Practical 1
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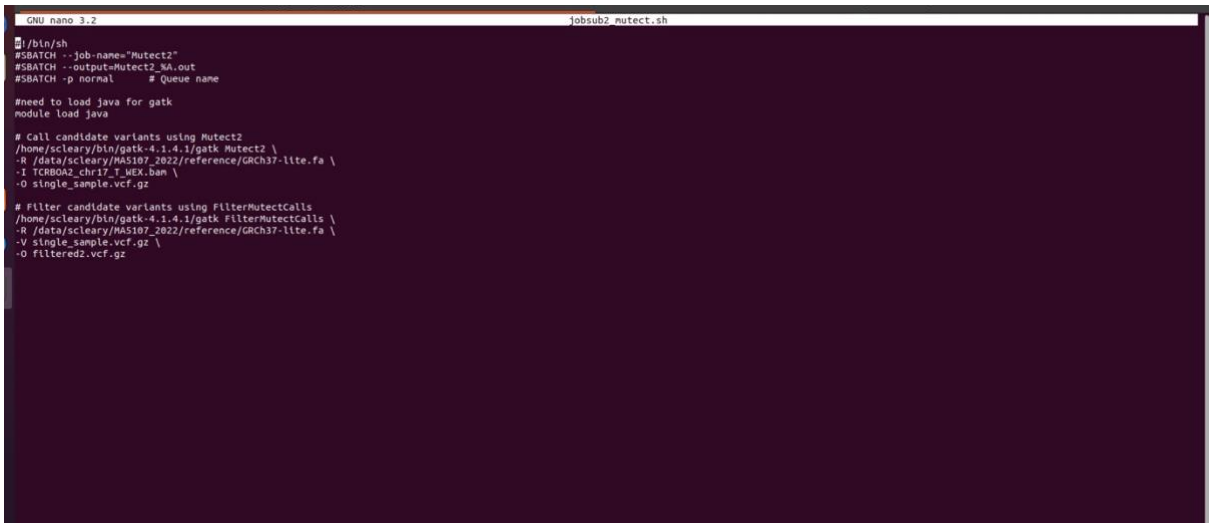
3.

4. Germline variants calling is direct. They vary against the reference. For somatic variants calling, it compares between two samples against the reference. Germline calling assumes fixed ploidy and calling consists of genotyping sites while somatic calling allows for varying ploidy. Somatic variants calling are both (a) different from control sample and (ii) different from the reference. Somatic variants calling(Mutect2) does not offer for the calculation of reference confidence which is a feature in Germline calling (HaplotypeCaller).

5. Mutect2 offers a joint analysis of multiple samples. SNVs and small indels can be detetcted via Mutect2. Mutect2 applies Bayesian somatic genotyping model while Mutect uses Bayesian classifier.

6.



7.

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normal_artifact 0.0     0.0     0.07    0.03
slippage        0.0     0.0     0.0     0.0
haplotype       0.0     0.0     0.0     0.0
germline        0.22    0.11    0.0     0.0
```

