

**The Hospital for Sick Children  
Technology Assessment at SickKids (TASK)**

**APPENDIX**

**A MICROCOSTING AND COST-CONSEQUENCE ANALYSIS OF GENOMIC TESTING STRATEGIES (INCLUDING TRIOS) IN AUTISM SPECTRUM DISORDER: AN UPDATE**

Authors:

Jathishinie Jegathisawaran, MHEcon  
Clinical Research Project Coordinator, Child Health Evaluative Sciences, The Hospital for Sick Children,  
Toronto, Canada

Kate Tsiplova, MSc  
Research Project Manager, Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto,  
Canada

Wendy J. Ungar, MSc, PhD  
Senior Scientist, Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada  
Professor, Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

**Report No. 2018-01**

**Date: February 06, 2019**

Co-investigators:

Christian R. Marshall, PhD

Associate Director, Genome Diagnostics, Department of Paediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, Canada

Assistant Professor, Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

Dimitri J. Stavropoulos, PhD

Co-Director, Cytogenetics, Department of Paediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, Canada

Assistant Professor, Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

Sergio L. Pereira, PhD

Research Core Manager, The Centre for Applied Genomics, Program in Genetics and Genome Biology, The Hospital for Sick Children, Toronto, Canada

Bhooma Thiruvahindrapuram, MSc

Facility Manger, Scientific Lead, The Centre for Applied Genomics, The Hospital for Sick Children, Toronto, Canada

**Acknowledgements:**

This research was supported by a grant for The Hospital for Sick Children's (SickKids) Centre for Genetic Medicine. We wish to thank Dr. Robin Hayeems, PhD, The Hospital for Sick Children, for valuable feedback and Stephanie Luca for her assistance with quality checks.

## **Appendix 1: Fact Sheet: Changes between the 2018 report update (2018-01) versus the 2016 report (2016-02.2)**

General for all platforms:

platforms in the 2018 report update: CMA, Illumina HiSeq® 2500, Illumina NextSeq® 550 and Illumina HiSeq X™; platforms in the 2016 report: CMA, Illumina HiSeq® 2500 and Illumina HiSeq X™:

- Overhead cost proportion: 22.3% vs. 23%
- No inflation adjustments were made for prices except labour from previous years for the 2018 report update; labour prices were adjusted by an annual 1.5% increase to 2017/2018. On the other hand, all prices were inflated for the 2016 report.

Exome and Genome analyses:

- Addition of filtration steps to analyze ~300-400 variants in order to flag variants of interest for both primary and secondary variants (impacts labour costing)

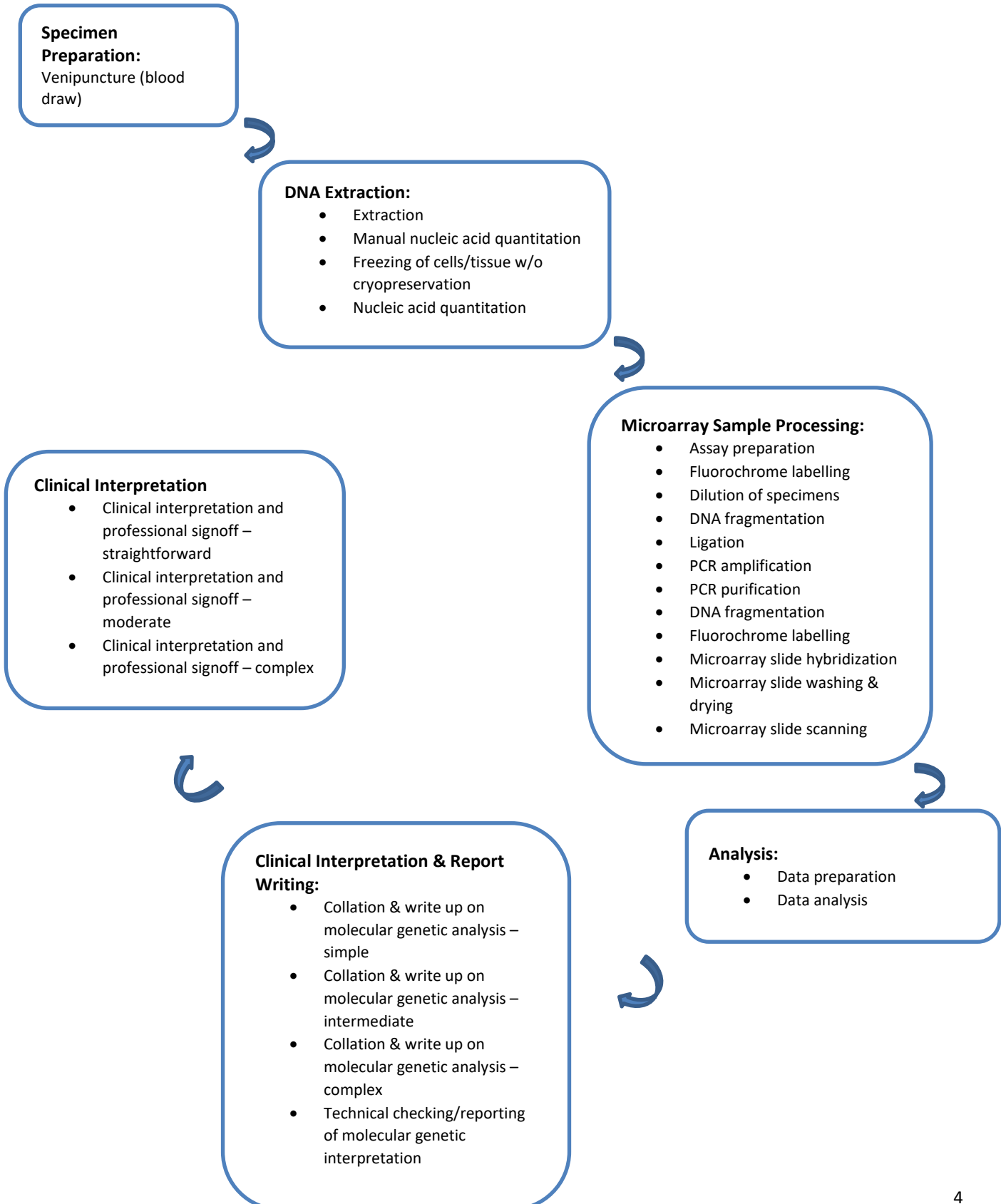
Whole Exome Sequencing:

- Addition of a new platform (NextSeq® 550)
- Exome output per month (NextSeq® 550): 80 (64-96)
- Exome output per month (HiSeq® 2500): 83 (70-95) vs. 87.5 (75-100)
- Bioinformatics
  - Pipeline: no change (Genome Analysis Toolkit (GATK))
  - Decrease of 1 step (temporary BAM files) for file storage
  - Additional 2 steps (extra step in recalibration; indel realignment) for computation use
  - Price per node: \$26,804 vs. \$9560

