Report of the RCPA Genetic Testing Survey 2011

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Executive summary

Under the current Pathology Funding Agreement, the Department of Health and Ageing (DoHA) set up a Genetics Working Party (GWP) to review the current genetic testing arrangements nationally and provide advice on possible reforms. To assist this process, the RCPA was contracted by DoHA to conduct its second survey of genetic testing in Australia (the first performed in 2007 (1)).

The principal aim of the "RCPA Genetic Testing Survey 2011" and the current report was to document the utilisation of genetic testing for medical purposes during 2011, by laboratories that have NATA accreditation in cytogenetics, biochemical genetics, molecular genetics, research and development, or specific molecular or genetic subtests in other disciplines of medical testing. Specifically, information was sought regarding volumes and types of testing available, the purposes of testing and sources of funding for tests performed during 2011.

All NATA accredited medical genetic testing laboratories providing medical genetic testing during 2011 were invited to participate (42 laboratories), and a 100% of eligible laboratories submitted data (39 in total). Data were collected using electronic survey instruments and then de-identified and collated for statistical analysis and comparison with 2006 data.

Key findings of the survey are presented in Box 1 (overleaf). Since 2006, there has been a 2.8 fold increase in volume of molecular genetic assays performed annually, and an increase in the number of targets tested (or types of tests available) from 437 to 546. However, other patterns observed in 2006 with regard to national provision of molecular genetic testing have not changed significantly, with a minority of tests performed by more than three laboratories or regions and relatively few assays performed by any one laboratory for interstate patients. The proportion of assays funded by the MBS has also remained at approximately 25%. Overseas testing remains as a very small proportion of total assays requested nationally, however some appears to overlap with testing available within Australia.

While participation was excellent, there are providers operating in Australia who were not NATA accredited in 2011 and therefore not included in the survey; the assumption has been made that these laboratories account for only a small proportion of the total volume of testing performed in Australia. It should also be acknowledged that data from some participants was incomplete. This stems mainly from the use of laboratory information systems that are not designed for extracting or tracking the data targeted by the survey. In future, this may be remedied by collecting data prospectively.

Finally, marked differences in some statistics were identified between the States/Territories during the initial data analysis; these were best explained by misclassification and differences in understanding of the scope of medical genetic testing, in particular biochemical genetics. Introduction of ongoing collection of national medical genetic testing data using a system that is shown to be valid and reliable may be worth considering.

Overall, the "RCPA Genetic Testing Survey 2011", through its 100% participation rate, has provided solid, representative data that can be used to effectively describe current practices and trends in volumes, types and funding of medical genetic testing in Australia.

Box 1: Summary outcomes

- 42 NATA accredited laboratories provided medical genetic testing during 2011. All of these laboratories responded to the invitation to participate in the RCPA Genetic Testing Survey 2011. Three were later excluded from participation; the remaining 39 all submitted survey data.
- There were 579,742 medical genetic assays performed during 2011, not including assays sent overseas, HLA-typing, newborn and maternal serum screening. In direct comparison to a total of 115,882 (excluding HLA-typing assays) molecular genetic assays performed in 2006, there were 327,193 molecular genetic assays performed in 2011, representing a 2.8-fold increase in assay volumes over five years.
- In 2011, 183 types of biochemical genetic tests, 174 cytogenetic tests and 546 molecular genetic tests were offered (compared to 437 molecular genetic tests in 2006).
- In comparison to 2006, where 10% of laboratories offered 40 or more types of test, in 2011 24% of molecular laboratories offered 40 or more types of test; overall, 35% offered 40 or more types of test.
- More than 50% of tests were offered by only one laboratory for each discipline. Thirteen per cent of molecular genetic tests were offered by more than three States/Territories (as was the case in 2006).
- The most common reason for performing medical genetic testing overall, and by discipline, in 2011 was for diagnostic or screening purposes. When broken down by discipline, prenatal and somatic testing also featured highly in cytogenetics.
- All States/Territories indicated that analysis of specific points in the genetic code was by far the most common scope of testing in 2011, except for Tasmania, where the most common scope was analysis of the entire genetic code due to the high proportion of karyotyping assays performed.
- Approximately 40% of assays performed on intra-State samples in 2011 were funded by the State/Territory, while approximately three-quarters of assays performed on interstate samples were funded by the referring laboratory. Biochemical genetic testing attracted negligible Federal funding. The costs for 11% of assays on interstate samples were apparently absorbed by the laboratory performing the testing.
- Laboratories reported performing 163,296 MBS funded assays (not including 17,882 HLA-typing assays). In comparison to 2006, the proportion of MBS funded molecular genetic assays increased marginally from 24% to 26% in 2011.
- Only 9.6% of assays in 2011 were performed on samples received from interstate patients. As a proportion of the number of assays performed on samples received from within-state patients, molecular assays performed for interstate patients have increased slightly from 9% in 2006, to 12% in 2011.
- In 2011, 2766 overseas requests were made for medical genetic testing. The majority of these were for molecular genetic assays. Of note, testing for a number of targets of overseas requests was also available within Australia in 2011. In comparison to 2006, the proportion of assays sent overseas increased, although remained a relatively small number of assays compared to the volume of assays performed within Australia.
- Only 1.4% of samples received by medical genetic laboratories were not tested due to inadequate resources or sample unsuitability. Fifty-four percent of laboratories reported operating under a formal or informal memorandum of understanding with a local clinical genetics service. A total of 1010.6 FTEs were employed in medical genetic laboratories in 2011.

Definitions and terminology

Survey

- Collection, cleaning and presentation of data from medical genetic testing laboratories

Survey instrument/s

- Spreadsheets used to collect data for the survey

NATA contact

- Person nominated by the laboratory to liaise with NATA for accreditation purposes

Test

- Name of the detection/interrogation of a given target.

Assay

- A single instance of detection/interrogation of a given target with a test.

Target

- The region detected or substance measured by the test (chromosome number, cytogenetic band, HGNC approved gene name, enzyme/protein/metabolite name).

Scope of testing

- The biological level or group at which testing is aimed, choosing from protein/enzyme, metabolite/s, genomic, chromosomes, gene or locus.

Method

- A description of the analytical approach used for testing, selected from:
    - **"specific assay - molec"** refers to any assay for a specific mutation or epimutation.
    - **"specific assay – biochem"** refers to any biochemical assay for a *specific* metabolite or enzyme activity.
    - **"mutation screen"** refers to screening for unspecified variants by an method that is recognised as potentially missing sequence variants.
    - **"multiple assays - molec"** and **"multiple assays – biochem"** refers to the use of multiple assays (specific or screening) on a single sample.
    - **"biochemical screen"** refers to qualitative or semi-quantitative screening.
    - **"light microscopy"** refers to cytogenetic analysis and includes standard karyotyping, special banding and chromosome breakage studies.
    - **"FISH"** refers to fluorescence in situ hybridisation used for the detection of altered dosage and

chromosomal rearrangements.

- **"array"** refers to microarray (CGH or SNP-based) for copy number variants.
- **"sent overseas"** refers to samples sent overseas (including New Zealand)
- **"other"** can be selected if it is not possible to assign one of the specified testing methods in the drop down list.

Purpose

- The reason for performing a test, selected from:
  - **"Diagnostic"** refers to testing of an affected patient (of any age) to determine the genetic basis for their disease. This includes diagnostic testing on post mortem specimens.
  - **"Predictive"** refers to testing of an unaffected person (of any age, not including prenatal) who is at increased risk of carrying the mutation on the basis of family history.
  - **"Screening"** refers to testing an unaffected person who is not recognised as being at increased risk of carrying a heritable mutation.
  - **"Prenatal/PGD"** refers to diagnostic testing on an embryo (prior to implantation) or foetus.
  - **"Somatic/Oncology"** refers to testing for non-heritable variants, typically in cancer tissue.
  - **"Other"** includes the following:
    i. **"Segregation study"** refers to testing to determine the segregation of genotypes or haplotypes with disease within a family.
    ii. **"Confirmation"** refers to confirmation of a result using a second method (for example FISH to confirm copy number variants identified on microarray analysis).
    iii. **"Monitoring"** refers to testing of a person over time with an identified molecular, cytogenetic or biochemical variant that may change in response to treatment, for example minimal residual disease monitoring.
    iv. **"Storage/banking"** refers to samples collected, extracted/cultured and stored for future analysis.
    v. **"Unknown"** refers to testing for unknown purposes

State samples

- Samples received from within the State during the 2011 calendar year.

