

Pipeline Report

J. Matthew Holt

April 8, 2022

Contents

| | | |
|----------|--|-----------|
| 1 | Metadata information | 2 |
| 1.1 | Constants | 2 |
| 1.2 | Dynamic | 2 |
| 2 | Summarized Small Variant Comparison | 3 |
| 2.1 | Preparation: “PCR-free-illumina” | 3 |
| 2.2 | Preparation: “PacBio-CCS-high” | 4 |
| 3 | Summarized SNP/Indel Comparison | 6 |
| 3.1 | Preparation: “PCR-free-illumina” | 6 |
| 3.2 | Preparation: “PacBio-CCS-high” | 8 |
| 4 | CMRG Comparison | 10 |
| 4.1 | Preparation: “PCR-free-illumina” | 10 |
| 4.2 | Preparation: “PacBio-CCS-high” | 11 |
| 5 | Summarized Haplotyper Comparison | 13 |
| 5.1 | Preparation: “PCR-free-illumina” | 13 |
| 5.2 | Preparation: “PacBio-CCS-high” | 13 |
| 6 | Summarized Deletion Comparisons | 15 |
| 6.1 | Restricted calls | 15 |
| 6.1.1 | Preparation: “PCR-free-illumina” | 15 |
| 6.1.2 | Preparation: “PacBio-CCS-high” | 16 |
| 6.2 | Unrestricted calls | 16 |
| 6.2.1 | Preparation: “PCR-free-illumina” | 16 |
| 6.2.2 | Preparation: “PacBio-CCS-high” | 17 |

1 Metadata information

1.1 Constants

The following information is not automatically updated in the report:

Build: b38 (hg38)

1.2 Dynamic

The following information is gathered dynamically when a report is generated:

| Library | Sample | Preparation | Gbp |
|-------------|---------|-------------------|--------|
| HALB3002753 | NA12878 | PCR-free-illumina | 181.14 |
| HALB3002754 | HG002 | PCR-free-illumina | 145.87 |
| HALB3002755 | HG003 | PCR-free-illumina | 149.77 |
| HALB3002756 | HG004 | PCR-free-illumina | 138.30 |
| HALB3002757 | HG005 | PCR-free-illumina | 159.85 |
| HALB3003200 | NA12878 | PCR-free-illumina | 167.53 |
| HALB3003201 | HG002 | PCR-free-illumina | 129.81 |
| HALB3003222 | HG003 | PCR-free-illumina | 156.20 |
| HALB3010451 | NA12878 | PacBio-CCS-high | 77.46 |
| HALB3010452 | HG002 | PacBio-CCS-high | 166.22 |
| HALB3010453 | HG003 | PacBio-CCS-high | 129.52 |
| HALB3010454 | HG004 | PacBio-CCS-high | 123.81 |
| HALB3010455 | HG005 | PacBio-CCS-high | 145.34 |
| HALB3010456 | HG006 | PacBio-CCS-high | 122.17 |
| HALB3010457 | HG007 | PacBio-CCS-high | 113.30 |

2 Summarized Small Variant Comparison

This section contains the summarized results of the small variant analysis. For each aligner-caller pair, we ran RTG on the Genome in a Bottle (GIAB) high confidence truth set ($\approx 3.6\text{M}$ variants). The following results are gathered from the RTG ‘summary.txt’ file using the final row (i.e. “None” indicating no variants were filtered) and with the `--all-records` option enabled.

2.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|--------------------------|---------------------------|---|----------------|----------------|----------------|
| clinical | sentieon-201808.07 | strelka-2.9.10 | 8 | 0.9923+-0.0014 | 0.9920+-0.0008 | 0.9922+-0.0010 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r11 | 8 | 0.9976+-0.0003 | 0.9920+-0.0006 | 0.9948+-0.0003 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r9 | 8 | 0.9976+-0.0003 | 0.9925+-0.0006 | 0.9950+-0.0004 |
| hg38_T2T_masked | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | 8 | 0.9984+-0.0003 | 0.9942+-0.0008 | 0.9963+-0.0005 |
| hg38_T2T_masked | dragmap-1.2.1 | octopus-0.7.4 | 8 | 0.9962+-0.0003 | 0.9899+-0.0008 | 0.9931+-0.0005 |
| hg38_T2T_masked | dragmap-1.2.1 | strelka-2.9.10 | 8 | 0.9893+-0.0039 | 0.9922+-0.0009 | 0.9907+-0.0023 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r11 | 8 | 0.9974+-0.0003 | 0.9927+-0.0009 | 0.9950+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r9 | 8 | 0.9974+-0.0003 | 0.9936+-0.0006 | 0.9955+-0.0004 |
| hg38_T2T_masked | sentieon-202112.01 | dnascope-1.0-202112.01-PO | 8 | 0.9983+-0.0003 | 0.9944+-0.0007 | 0.9963+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01 | octopus-0.7.4 | 8 | 0.9946+-0.0003 | 0.9903+-0.0007 | 0.9924+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01 | strelka-2.9.10 | 8 | 0.9869+-0.0039 | 0.9932+-0.0007 | 0.9900+-0.0022 |
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r11 | 8 | 0.9974+-0.0003 | 0.9918+-0.0010 | 0.9945+-0.0006 |
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r9 | 8 | 0.9974+-0.0003 | 0.9924+-0.0010 | 0.9949+-0.0006 |
| hg38_T2T_masked | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | 8 | 0.9986+-0.0002 | 0.9932+-0.0009 | 0.9959+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01-recal | octopus-0.7.4 | 8 | 0.9947+-0.0004 | 0.9903+-0.0008 | 0.9925+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01-recal | strelka-2.9.10 | 8 | 0.9905+-0.0016 | 0.9930+-0.0007 | 0.9918+-0.0011 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r11 | 8 | 0.9966+-0.0003 | 0.9921+-0.0011 | 0.9943+-0.0007 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r9 | 8 | 0.9966+-0.0003 | 0.9928+-0.0005 | 0.9947+-0.0004 |
| hg38_T2T_masked | snap-2.0.0 | dnascope-1.0-202112.01-PO | 8 | 0.9976+-0.0003 | 0.9943+-0.0006 | 0.9959+-0.0004 |
| hg38_T2T_masked | snap-2.0.0 | octopus-0.7.4 | 8 | 0.9938+-0.0003 | 0.9907+-0.0007 | 0.9922+-0.0004 |
| hg38_T2T_masked | snap-2.0.0 | strelka-2.9.10 | 8 | 0.9861+-0.0042 | 0.9934+-0.0007 | 0.9898+-0.0024 |
| hg38_asm5_alt | dragmap-1.2.1 | clair3-0.1-r11 | 8 | 0.9975+-0.0002 | 0.9695+-0.0012 | 0.9833+-0.0007 |
| hg38_asm5_alt | dragmap-1.2.1 | clair3-0.1-r9 | 8 | 0.9975+-0.0002 | 0.9705+-0.0008 | 0.9838+-0.0004 |
| hg38_asm5_alt | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | 8 | 0.9978+-0.0002 | 0.9735+-0.0010 | 0.9855+-0.0006 |
| hg38_asm5_alt | dragmap-1.2.1 | octopus-0.7.4 | 8 | 0.9969+-0.0002 | 0.9681+-0.0011 | 0.9823+-0.0006 |