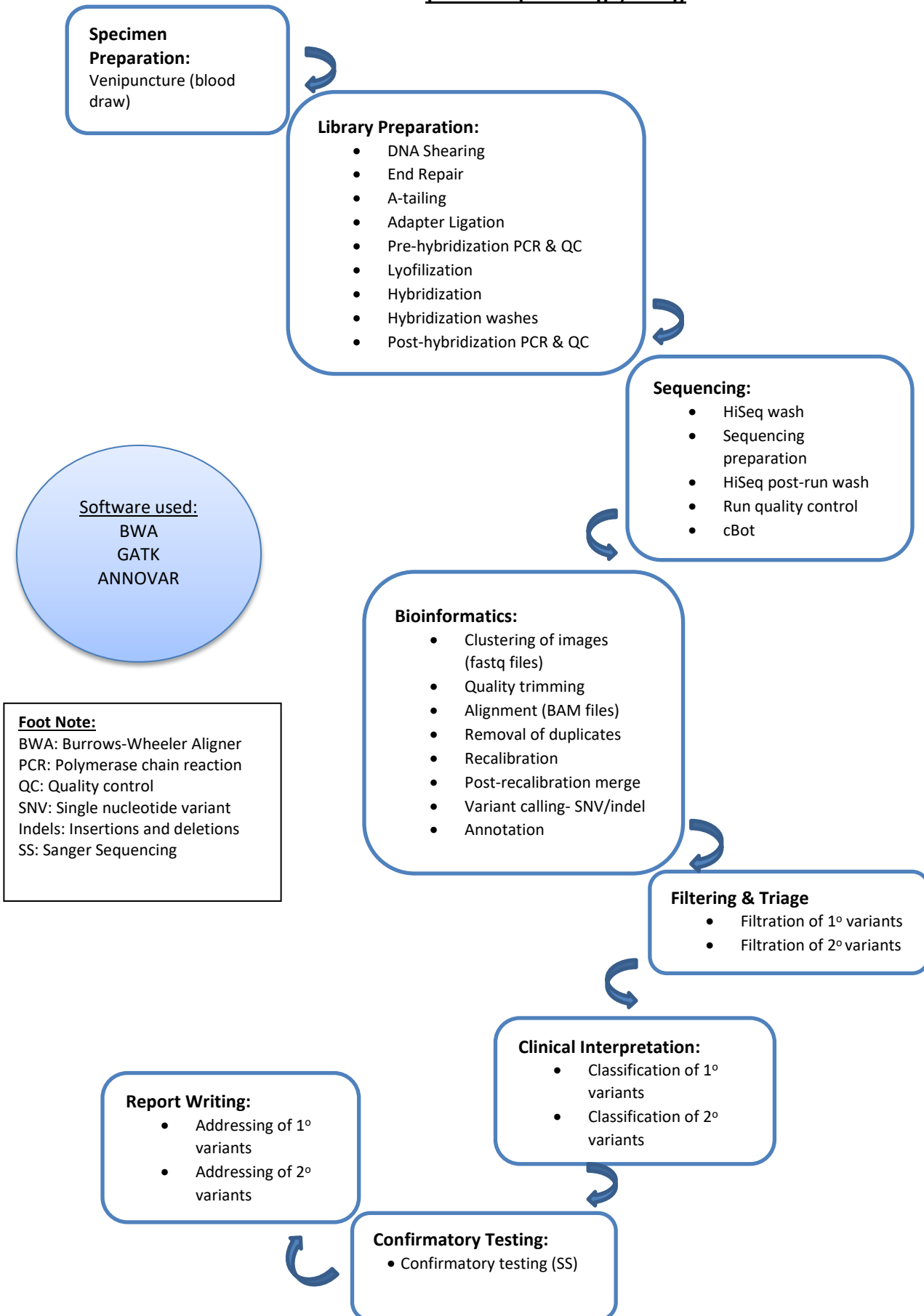
Whole Genome Sequencing:

- Elimination of platform HiSeq® 2500
- Inclusion of trio in addition to probands on the same platform (HiSeq X™)
  - Genome output per month 72 (64-96)
  - Proportion for follow-up testing (Sanger sequencing) is 10%
  - Small and large equipment volume: ½ of proband model
- Genome output per month 72 (64-96) vs. 150 (10% variability assigned)
- Bioinformatics
  - Pipeline: GATK vs. HAS
  - Additional 4 steps (recalibration; post-recalibration merge; CNV detection; SV detection) for computation use
  - Price per node: \$26,804 for all steps in 2018. In 2016, annotation was done on the old node (\$9560). Otherwise, same as 2018.

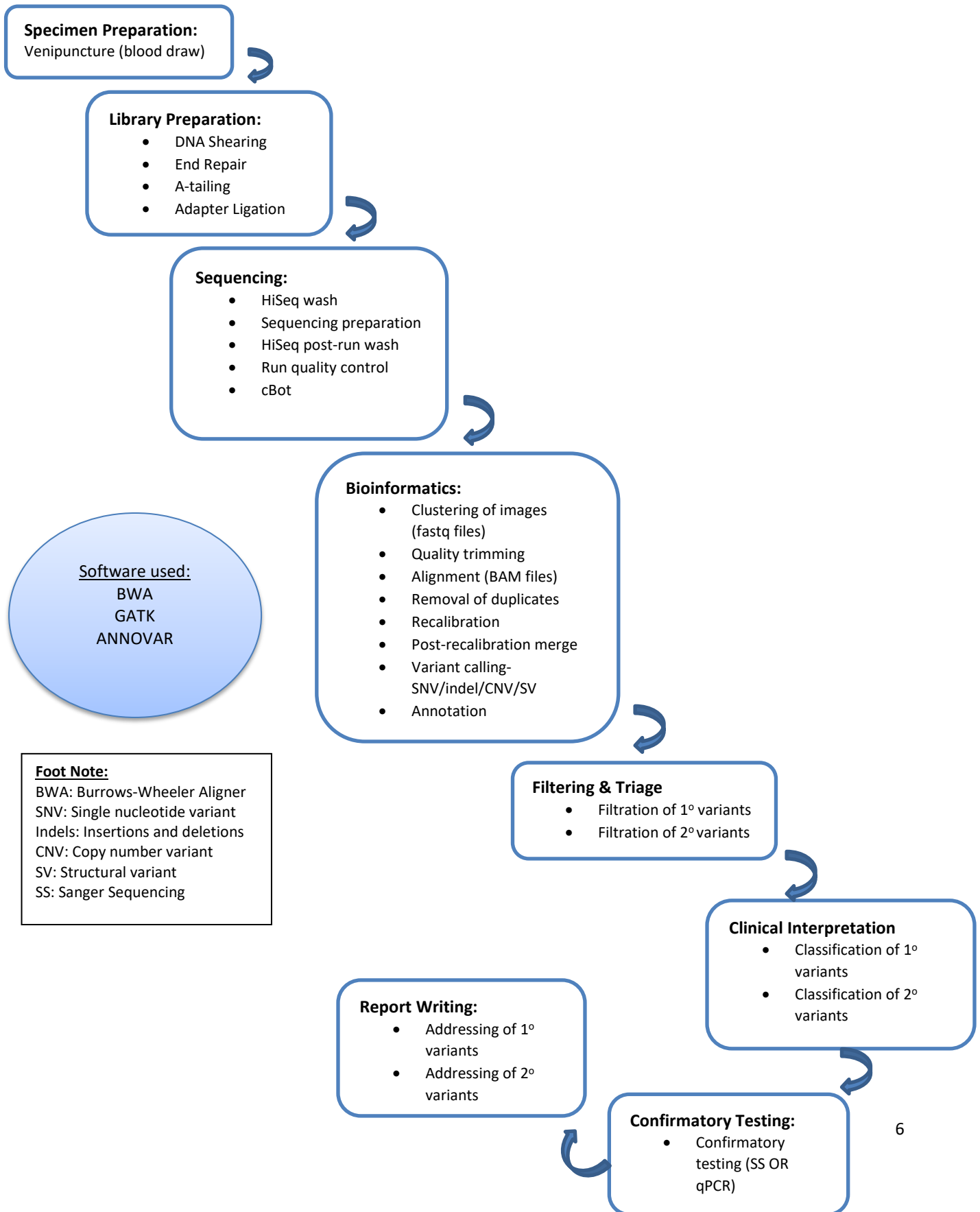
**Appendix 2: Chromosomal Microarray (CMA): Process Flow for Platform GeneChip® 3000Dx  
(Affymetrix (Santa Clara, USA))**