Interstate samples

- Samples received from outside the State (i.e. <u>other</u> Australian States or Territories) during the 2011 calendar year.

Funding source for State samples

- The source of funding for State sample test, selected from:
    - **"Federal"** refers to any form of Federal Government funding including Medicare and Veteran's Affairs.
    - **"State"** refers to State Government funding, irrespective of recharge arrangements between health units.
    - **"Grants"** refers to research or commercial funding
    - **"Patient"** refers to testing paid for by patients and their families.

Funding source for Interstate samples

- The source of funding for Interstate sample tests, selected from:
    - **"No charge"** refers to tests for which no cost was recovered.
    - **"Referring service"** refers to charges billed to the referring service (lab or clinical service).
    - **"Grants"** and **"Patients"** are defined as above.

Turn-around-time

- Time taken for testing to be performed, measured in days.

Introduction

Under the current Pathology Funding Agreement, the Department of Health and Ageing (DoHA) set up a Genetics Working Party (GWP) to review the current genetic testing arrangements nationally and provide advice on possible reforms by December 2012. The GWP includes nominees from the DOHA, RCPA, NCOPP, AAPP, HGSA, NHMRC, States and consumers.

To assist the GWP in their work, the RCPA was contracted by DoHA to conduct its second survey of genetic testing in Australia. The first survey, performed in 2007, provided a valuable snapshot of genetic testing nationally at that time; however a second survey was required in order to identify trends in this rapidly changing field of diagnostics.

The principal aim of the survey and report was to document the utilisation of genetic testing for medical purposes during 2011, by laboratories that have NATA accreditation in cytogenetics, biochemical genetics, molecular genetics, research and development, or specific molecular or genetic subtests in other disciplines of medical testing.

The ultimate purpose of collecting this information was to answer the following questions regarding genetic testing in Australia in 2011, and where possible in comparison to 2006:

- What variety of genetic tests (for both heritable and somatic variants) was offered across Australia?
- To what extent did laboratories provide testing for their own States versus test samples from interstate?
- What type and volume of genetic tests were sent to overseas laboratories?
- What was the volume of testing in different patient groups i.e. affected, unaffected/predictive, screening, somatic tests?
- Was the utilisation of these tests similar across the different States?
- What proportion of samples received was not tested because of inadequate resources, unsuitability of samples or inappropriate requests?
- What were the sources of funding for testing and what proportion of testing was funded by each of those sources?

The following report outlines the survey process and findings with respect to the above questions.

Methods

Instrument design

The survey instrument used in 2007 was modified in order to accommodate all medical genetic testing disciplines (molecular genetics, cytogenetics and biochemical genetics) and to include additional questions on sources of funding for testing of both samples received from within the State and from interstate (Appendix A). A second survey instrument was developed to capture information on untested samples, laboratory staffing and resources and an overall indication of the purpose for which medical genetic testing was performed for samples received by each laboratory (Appendix B).

Feedback on survey design was sought from multiple representatives across disciplines, States and the GWP, and incorporated where appropriate.

Survey participants

All NATA accredited laboratories that provided medical genetic testing in Australia in 2011 were eligible to participate. Medical genetic testing was defined as molecular, cytogenetic and biochemical genetic testing for medical purposes, including both heritable and non-heritable (somatic) genetic variants.

The survey included data on samples collected within Australia, and tested during the 2011 calendar year. The testing was either performed in an Australian laboratory, or sent from an Australian laboratory to an overseas laboratory (including New Zealand).

The survey excluded medical testing of non-human genes (e.g. microbial genetic testing), non-medical testing of human genes (eg paternity testing) and testing performed on samples received from overseas (including New Zealand). The GWP considered newborn screening to also be beyond the scope of the survey.

Confidentiality

Precautions were put in place to address potential sensitivities regarding the collection and use of medical genetic testing information. The raw data, as captured on the survey instruments, remained confidential and was not made available to the GWP, the RCPA, HGSA, or any State or Federal Government Department. De-identified data was made available to a restricted number of key experts to facilitate clarification of inconsistencies during analysis. In the report, the data are summarised and presented on an aggregated, mainly State-by-State basis, preventing within-State or between-laboratory comparisons. A confidentiality agreement stating these precautions was provided to participants, and on receipt by the survey coordinator was co-signed and the original returned.

Invitation and data collection process

NATA contacts for 42 laboratories providing accredited medical genetic testing were invited to participate in the survey. The invitation was sent by email and the survey instructions, instruments and confidentiality agreement delivered as attachments.

Invitees were asked to respond within 7 days to indicate their intention to participate. Follow-up emails were sent to non-responders, and those still not responding were contacted by telephone. Participating laboratories were given 7 weeks to collect and submit data to the study coordinator. A pre-emptive

reminder of the data submission deadline was sent to laboratories that had not yet submitted data one week prior to the submission deadline, and where necessary additional phone call reminders were made to maximise the participation rate. Additional time was provided on request and to allow for correction and resubmission of data where necessary.

Data analysis and validation

Data were collected in individually identified survey instruments and collated into a master spreadsheet for cleaning and manipulation.

It should be noted that each NATA contact frequently represented multiple smaller laboratories that each made separate submissions, but for the purposes of the survey these were collapsed down to be treated as a single entity.

Where any uncertainty regarding data occurred, clarification was sought by contacting the relevant participating laboratory. Any data remaining incomplete after this process was designated as “not provided”. Proportions were converted to numbers based on the assay volumes provided by the laboratories.

Best efforts were made to assign tests to one of the three disciplines; however it is acknowledged that the distinction, particularly between molecular genetic and cytogenetic testing, is sometimes blurred.

Where possible, data collected by the survey was validated against other national data collections, or assessed by consultation with key stakeholders.

Results

Participation

All invited laboratories agreed to participate and submitted data, except for three laboratories that were excluded from participation; two perform testing on behalf of another participating laboratory, and the other performs testing outside the scope of the survey.

The data submission deadline was met by 18 (45%) of participating laboratories. However, data submission gradually continued and the last submission, including submission of updated or corrected data, was on the 8th August.

Data was received from all States/Territories where medical genetic testing is known to be performed. No data was received from the Northern Territory and therefore it is not included as a distinct region in the tables and figures. A mix of public and privately funded laboratories participated.

Sixteen laboratories performed multidisciplinary testing. Testing in all three disciplines was represented in NSW, QLD, SA, VIC and WA.

Data cleaning and missing data

The main issues identified during data cleaning were with regard to naming of targets and missing information on turnaround times (TAT) and testing purposes.

There was frequent use of non-HGNC approved names for gene targets, and several instances of providing the number of targets detected by a test, rather than names of individual targets, or stating "mitochondrial DNA" rather than individual mtDNA genes.

Laboratories clearly struggled to provide TAT data, and anecdotally indicated that this was in part a consequence of the constraints of local LIMS. Also notably absent in many cases was the specific purpose of testing where the "other" category had been selected. Differences in classification of testing as diagnostic or screening between the States/Territories resulted in the necessary merge of these two categories for analysis.

Following preliminary data analysis, data on biochemical genetic testing was revisited due to inconsistencies in testing volumes across States/Territories. Data were adjusted to exclude 89,851 assays considered outside the scope of biochemical genetics, and 95% of these were performed in QLD.

Data was collected on PGD, HLA-typing and maternal serum screening however there is concern that representative coverage of these was not achieved. It is unclear as to whether there was good participation from all laboratories providing somatic testing, which is not always performed by genetic laboratories.

Aggregated (de-identified) data tables are available on request from the RCPA.

Medical genetic testing data analysis

The results of the data analysis are presented in the following pages.

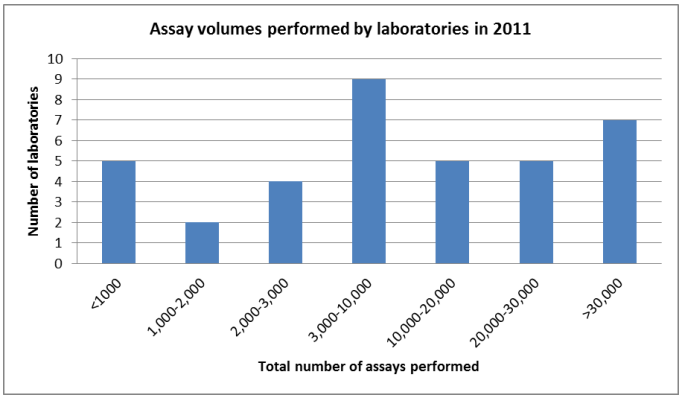
The main analysis excludes tissue-typing, newborn screening, maternal serum screening and testing sent overseas, unless indicated otherwise. Overseas testing is considered in a separate section. As a result of difficulties in achieving complete capture and absence of independent and readily available data sets for

validation of tissue-typing and newborn and maternal screening submissions, the data for these types of medical genetic testing are available as aggregated data only.

