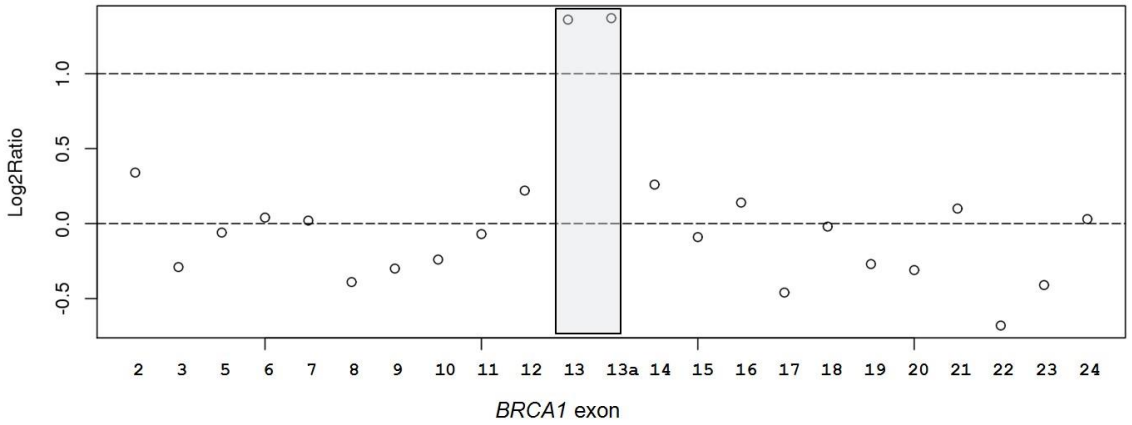
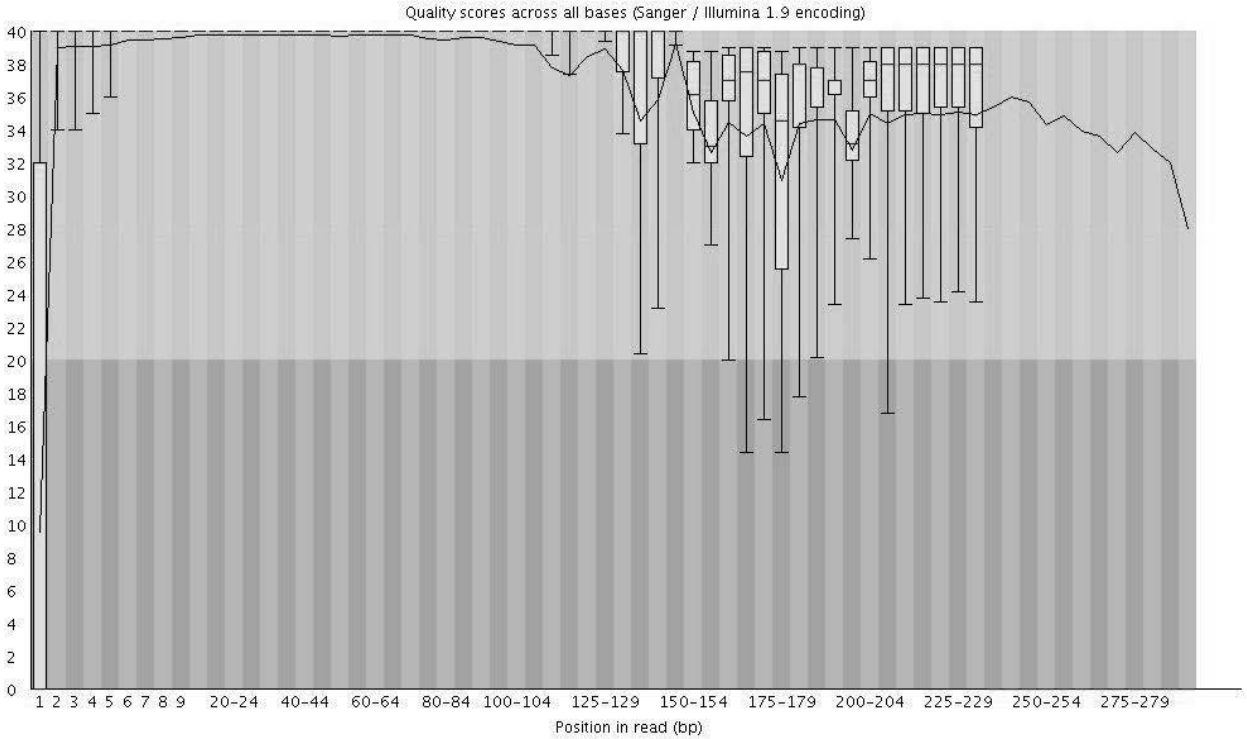
