# Remove studies "DYADG", "DYADM", "HAITI", and "GHANA"
df_analysis_severe_stunted <- subset(df_analysis_severe_stunted, !(study %in% c("DYADG", "DYADM", "HAITI", "GHANA")))
```

Fit a cubic splines model per study

```
#SS.Comb <- df_analysis %>%
# split(.$study) %>%
# map_dfr(function(df_analysis) {
#   study_name <- unique(df_analysis$study)
#   if (study_name %in% c(study_name)) {
#     model <- gam(severe_stunted ~ arm_primary + iwi * arm_primary + s(iwi, bs = "cr",
```

```

#                                     by = arm_primary),
#                                     data = df_analysis,
#                                     family = "gaussian", method = "REML")
# }
## Return a data frame with study_name and model
# data.frame(study = study_name, model = I(list(model)))
#})

SS.Comb_severe_stunted <- df_analysis_severe_stunted %>%
mutate(study = factor(study)) %>%
split(.$study) %>%
map_dfr(function(df_analysis_severe_stunted) {
  study_name <- unique(df_analysis_severe_stunted$study)
  if (study_name %in% c("DOSE")) {
    model <- gam(severe_stunted ~ arms_maternal + iwi * arms_maternal + s(iwi, bs = "cr",
                                                                    by = arms_maternal),
                data = df_analysis_severe_stunted,
                family = binomial("logit"), method = "REML")
  } else {
    model <- gam(severe_stunted ~ arms_maternal + iwi * arms_maternal + s(iwi, bs = "cr",
                                                                    by = arms_maternal) +
                s(cluster, bs = "re", by = dummy),
                data = df_analysis_severe_stunted,
                family = binomial("logit"), method = "REML")
  }
  # Return a data frame with study_name and model
  data.frame(study = study_name, model = I(list(model)))
})

new.data_severe_stunted <- df_analysis_severe_stunted %>%
select(study, cluster, arms_maternal) %>%
mutate(dummy = 0) %>%
distinct() %>%
expand_grid(iwi = seq(0, 70, by = 1))

predictions.SS.Comb_severe_stunted <- new.data_severe_stunted %>%
droplevels() %>%
arrange(desc(study)) %>%
group_by(study) %>%
nest() %>%
full_join(SS.Comb_severe_stunted, by = "study") %>%
group_by(study) %>%
do(augment(.$model[[1]], newdata = .$data[[1]], se_fit = T))

# View the resulting dataframe
print(predictions.SS.Comb_severe_stunted)

## # A tibble: 99,755 x 7
## # Groups:   study [12]
##   study cluster arms_maternal dummy   iwi .fitted .se.fit
##   <chr> <fct>   <fct>         <dbl> <dbl>   <dbl>   <dbl>