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|---------------|--------------------------|---------------------------|---|----------------|----------------|----------------|
| hg38_asm5_alt | dragmap-1.2.1 | strelka-2.9.10 | 8 | 0.9902+-0.0038 | 0.9699+-0.0011 | 0.9800+-0.0023 |
| hg38_asm5_alt | sentieon-202112.01 | clair3-0.1-r11 | 8 | 0.9977+-0.0002 | 0.9922+-0.0009 | 0.9949+-0.0005 |
| hg38_asm5_alt | sentieon-202112.01 | clair3-0.1-r9 | 8 | 0.9977+-0.0002 | 0.9926+-0.0007 | 0.9951+-0.0004 |
| hg38_asm5_alt | sentieon-202112.01 | dnascope-1.0-202112.01-PO | 8 | 0.9983+-0.0002 | 0.9938+-0.0007 | 0.9961+-0.0004 |
| hg38_asm5_alt | sentieon-202112.01 | octopus-0.7.4 | 8 | 0.9958+-0.0002 | 0.9893+-0.0008 | 0.9926+-0.0004 |
| hg38_asm5_alt | sentieon-202112.01 | strelka-2.9.10 | 8 | 0.9890+-0.0038 | 0.9921+-0.0007 | 0.9906+-0.0022 |
| hg38_asm5_alt | sentieon-202112.01-recal | clair3-0.1-r11 | 8 | 0.9978+-0.0002 | 0.9911+-0.0008 | 0.9944+-0.0005 |
| hg38_asm5_alt | sentieon-202112.01-recal | clair3-0.1-r9 | 8 | 0.9978+-0.0002 | 0.9916+-0.0008 | 0.9947+-0.0004 |
| hg38_asm5_alt | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | 8 | 0.9986+-0.0002 | 0.9926+-0.0008 | 0.9956+-0.0005 |
| hg38_asm5_alt | sentieon-202112.01-recal | octopus-0.7.4 | 8 | 0.9960+-0.0002 | 0.9893+-0.0008 | 0.9926+-0.0004 |
| hg38_asm5_alt | sentieon-202112.01-recal | strelka-2.9.10 | 8 | 0.9923+-0.0014 | 0.9920+-0.0008 | 0.9922+-0.0010 |
| hg38_asm5_alt | snap-2.0.0 | clair3-0.1-r11 | 8 | 0.9967+-0.0003 | 0.9920+-0.0008 | 0.9944+-0.0005 |
| hg38_asm5_alt | snap-2.0.0 | clair3-0.1-r9 | 8 | 0.9967+-0.0003 | 0.9927+-0.0005 | 0.9947+-0.0004 |
| hg38_asm5_alt | snap-2.0.0 | deepvariant-1.2.0 | 8 | 0.9984+-0.0002 | 0.9936+-0.0005 | 0.9960+-0.0003 |
| hg38_asm5_alt | snap-2.0.0 | dnascope-1.0-202112.01-PO | 8 | 0.9976+-0.0003 | 0.9941+-0.0006 | 0.9959+-0.0004 |
| hg38_asm5_alt | snap-2.0.0 | octopus-0.7.4 | 8 | 0.9944+-0.0003 | 0.9905+-0.0007 | 0.9925+-0.0004 |
| hg38_asm5_alt | snap-2.0.0 | strelka-2.9.10 | 8 | 0.9868+-0.0042 | 0.9932+-0.0007 | 0.9900+-0.0024 |

2.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|---------------|-----------------------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r11 | 7 | 0.9980+-0.0013 | 0.9987+-0.0006 | 0.9984+-0.0010 |
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r9 | 7 | 0.9980+-0.0013 | 0.9987+-0.0006 | 0.9983+-0.0010 |
| hg38_T2T_masked | minimap2-2.23 | dnascope_hifi-0.4-202112.01 | 7 | 0.9986+-0.0008 | 0.9986+-0.0006 | 0.9986+-0.0007 |
| hg38_T2T_masked | minimap2-2.23 | peppermargindv-r0.8 | 7 | 0.9983+-0.0009 | 0.9985+-0.0005 | 0.9984+-0.0007 |
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r11 | 7 | 0.9984+-0.0013 | 0.9987+-0.0006 | 0.9985+-0.0009 |
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r9 | 7 | 0.9984+-0.0013 | 0.9987+-0.0006 | 0.9985+-0.0009 |
| hg38_T2T_masked | pbmm2-1.7.0 | dnascope_hifi-0.4-202112.01 | 7 | 0.9987+-0.0008 | 0.9987+-0.0005 | 0.9987+-0.0007 |
| hg38_T2T_masked | pbmm2-1.7.0 | peppermargindv-r0.8 | 7 | 0.9985+-0.0009 | 0.9984+-0.0005 | 0.9985+-0.0007 |

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|------------------------|-----------------------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r11 | 7 | 0.9980+-0.0013 | 0.9987+-0.0006 | 0.9983+-0.0010 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r9 | 7 | 0.9980+-0.0013 | 0.9987+-0.0006 | 0.9983+-0.0010 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dnascope_hifi-0.4-202112.01 | 7 | 0.9986+-0.0008 | 0.9986+-0.0006 | 0.9986+-0.0007 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | peppermargindv-r0.8 | 7 | 0.9983+-0.0009 | 0.9985+-0.0005 | 0.9984+-0.0007 |

3 Summarized SNP/Indel Comparison

This section contains the summarized results of the small variant analysis when stratified by SNP/Indel. Files were filtered using `bcftools filter` to pair down to SNPs or Indels only. For each aligner-caller pair, we ran RTG on the Genome in a Bottle (GIAB) high confidence truth set (≈ 3.6 M variants). The following results are gathered from the RTG ‘summary.txt’ file using the final row (i.e. “None” indicating no variants were filtered) and with the `--all-records` option enabled.