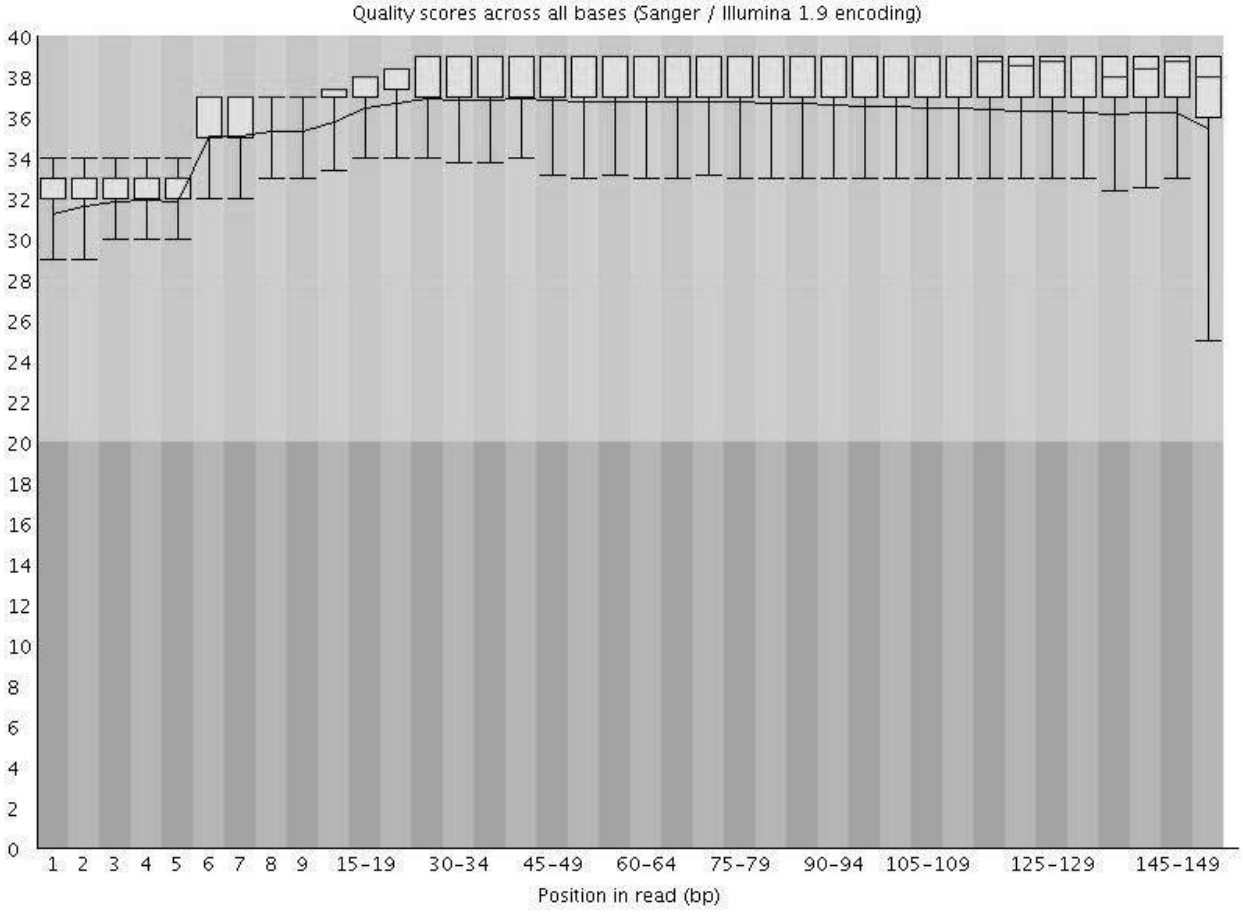