Assay volumes

A total of 579,742 assays were performed nationally in 2011. The median number of assays performed by individual laboratories was 9798 (range 110 - 55,374).

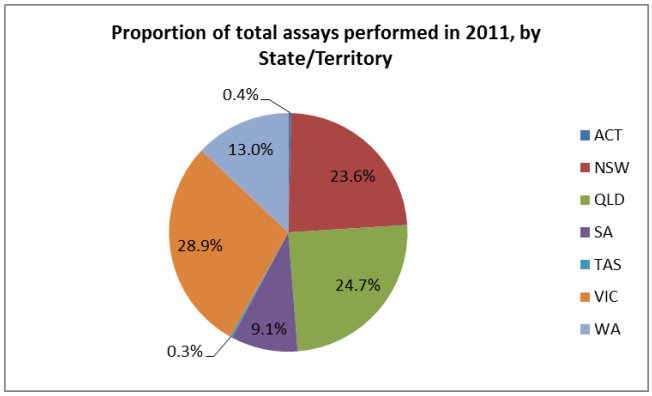
Figure 1: Distribution of assay volumes for 2011



Most laboratories (86%) performed more than 1,000 assays. Figure 1 indicates a spread of assay volumes across medium to high volumes. However it should be noted that some laboratories represent large networks of smaller testing units that may individually perform smaller numbers of assays annually.

The number of assays performed per State/Territory ranged from 1713 to 228,567 (Table 1). The proportions of assays performed by each State/Territory are displayed in Figure 2.

Figure 2: Assay volumes for 2011, proportions by State/Territory



QLD, SA, VIC and WA had similar per capita volumes that were slightly higher than the national total, while TAS and the ACT performed the lowest volumes of genetic assays as a proportion and on a per capita basis.

NSW has a lower per capita volume than that noted for other States performing higher volume testing, however it should be remembered that the volume analysis presented in Table 1 does not take complexity of testing into account. Differences could also reflect incomplete data collection, issues with reliability and validity of the survey instruments, and implementation of new technologies. Further analysis, beyond the scope of the current survey, would be required for clarification.

Table 1: Assay volumes per capita for 2011, by State/Territory

State/ Territory	Number of assays performed	2011 population '000	Assays percapita '000
ACT	2356	370.7	6.4
NSW	136869	7,247.7	18.9
QLD	143281	4,513.0	31.7
SA	52617	1,645.0	32.0
TAS	1713	511.7	3.3
VIC	167797	5,574.5	30.1
WA	75109	2,387.2	31.5
Total	579742	22,249.8	26.1

NB: On average, 6% of tests are performed for patients from outside the State/Territory (see section on National provision); 2011 population data is taken from Preliminary 2011 Census data, ABS.

The proportions of assays performed by biochemical genetics, cytogenetics and molecular genetics were 16%, 28% and 56% respectively. The highest volume assays for each of the three disciplines are provided in the table below.

Table 2: The targets for the tests with the highest assay volumes, by discipline

Biochemical genetics	Cytogenetics	Molecular genetics
amino acids	all chromosomes	HFE
organic acids	chr X	F2
glycosaminoglycans	chr Y	F5
alpha-1-antitrypsin	chr 21	CFTR
thiopurine methyltransferase	chr 18*	BCR-ABL
	chr 13*	

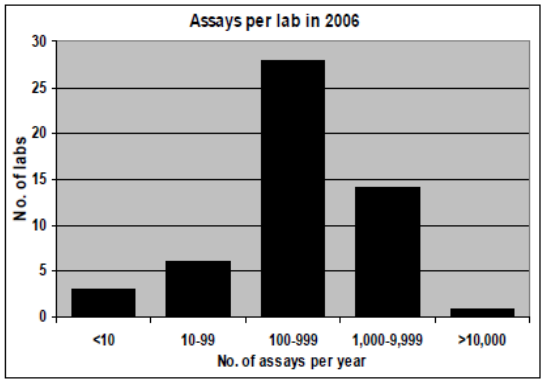
Note: A large number of assays for cytogenetics did not have target information (8% of cytogenetic assays).
**denotes equal volume of assays performed in 2011.*

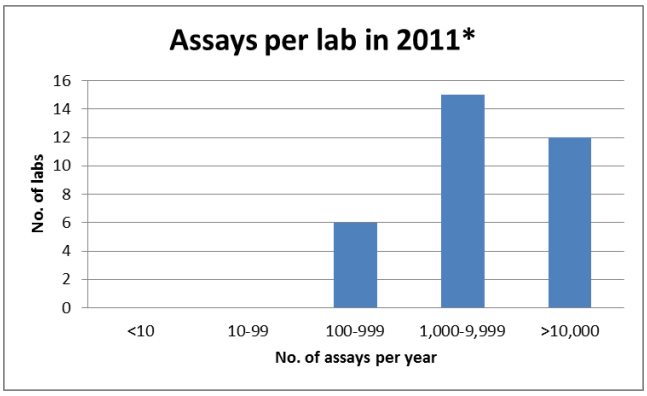
It should be noted that many of the high volume assays were performed as panels, which were separated out to better illustrate national testing volumes, either by the laboratory submitting the data, or during data analysis. This is particularly the case for aneuploidy testing in cytogenetics, where over 90% of assays for chromosomes 13, 18 and 21 were submitted as panel data, that is, most of the time these three targets are interrogated together. A similar pattern would be expected for F2 and F5 testing, however the data submitted by laboratories did not tend to indicate whether these targets were tested as part of a panel.

Comparison to 2006

In direct comparison to a total of 115,882 (excluding HLA-typing assays) molecular genetic assays performed in 2006, there were 327,193 molecular genetic assays performed in 2011, representing a 2.8-fold increase in testing volumes over five years.

In 2006, the median number of assays performed per laboratory was 424 (range 2 - 44,150) and most labs performed more than 100 assays per year. In 2011, the median for laboratories performing molecular genetic testing was 6406, all labs performed more than 100 assays per year, and a definite skewing of assay numbers towards much higher volumes is evident (see below). The skewing to higher volume reflects both increased volume AND pooling of data by NATA contacts i.e. in 2006, the data were laboratory by laboratory.





*molecular laboratories only

The highest volume diagnostic (F5, CFTR, HBA1, HBA2, HBB, HFE, SERPIN1A and subtelomeres) molecular tests in 2006 were similar to those observed in 2011, although subtelomere testing is now considerably less frequent, presumably due to the availability of microarray analysis. The highest volume somatic (BCL2, BCRABL1, IGH@, TRB@, TRG@) molecular tests in 2006 have changed significantly in 2011, to include BCRABL1, JAK2, KRAS, BRAF and EGFR, which reflects advances in knowledge in this field and associated companion diagnostic testing.

Scope and testing methods

The scope and testing methods used in each State/Territory are presented by total assay numbers and proportion of total assays in Tables 3 and 4.

Table 3: Assay volumes and proportions by scope

State/Territory &Scope	Number of assays	% of State/Territory total
ACT		
gene or locus	2356	100.0%
NSW		
chromosomes	18162	13.3%
gene or locus	80046	58.5%
genomic	19363	14.1%
metabolite/s	18944	13.8%
protein/enzyme	354	0.3%
QLD		
chromosomes	9890	6.9%
gene or locus	63547	44.4%
genomic	30159	21.0%
metabolite/s	18501	12.9%
protein/enzyme	21184	14.8%
SA		
chromosomes	3018	5.7%
gene or locus	26353	50.1%
genomic	7827	14.9%
metabolite/s	8414	16.0%
protein/enzyme	7005	13.3%
TAS		
gene or locus	821	47.9%
genomic	892	52.1%
VIC		
chromosomes	28305	16.9%
gene or locus	104296	62.2%
genomic	24809	14.8%
metabolite/s	7605	4.5%
protein/enzyme	2782	1.7%
WA		
chromosomes	11532	15.4%
gene or locus	46747	62.2%
genomic	8753	11.7%
metabolite/s	7995	10.6%
protein/enzyme	82	0.1%

Of note, all States/Territories except Tasmania indicated that the most common scope of testing was “gene or locus”. Tasmania’s most common scope was “genomic” but this includes the target of “all chromosomes”, i.e. karyotyping. This observation is supported by data in Table 4 (overleaf), indicating that more than 50% of assays in Tasmania were performed by light microscopy.