3.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Caller | Type | N | Precision | Sensitivity | F-measure |
|-----------------|--------------------------|---------------------------|-------|---|----------------|----------------|----------------|
| clinical | sentieon-201808.07 | strelka-2.9.10 | SNP | 8 | 0.9912+-0.0016 | 0.9922+-0.0007 | 0.9917+-0.0010 |
| | | | Indel | 8 | 0.9885+-0.0009 | 0.9839+-0.0018 | 0.9862+-0.0013 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r11 | SNP | 8 | 0.9976+-0.0003 | 0.9920+-0.0006 | 0.9948+-0.0003 |
| | | | Indel | 8 | 0.9949+-0.0006 | 0.9890+-0.0010 | 0.9920+-0.0008 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r9 | SNP | 8 | 0.9976+-0.0003 | 0.9925+-0.0006 | 0.9950+-0.0004 |
| | | | Indel | 8 | 0.9949+-0.0006 | 0.9896+-0.0011 | 0.9922+-0.0008 |
| hg38_T2T_masked | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9986+-0.0002 | 0.9940+-0.0008 | 0.9963+-0.0005 |
| | | | Indel | 8 | 0.9968+-0.0005 | 0.9946+-0.0008 | 0.9957+-0.0006 |
| hg38_T2T_masked | dragmap-1.2.1 | octopus-0.7.4 | SNP | 8 | 0.9961+-0.0003 | 0.9851+-0.0012 | 0.9906+-0.0006 |
| | | | Indel | 8 | 0.9476+-0.0026 | 0.9612+-0.0024 | 0.9544+-0.0024 |
| hg38_T2T_masked | dragmap-1.2.1 | strelka-2.9.10 | SNP | 8 | 0.9878+-0.0045 | 0.9924+-0.0009 | 0.9900+-0.0025 |
| | | | Indel | 8 | 0.9883+-0.0010 | 0.9841+-0.0019 | 0.9862+-0.0014 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r11 | SNP | 8 | 0.9973+-0.0003 | 0.9929+-0.0009 | 0.9951+-0.0005 |
| | | | Indel | 8 | 0.9948+-0.0006 | 0.9889+-0.0015 | 0.9918+-0.0010 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r9 | SNP | 8 | 0.9973+-0.0003 | 0.9938+-0.0006 | 0.9955+-0.0004 |
| | | | Indel | 8 | 0.9948+-0.0006 | 0.9900+-0.0012 | 0.9924+-0.0009 |
| hg38_T2T_masked | sentieon-202112.01 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9984+-0.0002 | 0.9942+-0.0007 | 0.9963+-0.0004 |
| | | | Indel | 8 | 0.9968+-0.0005 | 0.9946+-0.0008 | 0.9957+-0.0006 |
| hg38_T2T_masked | sentieon-202112.01 | octopus-0.7.4 | SNP | 8 | 0.9944+-0.0004 | 0.9854+-0.0011 | 0.9899+-0.0006 |
| | | | Indel | 8 | 0.9469+-0.0026 | 0.9612+-0.0023 | 0.9540+-0.0023 |
| hg38_T2T_masked | sentieon-202112.01 | strelka-2.9.10 | SNP | 8 | 0.9852+-0.0045 | 0.9935+-0.0006 | 0.9893+-0.0025 |
| | | | Indel | 8 | 0.9870+-0.0010 | 0.9844+-0.0018 | 0.9857+-0.0014 |
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r11 | SNP | 8 | 0.9974+-0.0003 | 0.9919+-0.0009 | 0.9947+-0.0005 |
| | | | Indel | 8 | 0.9942+-0.0008 | 0.9881+-0.0016 | 0.9911+-0.0011 |

| Reference | Aligner | Caller | Type | N | Precision | Sensitivity | F-measure |
|-----------------|--------------------------|---------------------------|-------|---|----------------|----------------|----------------|
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r9 | SNP | 8 | 0.9974+-0.0003 | 0.9927+-0.0009 | 0.9950+-0.0005 |
| | | | Indel | 8 | 0.9942+-0.0008 | 0.9889+-0.0016 | 0.9915+-0.0012 |
| hg38_T2T_masked | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9987+-0.0002 | 0.9931+-0.0009 | 0.9959+-0.0005 |
| | | | Indel | 8 | 0.9967+-0.0006 | 0.9927+-0.0014 | 0.9947+-0.0010 |
| hg38_T2T_masked | sentieon-202112.01-recal | octopus-0.7.4 | SNP | 8 | 0.9944+-0.0004 | 0.9854+-0.0011 | 0.9899+-0.0006 |
| | | | Indel | 8 | 0.9476+-0.0025 | 0.9613+-0.0023 | 0.9544+-0.0023 |
| hg38_T2T_masked | sentieon-202112.01-recal | strelka-2.9.10 | SNP | 8 | 0.9893+-0.0018 | 0.9933+-0.0006 | 0.9913+-0.0012 |
| | | | Indel | 8 | 0.9870+-0.0010 | 0.9844+-0.0018 | 0.9857+-0.0014 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r11 | SNP | 8 | 0.9964+-0.0003 | 0.9921+-0.0011 | 0.9942+-0.0006 |
| | | | Indel | 8 | 0.9943+-0.0006 | 0.9895+-0.0018 | 0.9919+-0.0012 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r9 | SNP | 8 | 0.9964+-0.0003 | 0.9929+-0.0005 | 0.9946+-0.0003 |
| | | | Indel | 8 | 0.9943+-0.0006 | 0.9903+-0.0012 | 0.9923+-0.0009 |
| hg38_T2T_masked | snap-2.0.0 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9977+-0.0002 | 0.9941+-0.0006 | 0.9959+-0.0004 |
| | | | Indel | 8 | 0.9962+-0.0004 | 0.9945+-0.0007 | 0.9953+-0.0005 |
| hg38_T2T_masked | snap-2.0.0 | octopus-0.7.4 | SNP | 8 | 0.9936+-0.0003 | 0.9858+-0.0011 | 0.9897+-0.0006 |
| | | | Indel | 8 | 0.9463+-0.0025 | 0.9609+-0.0023 | 0.9535+-0.0023 |
| hg38_T2T_masked | snap-2.0.0 | strelka-2.9.10 | SNP | 8 | 0.9845+-0.0048 | 0.9937+-0.0006 | 0.9891+-0.0026 |
| | | | Indel | 8 | 0.9853+-0.0009 | 0.9849+-0.0018 | 0.9851+-0.0014 |
| hg38_asm5.alt | dragmap-1.2.1 | clair3-0.1-r11 | SNP | 8 | 0.9975+-0.0002 | 0.9691+-0.0012 | 0.9831+-0.0006 |
| | | | Indel | 8 | 0.9948+-0.0006 | 0.9703+-0.0019 | 0.9824+-0.0012 |
| hg38_asm5.alt | dragmap-1.2.1 | clair3-0.1-r9 | SNP | 8 | 0.9975+-0.0002 | 0.9700+-0.0008 | 0.9836+-0.0004 |
| | | | Indel | 8 | 0.9949+-0.0006 | 0.9714+-0.0014 | 0.9830+-0.0010 |
| hg38_asm5.alt | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9980+-0.0002 | 0.9728+-0.0010 | 0.9853+-0.0006 |
| | | | Indel | 8 | 0.9966+-0.0006 | 0.9776+-0.0010 | 0.9870+-0.0007 |
| hg38_asm5.alt | dragmap-1.2.1 | octopus-0.7.4 | SNP | 8 | 0.9968+-0.0002 | 0.9628+-0.0016 | 0.9796+-0.0008 |
| | | | Indel | 8 | 0.9482+-0.0027 | 0.9436+-0.0024 | 0.9459+-0.0024 |
| hg38_asm5.alt | dragmap-1.2.1 | strelka-2.9.10 | SNP | 8 | 0.9886+-0.0044 | 0.9696+-0.0011 | 0.9790+-0.0026 |
| | | | Indel | 8 | 0.9894+-0.0009 | 0.9656+-0.0021 | 0.9773+-0.0015 |
| hg38_asm5.alt | sentieon-202112.01 | clair3-0.1-r11 | SNP | 8 | 0.9976+-0.0002 | 0.9923+-0.0009 | 0.9950+-0.0005 |
| | | | Indel | 8 | 0.9950+-0.0005 | 0.9890+-0.0012 | 0.9920+-0.0008 |
| hg38_asm5.alt | sentieon-202112.01 | clair3-0.1-r9 | SNP | 8 | 0.9976+-0.0002 | 0.9927+-0.0007 | 0.9952+-0.0004 |
| | | | Indel | 8 | 0.9950+-0.0005 | 0.9894+-0.0012 | 0.9922+-0.0009 |
| hg38_asm5.alt | sentieon-202112.01 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9984+-0.0002 | 0.9936+-0.0007 | 0.9960+-0.0004 |