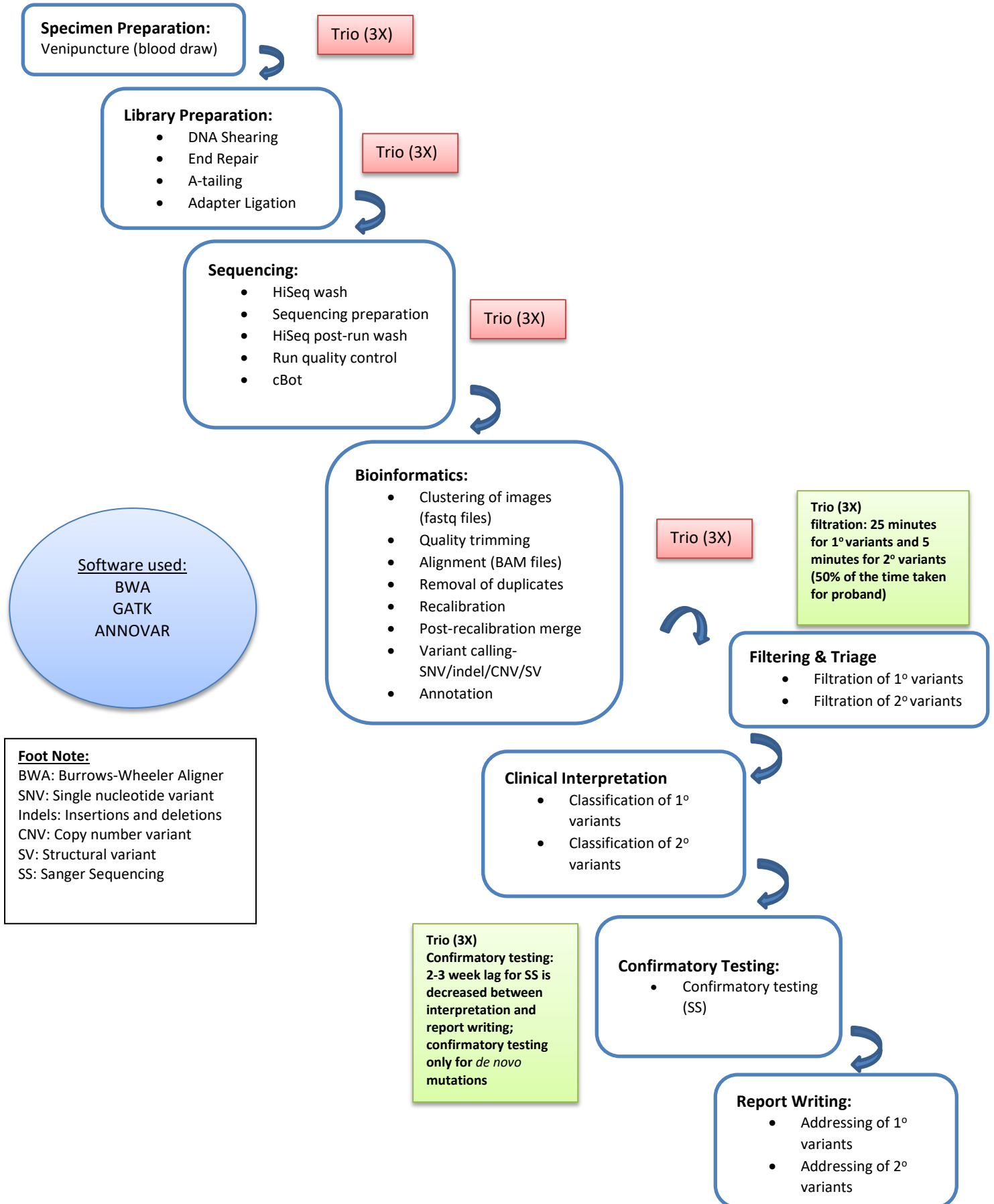
**Appendix 3: Whole Exome Sequencing (WES): Process Flow for Platform HiSeq® 2500  
(Illumina (San Diego, USA))**



**Appendix 4: Whole Genome Sequencing (WGS) (proband): Process Flow for Platform HiSeq X™ (Illumina (San Diego, USA))**



**Appendix 5: Whole Genome Sequencing (WGS) (trio): Process Flow for Platform HiSeq X™  
(Illumina (San Diego, USA))**



**Appendix 6. Resource use and unit prices for CMA inputs**

Cost Items	Quantity of Use per Sample			Price (CAD/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Labour</b>						
<b>Specimen Preparation (Units: minutes)</b>						
10120 Pediatric venipuncture	7.6	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11500 Service recipient primary registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
10360 Printing and sorting of specimen labels (per label)	0.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
88550 Creation of family/service recipient folder (add sample to existing family folder, assign a new number and retrieve or make a new folder) (once per folder)	5.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11500 Service recipient limited registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>DNA Extraction (Units: minutes)</b>						
85340 Extraction using an automated kit (once per specimen)	2.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
85360 Manual nucleic acid quantitation (once per specimen)	5.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
84510 Freezing of cells/tissue without cryopreservation	9.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018



Cost Items	Quantity of Use per Sample			Price (CAD/unit)		
	Estimate	Range	Source	Estimate	Range	Source
85370 Nucleic acid quantitation using spectrophotometer with sample retention tech (once per specimen)	1.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Microarray sample processing (Units: minutes)</b>						
85500 Assay preparation - manual worksheet prep (3 units for each assay and 1 per specimen)	2.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
83440 Fluorochrome labelling without dye swap	4.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
85560 Dilution of specimens (at the assay stage only, once per specimen)	2.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
DNA Fragmentation, by Restriction Enzyme Digestion	2.3	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
Ligation	1.5	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
PCR amplification	2.3	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
PCR purification by magnetic beads (once per sample)	12.4	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
DNA Fragmentation-by Restriction Enzyme Digestion	2.3	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
Fluorochrome labelling without dye swap.	1.1	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
Microarray Slide Hybridization	4.1	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
Microarray Slide Washing and Drying - Automated	8.0	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
Microarray slide scanning - Affymetrix scanner (once per slide)	10.0	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Analysis (Units: minutes)</b>						
Data preparation (includes transfer of data images)	8.0	Not assigned	Cytogenetics lab specialist	Confidential	-20% to +20%	SickKids wage information, 2018

Cost Items	Quantity of Use per Sample			Price (CAD/unit)		
	Estimate	Range	Source	Estimate	Range	Source
83550 Data analysis (includes review and analysis of each chromosome, prep prelim report, once per service recipient)	12.0	Not assigned	Lab technician	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Clinical interpretation and report writing (Units: minutes)</b>						
87760 Collation and write up on molecular genetic analysis - simple (60% of cases)	2.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
87760 Collation and write up on molecular genetic analysis - intermediate (20% of cases)	10.0	Not assigned	MIS Standards 2016	Confidential	-23% to +28%	Lab director, 2014; 1.5% annual increase to 2017/18
87760 Collation and write up on molecular genetic analysis - complex (20% of cases)	50.0	Not assigned	MIS Standards 2016	Confidential	-23% to +28%	Lab director, 2014; 1.5% annual increase to 2017/18
87770 Technical checking/reporting of molecular genetic interpretation (30% of cases)	5.0	Not assigned	Cytogenetics lab director	Confidential	-31% to +15%	Informatics facility manager, 2014; 1.5% annual increase to 2017/18
<b>Clinical interpretation (Units: minutes)</b>						
87780 Clinical interpretation and professional signoff (80% of cases, 10 minutes per case)	8.0	Not assigned	Cytogenetics lab director	Confidential	-20% to +20%	Public sector disclosure 2012; 1.5% annual increase to 2017/18
87780 Clinical interpretation and professional signoff (15% of cases, 20 minutes per case)	3.0	Not assigned	Cytogenetics lab director	Confidential	-20% to +20%	Public sector disclosure 2012; 1.5% annual increase to 2017/18
87780 Clinical interpretation and professional signoff (5% of cases, 60 minutes per case)	3.0	Not assigned	Cytogenetics lab director	Confidential	-20% to +20%	Public sector disclosure 2012; 1.5% annual increase to 2017/18
<b>Large Equipment</b>						
Affymetrix 1 GeneChip 3000Dx, 2 Fluidics stations, 1 hybridization oven	2/all tests	Not applicable	Lab manager	398,152	358,336.80-437,967.20	Affymetrix sales representative, 2018
1-year service contract	1/all tests	Not applicable	Affymetrix representative	89,277.20		Affymetrix sales representative, 2018