SA and QLD had a comparatively high proportion of assays under the scope of protein/enzyme, and this is reflected in Table 4 (overleaf) with a higher proportion of assays performed by specific biochemical genetic methods than the other States/Territories.

The comparatively lower per capita assay volumes in NSW noted previously may be partly accounted for by higher complexity or more extensive testing performed per assay. Table 4 indicates that NSW had a much higher proportion of testing attributed to multiple molecular genetic assays, compared to other high-volume States that performed a greater proportion of specific molecular assays and FISH.

Table 4: Proportion of assays by testing method

	State/Territory						
Method	**ACT**	**NSW**	**QLD**	**SA**	**TAS**	**VIC**	**WA**
array	0.0%	1.0%	1.1%	3.4%	0.0%	5.3%	2.0%
FISH	0.0%	5.2%	13.9%	7.5%	16.0%	19.3%	7.4%
light microscopy	0.0%	11.2%	14.2%	11.1%	52.1%	7.7%	8.1%
mutation screen	0.0%	2.1%	1.6%	2.4%	0.0%	10.3%	17.9%
specific assay – molecular	100.0%	33.9%	29.5%	28.6%	31.9%	30.1%	42.0%
multiple assays – molecular	0.0%	31.5%	5.8%	16.9%	0.0%	20.5%	11.4%
biochemical screen	0.0%	10.9%	7.5%	6.4%	0.0%	0.1%	4.4%
specific assay – biochemical	0.0%	3.2%	16.2%	22.3%	0.0%	4.0%	4.3%
multiple assays - biochemical	0.0%	0.1%	4.0%	0.6%	0.0%	2.0%	2.0%
other	0.0%	0.9%	6.2%	0.8%	0.0%	0.6%	0.4%

Comparison to 2006

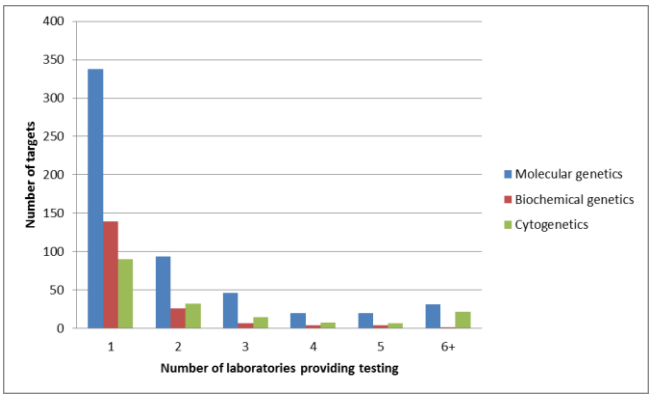
Differences in the detail collected on methods between 2006 and 2011 prevent useful comparisons. No equivalent data on scope was collected in 2006.

Variety and availability of testing for medical genetic targets

In 2011, testing was available for 183 biochemical genetic targets, 174 cytogenetic targets, and 546 molecular genetic targets. As is clear from Figure 3a below, the majority of those targets were tested by a single laboratory (77%, 52% and 62% of targets were tested by a single biochemical, cytogenetic or molecular laboratory respectively). Numbers of unique targets were similar across most States/Territories, except for the ACT and Tasmania, reflecting low levels of local testing (Figure 3b).

Figure 3: Availability of testing for medical genetic targets

a) Unique targets, by discipline



b) Unique targets, by State/Territory

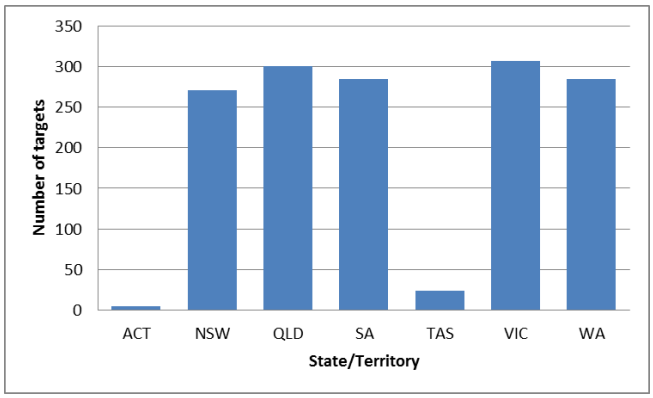


Table 5 lists the top five most widely tested targets for each discipline; these are all targets tested by 5 or more laboratories. No biochemical genetic target was tested by more than 6 different laboratories. "HFE" and "all chromosomes" were tested by 19 and 20 laboratories respectively.

Table 5: Top five most widely tested targets for each discipline

Biochemical genetics	Cytogenetics	Molecular genetics
amino acids	all chromosomes	HFE
pyruvate	IGH-MYC	F5
organic acids	chromosome X	F2
methylmalonic acid	chromosome Y	JAK2
carnitine	chromosome 21	MTHFR

Comparison to 2006

Since 2006, there has been a 25% increase in the number of types of molecular tests offered nationally.

In 2006, 19% of types of tests offered had 0 assays reported (i.e. weren't tested during 2006); this dropped to 9% in 2011.

Twelve per cent of molecular genetic tests were offered by more than three States/Territories (compared with 13% of tests offered by more than 3 States/Territories in 2006). In contrast to 2006, when no tests were available in all States/Territories, the three most widely available molecular tests (HFE, F5 and F2) were available in all States/Territories in 2011.

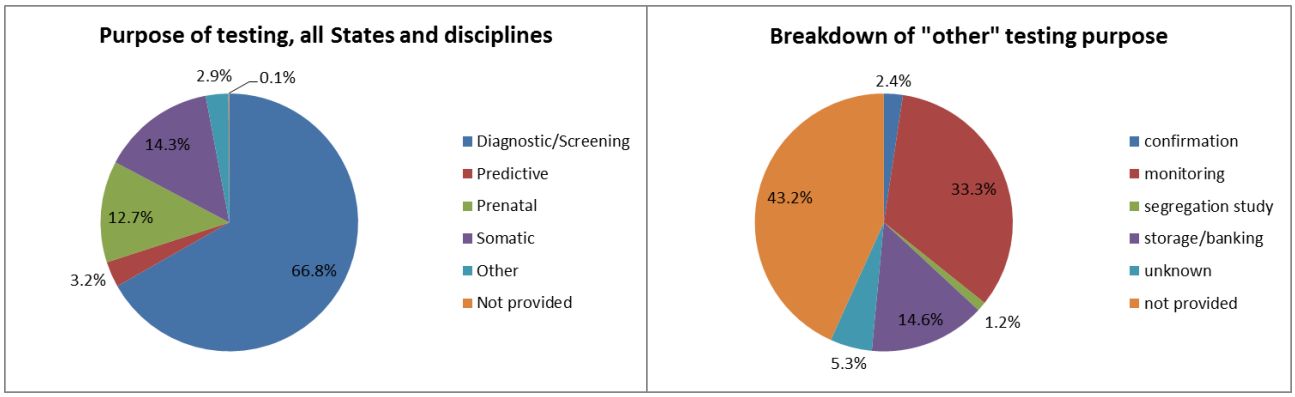
However, the overall availability of molecular genetic tests does not appear to have changed considerably; in 2006, 55% of molecular targets were tested by only 1 laboratory, 24% by 2 labs, and 5% by more than five, while in 2011, 62% of molecular targets were tested by only 1 laboratory, 17% by 2 labs, and 6% by more than five.

Purpose of testing

Overall, approximately two-thirds of all assays were performed for diagnostic or screening purposes (Figure 4). The remaining assays were predominantly performed for prenatal or somatic testing purposes.

While no additional detail was provided for 43% of assays classified as "other", the most common explanation for indicating this purpose was monitoring.