| Reference | Aligner | Caller | Type | N | Precision | Sensitivity | F-measure |
|---------------|--------------------------|---------------------------|-------|---|----------------|----------------|----------------|
| | | | Indel | 8 | 0.9970+-0.0004 | 0.9943+-0.0007 | 0.9957+-0.0006 |
| hg38_asm5.alt | sentieon-202112.01 | octopus-0.7.4 | SNP | 8 | 0.9957+-0.0002 | 0.9844+-0.0012 | 0.9900+-0.0006 |
| | | | Indel | 8 | 0.9478+-0.0025 | 0.9608+-0.0023 | 0.9543+-0.0023 |
| hg38_asm5.alt | sentieon-202112.01 | strelka-2.9.10 | SNP | 8 | 0.9874+-0.0043 | 0.9924+-0.0007 | 0.9899+-0.0024 |
| | | | Indel | 8 | 0.9884+-0.0008 | 0.9839+-0.0018 | 0.9861+-0.0013 |
| hg38_asm5.alt | sentieon-202112.01-recal | clair3-0.1-r11 | SNP | 8 | 0.9978+-0.0002 | 0.9912+-0.0008 | 0.9945+-0.0004 |
| | | | Indel | 8 | 0.9945+-0.0008 | 0.9880+-0.0011 | 0.9912+-0.0009 |
| hg38_asm5.alt | sentieon-202112.01-recal | clair3-0.1-r9 | SNP | 8 | 0.9978+-0.0002 | 0.9917+-0.0008 | 0.9948+-0.0004 |
| | | | Indel | 8 | 0.9945+-0.0008 | 0.9886+-0.0013 | 0.9916+-0.0010 |
| hg38_asm5.alt | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9988+-0.0001 | 0.9925+-0.0008 | 0.9956+-0.0004 |
| | | | Indel | 8 | 0.9968+-0.0006 | 0.9923+-0.0014 | 0.9946+-0.0010 |
| hg38_asm5.alt | sentieon-202112.01-recal | octopus-0.7.4 | SNP | 8 | 0.9958+-0.0002 | 0.9844+-0.0012 | 0.9901+-0.0006 |
| | | | Indel | 8 | 0.9486+-0.0024 | 0.9609+-0.0023 | 0.9547+-0.0022 |
| hg38_asm5.alt | sentieon-202112.01-recal | strelka-2.9.10 | SNP | 8 | 0.9912+-0.0016 | 0.9922+-0.0007 | 0.9917+-0.0010 |
| | | | Indel | 8 | 0.9885+-0.0009 | 0.9839+-0.0018 | 0.9862+-0.0013 |
| hg38_asm5.alt | snap-2.0.0 | clair3-0.1-r11 | SNP | 8 | 0.9966+-0.0003 | 0.9920+-0.0008 | 0.9943+-0.0005 |
| | | | Indel | 8 | 0.9944+-0.0006 | 0.9895+-0.0015 | 0.9919+-0.0010 |
| hg38_asm5.alt | snap-2.0.0 | clair3-0.1-r9 | SNP | 8 | 0.9966+-0.0003 | 0.9927+-0.0005 | 0.9946+-0.0003 |
| | | | Indel | 8 | 0.9944+-0.0006 | 0.9902+-0.0011 | 0.9923+-0.0008 |
| hg38_asm5.alt | snap-2.0.0 | deepvariant-1.2.0 | SNP | 8 | 0.9984+-0.0002 | 0.9936+-0.0005 | 0.9960+-0.0003 |
| | | | Indel | 8 | 0.9961+-0.0004 | 0.9920+-0.0009 | 0.9940+-0.0006 |
| hg38_asm5.alt | snap-2.0.0 | dnascope-1.0-202112.01-PO | SNP | 8 | 0.9977+-0.0002 | 0.9939+-0.0006 | 0.9958+-0.0004 |
| | | | Indel | 8 | 0.9963+-0.0004 | 0.9944+-0.0007 | 0.9953+-0.0005 |
| hg38_asm5.alt | snap-2.0.0 | octopus-0.7.4 | SNP | 8 | 0.9942+-0.0003 | 0.9856+-0.0011 | 0.9899+-0.0006 |
| | | | Indel | 8 | 0.9467+-0.0026 | 0.9608+-0.0023 | 0.9537+-0.0023 |
| hg38_asm5.alt | snap-2.0.0 | strelka-2.9.10 | SNP | 8 | 0.9852+-0.0048 | 0.9935+-0.0006 | 0.9894+-0.0026 |
| | | | Indel | 8 | 0.9860+-0.0009 | 0.9848+-0.0018 | 0.9854+-0.0013 |

3.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Caller | Type | N | Precision | Sensitivity | F-measure |
|-----------------|------------------------|-----------------------------|-------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r11 | SNP | 7 | 0.9979+-0.0003 | 0.9994+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9880+-0.0089 | 0.9859+-0.0064 | 0.9869+-0.0076 |
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r9 | SNP | 7 | 0.9978+-0.0003 | 0.9994+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9880+-0.0088 | 0.9859+-0.0063 | 0.9870+-0.0075 |
| hg38_T2T_masked | minimap2-2.23 | dnascope_hifi-0.4-202112.01 | SNP | 7 | 0.9993+-0.0002 | 0.9993+-0.0001 | 0.9993+-0.0001 |
| | | | Indel | 7 | 0.9935+-0.0049 | 0.9932+-0.0050 | 0.9934+-0.0049 |
| hg38_T2T_masked | minimap2-2.23 | peppermargindv-r0.8 | SNP | 7 | 0.9983+-0.0003 | 0.9990+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9886+-0.0056 | 0.9858+-0.0055 | 0.9872+-0.0055 |
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r11 | SNP | 7 | 0.9987+-0.0002 | 0.9993+-0.0002 | 0.9990+-0.0001 |
| | | | Indel | 7 | 0.9903+-0.0087 | 0.9913+-0.0059 | 0.9908+-0.0073 |
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r9 | SNP | 7 | 0.9987+-0.0002 | 0.9993+-0.0002 | 0.9990+-0.0001 |
| | | | Indel | 7 | 0.9903+-0.0087 | 0.9913+-0.0059 | 0.9908+-0.0073 |
| hg38_T2T_masked | pbmm2-1.7.0 | dnascope_hifi-0.4-202112.01 | SNP | 7 | 0.9993+-0.0003 | 0.9993+-0.0001 | 0.9994+-0.0001 |
| | | | Indel | 7 | 0.9940+-0.0046 | 0.9940+-0.0045 | 0.9940+-0.0046 |
| hg38_T2T_masked | pbmm2-1.7.0 | peppermargindv-r0.8 | SNP | 7 | 0.9989+-0.0002 | 0.9989+-0.0002 | 0.9989+-0.0001 |
| | | | Indel | 7 | 0.9908+-0.0055 | 0.9914+-0.0049 | 0.9911+-0.0052 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r11 | SNP | 7 | 0.9979+-0.0003 | 0.9994+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9880+-0.0089 | 0.9859+-0.0064 | 0.9869+-0.0076 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r9 | SNP | 7 | 0.9979+-0.0003 | 0.9994+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9880+-0.0089 | 0.9858+-0.0063 | 0.9869+-0.0076 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dnascope_hifi-0.4-202112.01 | SNP | 7 | 0.9993+-0.0002 | 0.9993+-0.0001 | 0.9993+-0.0001 |
| | | | Indel | 7 | 0.9935+-0.0049 | 0.9932+-0.0050 | 0.9934+-0.0049 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | peppermargindv-r0.8 | SNP | 7 | 0.9983+-0.0003 | 0.9990+-0.0001 | 0.9986+-0.0001 |
| | | | Indel | 7 | 0.9886+-0.0056 | 0.9858+-0.0055 | 0.9872+-0.0055 |

4 CMRG Comparison

GIAB recently released a pre-print describing Challenging Medically-Relevant Autosomal Genes (CMRG) benchmark. These regions are harder to capture than the typical GIAB benchmarks. This section contains the summarized results of the small variant analysis, specifically on the CMRG regions. For each aligner-caller pair, we ran RTG on the CMRG high confidence truth set (currently only for HG002 samples). The following results are gathered from the RTG ‘summary.txt’ file using the final row (i.e. “None” indicating no variants were filtered) and with the `--all-records` option enabled.

