Supplementary Material for:

Accuracy and Reproducibility of Somatic Point Mutation Calling in Clinical-Type Targeted Sequencing Data

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# Table 1: TST170–GM12878 default parameters

| Caller   | Rep | NumCalls | TP  | FP  | FN  | Sens.  | Prec.  |
|----------|-----|----------|-----|-----|-----|--------|--------|
| Mutect2  | 1   | 514      | 340 | 174 | 3   | 0.99125 | 0.66148 |
|          | 2   | 477      | 338 | 139 | 5   | 0.98542 | 0.7086  |
|          | 3   | 416      | 339 | 77  | 4   | 0.98834 | 0.8149  |
|          | 4   | 721      | 339 | 382 | 4   | 0.98834 | 0.47018 |
|          | 5   | 769      | 338 | 431 | 5   | 0.98542 | 0.43953 |
|          | 6   | 766      | 339 | 427 | 4   | 0.98834 | 0.44256 |
| Samtools | 1   | 325816   | 342 | 325474 | 1 | 0.99708 | 0.0010497 |
|          | 2   | 127858   | 341 | 127517 | 2 | 0.99417 | 0.002667 |
|          | 3   | 206361   | 341 | 206020 | 2 | 0.99417 | 0.0016254 |
|          | 4   | 145498   | 342 | 145156 | 1 | 0.99708 | 0.0023505 |
|          | 5   | 136664   | 342 | 136322 | 1 | 0.99708 | 0.0025025 |
|          | 6   | 138410   | 342 | 138068 | 1 | 0.99708 | 0.0024709 |
| VarDict  | 1   | 347      | 342 | 5   | 1   | 0.99708 | 0.98559 |
|          | 2   | 355      | 340 | 15  | 3   | 0.99125 | 0.95775 |
|          | 3   | 351      | 341 | 10  | 2   | 0.99417 | 0.97151 |
|          | 4   | 346      | 342 | 4   | 1   | 0.99708 | 0.98844 |
|          | 5   | 344      | 341 | 3   | 2   | 0.99417 | 0.99128 |
|          | 6   | 345      | 342 | 3   | 1   | 0.99708 | 0.9913  |
| VarScan2 | 1   | 729      | 342 | 387 | 1   | 0.99708 | 0.46914 |
|          | 2   | 552      | 339 | 213 | 4   | 0.98834 | 0.61413 |
|          | 3   | 593      | 340 | 253 | 3   | 0.99125 | 0.57336 |
|          | 4   | 662      | 342 | 320 | 1   | 0.99708 | 0.51662 |
|          | 5   | 629      | 342 | 287 | 1   | 0.99708 | 0.54372 |
|          | 6   | 639      | 342 | 297 | 1   | 0.99708 | 0.53521 |
| Pisces   | 1   | 1055     | 342 | 713 | 1   | 0.99708 | 0.32417 |
|          | 2   | 773      | 341 | 432 | 2   | 0.99417 | 0.44114 |
|          | 3   | 783      | 341 | 442 | 2   | 0.99417 | 0.4355  |
|          | 4   | 907      | 342 | 565 | 1   | 0.99708 | 0.37707 |
|          | 5   | 949      | 342 | 607 | 1   | 0.99708 | 0.36038 |
|          | 6   | 1045     | 342 | 703 | 1   | 0.99708 | 0.32727 |
# Table 2: TST170–GM12877 default parameters