Figure 4: Purpose of testing for 2011



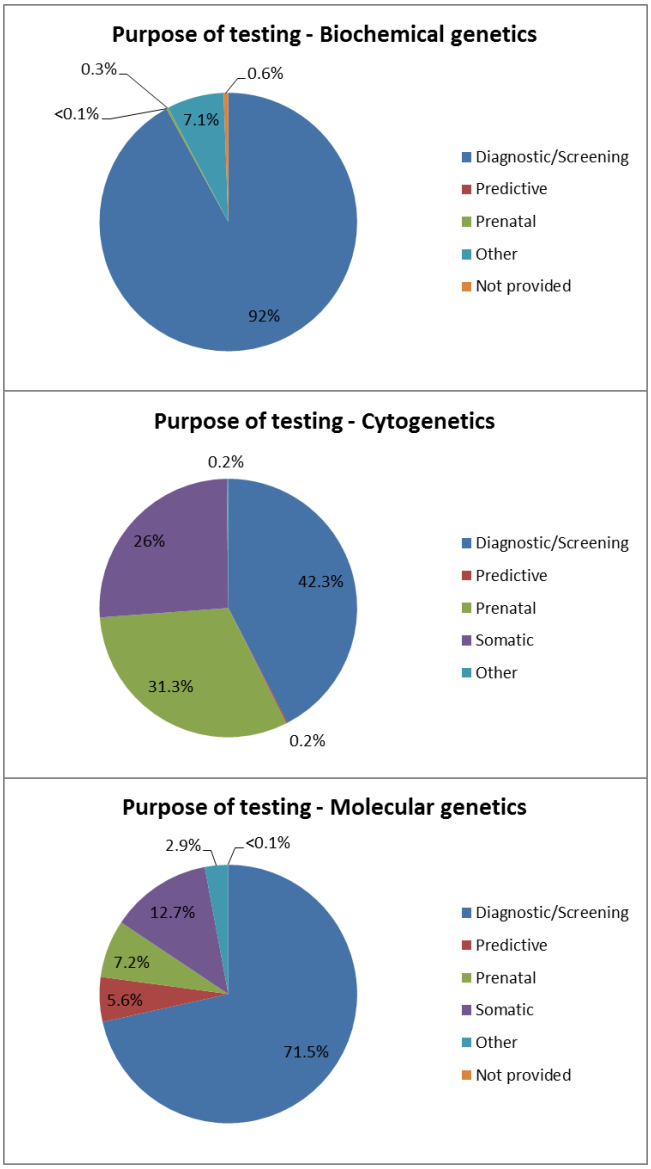
All States/Territories reported that the most common purpose for testing was diagnostic or screening (Table 6), and the majority of testing in the ACT and Tasmania fell in this category. Some variation in distribution of testing was observed across the remaining purpose categories; Victoria had the highest load of predictive and prenatal testing while QLD had the highest proportion of assays in the somatic testing category.

Although the survey instrument was designed to collect separate information on proportions of diagnostic testing and screening, evidence of misclassification during the initial data analysis necessarily resulted in merging of these purpose categories. It is unclear whether misclassification occurred due to interstate variation in everyday definitions of terms, interstate variation in request information or assumptions made regarding testing purpose at the laboratory level. However, as there may also be other inconsistencies in classification of testing purposes between States/Territories, caution should be taken when considering the data presented in Table 6.

Table 6: Purpose of testing, proportions by State/Territory

State/ Territory	Purpose of testing Diagnostic/ Screening	Predictive	Prenatal	Somatic	Other	Not provided
ACT	91.6%	0.0%	0.0%	8.4%	0.0%	0.0%
NSW	75.1%	0.7%	15.0%	7.4%	1.8%	0.0%
QLD	70.5%	1.8%	5.4%	19.5%	2.5%	0.4%
SA	79.6%	1.9%	3.1%	14.4%	1.0%	0.0%
TAS	97.7%	2.3%	0.0%	0.0%	0.0%	0.0%
VIC	51.4%	7.4%	19.8%	16.2%	5.1%	0.0%
WA	68.4%	2.3%	14.1%	13.3%	1.9%	0.0%

Figure 5: Purpose of testing, by discipline



When broken down by discipline, diagnosis or screening was still the most common reason for testing (Figure 5). In fact, this category accounted for the majority of biochemical genetic testing.

However, there were notable differences in other testing purpose categories.

Prenatal testing was far more common in cytogenetics, as was somatic (accounted for by FISH testing on tumour tissue). These purpose categories were selected less commonly in molecular testing and rarely reported in biochemical genetic testing.

Predictive testing accounted for approximately 5% of testing in molecular genetics but did not feature significantly in the disciplines of biochemical genetics or cytogenetics.

Comparison to 2006

The purpose behind molecular genetic testing was approached differently in 2006 and is addressed in the "Assay volumes" section of this document.

Funding

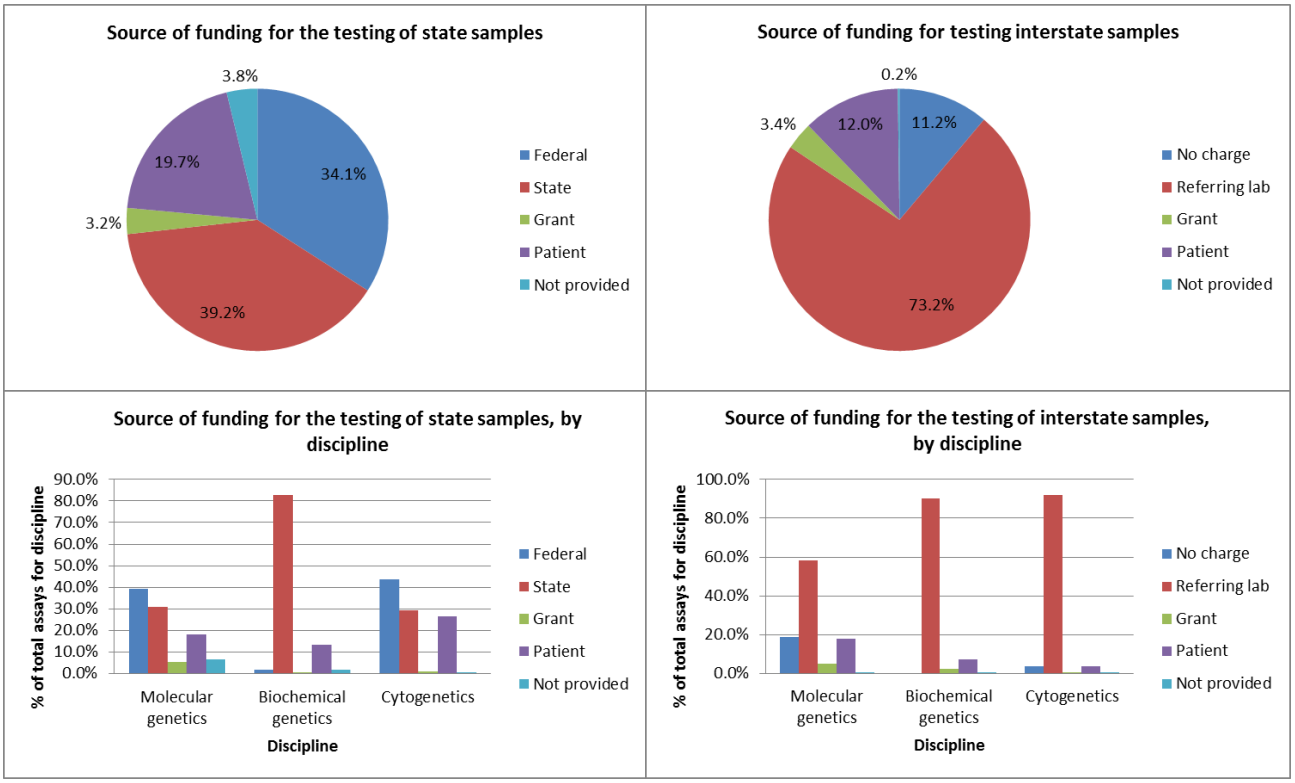
Approximately 40% of assays performed on State samples are funded by the State, while approximately three-quarters of assays performed on out-of-State samples are funded by the referring laboratory (Figure 6).

Patterns seen across the disciplines generally reflect the proportions observed overall, although:

- Biochemical genetic testing attracted negligible Federal funding
- Patient funding of medical genetic testing occurs across all disciplines and for state and interstate testing; this is particularly prominent for cytogenetic state testing (70% of this is prenatal karyotyping and aneuploidy testing).
- 11% of testing performed on samples (equivalent to 6,228 assays) from outside the State was done at no charge (at the cost of the laboratory) and 92% of this activity occurred in molecular genetics.

Information is not available on how referring laboratories paid for testing performed interstate.

Figure 6: Sources of funding for State and interstate samples



A total of 163,296 MBS funded assays were reported by participating laboratories (not including 17,882 HLA-typing assays). A cross-check with MBS data from 2010/2011 and 2011/2012 on numbers of services performed indicated similar overall assay volumes.