4.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|--------------------------|---------------------------|---|----------------|----------------|----------------|
| clinical | sentieon-201808.07 | strelka-2.9.10 | 2 | 0.9542+-0.0031 | 0.9512+-0.0007 | 0.9527+-0.0019 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r11 | 2 | 0.9708+-0.0001 | 0.9592+-0.0002 | 0.9650+-0.0000 |
| hg38_T2T_masked | dragmap-1.2.1 | clair3-0.1-r9 | 2 | 0.9708+-0.0001 | 0.9597+-0.0002 | 0.9652+-0.0002 |
| hg38_T2T_masked | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | 2 | 0.9753+-0.0001 | 0.9668+-0.0007 | 0.9710+-0.0004 |
| hg38_T2T_masked | dragmap-1.2.1 | octopus-0.7.4 | 2 | 0.9804+-0.0007 | 0.9634+-0.0009 | 0.9718+-0.0008 |
| hg38_T2T_masked | dragmap-1.2.1 | strelka-2.9.10 | 2 | 0.9405+-0.0033 | 0.9562+-0.0008 | 0.9482+-0.0021 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r11 | 2 | 0.9696+-0.0004 | 0.9594+-0.0010 | 0.9645+-0.0004 |
| hg38_T2T_masked | sentieon-202112.01 | clair3-0.1-r9 | 2 | 0.9697+-0.0004 | 0.9605+-0.0002 | 0.9650+-0.0000 |
| hg38_T2T_masked | sentieon-202112.01 | dnascope-1.0-202112.01-PO | 2 | 0.9750+-0.0009 | 0.9661+-0.0015 | 0.9706+-0.0011 |
| hg38_T2T_masked | sentieon-202112.01 | octopus-0.7.4 | 2 | 0.9734+-0.0016 | 0.9640+-0.0015 | 0.9687+-0.0016 |
| hg38_T2T_masked | sentieon-202112.01 | strelka-2.9.10 | 2 | 0.9357+-0.0045 | 0.9608+-0.0006 | 0.9481+-0.0025 |
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r11 | 2 | 0.9707+-0.0005 | 0.9564+-0.0010 | 0.9634+-0.0003 |
| hg38_T2T_masked | sentieon-202112.01-recal | clair3-0.1-r9 | 2 | 0.9707+-0.0005 | 0.9575+-0.0001 | 0.9640+-0.0001 |
| hg38_T2T_masked | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | 2 | 0.9767+-0.0015 | 0.9626+-0.0015 | 0.9695+-0.0015 |
| hg38_T2T_masked | sentieon-202112.01-recal | octopus-0.7.4 | 2 | 0.9738+-0.0001 | 0.9635+-0.0007 | 0.9687+-0.0005 |
| hg38_T2T_masked | sentieon-202112.01-recal | strelka-2.9.10 | 2 | 0.9449+-0.0026 | 0.9604+-0.0006 | 0.9526+-0.0017 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r11 | 2 | 0.9644+-0.0016 | 0.9586+-0.0011 | 0.9614+-0.0014 |
| hg38_T2T_masked | snap-2.0.0 | clair3-0.1-r9 | 2 | 0.9645+-0.0015 | 0.9601+-0.0002 | 0.9623+-0.0009 |
| hg38_T2T_masked | snap-2.0.0 | dnascope-1.0-202112.01-PO | 2 | 0.9704+-0.0012 | 0.9654+-0.0006 | 0.9679+-0.0009 |
| hg38_T2T_masked | snap-2.0.0 | octopus-0.7.4 | 2 | 0.9670+-0.0018 | 0.9652+-0.0007 | 0.9661+-0.0005 |
| hg38_T2T_masked | snap-2.0.0 | strelka-2.9.10 | 2 | 0.9269+-0.0055 | 0.9606+-0.0006 | 0.9435+-0.0031 |
| hg38_asm5_alt | dragmap-1.2.1 | clair3-0.1-r11 | 2 | 0.9750+-0.0001 | 0.8495+-0.0001 | 0.9080+-0.0001 |
| hg38_asm5_alt | dragmap-1.2.1 | clair3-0.1-r9 | 2 | 0.9750+-0.0001 | 0.8511+-0.0002 | 0.9088+-0.0002 |

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|---------------|--------------------------|---------------------------|---|----------------|----------------|----------------|
| hg38_asm5_alt | dragmap-1.2.1 | deepvariant-1.2.0 | 2 | 0.9854+-0.0003 | 0.8513+-0.0006 | 0.9134+-0.0002 |
| hg38_asm5_alt | dragmap-1.2.1 | dnascope-1.0-202112.01-PO | 2 | 0.9780+-0.0001 | 0.8656+-0.0008 | 0.9183+-0.0004 |
| hg38_asm5_alt | dragmap-1.2.1 | octopus-0.7.4 | 2 | 0.9747+-0.0000 | 0.8539+-0.0012 | 0.9103+-0.0007 |
| hg38_asm5_alt | dragmap-1.2.1 | strelka-2.9.10 | 2 | 0.9430+-0.0029 | 0.8447+-0.0010 | 0.8911+-0.0019 |
| hg38_asm5_alt | sentieon-202112.01 | clair3-0.1-r11 | 2 | 0.9777+-0.0004 | 0.9517+-0.0000 | 0.9646+-0.0002 |
| hg38_asm5_alt | sentieon-202112.01 | clair3-0.1-r9 | 2 | 0.9777+-0.0004 | 0.9517+-0.0000 | 0.9646+-0.0002 |
| hg38_asm5_alt | sentieon-202112.01 | dnascope-1.0-202112.01-PO | 2 | 0.9831+-0.0005 | 0.9622+-0.0012 | 0.9726+-0.0009 |
| hg38_asm5_alt | sentieon-202112.01 | octopus-0.7.4 | 2 | 0.9738+-0.0010 | 0.9551+-0.0014 | 0.9644+-0.0013 |
| hg38_asm5_alt | sentieon-202112.01 | strelka-2.9.10 | 2 | 0.9449+-0.0050 | 0.9516+-0.0007 | 0.9483+-0.0028 |
| hg38_asm5_alt | sentieon-202112.01-recal | clair3-0.1-r11 | 2 | 0.9789+-0.0002 | 0.9486+-0.0001 | 0.9635+-0.0002 |
| hg38_asm5_alt | sentieon-202112.01-recal | clair3-0.1-r9 | 2 | 0.9789+-0.0002 | 0.9486+-0.0001 | 0.9635+-0.0002 |
| hg38_asm5_alt | sentieon-202112.01-recal | dnascope-1.0-202112.01-PO | 2 | 0.9847+-0.0012 | 0.9589+-0.0010 | 0.9717+-0.0011 |
| hg38_asm5_alt | sentieon-202112.01-recal | octopus-0.7.4 | 2 | 0.9748+-0.0000 | 0.9550+-0.0013 | 0.9648+-0.0007 |
| hg38_asm5_alt | sentieon-202112.01-recal | strelka-2.9.10 | 2 | 0.9542+-0.0031 | 0.9512+-0.0007 | 0.9527+-0.0019 |
| hg38_asm5_alt | snap-2.0.0 | clair3-0.1-r11 | 2 | 0.9724+-0.0010 | 0.9505+-0.0005 | 0.9612+-0.0007 |
| hg38_asm5_alt | snap-2.0.0 | clair3-0.1-r9 | 2 | 0.9724+-0.0010 | 0.9520+-0.0002 | 0.9621+-0.0006 |
| hg38_asm5_alt | snap-2.0.0 | deepvariant-1.2.0 | 2 | 0.9869+-0.0007 | 0.9533+-0.0004 | 0.9698+-0.0001 |
| hg38_asm5_alt | snap-2.0.0 | dnascope-1.0-202112.01-PO | 2 | 0.9802+-0.0010 | 0.9583+-0.0003 | 0.9691+-0.0006 |
| hg38_asm5_alt | snap-2.0.0 | octopus-0.7.4 | 2 | 0.9666+-0.0018 | 0.9575+-0.0011 | 0.9620+-0.0003 |
| hg38_asm5_alt | snap-2.0.0 | strelka-2.9.10 | 2 | 0.9335+-0.0053 | 0.9525+-0.0008 | 0.9429+-0.0031 |