Cost Items	Quantity of Use per Sample			Price (CAD/unit)		
	Estimate	Range	Source	Estimate	Range	Source
					80,349.48 – 98,204.92	
<b>Supplies</b>						
Shipping & handling	1	Not assigned	FedEx	37.61	33.80 – 41.40	FedEx, 2018
Microarray slide & reagents per patient	1	Not assigned	Cytogeneticist	Confidential	-10% to +10%	Affymetrix sales representative, 2018
<b>Follow-up (proportion of cases)</b>						
Note: Price for FISH and qPCR tests includes three tests, proband and two parents						
FISH follow-up (proband and two parents)	0.1	Not assigned	Cytogeneticist	680.00	578.04 – 720.50	Cytogenetics lab director, 2018
qPCR follow-up (proband and two parents)	0.05	Not assigned	Cytogeneticist	223.90	201.51 – 246.29	Expert opinion, 2018

Abbreviations: CMA, Chromosomal Microarray Analysis; PCR, Polymerase chain reaction; MIS, Management Information Systems; qPCR, Real-time polymerase chain reaction; FISH, Fluorescence in situ hybridization.

**Appendix 7. Resource use and unit prices for WES inputs, Illumina HiSeq® 2500**

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Labour</b>						
<b>Specimen Preparation (Units: minutes)</b>						
10120 Pediatric venipuncture	7.6	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11500 Service recipient primary registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
10360 Printing and sorting of specimen labels (per label)	0.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
88550 Creation of family/service recipient folder (add sample to existing family folder, assign a new number and retrieve or make a new folder) (once per folder)	5.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11500 Service recipient limited registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Library preparation (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per batch. Resource use estimate was based on 8 samples per batch.						
DNA quantification (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-prep reagents (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Shearing (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Purification (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
End repair (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
A-tailing (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Adapter ligation (45 min)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-hybridization PCR (45 min)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Pre-hybridization QC (60 min)	7.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Lyophilization (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Hybridization (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Hybridization washes (150 min)	18.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Post-Hybridization PCR (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Post Hybridization QC (120 min)	15.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Sequencing (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per lane. Resource use estimate was based on 8 samples per lane.						
HiSeq wash (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Sequencing prep (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
HiSeq post-run wash (45 min)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Run quality control (15 min)	1.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
cBot (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Bioinformatics (Units: minutes)</b>						
Note: Resource use estimate was based on average output, 83 exomes per month. The lower bound was based on 95 exomes and the upper bound was based on 70 exomes.						
Variant calling (1 FTE hour for 70-95 exomes a month)	101.2	88.4-120.0	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (0.25 FTE hour for 70-95 exomes a month)	25.3	22.1-30.0	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Bioinformatics Maintenance (Units: minutes)</b>						
Note: One full time equivalent (FTE) hour to support one node per year was assumed. Resource use in minutes was calculated by multiplying the time to complete a job by the time needed to support the required number of nodes per job. For example, if a job required 0.5 hours and 3 nodes, then the resource use for the job is calculated as follows: 60 FTE minutes in an hour per year/(365*24 hours in a year)*3 hours to support 3 nodes*0.5 hours (i.e. number of minutes per year to support a 30 minute job on 3 nodes). The lower bound of resource use was based on 75% of the computation time and the upper bound was based on 125% of computation time.						
Alignment 0.5 hour (range: 0.4-0.6) 1 node	0.00342	0.00274-0.00411	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Mark Duplicates - PICARD 1 hour (range: 0.75-1.25) 1/20 nodes	0.00034	0.00026-0.00043	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Recalibration- GATK (step 1) 1.5 hours (range: 4-6) 1/20 nodes	0.00051	0.00043-0.00060	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Recalibration – GATK (step 2) 0.5 hour (range: 0.25-0.75) 2 nodes	0.00685	0.00342-0.0103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Post-recalibration merge – GATK 0.5 hour (range: 0.25-0.75) 1/20 nodes	0.000171	0.0000856-0.000257	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Indel Realignment (GATK) 0.5 hour (range: 0.25-0.75) 2 nodes	0.01	0.00342-0.0103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SNV/indel variant calling - (GATK haplotype caller) 0.33 hour (range: 0.3-0.37) 2 nodes	0.00456	0.00411-0.00507	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (ANNOVAR) 0.5 hour (range: 0.25-0.75) 0.2 nodes	0.00069	0.000342-0.00103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Filtering &amp; Triage (Units: minutes)</b>						
Filtration of primary variants	55	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Filtration of secondary variants	5	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Clinical Interpretation (Units: minutes)</b>						
Clinical classification of primary variants 15 minutes if no variants are found, otherwise 30 minutes per variant. On average, 2 variants are found (range: 0-4)	60	15-120	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Clinical classification of secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Report Writing (Units: minutes)</b>						

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Addressing primary variants 15 minutes base plus 15 minutes per variant. On average, 2 variants are found (range: 0-4)	45	15-75	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Addressing secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Large Equipment</b>						
Illumina HiSeq® 2500	1/all tests	Not applicable	TCAG lab manager	750000	700000-800000	TCAG lab manager, 2015
1-year service contract	1/all tests	Not applicable	TCAG lab manager	75000	50000-82500	TCAG lab manager, 2015
Agilent BioAnalyzer/Tape station	1/all tests	Not applicable	Agilent representative	38500	34000-43000	Agilent representative/TCAG lab manager, 2015
<b>Small Equipment</b>						
Tube microcentrifuge	1/all tests	Not applicable	TCAG lab manager	2250	2000-2500	TCAG lab manager, 2014
Plate microcentrifuge	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Thermomixer	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Vortex	1/all tests	Not applicable	TCAG lab manager	450	400-500	TCAG lab manager, 2014
Pipette sets	2/all tests	Not applicable	TCAG lab manager	1600	1400-2000	TCAG lab manager, 2014
Magnet particle concentrator for tubes	1/all tests	Not applicable	TCAG lab manager	700	630-770	TCAG lab manager, 2014
Thermocyclers	2/all tests	Not applicable	TCAG lab manager	3000	2700-3300	TCAG lab manager, 2014
<b>Supplies</b>						
Shipping & handling	1	Not assigned	TCAG lab Manager	37.61	33.80-41.40	FedEx, 2018
SureSelect Baits (96 reactions)	1	Not assigned	TCAG lab manager	195	175.50-214.50	TCAG lab manager, 2018
SureSelect Library prep (96 reactions)	1	Not assigned	TCAG lab manager	22.50	20.30-24.80	TCAG lab manager, 2018
Other library prep consumables	1	Not assigned	TCAG lab manager	70.0	63.00-77.00	TCAG lab manager, 2018
Sequencing reagents (8 samples per lane)	1	Not assigned	TCAG lab manager	337.50	303.80-371.30	TCAG lab manager 2018
<b>Follow-up (proportion of cases)</b>						

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Sanger sequencing (two tests per person, proband and two parents)	0.5	Not assigned	DPLM Associate director, Genomic Analysis	53.33	48.00-58.70	DPLM Associate director, Genomic Analysis, 2018
<b>Bioinformatics</b>						
<b>Bioinformatics File Storage (Units: GB per year)</b>						
Notes: 1. Resource use volume was calculated by multiplying the file size by the storage time (in years). 2. Price was given in dollars (\$) per GB per year.						
trimmed fastq file size: 9 GB; storage time: 9 months (range: 6-12)	6.75	4.5-9.0	TCAG Bioinformatics manager	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
final rem-dup, recalibrated, locally re-aligned BAM file file size: 9 GB; storage time: 9 months (range: 6-12)	4.5	3.0-6.0	TCAG Bioinformatics manager	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
<b>Bioinformatics Computation Use (Units: CPU time per hour)</b>						
Notes: 1. Resource use volume was calculated by multiplying the number of jobs by the number of cores per job and time (hours) required to complete a job. 25% (range 0 to 50%) was added to account for additional processing time to avoid operating at full capacity. 2. Scalar Decisions, Inc. quote of \$26,804 per node (20 cores) or \$1340.20 per core (including warranty) was used. A straight line depreciation method over 5 years was applied and the price per CPU per year was calculated to be \$5360.80. This price was converted to price per CPU per hour by dividing \$5360.80 by (365*24).						
Alignment 1 job, 54 GB RAM per job, 19 core per job, 0.5 hour to complete, >>1 node required	11.875	9.5-14.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Mark Duplicates – PICARD 1 job, 5 GB RAM per job, 2 cores per job, 1 hour to complete, >> 1/20 node required	2.5	2-3	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Recalibration- GATK (step 1) 1 job, 30 GB RAM per job, 1 core per job, 1.5 hours to complete, >>1/20 node required	1.875	1.5-2.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016



Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Recalibration – GATK (step 2) 23 jobs, 30 GB RAM per job, 1 core per job, 0.5 hour to complete, >>2 nodes required	14.375	11.5-17.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Post-recalibration merge - (GATK) 1 job, 10 GB RAM per job, 2 core per job, 0.5 hour to complete, >>1/20 node required	1.25	1-1.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Indel Realignment (GATK) 23 jobs, 10 GB RAM per job, 2 core per job, 0.5 hour to complete, >>2 nodes required	28.75	23-34.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
SNV/indel variant calling - GATK haplotype caller 23 jobs, 55 GB RAM per job, 1 core per job, 0.33 hour to complete, >>2 nodes required	9.58	7.67-11.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Annotation (ANNOVAR) 1 job, 32 GB RAM per job, 8 cores per job, 0.5 hour to complete, >>1/5 node required	5	4-6	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016

Abbreviations: WES, Whole Exome Sequencing; TCAG, The Centre for Applied Genomics; DPLM, The Department of Paediatric Laboratory Medicine; FTE, Full-time equivalent; MIS, Management Information Systems; GATK, Genome Analysis Toolkit; SNV, Single nucleotide variant.

**Appendix 8. Resource use and unit prices for WES inputs, Illumina NextSeq® 550**

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Labour</b>						
<b>Specimen Preparation (Units: minutes)</b>						
10120 Pediatric venipuncture	7.6	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11500 Service recipient primary registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
10360 Printing and sorting of specimen labels (per label)	0.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
88550 Creation of family/service recipient folder (add sample to existing family folder, assign a new number and retrieve or make a new folder) (once per folder)	5.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11500 Service recipient limited registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Library preparation (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per batch. Resource use estimate was based on 8 samples per batch.						
DNA quantification (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-prep reagents (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Shearing (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Purification (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
End repair (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
A-tailing (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Adapter ligation (45 min)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-hybridization PCR (45 min)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Pre-hybridization QC (60 min)	7.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Lyophilization (20 min)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Hybridization (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Hybridization washes (150 min)	18.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Post-Hybridization PCR (40 min)	5.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Post Hybridization QC (120 min)	15.0	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Sequencing (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per lane. Resource use estimate was based on 8 samples per lane.						
Sequencing prep (30 min)	3.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Run quality control (15 min)	1.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Bioinformatics (Units: minutes)</b>						
Note: Resource use estimate was based on the average output, 80 exomes per month. The lower bound was based on 96 exomes and the upper bound was based on 64 exomes.						
Variant calling (1 FTE hour for 64-96 exomes a month)	105	87.5-131.25	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (0.25 FTE hour for 64-96 exomes a month)	26.25	21.875-32.813	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Bioinformatics Maintenance (Units: minutes)</b>						
Note: One full time equivalent (FTE) hour to support one node per year was assumed. Resource use in minutes was calculated by multiplying the time to complete a job by the time needed to support the required number of nodes per job. For example, if a job required 0.5 hours and 3 nodes, then the resource use for the job is calculated as follows: 60 FTE minutes in an hour per year / (365*24 hours in a year) *3 hours to support 3 nodes*0.5 hours (i.e. number of minutes per year to support a 30 minute job on 3 nodes). The lower bound of resource use was based on 75% of the computation time and the upper bound was based on 125% of computation time.						
Alignment 0.5 hour (range: 0.4-0.6) 1 node	0.00342	0.00274-0.00411	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Mark Duplicates - PICARD 1 hour (range: 0.75-1.25) 1/20 nodes	0.00034	0.00026-0.00043	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Recalibration- GATK (step 1) 1.5 hours (range: 4-6) 1/20 nodes	0.00051	0.00043-0.00060	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Recalibration – GATK (step 2) 0.5 hour (range: 0.25-0.75) 2 nodes	0.00685	0.00342-0.0103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Post-recalibration merge – GATK 0.5 hour (range: 0.25-0.75) 1/20 nodes	0.000171	0.0000856-0.000257	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Indel Realignment (GATK) 0.5 hour (range: 0.25-0.75) 2 nodes	0.01	0.00342-0.0103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SNV/indel variant calling - (GATK haplotype caller) 0.33 hour (range: 0.3-0.37) 2 nodes	0.00456	0.00411-0.00507	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (ANNOVAR) 0.5 hour (range: 0.25-0.75) 0.2 nodes	0.00069	0.000342-0.00103	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Filtering &amp; Triage (Units: minutes)</b>						
Filtration of primary variants	55	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Filtration of secondary variants	5	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Clinical Interpretation (Units: minutes)</b>						
Clinical classification of primary variants 15 minutes if no variants are found, otherwise 30 minutes per variant. On average, 2 variants are found (range: 0-4)	60	15-120	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Clinical classification of secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Report Writing (Units: minutes)</b>						
Addressing primary variants	45	15-75	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
15 minutes base plus 15 minutes per variant. On average, 2 variants are found (range: 0-4)						
Addressing secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Large Equipment</b>						
Illumina NextSeq® 550	1/all tests	Not applicable	TCAG lab manager	201250	181125-221375	TCAG lab manager, 2018
1-year service contract	1/all tests	Not applicable	TCAG lab manager	17940	16146-19734	TCAG lab manager, 2018
Agilent BioAnalyzer/Tape station	1/all tests	Not applicable	Agilent representative	38500	34000-43000	Agilent representative/TCAG lab manager, 2015
<b>Small Equipment</b>						
Tube microcentrifuge	1/all tests	Not applicable	TCAG lab manager	2250	2000-2500	TCAG lab manager, 2014
Plate microcentrifuge	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Thermomixer	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Vortex	1/all tests	Not applicable	TCAG lab manager	450	400-500	TCAG lab manager, 2014
Pipette sets	2/all tests	Not applicable	TCAG lab manager	1600	1400-2000	TCAG lab manager, 2014
Magnet particle concentrator for tubes	1/all tests	Not applicable	TCAG lab manager	700	630-770	TCAG lab manager, 2014
Thermocyclers	2/all tests	Not applicable	TCAG lab manager	3000	2700-3300	TCAG lab manager, 2014
<b>Supplies</b>						
Shipping & Handling	1	Not assigned	TCAG lab manager	37.61	33.80-41.40	FedEx, 2018
SureSelect Baits (96 reactions)	1	Not assigned	TCAG lab manager	195	175.50-214.50	TCAG lab manager, 2018
SureSelect Library prep (96 reactions)	1	Not assigned	TCAG lab manager	22.50	20.30-24.80	TCAG lab manager, 2018
Other library prep consumables	1	Not assigned	TCAG lab manager	70.0	63.00-77.00	TCAG lab manager, 2018
Sequencing reagents (8 samples per lane)	1	Not assigned	TCAG lab manager	707.83	637.00-778.60	TCAG lab manager 2018
<b>Follow-up (proportion of cases)</b>						
Sanger sequencing (two tests per person, proband and two parents)	0.5	Not assigned	DPLM Associate director, Genomic Analysis	53.33	48.00-58.70	DPLM Associate director, Genomic Analysis, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Bioinformatics</b>						
<b>Bioinformatics File Storage (Units: GB per year)</b>						
Notes: 1. Resource use volume was calculated by multiplying the file size by the storage time (in years). 2. Price was given in dollars (\$) per GB per year.						
trimmed fastq file size: 9 GB; storage time: 9 months (range: 6-12)	6.75	4.5-9.0	TCAG Bioinformatics manager	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
final rem-dup, recalibrated, locally re-aligned BAM file file size: 9 GB; storage time: 9 months (range: 6-12)	4.5	3.0-6.0	TCAG Bioinformatics manager	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
<b>Bioinformatics Computation Use (Units: CPU time per hour)</b>						
Notes: 1. Resource use volume was calculated by multiplying the number of jobs by the number of cores per job and time (hours) required to complete a job. 25% (range 0 to 50%) was added to account for additional processing time to avoid operating at full capacity. 2. Scalar Decisions, Inc. quote of \$26,804 per node (20 cores) or \$1340.20 per core (including warranty) was used. A straight line depreciation method over 5 years was applied and the price per CPU per year was calculated to be \$5360.80. This price was converted to price per CPU per hour by dividing \$5360.80 by (365*24).						
Alignment 1 job, 54 GB RAM per job, 19 core per job, 0.5 hour to complete, >>1 nodes required	11.875	9.5-14.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Mark Duplicates – PICARD 1 job, 5 GB RAM per job, 2 cores per job, 1 hour to complete, >> 1/20 node required	2.5	2-3	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Recalibration- GATK (step 1) 1 job, 30 GB RAM per job, 1 core per job, 1.5 hours to complete, >>1/20 node required	1.875	1.5-2.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Recalibration – GATK (step 2)	14.375	11.5-17.25	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
23 jobs, 30 GB RAM per job, 1 core per job, 0.5 hour to complete, >>2 node required						
Post-recalibration merge - (GATK) 1 job, 10 GB RAM per job, 2 core per job, 0.5 hour to complete, >>1/20 node required	1.25	1-1.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Indel Realignment (GATK) 23 jobs, 10 GB RAM per job, 2 core per job, 0.5 hour to complete, >>2 node required	28.75	23-34.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
SNV/indel variant calling - GATK haplotype caller 23 jobs, 55 GB RAM per job, 1 core per job, 0.33 hour to complete, >>2 node required	9.58	7.67-11.5	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016
Annotation (ANNOVAR) 1 job, 32 GB RAM per job, 8 cores per job, 0.5 hour to complete, >>1/5 node required	5	4-6	TCAG Bioinformatics manager	0.612	0.551-0.673	Scalar quote, 2016