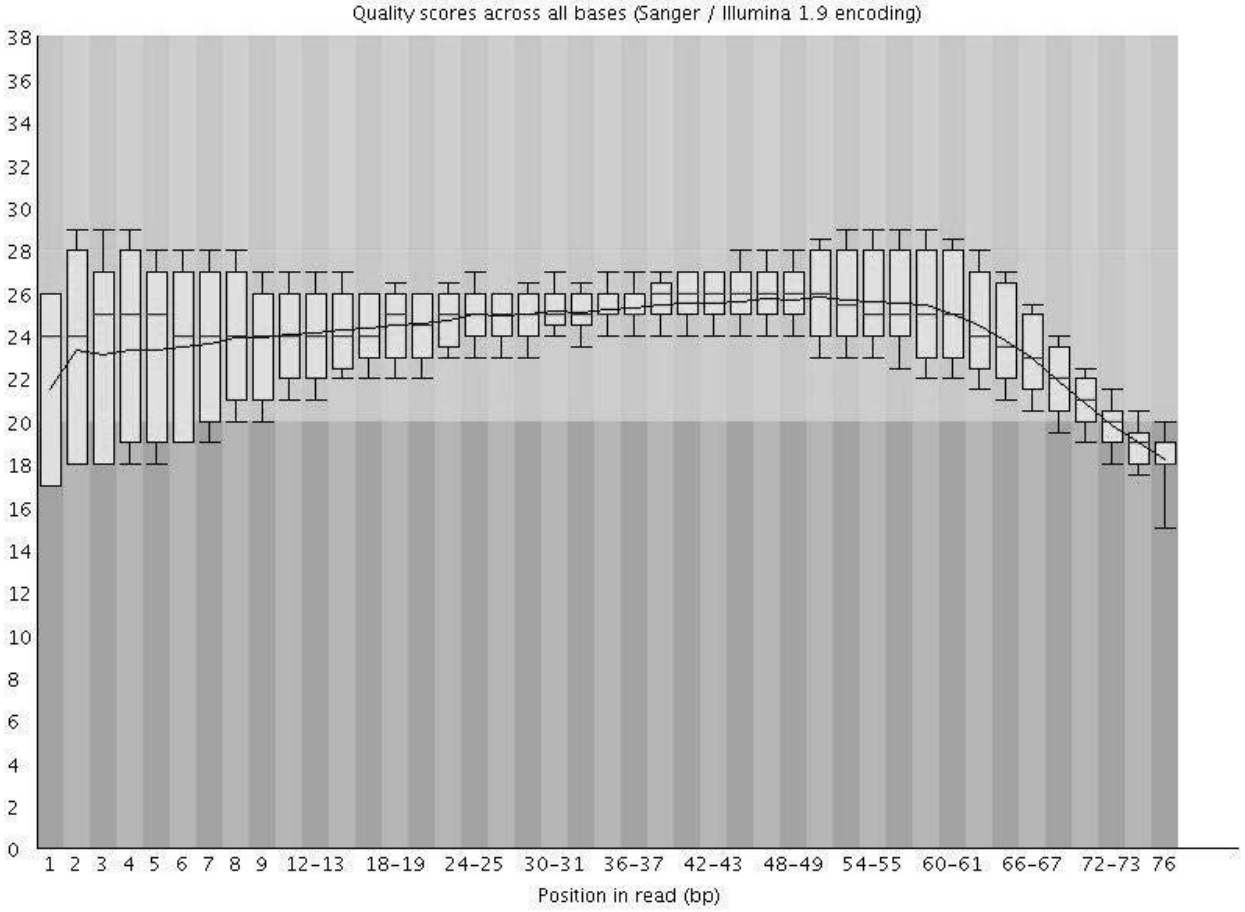

Supp. Figure S1: Copy number profile across *BRCA1* exons for sample S07 (reference laboratory).
Further evidence of copy number changes in *BRCA1* at exon 13 in sample 7 in the reference data analysed using Seq2C [20] with Log 2 values normalised by sample median. The boxed region indicates the location of the amplification.