4.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|---------------|-----------------------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r11 | 1 | 0.9661+-0.0000 | 0.9927+-0.0000 | 0.9792+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | clair3-0.1-r9 | 1 | 0.9671+-0.0000 | 0.9927+-0.0000 | 0.9797+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | dnascope_hifi-0.4-202112.01 | 1 | 0.9876+-0.0000 | 0.9894+-0.0000 | 0.9885+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | peppermargindv-r0.8 | 1 | 0.9862+-0.0000 | 0.9908+-0.0000 | 0.9885+-0.0000 |
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r11 | 1 | 0.9681+-0.0000 | 0.9902+-0.0000 | 0.9790+-0.0000 |

| Reference | Aligner | Caller | N | Precision | Sensitivity | F-measure |
|-----------------|------------------------|-----------------------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | pbmm2-1.7.0 | clair3-0.1-r9 | 1 | 0.9689+-0.0000 | 0.9904+-0.0000 | 0.9795+-0.0000 |
| hg38_T2T_masked | pbmm2-1.7.0 | dnascope_hifi-0.4-202112.01 | 1 | 0.9881+-0.0000 | 0.9889+-0.0000 | 0.9885+-0.0000 |
| hg38_T2T_masked | pbmm2-1.7.0 | peppermargindv-r0.8 | 1 | 0.9806+-0.0000 | 0.9888+-0.0000 | 0.9847+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r11 | 1 | 0.9661+-0.0000 | 0.9928+-0.0000 | 0.9792+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | clair3-0.1-r9 | 1 | 0.9669+-0.0000 | 0.9927+-0.0000 | 0.9796+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dnascope_hifi-0.4-202112.01 | 1 | 0.9876+-0.0000 | 0.9894+-0.0000 | 0.9885+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | peppermargindv-r0.8 | 1 | 0.9860+-0.0000 | 0.9908+-0.0000 | 0.9884+-0.0000 |

5 Summarized Haplotyper Comparison

This section contains the summarized results of the haplotype analysis. For each aligner-haplotyper pair, we attempted to run the haplotyper and gather the resulting prediction. “Output” is the percentage that generated an output file. This is most commonly below 100% when a tool crashes while trying to run. “Computed” is the percentage that generated a prediction in the output file. This is most commonly below 100% when a tool successfully runs, but it does not generate a prediction in the output file (e.g. “None”). “Matching” is the percentage that generated the correct haplotype prediction based on our lookup table. These haplotyping tools often assume a particular data type, and are not designed to work under all of the conditions tested by this benchmark.

5.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Haplotyper | N | Output (%) | Computed (%) | Matching (%) |
|-----------------|--------------------------|--------------|---|------------|--------------|--------------|
| hg38_T2T_masked | dragmap-1.2.1 | cyrius-1.1.1 | 8 | 100.0 | 75.0 | 75.0 |
| hg38_T2T_masked | sentieon-202112.01 | cyrius-1.1.1 | 8 | 100.0 | 87.5 | 87.5 |
| hg38_T2T_masked | sentieon-202112.01-recal | cyrius-1.1.1 | 8 | 100.0 | 87.5 | 87.5 |
| hg38_T2T_masked | snap-2.0.0 | cyrius-1.1.1 | 8 | 100.0 | 87.5 | 87.5 |
| hg38_asm5_alt | dragmap-1.2.1 | cyrius-1.1.1 | 8 | 25.0 | 0.0 | 0.0 |
| hg38_asm5_alt | sentieon-202112.01 | cyrius-1.1.1 | 8 | 100.0 | 100.0 | 100.0 |
| hg38_asm5_alt | sentieon-202112.01-recal | cyrius-1.1.1 | 8 | 100.0 | 100.0 | 100.0 |
| hg38_asm5_alt | snap-2.0.0 | cyrius-1.1.1 | 8 | 100.0 | 87.5 | 87.5 |

5.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Haplotyper | N | Output (%) | Computed (%) | Matching (%) |
|-----------------|---------------|--------------|---|------------|--------------|--------------|
| hg38_T2T_masked | minimap2-2.23 | cyrius-1.1.1 | 5 | 100.0 | 20.0 | 20.0 |
| hg38_T2T_masked | pbbmm2-1.7.0 | cyrius-1.1.1 | 5 | 100.0 | 40.0 | 40.0 |

| Reference | Aligner | Haplotyper | N | Output (%) | Computed (%) | Matching (%) |
|-----------------|------------------------|--------------|---|------------|--------------|--------------|
| hg38_T2T_masked | sentieon_mm2-202112.01 | cyrius-1.1.1 | 5 | 100.0 | 20.0 | 20.0 |

6 Summarized Deletion Comparisons

This section contains the summarized results of the deletion variant analysis. For each aligner-caller pair, we ran Truvari on the corresponding truth set with these options: “--pctsim 0.0 --sizemax 1000000000”. The following results are gathered from the Truvari “summary.txt” file.

6.1 Restricted calls

These evaluations are **RESTRICTED**, meaning that a BED file was used to limit the analysis regions, typically to “high-confidence” regions associated with the benchmark. This corresponds to the “--includebed” option in Truvari. As a result, benchmark sets that were not released with a corresponding BED file are excluded from this analysis. At this time, only the HG002 GIAB v0.6 benchmark is included in this analysis.