```
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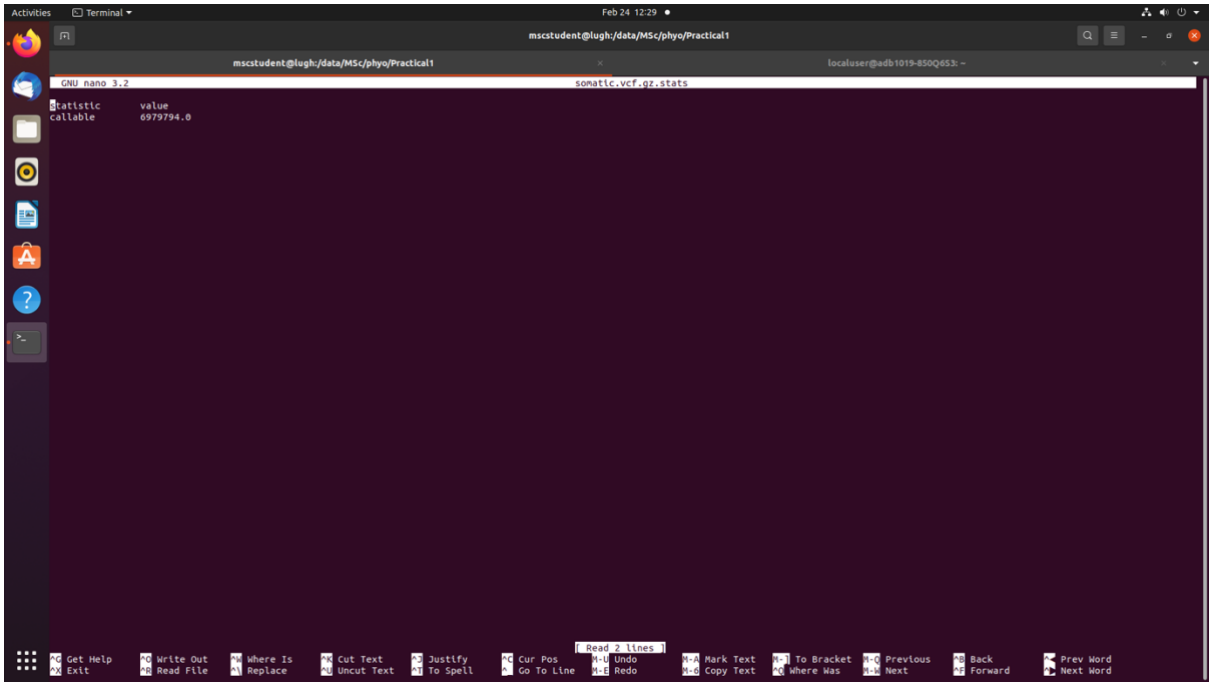
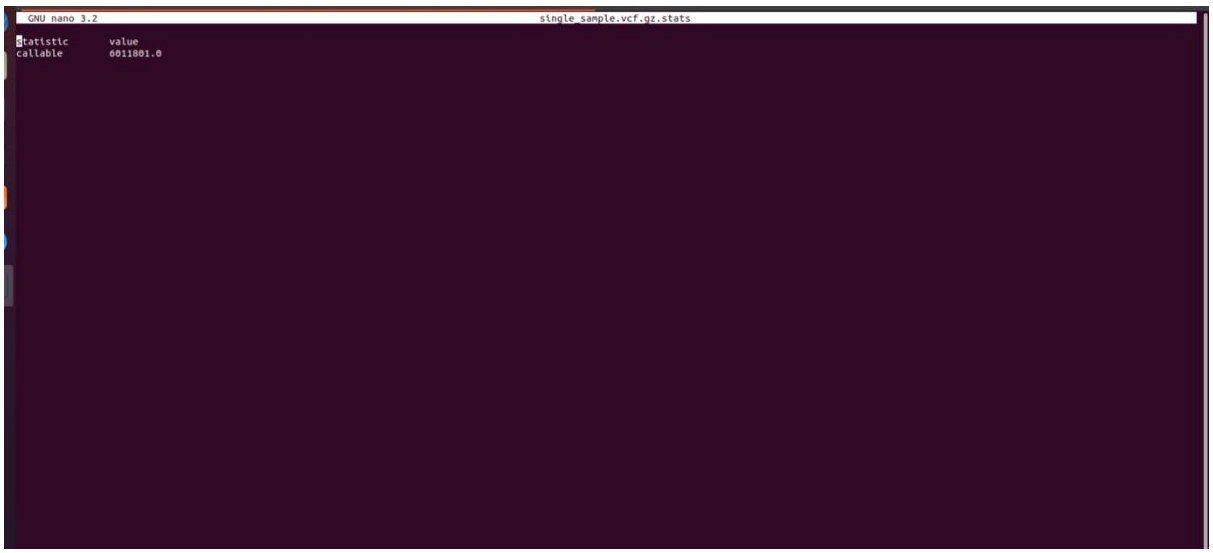
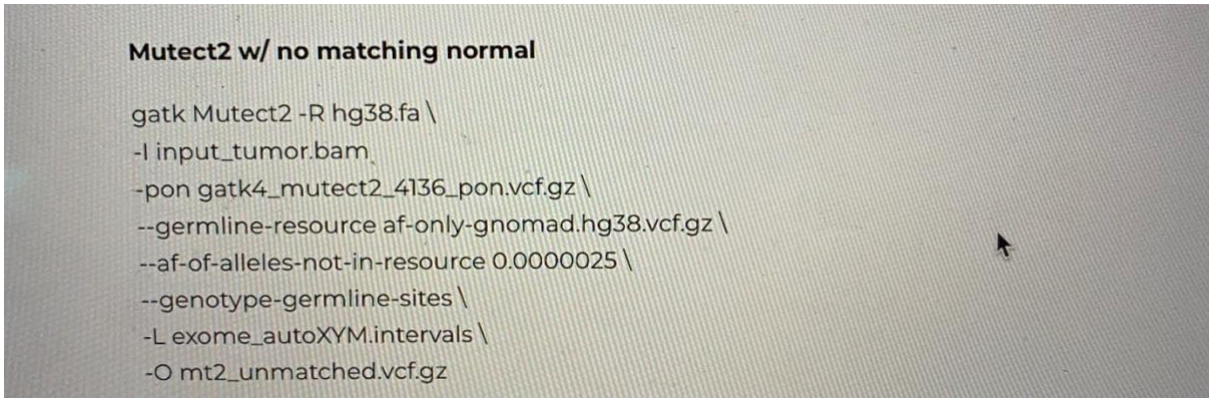
slippage        4.95    0.0     8.01    0.0
haplotype       13.0    0.0     6.99    0.0
germline        21.79   0.0     4.1     0.0
```





SNVs are different with 15.06 and 5.70 for steps 3 & 6 respectively. Moreover, fdr is also different with 0.503 & 0.081. Matched tumour normal variant calling is better for downstream analysis.

8.



We can remove possible germline mutations following the above code. Moreover, we can use population-based data if there is no matched normal sample.