| Caller   | Rep | NumCalls | TP  | FP  | FN  | Sens.    | Prec.    |
|----------|-----|----------|-----|-----|-----|----------|----------|
| Mutect2  | 1   | 1903     | 334 | 1569| 2   | 0.99405  | 0.17551  |
|          | 2   | 1773     | 335 | 1438| 1   | 0.99702  | 0.18895  |
|          | 3   | 1426     | 332 | 1094| 4   | 0.9881   | 0.23282  |
|          | 4   | 1330     | 335 | 995 | 1   | 0.99702  | 0.25188  |
|          | 5   | 2036     | 334 | 1702| 2   | 0.99405  | 0.16405  |
|          | 6   | 1626     | 335 | 1291| 1   | 0.99702  | 0.20603  |
| Samtools | 1   | 50468    | 336 | 50132| 0 | 1   | 0.006657 |
|          | 2   | 46565    | 336 | 46229| 0 | 1   | 0.0072157|
|          | 3   | 42572    | 335 | 42237| 1 | 0.99702  | 0.007869 |
|          | 4   | 62048    | 336 | 61712| 0 | 1   | 0.0054152|
|          | 5   | 71143    | 336 | 70807| 0 | 1   | 0.0047229|
|          | 6   | 62740    | 336 | 62404| 0 | 1   | 0.0053554|
| VarDict  | 1   | 355      | 336 | 19  | 0   | 1   | 0.94648  |
|          | 2   | 353      | 336 | 17  | 0   | 1   | 0.95184  |
|          | 3   | 364      | 335 | 29  | 1   | 0.99702  | 0.92033  |
|          | 4   | 351      | 336 | 15  | 0   | 1   | 0.95726  |
|          | 5   | 358      | 335 | 23  | 1   | 0.99702  | 0.93575  |
|          | 6   | 361      | 336 | 25  | 0   | 1   | 0.93075  |
| VarScan2 | 1   | 1242     | 335 | 907 | 1   | 0.99702  | 0.26973  |
|          | 2   | 1246     | 334 | 912 | 2   | 0.99405  | 0.26806  |
|          | 3   | 1138     | 334 | 804 | 2   | 0.99405  | 0.2935   |
|          | 4   | 1758     | 336 | 1422| 0   | 1   | 0.19113  |
|          | 5   | 1651     | 336 | 1315| 0   | 1   | 0.20351  |
|          | 6   | 1589     | 335 | 1254| 1   | 0.99702  | 0.21082  |
| Pisces   | 1   | 809      | 336 | 473 | 0   | 1   | 0.41533  |
|          | 2   | 813      | 336 | 477 | 0   | 1   | 0.41328  |
|          | 3   | 732      | 335 | 397 | 1   | 0.99702  | 0.45765  |
|          | 4   | 883      | 336 | 547 | 0   | 1   | 0.38052  |
|          | 5   | 883      | 336 | 547 | 0   | 1   | 0.38052  |
|          | 6   | 827      | 336 | 491 | 0   | 1   | 0.40629  |
### Table 3: OF–GM12878 default parameters

| Caller | Rep | NumCalls | TP   | FP   | FN   | Sens.  | Prec.  |
|--------|-----|----------|------|------|------|--------|--------|
| Mutect2 | 1   | 55       | 25   | 30   | 1    | 0.96154 | 0.45455 |
|         | 2   | 48       | 26   | 22   | 0    | 1      | 0.54167 |
|         | 3   | 41       | 26   | 15   | 0    | 1      | 0.63415 |
| Samtools | 1   | 21578    | 26   | 21552| 0    | 1      | 0.0012049 |
|         | 2   | 12704    | 26   | 12678| 0    | 1      | 0.0020466 |
|         | 3   | 9171     | 26   | 9145 | 0    | 1      | 0.002835 |
| VarDict | 1   | 27       | 26   | 1    | 0    | 1      | 0.96296 |
|         | 2   | 26       | 25   | 1    | 1    | 0.96154 | 0.96154 |
|         | 3   | 27       | 26   | 1    | 0    | 1      | 0.96296 |
| VarScan2 | 1   | 67       | 26   | 41   | 0    | 1      | 0.38806 |
|         | 2   | 145      | 26   | 119  | 0    | 1      | 0.17931 |
|         | 3   | 238      | 26   | 212  | 0    | 1      | 0.10924 |
| ITVC    | 1   | 315      | 25   | 290  | 1    | 0.96154 | 0.079365 |
|         | 2   | 315      | 25   | 290  | 1    | 0.96154 | 0.079365 |
|         | 3   | 314      | 25   | 289  | 1    | 0.96154 | 0.079618 |