6.1.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Caller | N | precision | recall | f1 |
|-----------------|--------------------------|----------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | dragmap-1.2.1 | dysgu-1.3.4 | 2 | 0.4324+-0.2752 | 0.7246+-0.0085 | 0.4853+-0.2265 |
| hg38_T2T_masked | dragmap-1.2.1 | dysgu-1.3.4-PO | 2 | 0.9105+-0.0212 | 0.7073+-0.0035 | 0.7960+-0.0059 |
| hg38_T2T_masked | dragmap-1.2.1 | manta-1.6.0 | 2 | 0.9561+-0.0011 | 0.6677+-0.0188 | 0.7862+-0.0127 |
| hg38_T2T_masked | sentieon-202112.01 | dysgu-1.3.4 | 2 | 0.4682+-0.2839 | 0.6704+-0.0047 | 0.4979+-0.2083 |
| hg38_T2T_masked | sentieon-202112.01 | dysgu-1.3.4-PO | 2 | 0.9025+-0.0211 | 0.6508+-0.0014 | 0.7562+-0.0064 |
| hg38_T2T_masked | sentieon-202112.01 | manta-1.6.0 | 2 | 0.9529+-0.0007 | 0.6909+-0.0153 | 0.8009+-0.0101 |
| hg38_T2T_masked | sentieon-202112.01-recal | dysgu-1.3.4 | 2 | 0.4737+-0.2870 | 0.6689+-0.0085 | 0.4999+-0.2072 |
| hg38_T2T_masked | sentieon-202112.01-recal | dysgu-1.3.4-PO | 2 | 0.9031+-0.0172 | 0.6516+-0.0060 | 0.7568+-0.0020 |
| hg38_T2T_masked | sentieon-202112.01-recal | manta-1.6.0 | 2 | 0.9518+-0.0009 | 0.6909+-0.0149 | 0.8005+-0.0097 |
| hg38_T2T_masked | snap-2.0.0 | dysgu-1.3.4 | 2 | 0.7011+-0.0512 | 0.6637+-0.0083 | 0.6806+-0.0199 |
| hg38_T2T_masked | snap-2.0.0 | dysgu-1.3.4-PO | 2 | 0.9420+-0.0040 | 0.6266+-0.0043 | 0.7526+-0.0018 |
| hg38_T2T_masked | snap-2.0.0 | manta-1.6.0 | 2 | 0.9490+-0.0008 | 0.6805+-0.0128 | 0.7925+-0.0084 |
| hg38_asm5_alt | dragmap-1.2.1 | dysgu-1.3.4 | 2 | 0.4355+-0.2775 | 0.7088+-0.0097 | 0.4825+-0.2235 |
| hg38_asm5_alt | dragmap-1.2.1 | dysgu-1.3.4-PO | 2 | 0.9146+-0.0191 | 0.6927+-0.0040 | 0.7882+-0.0045 |
| hg38_asm5_alt | dragmap-1.2.1 | manta-1.6.0 | 2 | 0.9616+-0.0007 | 0.6550+-0.0169 | 0.7791+-0.0117 |
| hg38_asm5_alt | sentieon-202112.01 | dysgu-1.3.4 | 2 | 0.4744+-0.2883 | 0.6665+-0.0052 | 0.5000+-0.2085 |
| hg38_asm5_alt | sentieon-202112.01 | dysgu-1.3.4-PO | 2 | 0.9061+-0.0184 | 0.6463+-0.0002 | 0.7544+-0.0062 |
| hg38_asm5_alt | sentieon-202112.01 | manta-1.6.0 | 2 | 0.9563+-0.0018 | 0.6899+-0.0149 | 0.8015+-0.0094 |
| hg38_asm5_alt | sentieon-202112.01-recal | dysgu-1.3.4 | 2 | 0.4791+-0.2912 | 0.6656+-0.0080 | 0.5016+-0.2078 |
| hg38_asm5_alt | sentieon-202112.01-recal | dysgu-1.3.4-PO | 2 | 0.9059+-0.0176 | 0.6464+-0.0042 | 0.7543+-0.0032 |
| hg38_asm5_alt | sentieon-202112.01-recal | manta-1.6.0 | 2 | 0.9547+-0.0018 | 0.6896+-0.0140 | 0.8007+-0.0088 |

| Reference | Aligner | Caller | N | precision | recall | f1 |
|---------------|------------|----------------|---|----------------|----------------|----------------|
| hg38_asm5_alt | snap-2.0.0 | dysgu-1.3.4 | 2 | 0.7062+-0.0531 | 0.6590+-0.0077 | 0.6805+-0.0207 |
| hg38_asm5_alt | snap-2.0.0 | dysgu-1.3.4-PO | 2 | 0.9430+-0.0048 | 0.6225+-0.0043 | 0.7500+-0.0016 |
| hg38_asm5_alt | snap-2.0.0 | manta-1.6.0 | 2 | 0.9509+-0.0022 | 0.6791+-0.0127 | 0.7923+-0.0079 |

6.1.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Caller | N | precision | recall | f1 |
|-----------------|------------------------|----------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | dysgu-1.3.4 | 1 | 0.8962+-0.0000 | 0.9811+-0.0000 | 0.9367+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | dysgu-1.3.4-PO | 1 | 0.9415+-0.0000 | 0.9731+-0.0000 | 0.9571+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | pbsv-2.8.0 | 1 | 0.9463+-0.0000 | 0.9847+-0.0000 | 0.9651+-0.0000 |
| hg38_T2T_masked | minimap2-2.23 | sniffles-2.0.2 | 1 | 0.9494+-0.0000 | 0.9808+-0.0000 | 0.9649+-0.0000 |
| hg38_T2T_masked | pbbmm2-1.7.0 | dysgu-1.3.4 | 1 | 0.8869+-0.0000 | 0.9760+-0.0000 | 0.9293+-0.0000 |
| hg38_T2T_masked | pbbmm2-1.7.0 | dysgu-1.3.4-PO | 1 | 0.9554+-0.0000 | 0.1849+-0.0000 | 0.3098+-0.0000 |
| hg38_T2T_masked | pbbmm2-1.7.0 | pbsv-2.8.0 | 1 | 0.9420+-0.0000 | 0.9859+-0.0000 | 0.9634+-0.0000 |
| hg38_T2T_masked | pbbmm2-1.7.0 | sniffles-2.0.2 | 1 | 0.9450+-0.0000 | 0.9811+-0.0000 | 0.9627+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dysgu-1.3.4 | 1 | 0.8955+-0.0000 | 0.9806+-0.0000 | 0.9361+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dysgu-1.3.4-PO | 1 | 0.9415+-0.0000 | 0.9727+-0.0000 | 0.9568+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | pbsv-2.8.0 | 1 | 0.9459+-0.0000 | 0.9847+-0.0000 | 0.9649+-0.0000 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | sniffles-2.0.2 | 1 | 0.9492+-0.0000 | 0.9808+-0.0000 | 0.9647+-0.0000 |

6.2 Unrestricted calls

These evaluations are **UNRESTRICTED**, meaning that there is no BED file used to limit the analysis to a subset of the genome (e.g. no high-confidence region applied). As a result, precision results are skewed downwards and should be considered a lower-bound on precision with respect to the full benchmark dataset. However, this allows us to add benchmarks that were not released with a BED file, specifically HG001/NA12878’s Personalis benchmark set.

