EDA: MS ComBat-GAM

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Objective

To visualize effects of ComBat-GAM applied on the MS data relative to the raw 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]  49 160
```

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

Datasets: HC

Dimensions HC (no PNC):

```
## [1]  94 160
```

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] 143 160
```

Count per site:

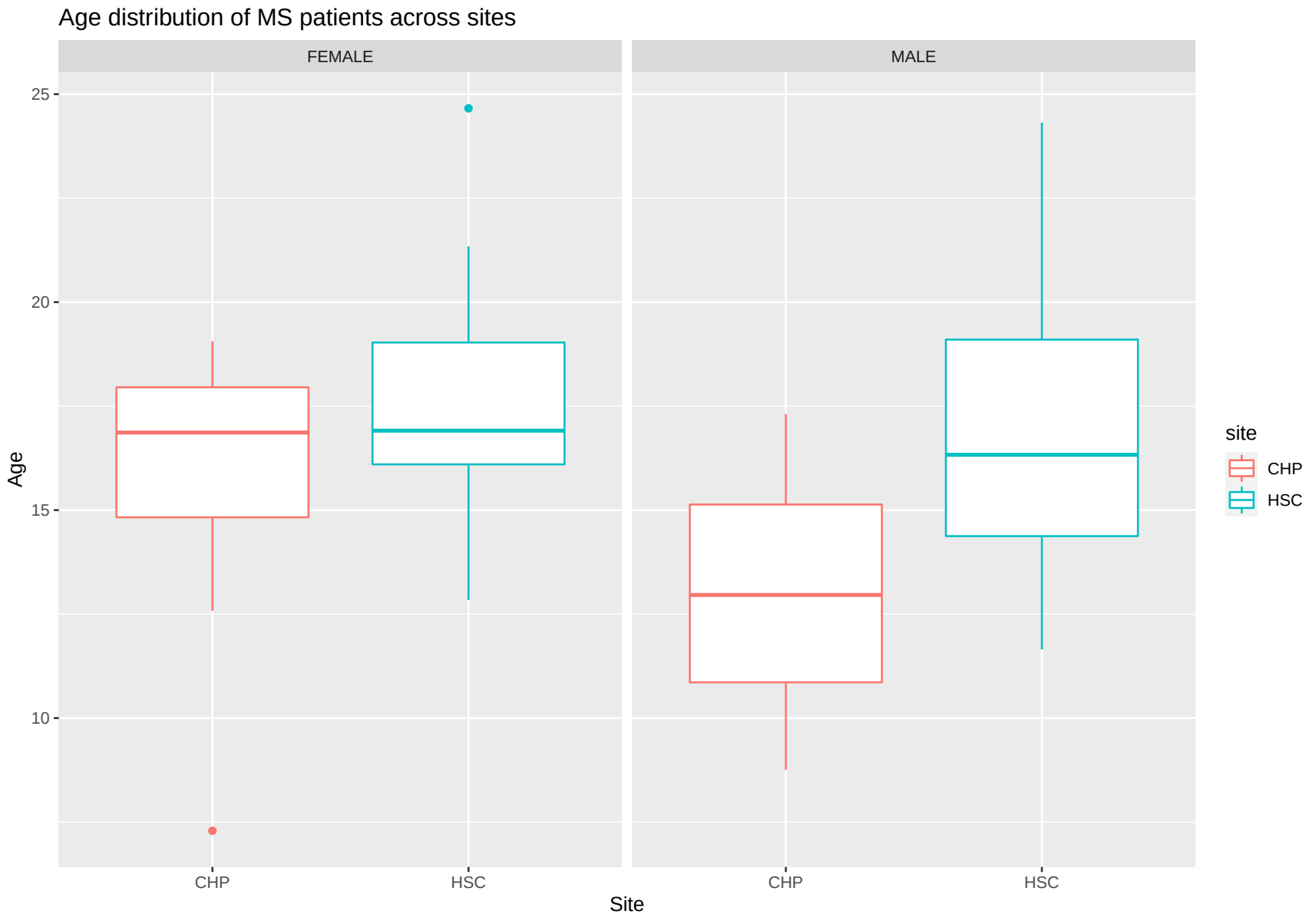
site	n
CHP	57
HSC	86

Count by sex and site:

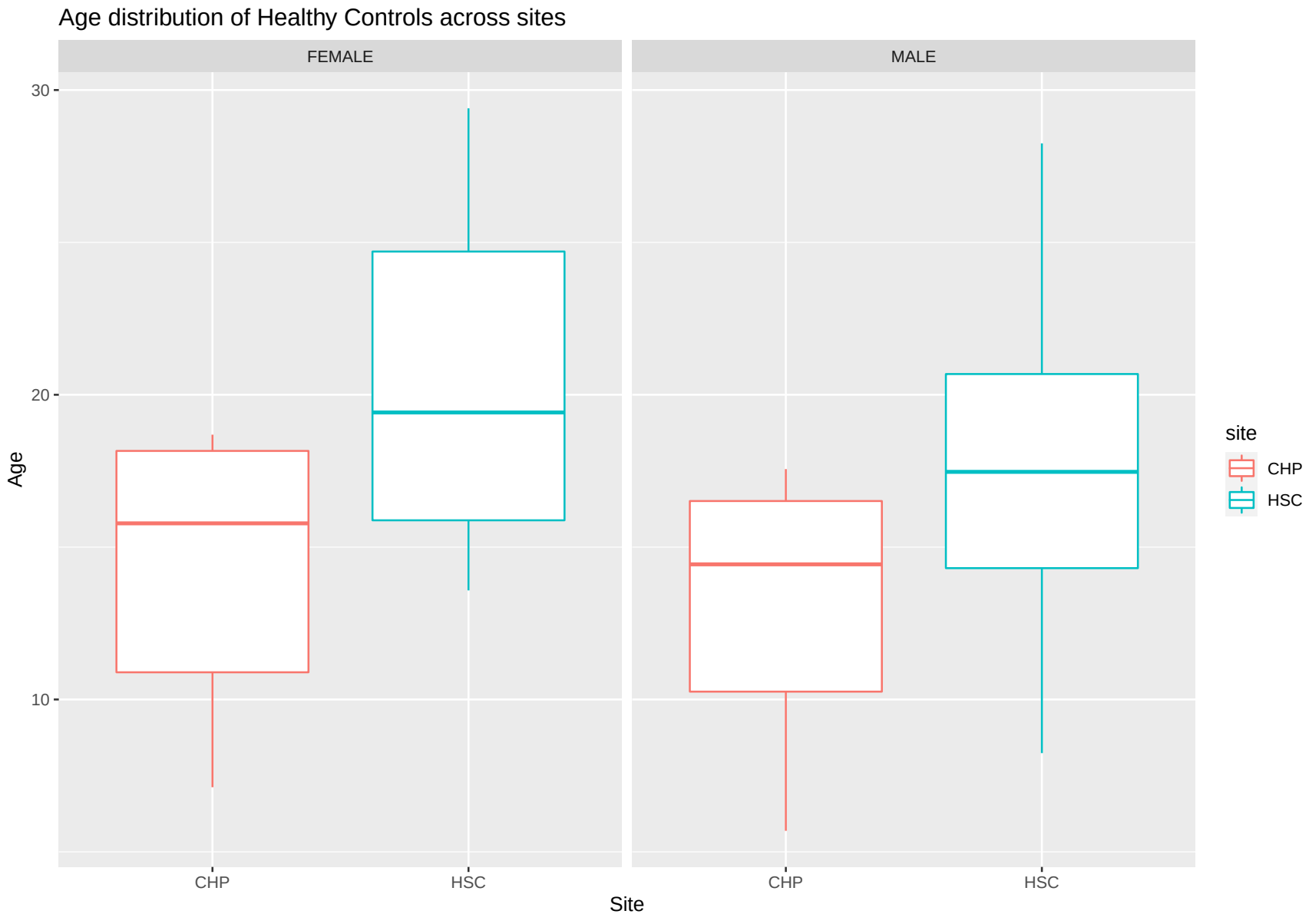
site	sex	n
CHP	FEMALE	42
CHP	MALE	15
HSC	FEMALE	54
HSC	MALE	32

Totals: Females 61; Males 33

Age across sites [MS]



Age across sites [HC]



Harmonization Approach

Adjusted data are shown for the following approach:
* Split the HC data into males and females
* Run ComBat-GAM on both datasets.
* Apply resulting models to MS data in males and females respectively.

Checking site effects

Site effects were tested with different models and data splits.

For full datasets, either sex and interactions terms (x $\sim$ sex + age + age2 + age *x* sex + age2 *x* sex) were included or only age terms (x $\sim$ age + age2).

For datasets split by sex, only age terms were included.

Site effects: MS raw

Number of ROIs showing site effects:

Full covariate model:

FDR	Bonferroni	Uncorrected P
1	1	22

Sex not considered:

FDR	Bonferroni	Uncorrected P
6	3	14

Site effects: MS adj

Full covariate model:

FDR	Bonferroni	Uncorrected P
6	2	37

Sex not considered:

FDR	Bonferroni	Uncorrected P
0	0	5

Site effects by sex: MS adj

Females:

FDR	Bonferroni	Uncorrected P
0	0	11

Males:

FDR	Bonferroni	Uncorrected P
44	7	67

Site effects: HC raw

Full model:

FDR	Bonferroni	Uncorrected P
50	21	61

Sex not considered:

FDR	Bonferroni	Uncorrected P
53	24	68

Site effects: HC adj

Number of ROIs showing site effects:

Full model:

FDR	Bonferroni	Uncorrected P
0	0	0

Sex not considered:

FDR	Bonferroni	Uncorrected P
0	0	0

Site effects by sex: HC adj

Females:

FDR	Bonferroni	Uncorrected P
0	0	0

Males:

FDR	Bonferroni	Uncorrected P
0	0	0

Conclusions

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

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