Quality scores across all bases (Sanger / Illumina 1.9 encoding)
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
1 2 3 4 5 6 7 8 9
20-24
40-44
60-64
80-84
100-104
125-129
150-154
175-179
200-204
225-229
250-254
275-279
Position in read (bp)

a)

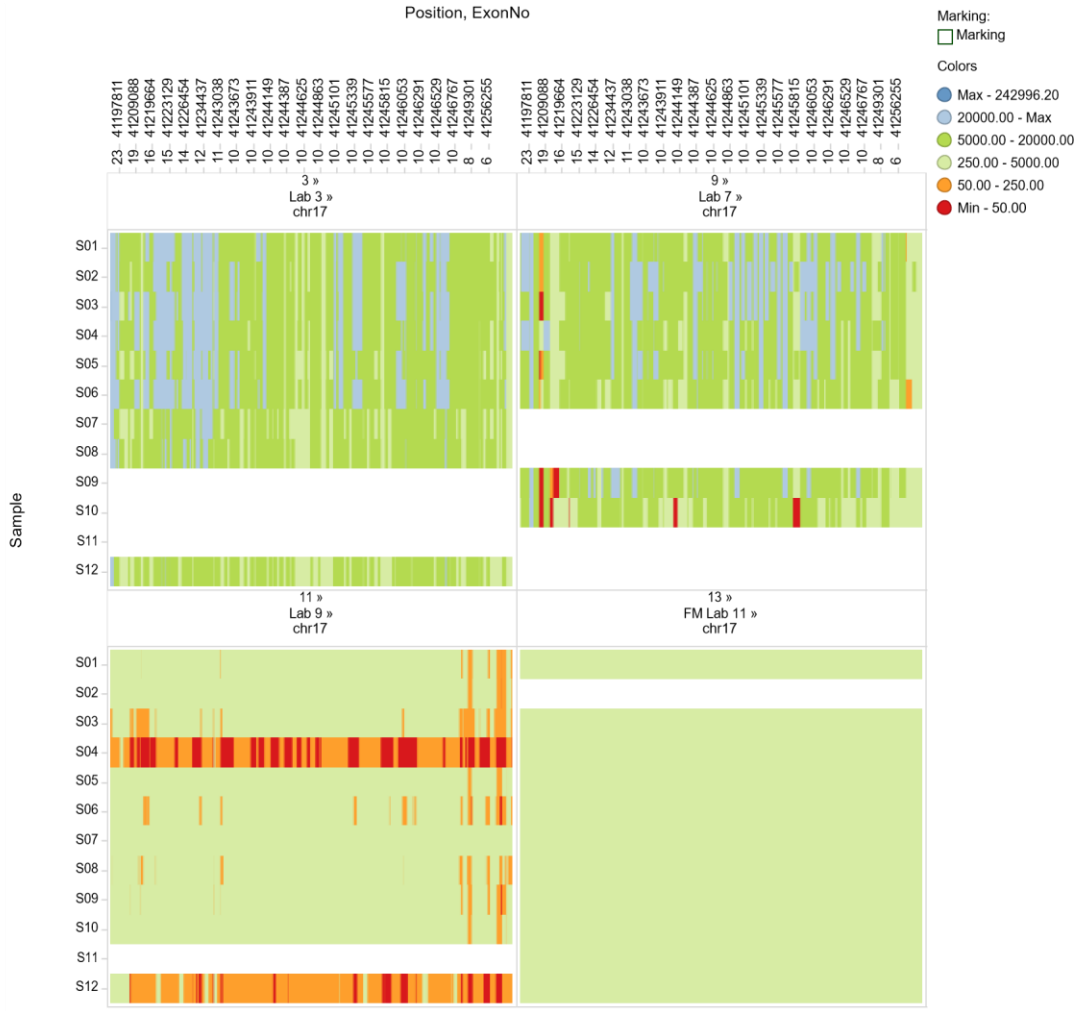

Quality scores across all bases (Sanger / Illumina 1.9 encoding)
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
1 2 3 4 5 6 7 8 9 15-19 30-34 45-49 60-64 75-79 90-94 105-109 125-129 145-149
Position in read (bp)

b)