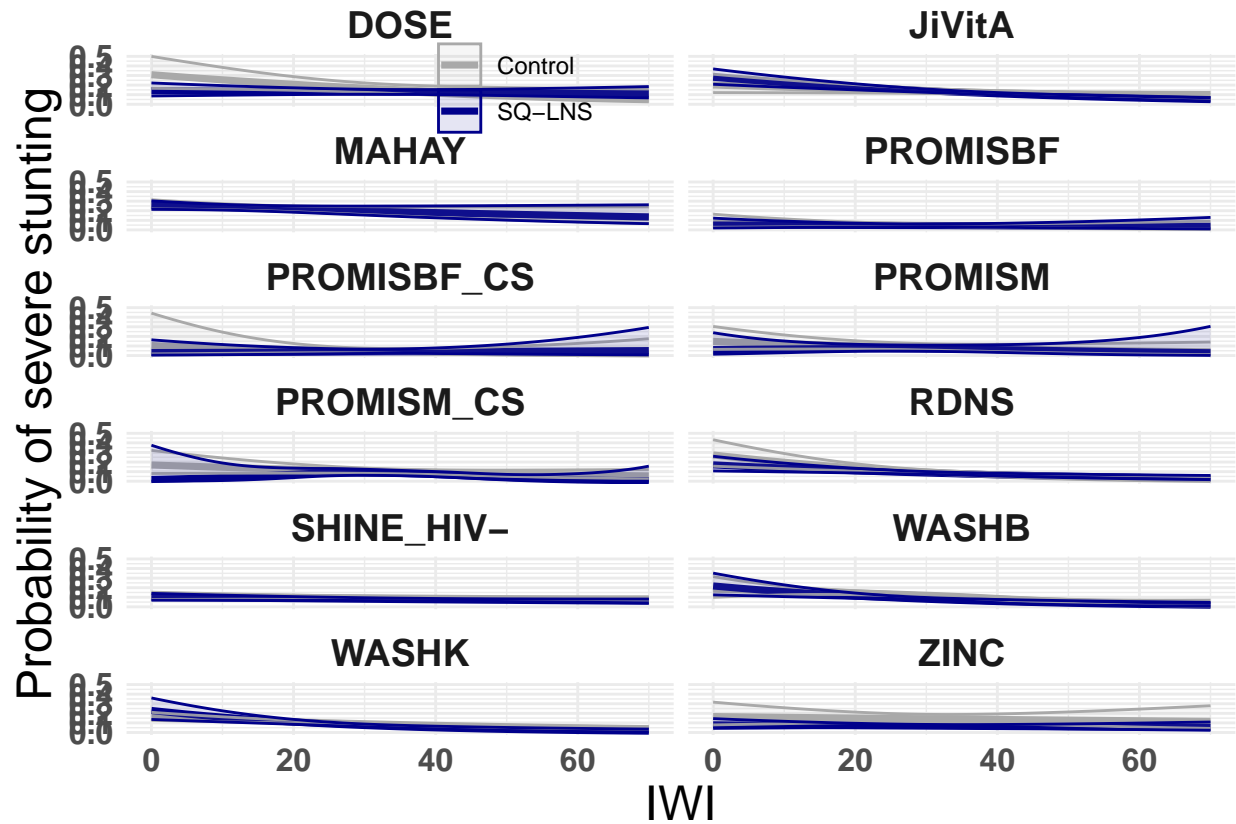
```

```
## 1 DOSE "" SQ-LNS 0 0 -1.81 0.283
## 2 DOSE "" SQ-LNS 0 1 -1.81 0.276
## 3 DOSE "" SQ-LNS 0 2 -1.81 0.269
## 4 DOSE "" SQ-LNS 0 3 -1.82 0.262
## 5 DOSE "" SQ-LNS 0 4 -1.82 0.255
## 6 DOSE "" SQ-LNS 0 5 -1.82 0.248
## 7 DOSE "" SQ-LNS 0 6 -1.83 0.242
## 8 DOSE "" SQ-LNS 0 7 -1.83 0.235
## 9 DOSE "" SQ-LNS 0 8 -1.84 0.228
## 10 DOSE "" SQ-LNS 0 9 -1.84 0.222
## # i 99,745 more rows
```

```
#write_csv(predictions.SS.Comb, here::here("output", "predictions_SSComb.csv"))
#write_csv(predictions.SS.Comb, here::here("output", "predictions_SSComb_nocluster.csv"))

plot_study_severe_stunted <- predictions.SS.Comb_severe_stunted%>%
  ggplot(., aes(iwi,expit(.fitted), color= arms_maternal))+
  geom_line(size=1.25)+
  facet_wrap(~study, ncol = 2, nrow = 6) +
  scale_colour_manual(values = c('darkgrey','darkblue')) +
  scale_fill_manual(values = c('darkgrey','darkblue')) +
  geom_ribbon(mapping = aes(ymin= expit(.fitted - 1.96*.se.fit),
                           ymax = expit(.fitted + 1.96*.se.fit),
                           fill= arms_maternal), alpha= 0.1)+
  ylab("Probability of severe stunting") +
  xlab("IWI") +
  labs(color='Treatment',fill='Treatment') +
  theme_minimal() +
  theme(legend.position = c(0.35,0.95),
        #"none",
        legend.title = element_blank(),
        axis.title.y = element_text(size = 18),
        axis.title.x = element_text(size = 18),
        strip.text = element_text(face="bold", size=14, hjust = 0.5),
        axis.text.y = element_text(face="bold", size=12),
        axis.text.x = element_text(face="bold", size=12))

print(plot_study_severe_stunted)
```



```
table(df_analysis_severe_stunted$study, df_analysis_severe_stunted$severe_stunted)
```

```
##
##           0      1
## DOSE      811  126
## JiVitA    3651  483
## MAHAY     2588  796
## PROMISBF  1695   82
## PROMISBF_CS 828   39
## PROMISM    926   86
## PROMISM_CS 1726  163
## RDNS      2269  209
## SHINE_HIV- 3372  302
## WASHB      4069  492
## WASHK      6013  581
## ZINC      2383  224
```

Point-wise Meta-analysis

```
# Create a new dataframe for the pointwise meta-analysis
# Since the predicted outcomes are similar with or without the random effect for the cluster variable,
new.data_severe_stunted <- df_analysis_severe_stunted %>%
  select(study, cluster, arms_maternal) %>%
```

```

mutate(dummy = 0) %>%
mutate(cluster = rep(unique(cluster), length.out = 1)) %>%
distinct() %>%
expand_grid(iwi = seq(0, 70, by = 1))

predictions.SS.Comb_severe_stunted <- new.data_severe_stunted %>%
  droplevels() %>%
  arrange(desc(study)) %>%
  group_by(study) %>%
  nest() %>%
  full_join(SS.Comb_severe_stunted, by = "study") %>%
  group_by(study) %>%
  do(augment(.$model[[1]], newdata = .$data[[1]], se_fit = T))

point.wise.DF.SS.Comb_severe_stunted = pointwise.ma(predictions.SS.Comb_severe_stunted,
  clustering.variable = "study",
  combining.variables = c("iwi", "arms_maternal"),
  predicted.outcome = ".fitted",
  predicted.outcome.se = ".se.fit",
  predicted.outcome.CI = NULL,
  tau.method = "REML")