### Table 4: OF–GM12877 default parameters

| Caller | Rep | NumCalls | TP   | FP   | FN   | Sens.  | Prec.  |
|--------|-----|----------|------|------|------|--------|--------|
| Mutect2 | 1   | 40       | 22   | 18   | 2    | 0.91667 | 0.55   |
|         | 2   | 52       | 23   | 29   | 1    | 0.95833 | 0.44231 |
|         | 3   | 56       | 22   | 34   | 2    | 0.91667 | 0.39286 |
| Samtools | 1   | 17770    | 24   | 17746| 0    | 1      | 0.0013506 |
|         | 2   | 20949    | 24   | 20925| 0    | 1      | 0.0011456 |
|         | 3   | 24386    | 24   | 24362| 0    | 1      | 0.00098417 |
| VarDict | 1   | 23       | 23   | 0    | 1    | 0.95833 | 1      |
|         | 2   | 24       | 23   | 1    | 1    | 0.95833 | 0.95833 |
|         | 3   | 24       | 23   | 1    | 1    | 0.95833 | 0.95833 |
| VarScan2 | 1   | 49       | 24   | 25   | 0    | 1      | 0.4898 |
|         | 2   | 53       | 24   | 29   | 0    | 1      | 0.45283 |
|         | 3   | 50       | 24   | 26   | 0    | 1      | 0.48   |
| ITVC    | 1   | 325      | 23   | 302  | 1    | 0.95833 | 0.070769 |
|         | 2   | 325      | 23   | 302  | 1    | 0.95833 | 0.070769 |
|         | 3   | 325      | 23   | 302  | 1    | 0.95833 | 0.070769 |
Table 5: TST170–GM12878 consistent parameters

| Caller   | Rep | NumCalls | TP  | FP  | FN  | Sens.  | Prec.  |
|----------|-----|----------|-----|-----|-----|--------|--------|
| Mutect2  | 1   | 502      | 341 | 161 | 2   | 0.99417| 0.67928|
|          | 2   | 472      | 337 | 135 | 6   | 0.98251| 0.71398|
|          | 3   | 409      | 339 | 70  | 4   | 0.98834| 0.82885|
|          | 4   | 703      | 340 | 363 | 3   | 0.99125| 0.48364|
|          | 5   | 755      | 340 | 415 | 3   | 0.99125| 0.45033|
|          | 6   | 754      | 340 | 414 | 3   | 0.99125| 0.45093|
| Samtools | 1   | 784      | 343 | 441 | 0   | 1      | 0.4375 |
|          | 2   | 1354     | 340 | 1014| 3   | 0.99125| 0.25111|
|          | 3   | 1079     | 342 | 737 | 1   | 0.99708| 0.31696|
|          | 4   | 700      | 343 | 357 | 0   | 1      | 0.49   |
|          | 5   | 731      | 343 | 388 | 0   | 1      | 0.46922|
|          | 6   | 715      | 343 | 372 | 0   | 1      | 0.47972|
| VarDict  | 1   | 378      | 343 | 35  | 0   | 1      | 0.90741|
|          | 2   | 679      | 340 | 339 | 3   | 0.99125| 0.50074|
|          | 3   | 546      | 342 | 204 | 1   | 0.99708| 0.62637|
|          | 4   | 415      | 343 | 72  | 0   | 1      | 0.82651|
|          | 5   | 465      | 342 | 123 | 1   | 0.99708| 0.73548|
|          | 6   | 435      | 343 | 92  | 0   | 1      | 0.78851|
| VarScan2 | 1   | 685      | 343 | 342 | 0   | 1      | 0.50073|
|          | 2   | 540      | 338 | 202 | 5   | 0.98542| 0.62593|
|          | 3   | 580      | 341 | 239 | 2   | 0.99141| 0.58793|
|          | 4   | 636      | 343 | 293 | 0   | 1      | 0.53931|
|          | 5   | 605      | 343 | 262 | 0   | 1      | 0.56694|
|          | 6   | 615      | 343 | 272 | 0   | 1      | 0.55772|
| Pisces   | 1   | 961      | 343 | 618 | 0   | 1      | 0.35692|
|          | 2   | 707      | 340 | 367 | 3   | 0.99125| 0.48091|
|          | 3   | 699      | 342 | 357 | 1   | 0.99708| 0.48927|
|          | 4   | 804      | 343 | 461 | 0   | 1      | 0.42662|
|          | 5   | 849      | 343 | 506 | 0   | 1      | 0.404  |
|          | 6   | 780      | 343 | 437 | 0   | 1      | 0.43974|
Table 6: TST170–GM12877 consistent parameters