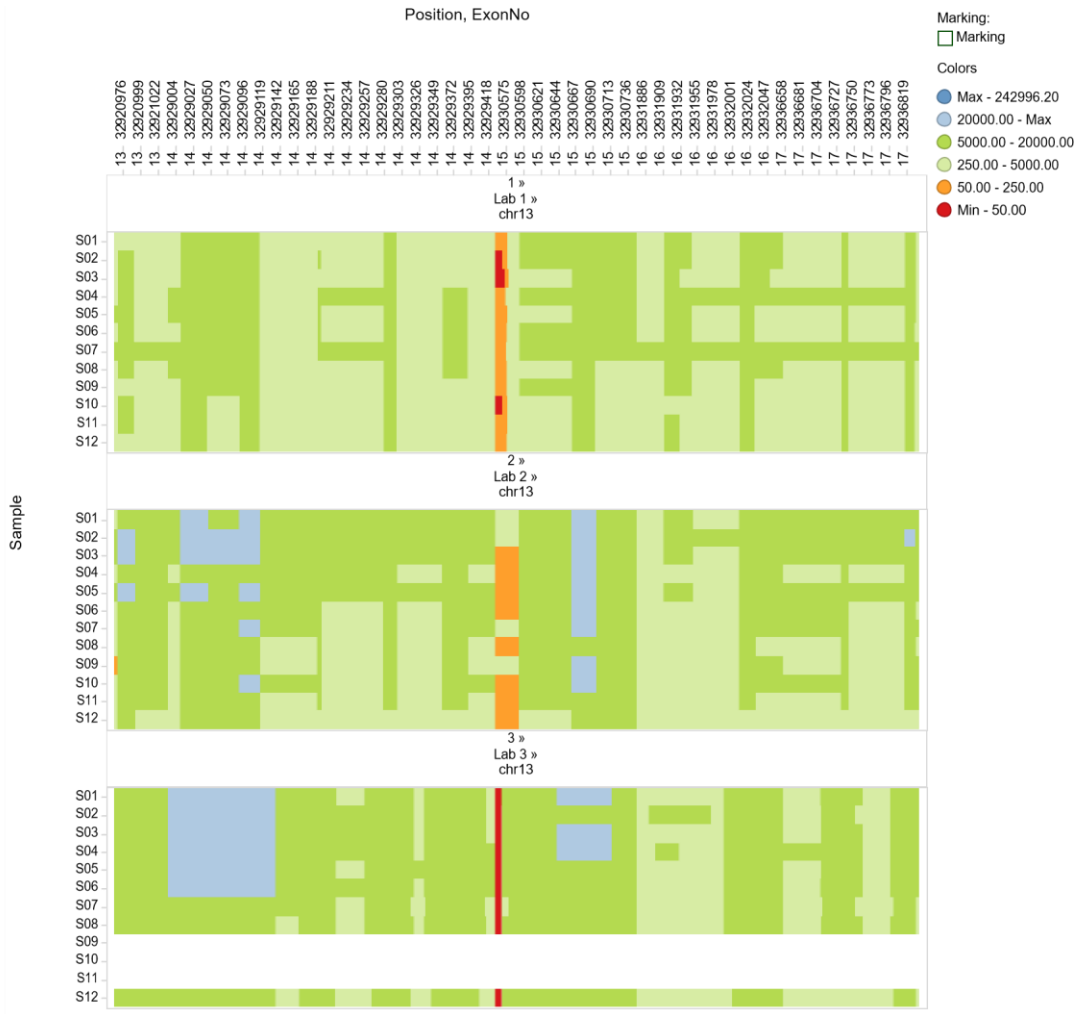



c)

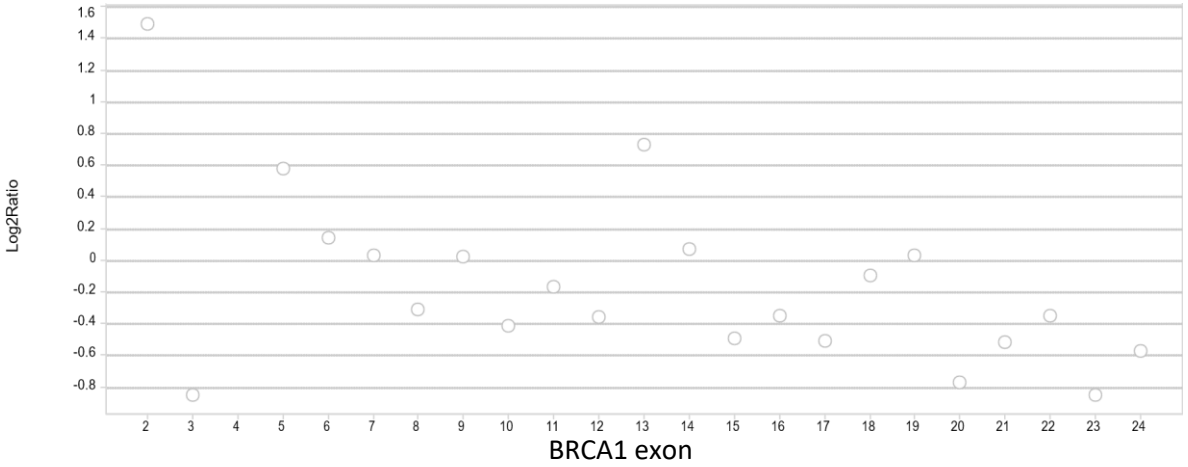
Supp. Figure S2: Base quality profiles for sample S01 across three participants (labs 2 (a), 3 (b) and 9(c)) to highlight systematic differences. The x-axis reflects the sequencer cycles (up to read length) and y-axis the Phred base quality.