Abbreviations: WES, Whole Exome Sequencing; TCAG, The Centre for Applied Genomics; DPLM, The Department of Paediatric Laboratory Medicine; FTE, Full-time equivalent; MIS, Management Information Systems; GATK, Genome Analysis Toolkit; SNV, Single nucleotide variant.

**Appendix 9. Resource use and unit prices for WGS-proband inputs, Illumina HiSeq X™**

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Labour</b>						
<b>Specimen Preparation (Units: minutes)</b>						
10120 Pediatric venipuncture	7.6	Not assigned	MIS Standards 2016	Confidential	-22%to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11500 Service recipient primary registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
10360 Printing and sorting of specimen labels (per label)	0.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
88550 Creation of family/service recipient folder (add sample to existing family folder, assign a new number and retrieve or make a new folder) (once per folder)	5.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11090 Packaging with testing documentation	1.0	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11500 Service recipient limited registration	1.8	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Library preparation (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per batch. The number of samples per batch was assumed to be 48.						
DNA quantification (20 min total)	0.4	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-prep reagents (20 min total)	0.4	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Shearing (20 min total)	0.4	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Purification (40 min total)	0.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
End repair (40 min total)	0.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
A-tailing (40 min total)	0.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Adapter ligation (45 min total)	0.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018



Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Sequencing (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per lane. The number of samples per lane was assumed to be 16.						
HiSeq wash (30 min total)	1.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Sequencing prep (30 min total)	1.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
HiSeq post-run wash (45 min total)	2.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Run quality control (15 min total)	0.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
cBot (30 min total)	1.9	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Bioinformatics (Units: minutes)*</b>						
Note: resource use estimate is based on average output, 72 genomes per month. The lower bound was based on 96 genomes and the upper bound was based on 64 genomes.						
Variant calling (1 FTE hour for 64-96 genomes a month)	116.67	87.5-131.25	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (0.25 FTE hour for 64-96 genomes a month)	29.17	21.875-32.813	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Bioinformatics Maintenance (Units: minutes)*</b>						
Note: One full time equivalent (FTE) hour to support one node per year was assumed. Resource use in minutes was calculated by multiplying the time to complete a job by the time needed to support the required number of nodes per job. For example, if a job required 3.2 hours and 1 node, then the resource use for the job is calculated as follows: 60 FTE minutes in an hour per year/ (365*24 hours in a year) *1 hour to support 1 node*3.2 hours (i.e. number of minutes per year to support a 192 minutes job on 1 node). The lower bound of resource use was based on 75% of the computation time and the upper bound was based on 125% of computation time.						
Alignment 12 hours (range: 9.0-15.0) 1 node	0.0822	0.06-0.10	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Mark Duplicates -PICARD 5 hours (range: 3.75-6.25) 1/20 nodes	0.0017	0.0013-0.0021	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Recalibration (GATK) 2 hours (range: 1.5-2.5) 2 nodes	0.0274	0.0205-0.0342	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Post-recalibration merge - Genome Analysis Toolkit (GATK) 1 hour (range: 0.75-1.25) 1/20 nodes	0.0003	0.0003-0.0004	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Indel Realignment (GATK) 1.5 hours (range: 1.13-1.875) 2 nodes	0.0205	0.0154-0.0257	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SNV/indel variant calling - (GATK haplotype caller) 3 hours (range: 2.25-3.75) 2 nodes	0.0411	0.0308-0.0514	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (ANNOVAR) 1.5 hours (range: 1.13-1.875) 1/5 nodes	0.0021	0.0015-0.0026	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
CNV Detection (Custom) 15 hours (range: 11.25-18.75) 1/20 nodes	0.0051	0.0039-0.0064	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
CNV Annotation (Custom) 1/12 hours (range: 0.0625-0.104) 1/20 nodes	0.0000285	0.000021-0.000036	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SV Detection (MANTA) 1 hour (range: 0.75-1.25) 1 node	0.0068	0.0051-0.0086	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SV Annotation (Custom) 1/12 hours (range: 0.0625-0.104) 1/20 nodes	0.0000285	0.000021-0.000036	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Filtering &amp; Triage (Units: minutes)</b>						
Filtration of primary variants	55	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Filtration of secondary variants	5	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Clinical Interpretation (Units: minutes)</b>						
Clinical classification of primary variants	75	15-135	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
15 minutes base plus 30 minutes per variant. On average, 2 variants are found (range: 0-4)						
Clinical classification of secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Report Writing (Units: minutes)</b>						
Addressing primary variants 15 minutes base plus 15 minutes per variant. On average, 2 variants are found (range: 0-4)	45	15-75	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Addressing secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Large Equipment</b>						
Illumina HiSeq X™	1/all tests	Not applicable	TCAG Lab manager	1150000	1035000-1265000	TCAG Lab manager, 2015
1-year service contract	1/all tests	Not applicable	TCAG Lab manager	119025	107123-130928	TCAG Lab manager, 2015
Agilent BioAnalyzer/Tape station	1/all tests	Not applicable	Agilent representative	38500	34000-43000	Agilent representative/TCAG Lab manager, 2015
<b>Small Equipment</b>						
Tube microcentrifuge	1/all tests	Not applicable	TCAG lab manager	2250	2000-2500	TCAG lab manager, 2014
Plate microcentrifuge	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Thermomixer	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Vortex	1/all tests	Not applicable	TCAG lab manager	450	400-500	TCAG lab manager, 2014
Pipette sets	2/all tests	Not applicable	TCAG lab manager	1600	1400-2000	TCAG lab manager, 2014
Magnet particle concentrator for tubes	1/all tests	Not applicable	TCAG lab manager	700	630-770	TCAG lab manager, 2014
Thermocyclers	2/all tests	Not applicable	TCAG lab manager	3000	2700-3300	TCAG lab manager, 2014
<b>Supplies</b>						
Shipping & handling	1	Not assigned	TCAG lab manager	37.61	33.80-41.40	FedEx, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Illumina Nano DNA library prep	1	Not assigned	TCAG lab manager	30.0	27.0-33.0	TCAG lab manager, 2015
Other library prep consumables per sample	1	Not assigned	TCAG lab manager	50.0	45.00-55.00	TCAG lab manager, 2015
Sequencing reagents (1 sample per lane)	1	Not assigned	TCAG lab manager	1290.0	1161.0-1419.0	TCAG lab manager, 2015
<b>Follow-up (proportion of cases)</b>						
Note: Price for Sanger sequencing and qPCR test included three tests, proband and two parents, with two sequences per person						
Sanger sequencing (two tests per person, proband and two parents)	0.5	Not assigned	DPLM Associate director, Genomic Analysis	53.33	48.00-58.67	DPLM Associate director, Genomic Analysis, 2018
qPCR follow-up (proband and two parents)	0.1	Not assigned	Team leader, Molecular Genetics	223.90	201.51-246.29	Expert opinion, 2018
<b>Bioinformatics*</b>						
<b>Bioinformatics File Storage (Units: GB/year)</b>						
Notes: 1. Resource use volume was calculated by multiplying the file size by the storage time (in years). 2. Price was given in dollars (\$) per GB per year.						
trimmed fastq file size: 120 GB; average storage time: 9 months (range: 6-12)	90	60-120	TCAG Bioinformatics analyst	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
final rem-dup, recalibrated, locally re-aligned BAM file file size: 80 GB; average storage time: 9 months (range: 6-12)	60	40-80	TCAG Bioinformatics analyst	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
<b>Bioinformatics Computation Use (Units: CPU time per hour)</b>						
Notes: 1. Resource use volume was calculated by multiplying the number of jobs by the number of cores per job and time (hours) required to complete a job. 25% (range 0 to 50%) was added to account for additional processing time to avoid operating at full capacity. 2. The cost of each compute node to TCAG was \$26,804, including warranty. A straight line depreciation method over 5 years was applied and the price per CPU per year was calculated to be \$5,360.80. This price was converted to price per CPU per hour by dividing \$5360.80 by (365*24).						
Alignment (BWA) 1 job, 54 GB RAM per job, 19 core per job, 12 hours to complete, 1 node required	285	228-342	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Mark Duplicates -PICARD	12.5	10-15	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
1 job, 5 GB RAM per job, 2 core per job, 5 hours to complete, 1/20 node required						
Recalibration (GATK) 23 jobs, 30 GB RAM per job, 1 core per job, 2 hours to complete, 2 nodes required	57.5	46-69	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Post-recalibration merge - Genome Analysis Toolkit (GATK) 1 job, 10 GB RAM per job, 2 core per job, 1 hour to complete, 1/20 node required	2.5	2.0-3.0	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Indel Realignment (GATK) 23 jobs, 10 GB RAM per job, 2 core per job, 1.5 hours to complete, 2 nodes required	86.25	69-103.5	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
SNV/indel variant calling - (GATK haplotype caller) 23 jobs, 55 GB RAM per job, 1 core per job, 3 hours to complete, 2 nodes required	86.25	69-103.5	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Annotation (ANNOVAR) 1 job, 32 GB RAM per job, 8 core per job, 1.5 hours to complete, 1/5 node required	15	12-18	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
CNV Detection (Custom) 2 jobs, 32 GB RAM per job, 1 core per job, 15 hours to complete, 1/20 node required	37.5	30-45	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
CNV Annotation (Custom)	0.104	0.083-0.125	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
1 job, 16 GB RAM per job, 1 core per job, 1/12 hours to complete, 1/20 node required						
SV Detection (MANTA) 1 job, 40 GB RAM per job, 20 core per job, 1 hour to complete, 1 node required	25	20-30	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
SV Annotation (Custom) 1 job, 16GB RAM per job, 1 core per job, 1/12 hour to complete, 1/20 node required	0.104	0.083-0.125	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Abbreviations: WGS, Whole Genome Sequencing; TCAG, The Centre for Applied Genomics; DPLM, The Department of Paediatric Laboratory Medicine; FTE, Full-time equivalent; qPCR, Real-time polymerase chain reaction; MIS, Management Information Systems; GATK, Genome Analysis Toolkit; SNV, Single nucleotide variant.

**Appendix 10. Resource use and unit prices for WGS-trio inputs, Illumina HiSeq X™**

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Labour</b>						
<b>Specimen Preparation (Units: minutes)</b>						
10120 Pediatric venipuncture	22.8	Not assigned	MIS Standards 2016	Confidential	-22%to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11090 Packaging with testing documentation	3	Not assigned	MIS Standards 2016	Confidential	-22% to +28%	SickKids wage information, 2014; 1.5% annual increase to 2017/18
11500 Service recipient primary registration	5.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
10360 Printing and sorting of specimen labels (per label)	1.2	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
88550 Creation of family/service recipient folder (add sample to existing family folder, assign a new number and retrieve or make a new folder) (once per folder)	15	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11090 Packaging with testing documentation	3	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
11500 Service recipient limited registration	5.4	Not assigned	MIS Standards 2016	Confidential	-20% to +20%	SickKids wage information, 2018
<b>Library preparation (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per batch. The number of samples per batch was assumed to be 48.						
DNA quantification (20 min total)	1.3	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Pre-prep reagents (20 min total)	1.3	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Shearing (20 min total)	1.3	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Purification (40 min total)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
End repair (40 min total)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
A-tailing (40 min total)	2.5	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Adapter ligation (45 min total)	2.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
<b>Sequencing (Units: minutes)</b>						
Note: Total time per task was divided by the number of samples per lane. The number of samples per lane was assumed to be 16.						
HiSeq wash (30 min total)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Sequencing prep (30 min total)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
HiSeq post-run wash (45 min total)	8.4	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
Run quality control (15 min total)	2.8	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
cBot (30 min total)	5.6	Not assigned	TCAG lab manager	Confidential	-10% to +10%	TCAG lab manager, 2018
<b>Bioinformatics (Units: minutes)*</b>						
Note: resource use estimate is based on average output, 72 genomes per month. The lower bound was based on 96 genomes and the upper bound was based on 64 genomes.						
Variant calling (1 FTE hour for 64-96 genomes a month)	116.67	87.5-131.25	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (0.25 FTE hour for 64-96 genomes a month)	29.17	21.875-32.813	TCAG Bioinformatics manager	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Bioinformatics Maintenance (Units: minutes)*</b>						
Note: One full time equivalent (FTE) hour to support one node per year was assumed. Resource use in minutes was calculated by multiplying the time to complete a job by the time needed to support the required number of nodes per job. For example, if a job required 3.2 hours and 1 nodes, then the resource use for the job is calculated as follows: 60 FTE minutes in an hour per year/ (365*24 hours in a year)*1 hour to support 1 node*3.2 hours (i.e. number of minutes per year to support a 192 minute job on 1 node). The lower bound of resource use was based on 75% of the computation time and the upper bound was based on 125% of computation time.						
Alignment 12 hours (range: 9.0-15.0) 1 node	0.25	0.18-0.31	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Mark Duplicates –PICARD 5 hours (range: 3.75-6.25) 1/20 nodes	0.01	0.004-0.01	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Recalibration (GATK) 2 hours (range: 1.5-2.5) 2 nodes	0.08	0.06-0.10	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Post-recalibration merge - Genome Analysis Toolkit (GATK) 1 hour (range: 0.75-1.25) 1/20 nodes	0.0010	0.00077-0.00128	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018



Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Indel Realignment (GATK) 1.5 hours (range: 1.13-1.875) 2 nodes	0.06	0.05-0.08	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SNV/indel variant calling - (GATK haplotype caller) 3 hours (range: 2.25-3.75) 2 nodes	0.12	0.09-0.15	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
Annotation (ANNOVAR) 1.5 hours (range: 1.13-1.875) 1/5 nodes	0.01	0.00462-0.0077	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
CNV Detection (Custom) 15 hours (range: 11.25-18.75) 1/20 nodes	0.02	0.012-0.019	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
CNV Annotation (Custom) 1/12 hours (range: 0.0625-0.104) 1/20 nodes	0.0000856	0.0000642-0.000107	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SV Detection (MANTA) 1 hour (range: 0.75-1.25) 1 node	0.02	0.0154-0.0257	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
SV Annotation (Custom) 1/12 hours (range: 0.0625-0.104) 1/20 nodes	0.0000856	0.0000642-0.000107	TCAG Bioinformatics manager, 2018	Confidential	-20% to +20%	TCAG Bioinformatics manager, 2018
<b>Filtering &amp; Triage (Units: minutes)</b>						
Filtration of primary variants	25	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Filtration of secondary variants	5	Not assigned	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Clinical Interpretation (Units: minutes)</b>						
Clinical classification of primary variants 15 minutes base plus 30 minutes per variant. On average, 2 variants are found (range: 0-4)	75	15-135	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Clinical classification of secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Report Writing (Units: minutes)</b>						
Addressing primary variants 15 minutes base plus 15 minutes per variant. On average, 2 variants are found (range: 0-4)	45	15-75	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
Addressing secondary variants 30 minutes per case (range: 20-40), found in 4% of cases (range: 3-5%)	1.2	0.6-2.0	DPLM Associate director, Genomic Analysis	Confidential	-20% to +20%	Public Sector Salary Disclosure, 2017
<b>Large Equipment</b>						
Illumina HiSeq X™	1/all tests	Not applicable	TCAG Lab manager	1150000	1035000- 1265000	TCAG Lab manager, 2015
1-year service contract	1/all tests	Not applicable	TCAG Lab manager	119025	107123- 130928	TCAG Lab manager, 2015
Agilent BioAnalyzer/Tape station	1/all tests	Not applicable	Agilent representative	38500	34000-43000	Agilent representative/ TCAG Lab manager, 2015
<b>Small Equipment</b>						
Tube microcentrifuge	1/all tests	Not applicable	TCAG lab manager	2250	2000-2500	TCAG lab manager, 2014
Plate microcentrifuge	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Thermomixer	1/all tests	Not applicable	TCAG lab manager	5000	4500-5500	TCAG lab manager, 2014
Vortex	1/all tests	Not applicable	TCAG lab manager	450	400-500	TCAG lab manager, 2014
Pipette sets	2/all tests	Not applicable	TCAG lab manager	1600	1400-2000	TCAG lab manager, 2014
Magnet particle concentrator for tubes	1/all tests	Not applicable	TCAG lab manager	700	630-770	TCAG lab manager, 2014
Thermocyclers	2/all tests	Not applicable	TCAG lab manager	3000	2700-3300	TCAG lab manager, 2014
<b>Supplies</b>						
Shipping & Handling	3	Not assigned	TCAG lab manager	37.61	33.80-41.40	FedEx, 2018
Illumina Nano DNA library prep	3	Not assigned	TCAG lab manager	30.0	27.0-33.0	TCAG lab manager, 2015
Other library prep consumables per sample	3	Not assigned	TCAG lab manager	50.0	45.00-55.00	TCAG lab manager, 2015

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Sequencing reagents (1 sample per lane)	3	Not assigned	TCAG lab manager	1290.0	1161.0-1419.0	TCAG lab manager, 2015
<b>Follow-up (proportion of cases)</b>						
Note: Price for Sanger sequencing and qPCR test included three tests, proband and two parents, with two sequences per person						
Sanger sequencing (two tests per person, proband and two parents)	0.1	Not assigned	DPLM Associate director, Genomic Analysis	53.33	48.00-58.67	DPLM Associate director, Genomic Analysis, 2018
qPCR followup (proband and two parents)	0.3	Not assigned	Team Leader, Molecular Genetics	223.90	201.51-246.29	Expert opinion, 2018
<b>Bioinformatics*</b>						
<b>Bioinformatics File Storage (Units: GB/year)</b>						
Notes: 1. Resource use volume was calculated by multiplying the file size by the storage time (in years). 2. Price was given in dollars (\$) per GB per year.						
trimmed fastq file size: 120 GB; average storage time: 9 months (range: 6-12)	270	180-360	TCAG Bioinformatics analyst	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
final rem-dup, recalibrated, locally re-aligned BAM file file size: 80 GB; average storage time: 9 months (range: 6-12)	180	120-240	TCAG Bioinformatics analyst	0.4	0.36-0.44	TCAG Bioinformatics manager, 2014
<b>Bioinformatics Computation Use (Units: CPU time per hour)</b>						
Notes: 1. Resource use volume was calculated by multiplying the number of jobs by the number of cores per job and time (hours) required to complete a job. 25% (range 0 to 50%) was added to account for additional processing time to avoid operating at full capacity. 2. The cost of each compute node to TCAG was \$26,804, including warranty. A straight line depreciation method over 5 years was applied and the price per CPU per year was calculated to be \$5,360.80. This price was converted to price per CPU per hour by dividing \$5360.80 by (365*24).						
Alignment (BWA) 1 job, 54 GB RAM per job, 19 core per job, 12 hours to complete, 1 node required	855	684-1026	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Mark Duplicates –PICARD 1 job, 5 GB RAM per job, 2 core per job, 5 hours to complete, 1/20 node required	37.5	30-45	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
Recalibration (GATK) 23 jobs, 30 GB RAM per job, 1 core per job, 2 hours to complete, 2 nodes required	172.5	138-207	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Post-recalibration merge - Genome Analysis Toolkit (GATK) 1 job, 10 GB RAM per job, 2 core per job, 1hour to complete, 1/20 node required	7.5	6-9	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Indel Realignment (GATK) 23 jobs, 10 GB RAM per job, 2 core per job, 1.5 hours to complete, 2 nodes required	258.75	207-310.5	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
SNV/indel variant calling - (GATK haplotype caller) 23 jobs, 55 GB RAM per job, 1 core per job, 3 hours to complete, 2 nodes required	258.75	207-310.5	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
Annotation (ANNOVAR) 1 job, 32 GB RAM per job, 8 core per job, 1.5 hours to complete, 1/5 node required	45	36-54	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
CNV Detection (Custom) 2 jobs, 32 GB RAM per job, 1 core per job, 15 hours to complete, 1/20 node required	112.5	90-135	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
CNV Annotation (Custom) 1 job, 16 GB RAM per job, 1 core per job, 1/12 hour to complete, 1/20 node required	0.3125	0.25-0.375	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016
SV Detection (MANTA)	75	60-90	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Cost Items	Quantity of Use per Sample			Price (CAD \$/unit)		
	Estimate	Range	Source	Estimate	Range	Source
1 job, 40 GB RAM per job, 20 core per job, 1 hour to complete, 1 node required						
SV Annotation (Custom) 1 job, 16GB RAM per job, 1 core per job, 1/12 hour to complete, 1/20 node required	0.3125	0.25-0.375	TCAG Bioinformatics manager	0.612	0.551-0.673	TCAG Bioinformatics analyst, 2016

Abbreviations: WGS, Whole Genome Sequencing; TCAG, The Centre for Applied Genomics; DPLM, The Department of Paediatric Laboratory Medicine; FTE, Full-time equivalent; qPCR, Real-time polymerase chain reaction; MIS, Management Information Systems; GATK, Genome Analysis Toolkit; SNV, Single nucleotide variant.