| Caller     | Rep | NumCalls | TP  | FP  | FN  | Sens.  | Prec.  |
|------------|-----|----------|-----|-----|-----|--------|--------|
| Mutect2    | 1   | 1873     | 333 | 1540| 3   | 0.99107| 0.17779|
|            | 2   | 1751     | 333 | 1418| 3   | 0.99107| 0.19018|
|            | 3   | 1422     | 331 | 1091| 5   | 0.98512| 0.23277|
|            | 4   | 1297     | 335 | 962 | 1   | 0.99702| 0.25829|
|            | 5   | 1978     | 334 | 1644| 2   | 0.99405| 0.16886|
|            | 6   | 1595     | 334 | 1261| 2   | 0.99405| 0.2094 |
| Samtools   | 1   | 3909     | 335 | 3574| 1   | 0.99702| 0.0857 |
|            | 2   | 4419     | 334 | 4085| 2   | 0.99405| 0.07558|
|            | 3   | 4494     | 334 | 4160| 2   | 0.99405| 0.07432|
|            | 4   | 3883     | 336 | 3547| 0   | 1      | 0.08653|
|            | 5   | 3471     | 336 | 3135| 0   | 1      | 0.09680|
|            | 6   | 4571     | 335 | 4236| 1   | 0.99702| 0.07328|
| VarDict    | 1   | 1406     | 335 | 1071| 1   | 0.99702| 0.23826|
|            | 2   | 1518     | 334 | 1184| 2   | 0.99405| 0.22003|
|            | 3   | 2038     | 334 | 1704| 2   | 0.99405| 0.16389|
|            | 4   | 1164     | 336 | 828 | 0   | 1      | 0.28866|
|            | 5   | 1056     | 335 | 721 | 1   | 0.99702| 0.31723|
|            | 6   | 1101     | 335 | 766 | 1   | 0.99702| 0.30427|
| VarScan2   | 1   | 1162     | 335 | 827 | 1   | 0.99702| 0.2883 |
|            | 2   | 1194     | 333 | 861 | 3   | 0.99107| 0.27889|
|            | 3   | 1073     | 333 | 740 | 3   | 0.99107| 0.31034|
|            | 4   | 1567     | 336 | 1231| 0   | 1      | 0.21442|
|            | 5   | 1485     | 336 | 1149| 0   | 1      | 0.22626|
|            | 6   | 1428     | 335 | 1093| 1   | 0.99702| 0.23459|
| Pisces     | 1   | 676      | 335 | 341 | 1   | 0.99702| 0.49556|
|            | 2   | 655      | 334 | 321 | 2   | 0.99405| 0.50992|
|            | 3   | 626      | 334 | 292 | 2   | 0.99405| 0.53355|
|            | 4   | 720      | 336 | 384 | 0   | 1      | 0.46667|
|            | 5   | 743      | 336 | 407 | 0   | 1      | 0.45222|
|            | 6   | 689      | 335 | 354 | 1   | 0.99702| 0.48621|
### Table 7: OF–GM12878 consistent parameters