Federally funded testing consisted of 60% molecular genetic assays, 39% cytogenetic assays and 1% biochemical genetic assays. Almost half of molecular genetic assays were described as specific molecular assays, reflecting the nature of the targets included in Federally funded testing (typically specific variants causing disease or chemotherapeutic drug sensitivity). Supporting this, tests that attracted Federal funding were most commonly diagnostic or screening (68%) followed by somatic (18%).

Comparison to 2006

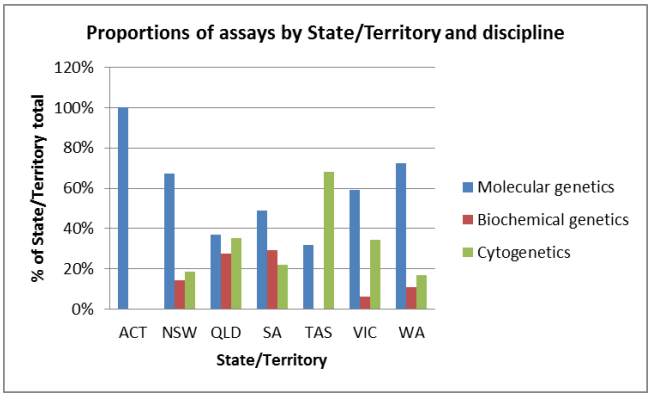
Specific sources of funding were not addressed by the 2006 survey, other than the distinction between Federal (MBS) funding and non-MBS funded molecular genetic tests.

In 2006, 41,497 MBS funded molecular genetic assays were performed (24% of total assays). In comparison, 116,532 MBS funded molecular genetic assays (including HLA-typing) were performed in 2011 (26% of molecular assays), indicating that the proportion of assays attracting Federal funding has not changed significantly over the last five years, despite the introduction of a number of additional tests to the MBS.

National test provision

All States/Territories provided molecular testing; all but the smallest two, by population, provided testing from all three disciplines (Figure 7).

Figure 7: Proportions of assays performed across disciplines, by State/Territory

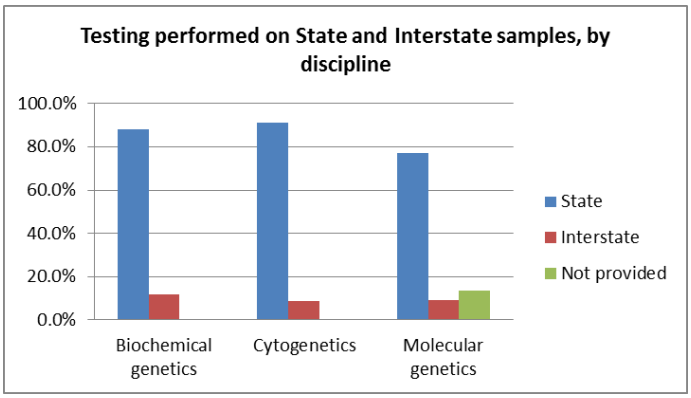


Overall, 83% of testing was performed on samples received from within the State/Territory, while 9% was performed on interstate samples (the distinction of intra-State versus outside-the-State samples was not provided for 8% of assays (all being molecular genetic assays).

Similar proportions of interstate testing were performed for molecular genetics and cytogenetics, and a slightly smaller proportion for biochemical genetics (see Figure 8a).

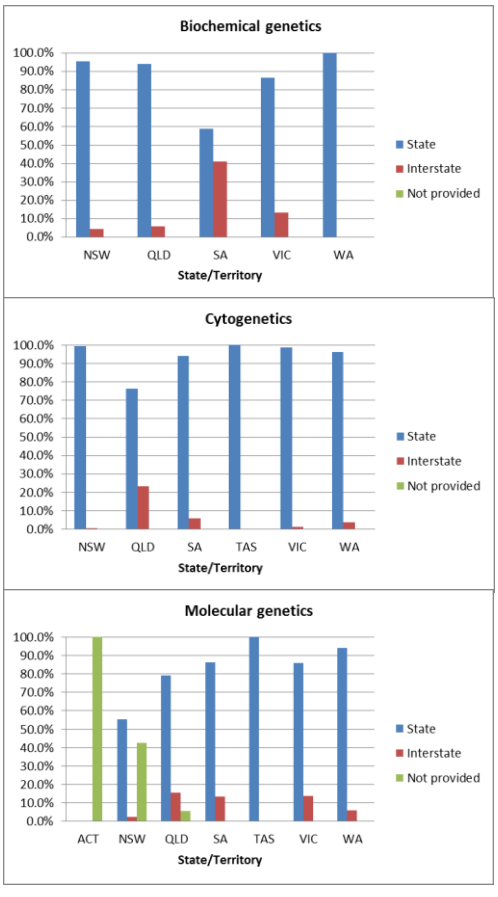
Figure 8: Proportion of testing performed on state and interstate samples

a) Overall by discipline



Tasmania did not perform any interstate testing, and the ACT did not provide any data on sample origin (Figure 8b). SA reported the highest proportion of interstate testing of the remaining states, while NSW reported the lowest; however information on the origin of samples for NSW was unavailable for almost 30%. The comparatively high numbers of interstate assays performed by SA were mostly of a biochemical genetic nature.

b) By discipline and State/Territory



Comparison to 2006

In 2006, 6,941 interstate samples were tested, equivalent to 9% of within state samples, but interstate assay volumes were greater for the types of test that were offered by a limited number of regions. The average proportion of assays performed on interstate samples for single region tests was 5% implied that there was not equal access to those tests across Australia. When data from 2011 is manipulated in a similar manner, 30,719 interstate molecular genetics assays were performed (the equivalent of 12% of within state assays), and again there is evidence that access to tests performed within a single state/Territory are not highly accessed by other States (average proportion of assays performed on interstate samples for single region tests was 15%), although there has been some improvement since 2006. Reasons for this discrepancy cannot be answered directly by the data; however, more stringent criteria for testing may be applied to "sendaway" samples, and there is evidence that some testing available in Australia is sent overseas (see "Overseas testing" section). The improvement noted since 2006 may have been facilitated by better communication of national test availability through mechanisms such as the RCPA Genetic Tests Catalogue.

Median turnaround-times (TATs)

TAT is a product of multiple factors, including the complexity of testing and interpretation, batching practices, and the clinical urgency of the result. Trends in the data collected support this; higher average median TATs were observed in more complex/multiple assay tests, and lower average median TATs were observed in methods with a large prenatal component (see Table 7). However, the design of the survey instrument prevented clear separation of TAT for assays by purpose or other factors.

Table 7: Turnaround-times by method and prenatal testing load

Method	Average Median TAT (days)	Proportion of total assays for prenatal testing (%)
FISH	10	52.1%
light microscopy	17	19.5%
array	42	10.8%
mutation screen	39	0.5%
specific assay – molecular	28	7.8%
multiple assays – molecular	36	8.4%
biochemical screen	15	0.0%
specific assay – biochemical	27	0.4%
multiple assays – biochemical	17	0.0%
other	100	1.1%

Accurate TAT data was difficult for many laboratories to access, and was not provided for 32,949 (6%) assays.

Comparison to 2006

Data on turnaround times was not collected in the 2006 survey.

Testing on samples sent overseas

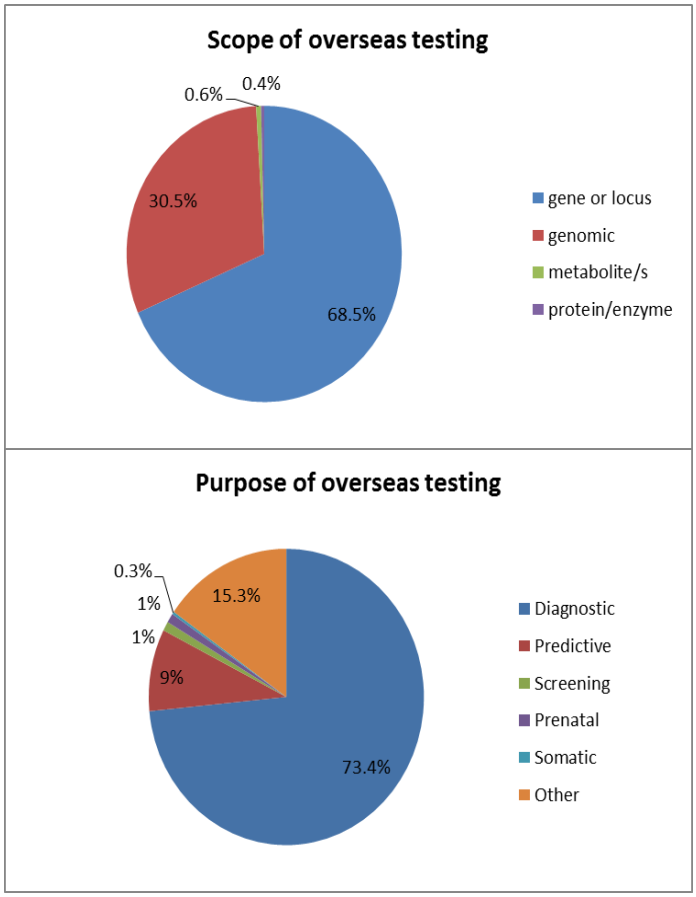
Assay volumes, scope and purpose of testing

During 2011, 2766 overseas assays were requested, 2431 on intra-State samples and 335 on out-of-State samples. 98.7% of the tests were for molecular genetic assays. The vast majority of requests were for genomic and gene or locus tests (see Table 8 and Figure 9); this holds true overall and when broken down to a State/Territory basis.