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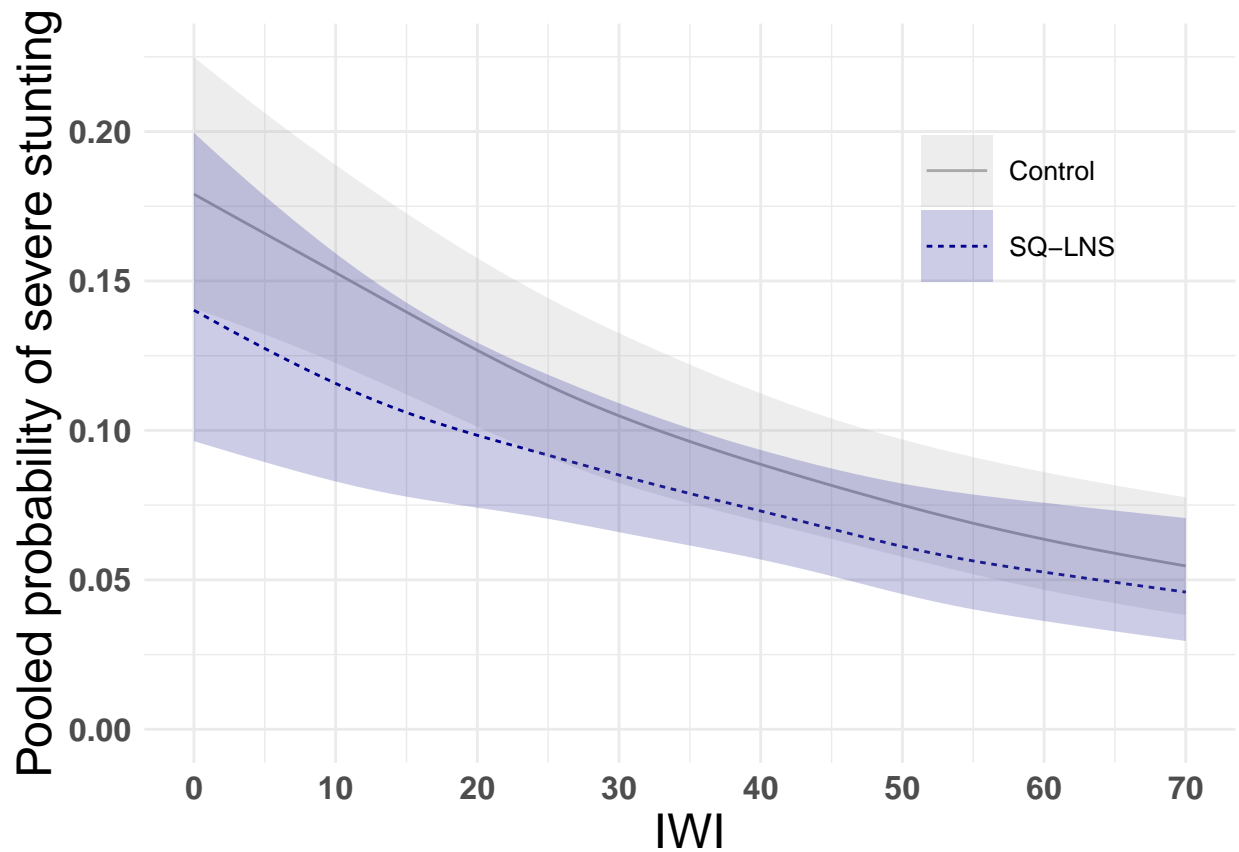
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```
## Backtransform predicted outcomes and their corresponding confidence intervals
```

```
point.wise.DF.SS.Comb_severe_stunted$RE.meta = expit(point.wise.DF.SS.Comb_severe_stunted$RE.me
point.wise.DF.SS.Comb_severe_stunted$RE.meta.upper = expit(point.wise.DF.SS.Comb_severe_stunted$RE.me
point.wise.DF.SS.Comb_severe_stunted$RE.meta.lower = expit(point.wise.DF.SS.Comb_severe_stunted$RE.me
```

```
point.wise.DF.SS.Comb.plot_severe_stunted = point.wise.DF.SS.Comb_severe_stunted%>%
  mutate(Treatment = as.factor(arms_maternal)) %>%
  ggplot(aes(x = iwi, y = RE.meta, fill = Treatment, linetype = Treatment)) +
  geom_line(size=0.5, aes(colour = Treatment))+
  scale_color_manual(values = c('darkgrey','darkblue')) +
  scale_fill_manual(values = c('darkgrey','darkblue')) +
  geom_ribbon(aes(ymin = RE.meta.lower,ymax=RE.meta.upper),alpha=0.2) +
  #scale_color_jama(name= "Treatment")+
  #scale_linetype_discrete(name="Treatment")+ylab("") +
  #scale_linetype_manual(values=c("solid","dashed")) +
  labs(color='Treatment', fill='Treatment', linetype='Treatment') +
  xlab(bquote('IWI')) +
  ylab(bquote('Pooled probability of severe stunting')) +
  theme_minimal() +
  theme(legend.position = c(0.80,0.75),
        legend.title = element_blank(),
        axis.title.y = element_text(size = 18),
        axis.title.x = element_text(size = 18),
        strip.text = element_text(face="bold", size=14, hjust = 0.5),
        axis.text.y = element_text(face="bold", size=12),
        axis.text.x = element_text(face="bold", size=12),
        legend.key.size = unit(1, "cm"),
        legend.key.width = unit(1,"cm"),
        legend.text=element_text(size=10, hjust = 0)) + ylim(c(0,NA)) +
  scale_x_continuous(breaks = seq(min(point.wise.DF.SS.Comb_severe_stunted$iwi), max(point.wise.DF.SS.C

print(point.wise.DF.SS.Comb.plot_severe_stunted)
```



```
# Save the plot
#ggsave(here::here("output", "gam_pooled_pointwise_wasted.png"),
#       plot = point.wise.DF.SS.Comb.plot, width = 6, height = 6, dpi = 300)
```

Absolute treatment effect