Supp. Figure S3: *BRCA1* coverage profiles for the 12 samples for four participants highlighting differences between amplicon (top row) and hybrid capture approaches (bottom row). Exon 19 drop out in lab P7 data can be observed across the samples.




Supp. Figure S4: *BRCA2* coverage profile drop outs in GeneRead amplicon panel data in chromosome 15.




Supp. Figure S5: Copy number profile for an amplicon capture, sample S07.

Table S1: Variant calls per sample by central bioinformatic analysis prior to BRCA specific filtering using 5% as the allele fraction cutoff. Green colouring is used to indicate one correct detected variant. Red colouring represents discordant results.

| | Lab 1 | Lab 2 | Lab 3 | Lab 4 | Lab 8 | Lab 8 | Lab 5 | Lab 5 | Lab 6 | Lab 7 | Lab 9 | Lab 10 | Lab 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| S01 | 1 | 1 | 1 | 1 | 3 | 1 | | | | 37 | 1 | 2 | 1 |
| S02 | | | | | 2 | | | | | | | | |
| S03 | | | | 1 | 2 | 2 | | | | 34 | | | |
| S04 | 1 | 1 | 1 | | 2 | 3 | | | | 67 | | 1 | 1 |
| S05 | 1 | 1 | 1 | 1 | 2 | 3 | | | | 31 | 1 | 1 | 1 |
| S06 | | 1 | 1 | 1 | 2 | 5 | 2 | 1 | | 125 | 1 | 4 | 1 |
| S07 | | | | 1 | 63 | 60 | | 1 | | | | 1 | |
| S08 | | | | | 105 | 112 | | | | | | 1 | |
| S09 | 1 | 1 | | | 12 | 13 | | | | 225 | | 2 | 1 |
| S10 | | | | | 14 | 15 | | | | 203 | | 2 | |
| S11 | 1 | 1 | | 1 | 2 | 3 | 2 | 2 | | | | 1 | |
| S12 | 1 | 1 | 1 | 1 | 82 | 87 | | | | | | | 1 |

Table S2: Variant calls per sample by central bioinformatic analysis prior to BRCA specific filtering using 20% as the allele fraction cutoff. Green colouring is used to indicate one correct detected variant. Red colouring represents discordant results.

| | Lab 1 | Lab 2 | Lab 3 | Lab 4 | Lab 8 | Lab 8 | Lab 5 | Lab 5 | Lab 6 | Lab 7 | Lab 9 | Lab 10 | Lab 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| S01 | 1 | 1 | 1 | 1 | 1 | | | | | 1 | 1 | 1 | 1 |
| S02 | | | | | | | | | | | | | |
| S03 | | | | | | | | | | | | | |
| S04 | 1 | 1 | 1 | | 1 | 1 | | | | 10 | | 1 | 1 |
| S05 | 1 | 1 | 1 | 1 | 1 | 1 | | | | 11 | 1 | 1 | 1 |
| S06 | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | 5 | 1 | 1 | 1 |
| S07 | | | | | 9 | | | | | | | | |
| S08 | | | | | 5 | 5 | | | | | | | |
| S09 | 1 | 1 | | | | 1 | | | | 6 | | 1 | 1 |
| S10 | | | | | 1 | | | | | 47 | | | |
| S11 | | | | | | | | | | | | | |
| S12 | 1 | 1 | 1 | 1 | 3 | 2 | | | | | | | 1 |