| Caller    | Rep | NumCalls | TP  | FP  | FN  | Sens.  | Prec.  |
|-----------|-----|----------|-----|-----|-----|--------|--------|
| Mutect2   | 1   | 55       | 25  | 30  | 1   | 0.96154| 0.45455|
|           | 2   | 55       | 25  | 30  | 1   | 0.96154| 0.45455|
|           | 3   | 55       | 25  | 30  | 1   | 0.96154| 0.45455|
| Samtools  | 1   | 63       | 26  | 37  | 0   | 1      | 0.4127 |
|           | 2   | 63       | 26  | 37  | 0   | 1      | 0.4127 |
|           | 3   | 63       | 26  | 37  | 0   | 1      | 0.4127 |
| VarDict   | 1   | 34       | 26  | 8   | 0   | 1      | 0.76471|
|           | 2   | 34       | 26  | 8   | 0   | 1      | 0.76471|
|           | 3   | 34       | 26  | 8   | 0   | 1      | 0.76471|
| VarScan2  | 1   | 64       | 26  | 38  | 0   | 1      | 0.40625|
|           | 2   | 64       | 26  | 38  | 0   | 1      | 0.40625|
|           | 3   | 64       | 26  | 38  | 0   | 1      | 0.40625|
| ITVC      | 1   | 23       | 19  | 4   | 7   | 0.73077| 0.82609|
|           | 2   | 25       | 21  | 4   | 5   | 0.80769| 0.84   |
|           | 3   | 22       | 19  | 3   | 7   | 0.73077| 0.86364|

### Table 8: OF–GM12877 consistent parameters

| Caller    | Rep | NumCalls | TP  | FP  | FN  | Sens.  | Prec.  |
|-----------|-----|----------|-----|-----|-----|--------|--------|
| Mutect2   | 1   | 41       | 22  | 19  | 2   | 0.91667| 0.53659|
|           | 2   | 53       | 23  | 30  | 1   | 0.95833| 0.43396|
|           | 3   | 58       | 22  | 36  | 2   | 0.91667| 0.37931|
| Samtools  | 1   | 53       | 24  | 29  | 0   | 1      | 0.45283|
|           | 2   | 60       | 24  | 36  | 0   | 1      | 0.4    |
|           | 3   | 48       | 24  | 24  | 0   | 1      | 0.5    |
| VarDict   | 1   | 27       | 24  | 3   | 0   | 1      | 0.88889|
|           | 2   | 27       | 24  | 3   | 0   | 1      | 0.88889|
|           | 3   | 26       | 24  | 2   | 0   | 1      | 0.92308|
| VarScan2  | 1   | 46       | 24  | 22  | 0   | 1      | 0.52174|
|           | 2   | 49       | 24  | 25  | 0   | 1      | 0.4898 |
|           | 3   | 47       | 24  | 23  | 0   | 1      | 0.51064|
| ITVC      | 1   | 22       | 20  | 2   | 4   | 0.83333| 0.90909|
|           | 2   | 22       | 20  | 2   | 4   | 0.83333| 0.90909|
|           | 3   | 22       | 20  | 2   | 4   | 0.83333| 0.90909|
Table 9: Average sensitivity and precision on TST170 data when calls from different combinations of algorithms are intersected