```
predictions.SS.Comb_severe_stunted=predictions.SS.Comb_severe_stunted%>%
  mutate(Lower = .fitted - 1.96*.se.fit,
         Upper = .fitted + 1.96*.se.fit)%>%
  mutate(fit = expit(.fitted), Lower = expit(Lower), Upper = expit(Upper)) %>%
  mutate(iwi = as.character(iwi))

absolute_diff_SS.Comb_severe_stunted = risk.diff.creator(dataframe = predictions.SS.Comb_severe_stunted,
  treatment = "arms_maternal", outcome = NULL,
  matching.variables = c("iwi","study"),
  predicted.outcome = "fit",
  predicted.CI = c("Lower","Upper"))

absolute_diff_SS.Comb_severe_stunted= absolute_diff_SS.Comb_severe_stunted%>%
  select(study, iwi, fit.diff, diff.lower, diff.upper)
```

```

point.wise.absolute_diff_SS.Comb_severe_stunted = pointwise.ma(data = absolute_diff_SS.Comb_severe_stunted,
  clustering.variable = "study",
  combining.variables = c("iwi"),
  predicted.outcome = "fit.diff",
  predicted.outcome.se = NULL,
  predicted.outcome.CI = c("diff.lower", "diff.upper"),
  tau.method = "REML"
)

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```

```
point.wise.absolute_diff_SS.Comb_severe_stunted = point.wise.absolute_diff_SS.Comb_severe_stunted%>%
  mutate(iwi = as.numeric(iwi))
```

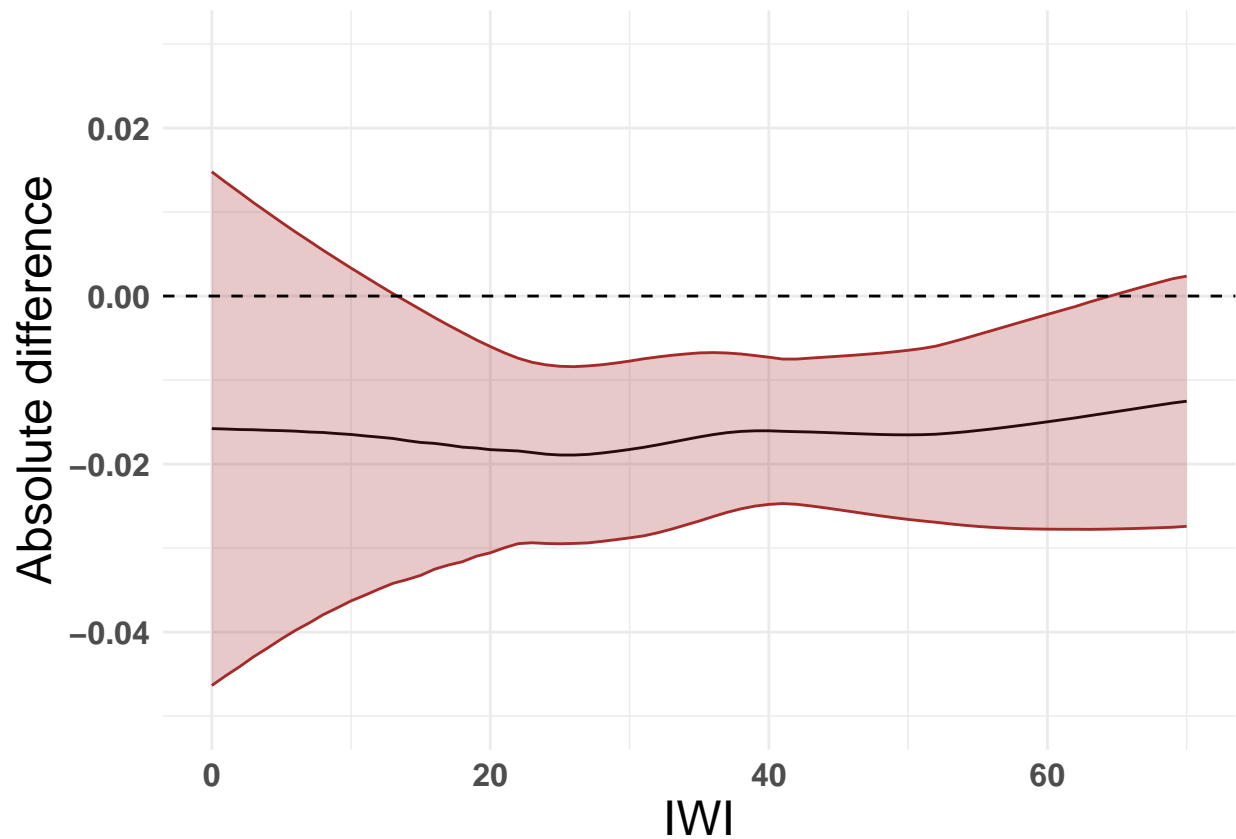
```
point.wise.DF.SS.Comb.diff.plot_severe_stunted=point.wise.absolute_diff_SS.Comb_severe_stunted%>%
  ggplot(aes(x = iwi,y=RE.meta)) + geom_line(size=0.5)+
  geom_ribbon(mapping = aes(ymin=RE.meta.lower, ymax=RE.meta.upper),alpha=0.25,
             color="brown", fill="brown")+
  geom_hline(yintercept = 0, linetype=2)+ylab("") +
  xlab(bquote('IWI')) +
```

```

ylab(bquote('Absolute difference')) +
theme_minimal() +
theme(axis.title.y = element_text(size = 18),
      axis.title.x = element_text(size = 18),
      strip.text = element_text(face="bold", size=14, hjust = 0.5),
      axis.text.y = element_text(face="bold", size=12),
      axis.text.x = element_text(face="bold", size=12)) + ylim(c(-0.05,0.03))

print(point.wise.DF.SS.Comb.diff.plot_severe_stunted)

