EDA: MS ComBat GAM vs Linear

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Objective

To compare effects of applying ComBat-GAM vs ComBat-Linear in the MS data.

IMPORTANT

MS patients from the *HSC* site that were scanned in a *SIEMENSTIMTRIO* scanner were excluded from the current harmonization.

```
[1] "In MS:"
```

	CHP	HSC
SIEMENSPRISMAFIT	0	28
SIEMENSTIMTRIO	0	18
SIEMENSVERIO	21	0

IMPORTANT (cont.)

The corresponding group in the Healthy Control data was similarly excluded when modeling site effects with ComBat-GAM.

```
[1] "In HC:"
```

	CHP	HSC	PNC
SIEMENSPRISMAFIT	0	58	0
SIEMENSTIMTRIO	0	7	1185
SIEMENSVERIO	36	0	0

Datasets: MS

MS (dimensions):

```
## [1]  49 161
```

MS (count by site)

site	n
CHP	21
HSC	28

MS (count by sex)

sex	site	n
FEMALE	CHP	18
FEMALE	HSC	17
MALE	CHP	3
MALE	HSC	11

Totals: Females = 35; Males = 14

Datasets: HC

Dimensions HC (no PNC):

```
## [1]  94 161
```

Count per site:

site	n
CHP	36
HSC	58

Count by sex and site:

site	sex	n
CHP	FEMALE	24
CHP	MALE	12
HSC	FEMALE	37
HSC	MALE	21

Totals: Females 61; Males 33

Datasets: HC + MS

Dimensions (no PNC):

```
## [1] 143 161
```

Count per site:

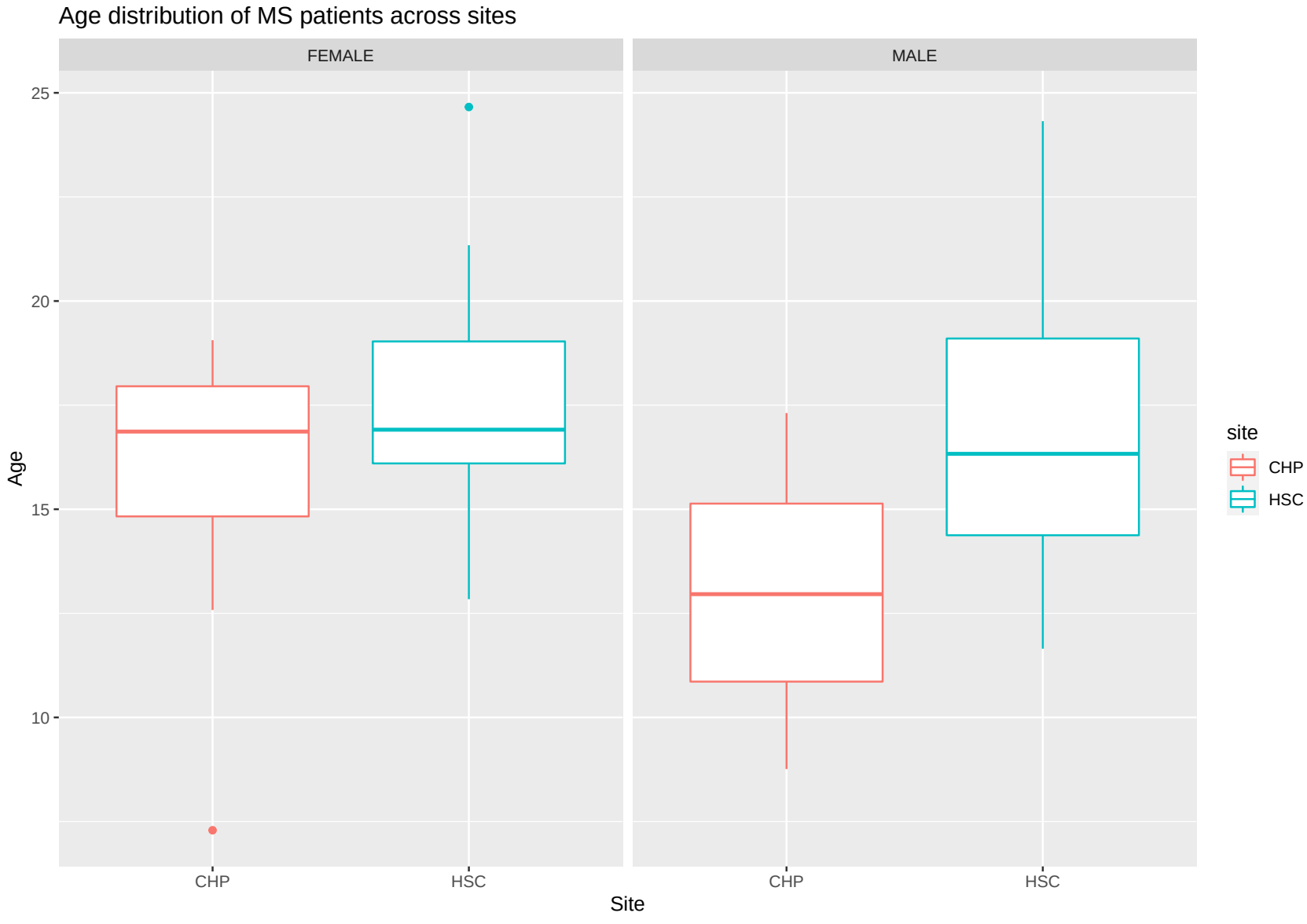
site	n
CHP	57
HSC	86

Count by sex and site:

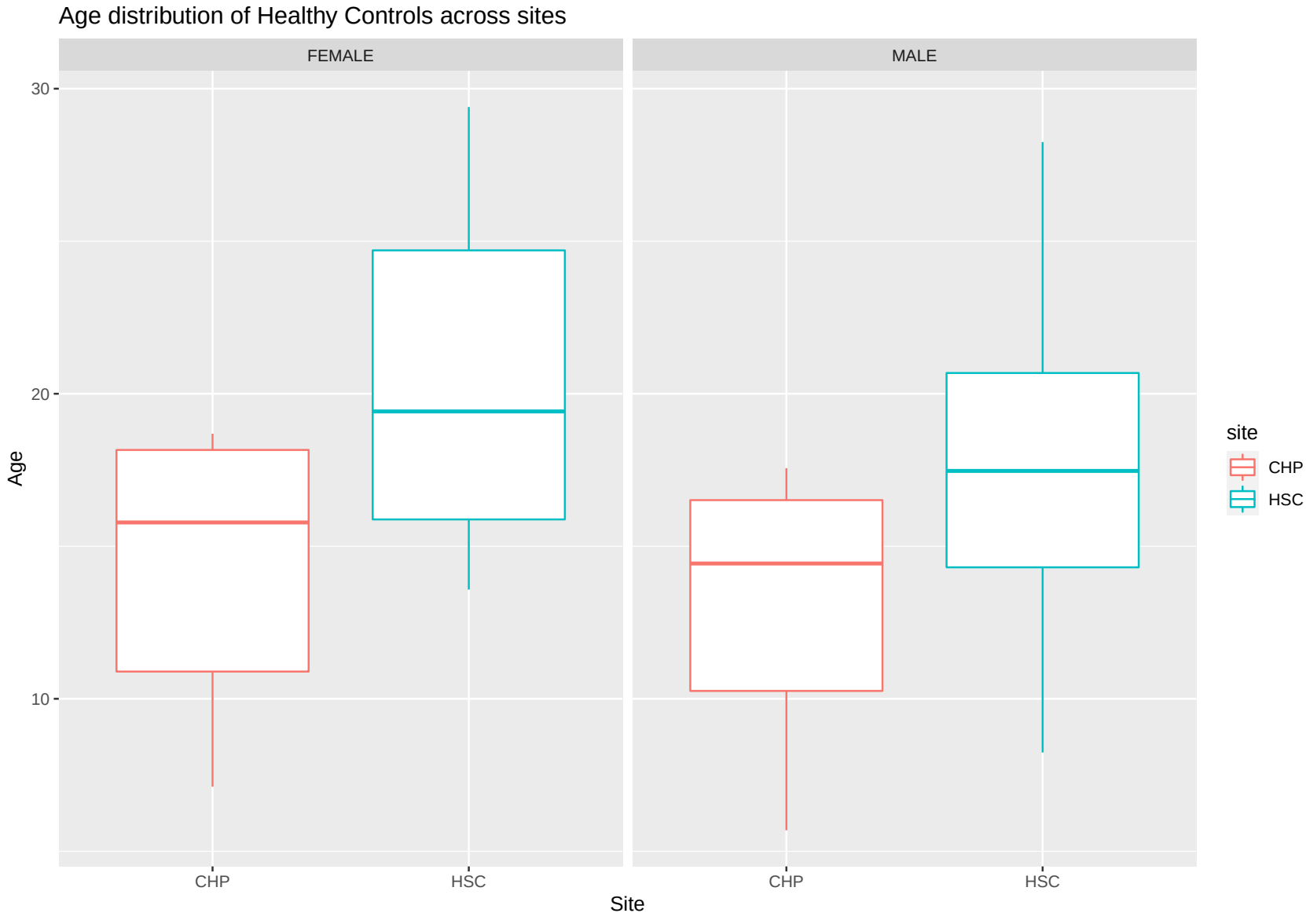
site	sex	n
CHP	FEMALE	42
CHP	MALE	15
HSC	FEMALE	54
HSC	MALE	32

Totals: Females 61; Males 33

Age across sites [MS]



Age across sites [HC]



Harmonization Approach

Adjusted data are shown for the following approach:

- Join HC and MS data into one dataset
- Split this dataset into males and females
- Run ComBat (GAM and Linear) on in parallel on males and females.

Models used in harmonization

- GAM: s(age) + MS
- Linear: age + age^2 + MS

Site effects: MS + HC [GAM]

Number of ROIs showing site effects:

Full covariate model:

[1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Ignore sex: [1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects by sex: MS + HC [GAM]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects: MS + HC [Linear]

Full covariate model:

[1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Sex not considered: [1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects by sex: MS + HC [Linear]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects: MS [GAM]

Full model:

[1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	9

Ignore sex:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects: MS [Linear]

Number of ROIs showing site effects:

Full model: [1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	11

Sex not considered: [1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects by sex: MS [GAM]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	1

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
16	1	54

Site effects by sex: MS [Linear]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	0

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
18	2	56

Site effects: HC [GAM]

Full model:

[1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	7

Sex not considered:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	15

Site effects by sex: HC [GAM]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	2

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	2

Site effects: HC [Linear]

Number of ROIs showing site effects:

Full model: [1] "~ age + age2 + sex + MS"

FDR	Bonferroni	Uncorrected P
0	0	3

Sex not considered: [1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	11

Site effects by sex: HC [Linear]

Females:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	2

Males:

[1] "~ age + age2 + MS"

FDR	Bonferroni	Uncorrected P
0	0	1

Conclusions

Harmonization seems to be effective for Females in HC and MS.

With the current approach, MS Males are not harmonized correctly.