| Combination             | Sensitivity | Precision |
|-------------------------|-------------|-----------|
| VarDict                 | 0.99705     | 0.49311   |
| MuTect2                 | 0.99093     | 0.40369   |
| Pisces                  | 0.99754     | 0.4618    |
| SAMtools                | 0.99754     | 0.24473   |
| VarScan2                | 0.99632     | 0.41095   |
| VarDict Pisces          | 0.99705     | 0.96484   |
| VarDict VarScan2        | 0.99582     | 0.84388   |
| MuTect2 VarDict         | 0.99093     | 0.75731   |
| MuTect2 Pisces          | 0.99093     | 0.94935   |
| MuTect2 SAMtools        | 0.99093     | 0.8493    |
| MuTect2 VarScan2        | 0.99019     | 0.86984   |
| SAMtools VarDict        | 0.99705     | 0.62907   |
| SAMtools Pisces         | 0.99754     | 0.75762   |
| SAMtools VarScan2       | 0.99632     | 0.44677   |
| VarScan2 Pisces         | 0.99632     | 0.78136   |
| VarDict VarScan2 Pisces | 0.99582     | 0.97315   |
| MuTect2 VarDict Pisces  | 0.99093     | 0.9823    |
| MuTect2 VarDict VarScan2| 0.99019     | 0.94007   |
| MuTect2 SAMtools VarDict| 0.99093     | 0.92933   |
| MuTect2 SAMtools Pisces | 0.99093     | 0.95357   |
| MuTect2 SAMtools VarScan2| 0.99019     | 0.87255   |
| MuTect2 VarScan2 Pisces | 0.99019     | 0.9538    |
| SAMtools VarDict Pisces | 0.99705     | 0.96968   |
| SAMtools VarDict VarScan2| 0.99582     | 0.84519   |
| SAMtools VarScan2 Pisces| 0.99632     | 0.79227   |
| MuTect2 VarDict VarScan2Pisces | 0.99019 | 0.98277 |
| MuTect2 SAMtools VarDictPisces | 0.99093 | 0.98301 |
| MuTect2 SAMtools VarDict VarScan2 | 0.99019 | 0.94115 |
| MuTect2 SAMtools VarScan2Pisces | 0.99019 | 0.95421 |
| SAMtools VarDict VarScan2Pisces | 0.99582 | 0.97361 |
| MuTect2 SAMtools VarDict VarScan2Pisces | 0.99019 | 0.98324 |
Table 10: Average sensitivity and precision on OF data when calls from different combinations of algorithms are intersected

| Combination                                      | Sensitivity | Precision  |
|--------------------------------------------------|-------------|------------|
| VarDict                                          | 1           | 0.8325     |
| MuTect2 1                                        | 0.94605     | 0.45225    |
| ITVC                                             | 0.79487     | 0.87617    |
| SAMtools 1                                      | 1           | 0.43182    |
| VarScan2 1                                      | 1           | 0.45682    |
| VarDict ITVC                                    | 0.79487     | 0.93749    |
| VarDict VarScan2 1                              | 1           | 0.83819    |
| MuTect2 VarDict 1                               | 0.94605     | 0.92585    |
| MuTect2 ITVC                                    | 0.7687      | 0.88519    |
| MuTect2 SAMtools 1                              | 0.94605     | 0.86473    |
| MuTect2 VarScan2 1                              | 0.94605     | 0.86473    |
| SAMtools VarDict 1                              | 1           | 0.84389    |
| SAMtools ITVC                                    | 0.79487     | 0.87617    |
| SAMtools VarScan2 1                             | 1           | 0.47836    |
| VarScan2 ITVC                                    | 0.79487     | 0.87617    |
| VarDict VarScan2 ITVC                           | 0.79487     | 0.93749    |
| MuTect2 VarDict ITVC                            | 0.7687      | 0.95036    |
| MuTect2 VarDict VarScan2 1                      | 0.94605     | 0.92585    |
| MuTect2 SAMtools VarDict 1                      | 0.94605     | 0.92585    |
| MuTect2 SAMtools ITVC                           | 0.7687      | 0.88519    |
| MuTect2 VarScan2 ITVC                           | 0.7687      | 0.88519    |
| SAMtools VarDict ITVC                           | 0.79487     | 0.93749    |
| SAMtools VarDict VarScan2 1                     | 1           | 0.84389    |
| SAMtools VarScan2 ITVC                          | 0.79487     | 0.87617    |
| MuTect2 VarDict VarScan2 ITVC                   | 0.7687      | 0.95036    |
| MuTect2 SAMtools VarDict ITVC                   | 0.7687      | 0.95036    |
| MuTect2 SAMtools VarDict VarScan2 1             | 0.94605     | 0.92585    |
| MuTect2 SAMtools VarScan2 ITVC                  | 0.7687      | 0.88519    |
| SAMtools VarDict VarScan2 ITVC                  | 0.79487     | 0.93749    |