```

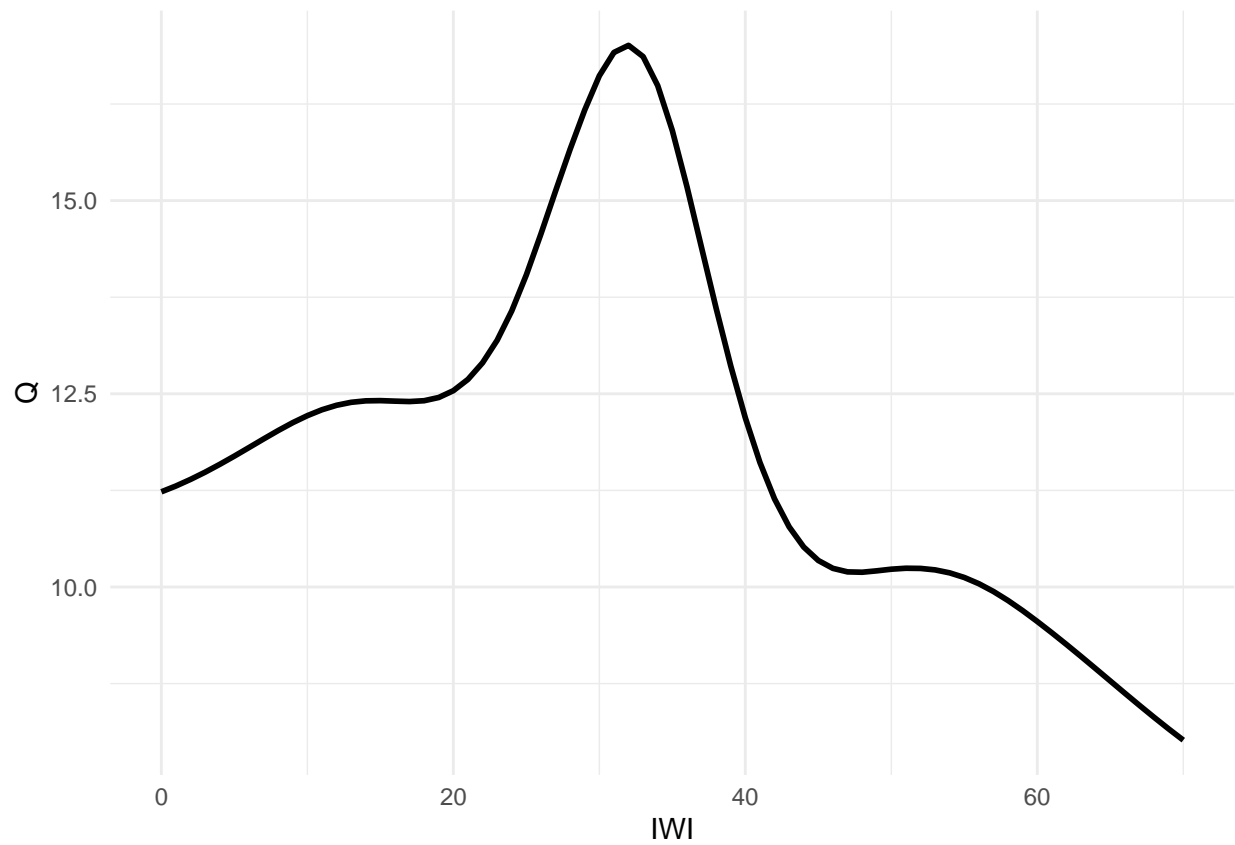


```

point.wise.Q.plot_severe_stunted=point.wise.absolute_diff_SS.Comb_severe_stunted%>%
  ggplot(aes(x = iwi,y=Q)) + geom_line(size=1)+
  xlab(bquote('IWI')) +
  theme_minimal()

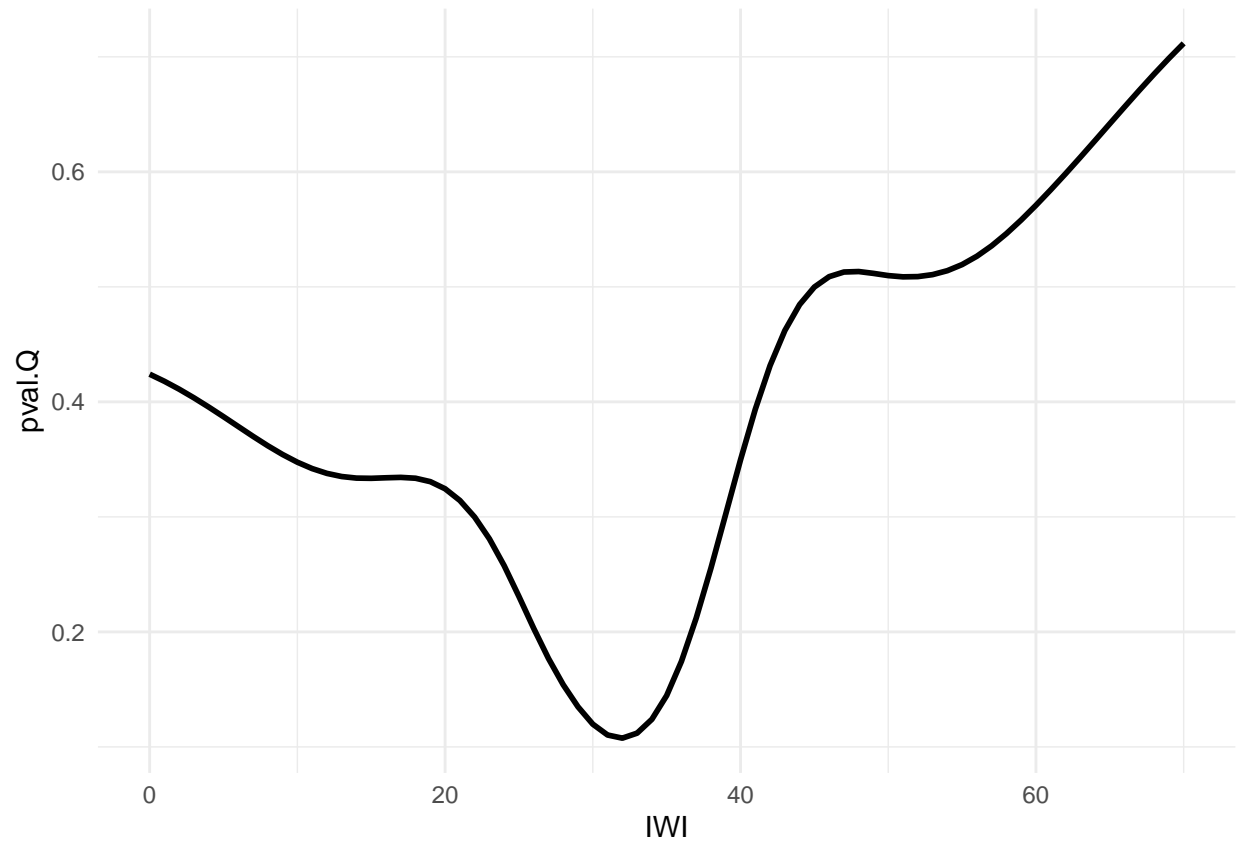
print(point.wise.Q.plot_severe_stunted)