6.2.1 Preparation: “PCR-free-illumina”

| Reference | Aligner | Caller | N | precision | recall | f1 |
|-----------------|--------------------------|----------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | dragmap-1.2.1 | dysgu-1.3.4 | 4 | 0.2646+-0.0970 | 0.8008+-0.1597 | 0.3829+-0.0991 |
| hg38_T2T_masked | dragmap-1.2.1 | dysgu-1.3.4-PO | 4 | 0.5682+-0.0907 | 0.7865+-0.1645 | 0.6380+-0.0072 |
| hg38_T2T_masked | dragmap-1.2.1 | manta-1.6.0 | 4 | 0.5691+-0.0968 | 0.7417+-0.1500 | 0.6221+-0.0078 |
| hg38_T2T_masked | sentieon-202112.01 | dysgu-1.3.4 | 4 | 0.2468+-0.0789 | 0.7535+-0.1552 | 0.3599+-0.0782 |
| hg38_T2T_masked | sentieon-202112.01 | dysgu-1.3.4-PO | 4 | 0.5693+-0.0916 | 0.7369+-0.1598 | 0.6199+-0.0078 |
| hg38_T2T_masked | sentieon-202112.01 | manta-1.6.0 | 4 | 0.5404+-0.0990 | 0.7589+-0.1444 | 0.6098+-0.0175 |
| hg38_T2T_masked | sentieon-202112.01-recal | dysgu-1.3.4 | 4 | 0.2484+-0.0787 | 0.7525+-0.1552 | 0.3615+-0.0774 |
| hg38_T2T_masked | sentieon-202112.01-recal | dysgu-1.3.4-PO | 4 | 0.5692+-0.0924 | 0.7371+-0.1589 | 0.6198+-0.0064 |
| hg38_T2T_masked | sentieon-202112.01-recal | manta-1.6.0 | 4 | 0.5392+-0.0979 | 0.7588+-0.1451 | 0.6092+-0.0167 |
| hg38_T2T_masked | snap-2.0.0 | dysgu-1.3.4 | 4 | 0.2768+-0.0463 | 0.7310+-0.1515 | 0.3903+-0.0248 |
| hg38_T2T_masked | snap-2.0.0 | dysgu-1.3.4-PO | 4 | 0.6057+-0.0977 | 0.6900+-0.1455 | 0.6229+-0.0111 |
| hg38_T2T_masked | snap-2.0.0 | manta-1.6.0 | 4 | 0.4960+-0.0947 | 0.7504+-0.1473 | 0.5758+-0.0217 |
| hg38_asm5_alt | dragmap-1.2.1 | dysgu-1.3.4 | 4 | 0.2714+-0.1009 | 0.7783+-0.1542 | 0.3868+-0.1000 |
| hg38_asm5_alt | dragmap-1.2.1 | dysgu-1.3.4-PO | 4 | 0.5745+-0.0922 | 0.7648+-0.1575 | 0.6346+-0.0062 |
| hg38_asm5_alt | dragmap-1.2.1 | manta-1.6.0 | 4 | 0.5851+-0.1027 | 0.7229+-0.1443 | 0.6242+-0.0073 |
| hg38_asm5_alt | sentieon-202112.01 | dysgu-1.3.4 | 4 | 0.2164+-0.0636 | 0.7461+-0.1528 | 0.3261+-0.0658 |
| hg38_asm5_alt | sentieon-202112.01 | dysgu-1.3.4-PO | 4 | 0.5629+-0.0909 | 0.7279+-0.1555 | 0.6130+-0.0078 |
| hg38_asm5_alt | sentieon-202112.01 | manta-1.6.0 | 4 | 0.5502+-0.1032 | 0.7558+-0.1430 | 0.6148+-0.0182 |
| hg38_asm5_alt | sentieon-202112.01-recal | dysgu-1.3.4 | 4 | 0.2178+-0.0639 | 0.7458+-0.1533 | 0.3276+-0.0656 |
| hg38_asm5_alt | sentieon-202112.01-recal | dysgu-1.3.4-PO | 4 | 0.5628+-0.0919 | 0.7274+-0.1549 | 0.6126+-0.0057 |
| hg38_asm5_alt | sentieon-202112.01-recal | manta-1.6.0 | 4 | 0.5492+-0.1020 | 0.7553+-0.1435 | 0.6141+-0.0173 |
| hg38_asm5_alt | snap-2.0.0 | dysgu-1.3.4 | 4 | 0.2781+-0.0471 | 0.7277+-0.1532 | 0.3908+-0.0252 |
| hg38_asm5_alt | snap-2.0.0 | dysgu-1.3.4-PO | 4 | 0.6027+-0.0977 | 0.6880+-0.1475 | 0.6199+-0.0122 |
| hg38_asm5_alt | snap-2.0.0 | manta-1.6.0 | 4 | 0.4999+-0.0970 | 0.7479+-0.1467 | 0.5774+-0.0223 |

6.2.2 Preparation: “PacBio-CCS-high”

| Reference | Aligner | Caller | N | precision | recall | f1 |
|-----------------|---------------|----------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | dysgu-1.3.4 | 2 | 0.2508+-0.0756 | 0.9544+-0.0156 | 0.3906+-0.0938 |
| hg38_T2T_masked | minimap2-2.23 | dysgu-1.3.4-PO | 2 | 0.4148+-0.1336 | 0.9438+-0.0201 | 0.5618+-0.1264 |

| Reference | Aligner | Caller | N | precision | recall | f1 |
|-----------------|------------------------|----------------|---|----------------|----------------|----------------|
| hg38_T2T_masked | minimap2-2.23 | pbsv-2.8.0 | 2 | 0.3681+-0.1158 | 0.9564+-0.0071 | 0.5204+-0.1206 |
| hg38_T2T_masked | minimap2-2.23 | sniffles-2.0.2 | 2 | 0.3764+-0.1182 | 0.9473+-0.0192 | 0.5265+-0.1189 |
| hg38_T2T_masked | pbbmm2-1.7.0 | dysgu-1.3.4 | 2 | 0.2589+-0.0754 | 0.9506+-0.0092 | 0.4008+-0.0926 |
| hg38_T2T_masked | pbbmm2-1.7.0 | dysgu-1.3.4-PO | 2 | 0.6125+-0.0607 | 0.4066+-0.2475 | 0.4280+-0.1706 |
| hg38_T2T_masked | pbbmm2-1.7.0 | pbsv-2.8.0 | 2 | 0.3813+-0.1210 | 0.9593+-0.0087 | 0.5338+-0.1234 |
| hg38_T2T_masked | pbbmm2-1.7.0 | sniffles-2.0.2 | 2 | 0.3836+-0.1205 | 0.9486+-0.0172 | 0.5339+-0.1203 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dysgu-1.3.4 | 2 | 0.2497+-0.0748 | 0.9540+-0.0156 | 0.3893+-0.0929 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | dysgu-1.3.4-PO | 2 | 0.4148+-0.1338 | 0.9434+-0.0201 | 0.5617+-0.1265 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | pbsv-2.8.0 | 2 | 0.3672+-0.1156 | 0.9561+-0.0070 | 0.5195+-0.1206 |
| hg38_T2T_masked | sentieon_mm2-202112.01 | sniffles-2.0.2 | 2 | 0.3761+-0.1180 | 0.9473+-0.0192 | 0.5262+-0.1187 |