Table 8: Scope of overseas testing, by State/Territory

State or Territory	Number of assays	% of State/Territory total
ACT		
gene or locus	39	100%
NSW		
gene or locus	428	49.5%
genomic	420	48.6%
metabolite/s	14	1.6%
protein/enzyme	3	0.3%
QLD		
gene or locus	870	99.1%
genomic	8	0.9%
SA		
gene or locus	252	95.8%
genomic	2	0.8%
metabolite/s	2	0.8%
protein/enzyme	7	2.7%
VIC		
gene or locus	66	13.7%
genomic	415	86.3%
WA		
gene or locus	240	100%

Figure9: Scope and purpose of testing, overall



The purpose of testing was most commonly diagnostic, although small numbers for all other testing purposes were noted (Figure 9). It is clear from Table 9 that the majority of assays were molecular and therefore overall numbers biased by overseas requests from this discipline. Numbers of biochemical genetics requests for screening purposes were similar to those for diagnostic purposes. "Other" reasons for molecular genetic testing were predominantly segregation studies.

Table 9: Purpose of overseas testing, by discipline

Discipline	Diagnostic	Predictive	Screening	Prenatal	Somatic	Other	All	% of total
Biochemical genetics	17	0	14	1	1	0	33	1.2%
Cytogenetics	1	0	0	1	0	0	2	0.1%
Molecular genetics	2014	248	14	26	7	422	2731	98.7%
Total	**2032**	**248**	**28**	**28**	**8**	**422**	**2766**	**100.0%**

Funding sources

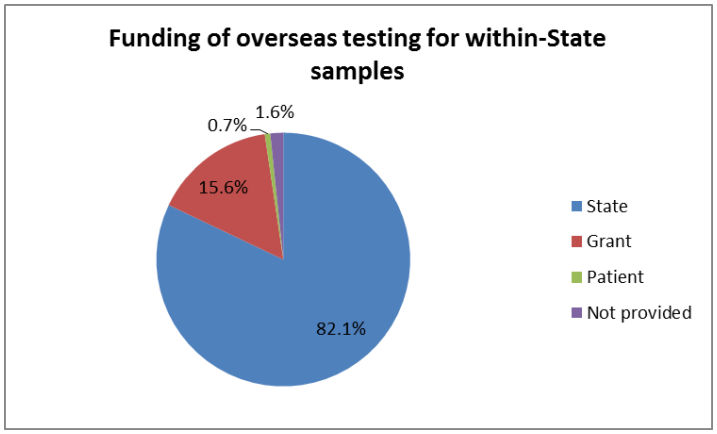
A total of 73 overseas requests were made for out-of-state samples; all but one was funded by referring laboratories. The majority of overseas tests were requests for within-state samples that were funded by the State (82.1%), with a smaller proportion funded from grants (see Table 10 and Figure 10).

Table 10: Funding sources for overseas testing of within-state samples, by State/Territory

State/ Territory	Number of tests funded by:						
	State	Grants	Patient	Federal	NP*	All	% of total
ACT	0	0	0	0	19	19	0.8%
NSW	839	19	1	0	5	864	35.5%
QLD	862	0	16	0	0	878	36.1%
SA	48	0	0	0	0	48	2.0%
VIC	6	360	0	0	16	382	15.7%
WA	240	0	0	0	0	240	9.9%
Total	**1995**	**379**	**17**	**0**	**40**	**2431**	**100.0%**

*Not provided

Figure 10: Funding of overseas testing



Test Targets

Data was unavailable on the specific targets of 1104 (40%) requests. The remaining 60% of requests were for 376 unique targets. Testing was available for 124 of these targets within Australia in 2011. While data was not specifically collected on the reason for choosing to send samples overseas, tests available in Australia may not be considered to be equivalent to those available overseas due to differences in cost or comprehensiveness of testing, or the requestor may simply not be aware that testing is available in Australia.

Comparison to 2006

Detailed data on overseas testing was not collected in 2006, however, the total volume of tests was estimated at 0.3% of total assays performed. There was concern at the time that this figure underestimated the true volume because laboratories had difficulty providing accurate data. Data from the 2011 survey provides an estimate of 0.8% of total assays performed; this is an increase since 2006 although it still represents a very small number of samples sent overseas compared to the volumes of molecular genetic assays performed in Australia. There is no evidence to suggest that data on numbers overseas requests are underestimated in the current survey; in fact, extrapolation of data provided by key requestors of overseas testing in one Australian State indicates that the estimate derived from the survey data is likely to be accurate.

Resourcing, qualifications and partnerships

The total number of samples received by participating laboratories in 2011 was 1,280,386 (average 32,830; standard deviation +/- 79,120; range 110-442,352). Laboratories reported that only a very small proportion of those samples were not tested because of inadequate resources or unsuitability for testing, or that were for storage purposes only (Table 11). These figures were reasonably consistent across States/Territories, although Tasmania stored a higher proportion of samples than elsewhere, and Victoria reported a higher proportion of samples that were unsuitable for testing.

It is important to note that a proportion of these samples will not have undergone medical genetic testing, as a number of biochemical tests deemed outside the scope of medical genetic testing were excluded only after data collection was complete, and the data in Table 11 could not be adjusted accordingly.

Table 11: Proportions of samples not tested, by State/Territory

State	Unsuitable for testing	Not tested due to inadequate resources	Storage only	Samples tested
NSW	0.5%	0.0%	2.5%	97.0%
QLD	1.0%	0.1%	0.3%	98.6%
SA	0.5%	0.0%	0.3%	99.2%
TAS	0.1%	0.0%	5.7%	94.2%
VIC	2.4%	1.3%	0.6%	95.7%
WA	0.4%	0.1%	1.0%	98.5%
Total	**1.1%**	**0.3%**	**0.7%**	97.9%

Table 12: Qualifications of staff in medical genetic laboratories

State	Total FTE*	FRCPA (genetics)	FRCPA (other)	FHGSA	Other Fellow	MHGSA	Other Med Scientist	Technician
NSW Total	238.6	3.8	5.2	18.2	3.1	24.8	160.9	22.7
QLD Total	230.2	4.2	10.6	8.5	6.0	28.4	143.2	29.3
SA Total	174.4	2.0	1.0	3.0	7.0	17.0	62.1	82.3
TAS Total	9.2	0.0	0.0	0.0	0.0	2.0	4.0	3.2
VIC Total	221.5	0.1	3.7	16.2	4.0	25.6	133.9	38.0
WA Total	136.8	3.4	13.0	5.0	6.0	16.0	70.4	23.0
Total	**1010.7**	**13.5**	**33.5**	**50.8**	**26.1**	**113.8**	**574.5**	**198.5**

*Full time equivalents

Staffing of medical genetic laboratories is provided in Table 12. Only 8 laboratories indicated that they had a Genetic Pathologist on staff. An additional 9 laboratories indicated that they employed a Pathologist from another discipline. There may be some confusion in classification due to the recent introduction of the Faculty of Science membership by the RCPA.

Of the total number of scientists i.e. those with FHGSA, other Fellow, MHGSA and other medical scientist, only 25% had a Fellowship or Membership; it is recognised that a proportion of the remaining scientists may have research degree.

The proportion of laboratories with a formal MOU or informal relationship with a clinical genetics service was 60%, however a third of these indicated that the MOU included only some units of the laboratory. While only one-quarter of assays were performed by laboratories without an MOU, several of these labs performed more than 10,000 assays during 2011.