```

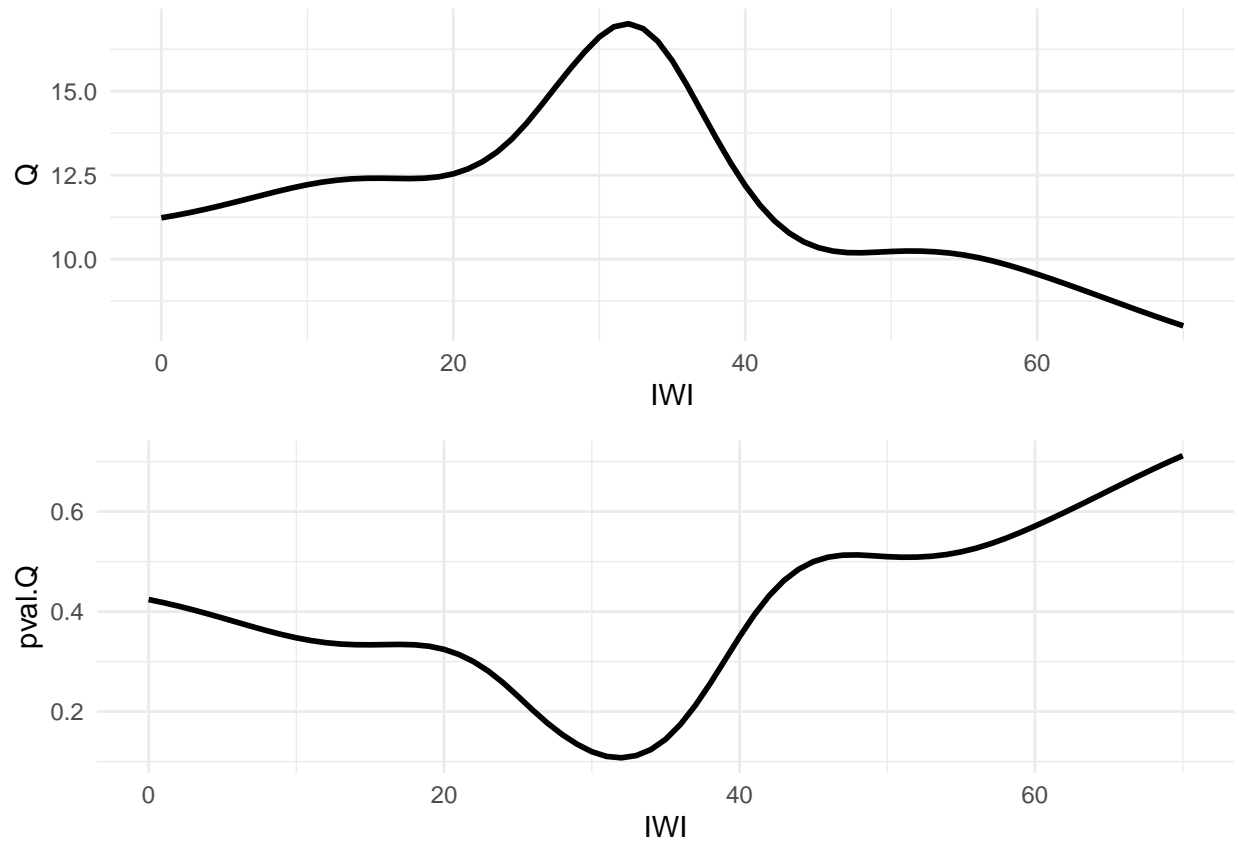


```
point.wise.pvalQ.plot_severe_stunted=point.wise.absolute_diff_SS.Comb_severe_stunted%>%
  ggplot(aes(x = iwi,y=pval.Q)) + geom_line(size=1)+
  xlab(bquote('IWI')) +
  theme_minimal()

print(point.wise.pvalQ.plot_severe_stunted)
```



```
plot_composite_hetero_severe_stunted <- plot_grid(point.wise.Q.plot_severe_stunted, point.wise.pvalQ.pl  
          nrow=2, align = "h")  
plot_composite_hetero_severe_stunted
```

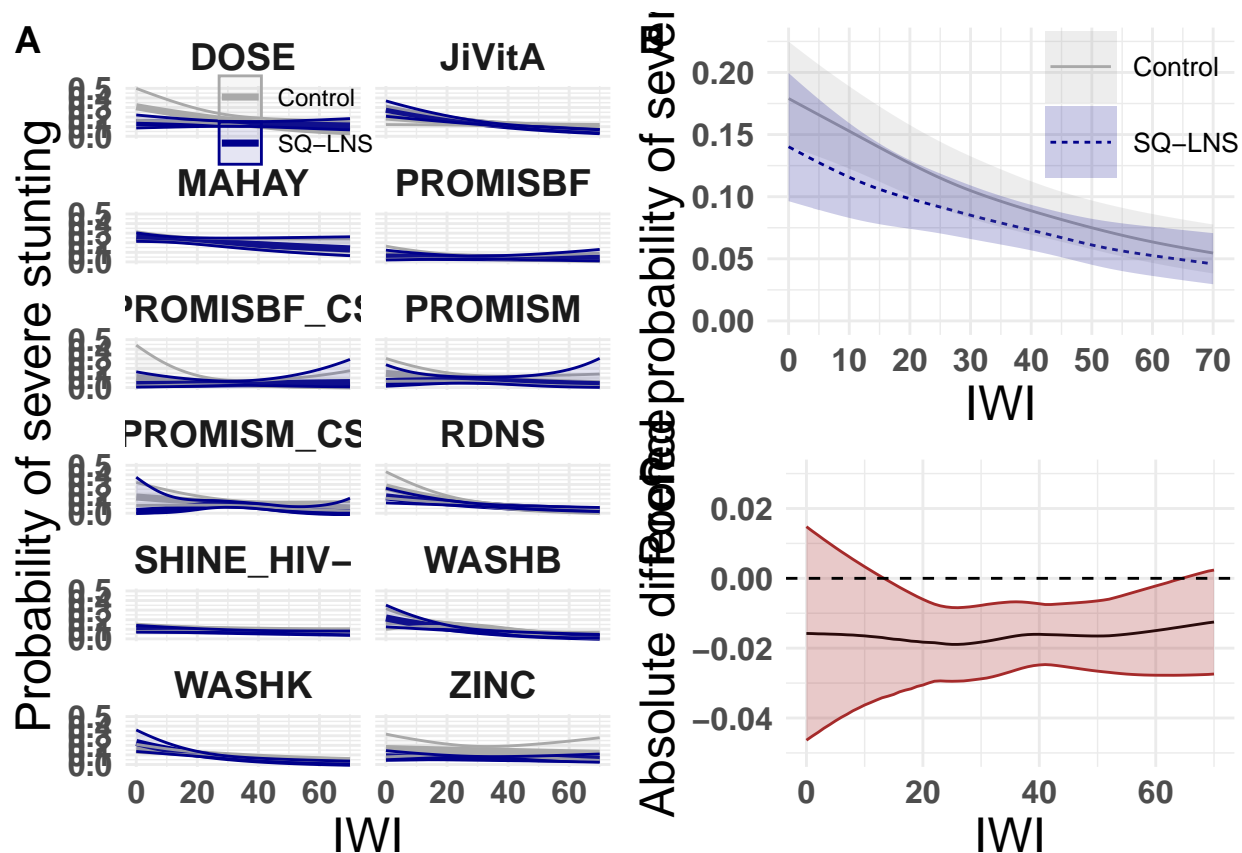



```
# Save the plot
#ggsave(here::here("output", "qplot_pooled_pointwise_wasted.png"),
#       plot = point.wise.Q.plot, width = 6, height = 6, dpi = 300)

plot_comp_effect_severe_stunted <- plot_grid(point.wise.DF.SS.Comb.plot_severe_stunted, point.wise.DF.SS.Comb.plot_severe_stunted,
                                              ncol=2, labels = c("A", "", ""))

plot_composite_severe_stunted <- plot_grid(plot_study_severe_stunted, plot_comp_effect_severe_stunted,
                                              ncol=2, labels = c("A", "", ""))

plot_composite_severe_stunted
```



```
# Save the plot
#ggsave(here::here("output", "gam_pooled_pointwise_severe_stunted_arm_maternal.png"),
# plot = plot_composite_severe_stunted, width = 14, height = 16, dpi = 300)
```

Session info

```
sessionInfo()
```

```
## R version 4.3.3 (2024-02-29)
## Platform: aarch64-apple-darwin20 (64-bit)
## Running under: macOS Sonoma 14.5
##
## Matrix products: default
## BLAS: /System/Library/Frameworks/Accelerate.framework/Versions/A/Frameworks/vecLib.framework/Versions/A/
## LAPACK: /Library/Frameworks/R.framework/Versions/4.3-arm64/Resources/lib/libRlapack.dylib; LAPACK v
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## time zone: America/Los_Angeles
## tzcode source: internal
##
## attached base packages:
## [1] stats graphics grDevices utils datasets methods base
##
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## other attached packages:
## [1] geepack_1.3.10      estimatr_1.0.4      sandwich_3.1-0      msm_1.7.1
## [5] lmtest_0.9-40       zoo_1.8-12          tidymv_3.4.2        meta_7.0-0
## [9] metadat_1.2-0       mgcv_1.9-1          nlme_3.1-164        patchwork_1.2.0
## [13] RColorBrewer_1.1-3  cowplot_1.1.3       gridExtra_2.3        ggrepel_0.9.5
## [17] ggsci_3.0.1         broom_1.0.5         rmarkdown_2.26       skimr_2.1.5
## [21] readxl_1.4.3        lubridate_1.9.3     forcats_1.0.0       stringr_1.5.1
## [25] purrr_1.0.2         readr_2.1.5         tidyr_1.3.1         tibble_3.2.1
## [29] ggplot2_3.5.1       tidyverse_2.0.0     haven_2.5.4         table1_1.4.3
## [33] dplyr_1.1.4         here_1.0.1
##
## loaded via a namespace (and not attached):
## [1] tidyselect_1.2.1    farver_2.1.2        fastmap_1.1.1       CompQuadForm_1.4.3
## [5] mathjaxr_1.6-0      digest_0.6.35       timechange_0.3.0    lifecycle_1.0.4
## [9] survival_3.5-8      magrittr_2.0.3      compiler_4.3.3      sass_0.4.9
## [13] rlang_1.1.4         tools_4.3.3         utf8_1.2.4          yaml_2.3.8
## [17] knitr_1.45          labeling_0.4.3       xml2_1.3.6          repr_1.1.7
## [21] expm_0.999-9        withr_3.0.0         numDeriv_2016.8-1.1 grid_4.3.3
## [25] fansi_1.0.6         colorspace_2.1-0    scales_1.3.0        MASS_7.3-60.0.1
## [29] tinytex_0.50        cli_3.6.2           mvtnorm_1.2-4       metafor_4.6-0
## [33] ragg_1.3.0          generics_0.1.3      rstudioapi_0.15.0   tzdb_0.4.0
## [37] cachem_1.0.8        minqa_1.2.6         splines_4.3.3       cellranger_1.1.0
## [41] base64enc_0.1-3     vctrs_0.6.5         boot_1.3-29         Matrix_1.6-5
## [45] jsonlite_1.8.8      hms_1.1.3           Formula_1.2-5       systemfonts_1.0.6
## [49] jquerylib_0.1.4     glue_1.7.0          nloptr_2.0.3        stringi_1.8.4
## [53] gtable_0.3.5        lme4_1.1-35.1       munsell_0.5.1       pillar_1.9.0
## [57] htmltools_0.5.7     R6_2.5.1            textshaping_0.3.7   rprojroot_2.0.4
## [61] evaluate_0.23       lattice_0.22-5      highr_0.10          backports_1.4.1
## [65] bslib_0.6.1         Rcpp_1.0.12         xfun_0.42           pkgconfig_2.0.3

```