Comparison to 2006

No equivalent data was collected in 2006 for comparison.

Discussion

Study outcomes and limitations

The principle aim of the "RCPA Genetic Testing Survey 2011" and the current report was to document the utilisation of genetic testing for medical purposes during 2011, by laboratories that have NATA accreditation. A combination of effective engagement with medical genetic testing laboratories and attentive follow-up, resulted in 100% participation from eligible laboratories. Data was successfully captured from all States and disciplines, ensuring analysis of nationally representative data.

Where possible, survey data was validated by comparison with independent data sets. This process confirmed that the overall assay volume derived from the survey data was similar to (although slightly underestimated) the number of services counted under MBS P07 group items over the same time period. Small differences between the values would be expected due to the counting of services at the time of performance versus time of charging (time-lag) and claiming of multiple tests under a single MBS item. Underestimation may also reflect incomplete data capture. The exercise of identifying methods for independently validating the data collected by the Survey also revealed the absence of a national data set or registry for maternal serum screening in Australia.

Marked differences in some statistics were identified, and corrected, between the States/Territories during initial data analysis. These were best explained as the result of misclassification of testing purposes and variation in testing included under the scope of biochemical genetics. These discrepancies were dealt with by review and consolidation of the data (to exclude non-biochemical genetic tests in a systematic manner), and merging of testing purpose categories (to combine diagnostic testing and screening as a single entity). Some differences remained between the States/Territories that could reflect further methodological issues, or real variations in medical genetic testing. These challenges in data collection and interpretation highlight a tangible need for a nationally agreed definition of the scope of medical genetic testing, and a reliable system, using appropriate key indicators, for counting and performance monitoring.

There was an accepted, but minimal, risk of incomplete data capture due to the decision to target NATA accredited laboratories, imposed for ease of recruitment of laboratories to the survey. Some laboratories reported difficulties in providing some types of data, particularly TATs and information on overseas requests, due to functional constraints of local laboratory information systems that are not designed for extracting or tracking data required for the Survey; this may be overcome in future surveys by employing a prospective study design. Finally, data on maternal serum screening and HLA-typing was contributed by some, but not all States, possibly due to confusion as to whether or not this form of screening was within scope of the Survey. For this reason, analysis of this data was not included in the current report.

Changes since 2006

Key comparisons with data from 2006 are summarised throughout the current report. Since 2006, there has been a 2.8 fold increase in volume of molecular genetic assays performed annually, and an increase in the number of targets tested (or types of tests available) from 437 to 546. However, other patterns observed in 2006 with regard to national provision of molecular genetic testing have not changed significantly, with a minority of tests performed by more than three laboratories or regions and relatively few assays performed by any one laboratory for interstate patients.

The proportion of assays funded by the MBS has also remained at approximately 25%. However, this survey was restricted to laboratories with NATA accreditation (essential for obtaining Medicare rebates). If genetic

testing activity from non-accredited laboratories had been included, the proportion of MBS-rebated testing would have been less than 25%.

Overseas testing remains as a very small proportion of total assays requested nationally. Some of this testing appears to overlap with testing available within Australia. Many tests also available in Australia may not be considered equivalent to those performed overseas, due to less extensive testing of the target (selected variants versus whole gene or genome approach) or less comprehensive testing (single-target versus multi-target panels) being offered, or pricing differences. However it is not possible to determine the reason for overseas requesting behaviour of Australian laboratories from the data collected.

Overall, the "RCPA Genetic Testing Survey 2011", through its 100% participation rate, provided solid, representative data that can be used to effectively describe current practices and trends in volumes, types and funding of medical genetic testing in Australia. Introduction of the ongoing collection of national medical genetic testing data, including maternal and neonatal screening, may be worth considering. However, it is recommended that scope and classification issues, highlighted by this report, be addressed first.

References

1. Suthers G (on behalf of The Royal College of Pathologists of Australasia). Report of the Australian Genetic Testing Survey 2006.Version date 2 September 2008.

Acknowledgements

We would like express our sincere thanks and appreciation for the time and effort contributed willingly by participating medical genetic testing laboratories throughout Australia, and the contributions made by representatives of the HGSA and other key stakeholders during the survey process.

Appendices

Appendix A – Main survey instrument

Name of test	Scope	Target	Method	Total number of tests performed	Purpose (%)							Tests on State samples	Funding source State samples(%)				Tests on Interstate samples	Funding source Interstate samples(%)				Median TAT (days)	Data Check
					Diagnostic	Predictive	Screening	Prenatal	Somatic/ Oncology	Other (select)	Other (%)		Federal	State	Grants	Patient		No charge	Referring service	Grants	Patient		
CF testing	gene or locus	CFTR	multiple assays - molec	48	50	50	0	0	0	nil	0	24	0	100	0	0	24	0	100	0	0		
CF testing	gene or locus	CFTR	mutation screen	6	75	0	0	10	0	unknown	15	0	0	0	0	0	6	0	100	0	0	42	
CF genotyping	gene or locus	CFTR	specific assay - molec	500	25	75	0	0	0	nil	0	500	0	100	0	0	0	0	0	0	0	7	
DMD	gene or locus	DMD	specific assay - molec	150	90	0	0	10	0	nil	0	150	0	100	0	0	0	0	0	0	0	5	
DMD	gene or locus	DMD	sent overseas	4	100	0	0	0	0	nil	0	4	0	100	0	0	0	0	0	0	0	150	
Hereditary pancreatitis	gene or locus	PRSS1	specific assay - molec	25	100	0	0	0	0	nil	0	20	0	100	0	0	5	0	100	0	0	42	
Hereditary pancreatitis	gene or locus	SPINK1	specific assay - molec	25	100	0	0	0	0	nil	0	20	0	100	0	0	5	0	100	0	0	42	
FISH (array confirmation)	gene or locus	14q11.2	FISH	50	100	0	0	0	0	nil	0	50	0	100	0	0	0	0	0	0	0	100	
FISH	gene or locus	22q12 (EWSR1)	FISH	0	0	0	0	0	0	nil	0	0	0	0	0	0	0	0	0	0	0	0	
Cholinesterase phenotype	protein/enzyme	BCHE	specific assay - biochem	10	50	50	0	0	0	nil	0	10	0	100	0	0	0	0	0	0	0	39	
Microarray analysis	genomic	whole genome	array	300			20			nil	0	300	100	0	0	0	0	0	50	0	0	56	
Maternal serum screening (MSS1)	protein/enzyme	b-hCG	specific assay - biochem	1000	0	0	100	0	0	nil	0	1000	0	100	0	0	0	0	0	0	0	1	
Maternal serum screening (MSS1)	protein/enzyme	PAPP-A	specific assay - biochem	1000	0	0	100	0	0	nil	0	1000	0	100	0	0	0	0	0	0	0	1	
Maternal cell contamination	genomic	maternal DNA	specific assay - molec	70	0	0	0	100	0	nil	0	60	30	0	0	30	10	100	0	0	0	2	

Notes:

Examples were provided to assist laboratories in completion of the survey instrument (light green shaded rows).

Red shading was formatted to appear in the spreadsheet to highlight missing or inconsistent data.

Appendix B - Additional questions instrument

RCPA Genetics Survey 2011 - Additional questions

DATA INCOMPLETE

Please complete the following questions by entering a number value in all white boxes.

Question 1

a) How many samples did your laboratory receive in 2011?

b) Of the samples received, how many were not tested because

i. Unsuitable sample, or inappropriate request

ii. Inadequate resources (inlcuding staffing, equipment and funding)

c) Of the samples received, how many were extracted or cultured for storage only

Question 2

Overall, what proportions of samples tested by your laboratory were tested for the following purposes *(must add up to 100%)* :

a) diagnostic

b) predictive

c) prenatal

d) somatic/oncology

e) other

f) unknown

0%

Question 3

How many FTEs (full-time equivalents) does your laboratory employ?

a) FRCPA (Genetics)

b) FRCPA (Other)

c) FHGSA

d) Other Fellowship

e) MHGSA

f) Other medical scientist

g) Technician/Assistant

Please complete the following questions by selecting YES or NO from the drop down list .

Question 4

Does your laboratory formally liaise, or have an MOU, with a clinical genetics service?

Remember to save your answers before returning this spreadsheet to genetics.survey2011@rcpa.edu.au

Notes:

"DATA INCOMPLETE" and a box summing the percentages provided in question 2 boxes were included to flag inconsistent or incomplete data.