384-388 Albert Street, East Melbourne 3002

17 July 2020

Select Committee on Autism

To whom it may concern,

BioAutism is please to make this submission to the Select Committee on Autism. The purpose of our submission is to provide specific responses to the Terms of Reference [ToR] a,b,e,g,i,j. It proposes recommendations for incorporation into the proposed National Autism Strategy, with particular regard to the need to understand the aetiology of autism in the face of its apparent increasing prevalence.

Better understanding will lead to earlier diagnosis and intervention using better, more individualised, treatments and therapies.

BioAutism is a Health Promotion Charity with Deductible Gift Recipient status in Australia. Our objective is to help fund research into the underlying causes of autism so that in the future we may all benefit from improved diagnosis and treatments. BioAutism advocates for more funding in this area. It is the also only charity in Australia solely dedicated to supporting autism research.

If you have any queries or would like to follow up any information contained in our submission please contact us through or call Michael Stapleton (director) on .

Sincerely,

Robert Klupacs
Chief Executive, BioAutism Limited

Submission to the select committee on autism to inquire into and report on the services, support and life outcomes for autistic people

BioAutism Limited

17 July 2020

BioAutism Ltd 384-388 Albert St East Melbourne Victoria 3002

ABN 68 161 601 092

BioAutism
the key ...Unlocking the mystery

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EXECUTIVE SUMMARY

The purpose of this submission is to provide specific responses to the Terms of Reference [ToR] a,b,e,g,i,j. It proposes recommendations for incorporation into the proposed National Autism Strategy, with particular regard to the need to understand the aetiology of autism in the face of its apparent increasing prevalence. Better understanding will lead to earlier diagnosis and intervention using better, more individualised, treatments and therapies.

Some additional background information is provided for each recommendation for readers who may not be familiar with the complexities of autism.

The main recommendation proposed is the establishment of a compulsory National Autism Register (similar to the existing Western Australian Autism Register) in order to keep track of numbers in real time, so that Governments at all levels can formulate policy with regard to education, employment and care requirements with confidence.

In parallel, the existing biobank established by the Cooperative Research Centre for Autism should be expanded in capacity in order to accommodate and analyse a substantial increase in biological specimens.

A generous Medicare supplementation scheme should be used to encourage participation by the autistic community in the supply of biological specimens which will help identify any underlying pathology. These specimens will be used to provide early psychology and biology-based interventions, as well as provide a vital source of information, suitably de-identified, for researchers to investigate autism's aetiology, both genetic and environmental.

The case is also made for a substantial increase in Government funding ($300 million over five years) for this essential biological research.

A list of more detailed recommendations for each ToR can be found on the next page.

LIST OF ABBREVIATIONS

ABA	Applied Behaviour Analysis
ASD	Autism Spectrum Disorder
ATSI	Aboriginal and Torres Strait Islanders
CALD	Culturally and Linguistically Diverse
DSM	Diagnostic and Statistical Manual
ESDM	Early Start Denver Model
HCWA	Helping Children With Autism
ICD	International Classification of Diseases
MCHN	Maternal & Child Health Nurse
NDIS	National Disability Insurance Scheme
NGADASD	National Guidelines for Assessment and Diagnosis of ASD
NHMRC	National Health and Medical Research Council
OTARC	Olga Tennyson Autism Research Centre
SDAC	Survey of Disability, Ageing, and Caring
WGS	Whole Genome Sequencing

SUMMARY OF RECOMMENDATIONS

[ToR a] Current approaches and barriers to consistent, timely and best practice autism diagnosis

I. Some of the reasons for delays in obtaining a diagnosis, and the journey through the maze of dealing with various health professionals (sometimes called "Odyssey of Diagnosis") are briefly discussed. Proposals to overcome these problems, based on biomarker research, are given in response to [ToR j]

II. All those studying to become health professionals should be given sufficient education and training to recognise the behavioural aspects of autism, as well as its accompanying physical health co-morbidities. This training should also be made available to the ATSI and CALD communities, as it is suspected that a proportion of newcomers to Australia may not be familiar with the many presentations of autism behaviour and accompanying co-morbidities.

[ToR b] The Prevalence of Autism in Australia

I. A National Autism Register needs to be established in order to collect real time information, and to obtain an understanding of the longitudinal development of autism with age.

II. A concerted effort needs to be made to ensure that the ATSI community is well served with health professionals able to assess and diagnose autism.

[ToR e] The Demand for, and Adequacy of Commonwealth, State and Local Government Services to meet the Needs of Autistic People at all Life Stages

A National Autism Register of all people with ASD needs to be established in order to provide sufficient services for the ASD, now and in the future. This Register needs to be established to operate

in real time, as soon as people receive an official diagnosis. Their development over the years can be followed, at say, 5 year periods, so that their needs can be refined with their age, taking into account the impact of any medical treatments. These longitudinal data will provide much needed information about their social, educational, employment, and housing needs, as well as a record of their changing abilities and health. It will also contribute to better forecasting of NDIS funding needs. A similar project, relating only to medical incidents, is already being developed in the UK, linking the National Down Syndrome Cytogenetic Register to Hospital Episode Statistics.

The paucity of data relating to Aboriginal and Torres Strait Islanders (ATSI) shows that a concerted effort needs to be made to ensure that this community is well served with health professionals able to assess and diagnose autism.

[ToR g] The social and economic cost of failing to provide adequate and appropriate services, including to support key life stage transitions of autistic people

I. The Productivity Commission should review the educational, housing, employment, health, and care needs of the autism community every five or ten years using the data to be collected through the above proposed National Autism Register.
II. Further research should be carried out on the social impact of having an autistic child, especially the effects on parents and siblings, through longitudinal studies.
III. Further research is also needed to investigate the proportion of those in prison with autism, with the aim of providing appropriate psychological support, health checks, and therapies.
IV. The proposed National Autism Register of children born with autism in Australia, should also be used to keep a record of attempted suicides, actual suicides and deaths from other

causes. It is anticipated that it will eventually be able to help identify people at a higher risk of early mortality when combined with medical data.

V. Contact with the justice system could also be recorded in the proposed register for research purposes.

[ToR i] The development of a National Autism Strategy and its interaction with the next phase of the National Disability Strategy

I. The key element for establishing a National Autism Strategy is to have a Compulsory National Register as a single source of reliable information for use by all levels of government.

II. Sufficient, sustainable funding for research into producing a biological Autism Matrix with which to obtain a very early diagnosis, thus enabling the provision of tailored, early intervention. This Matrix would be based on say, several types of biomarkers, which distinguish them from average (referent) values for non-autistic children and adults of different sex and ages. The objective of the program is to produce an accurate forecast of whether a child is likely to be autistic as soon as possible after birth, so that early intervention can be started straight away.

III. In order to encourage cooperation by those in the autism community, all those diagnosed with ASD, or suspected of having ASD should be offered Whole Genome Sequence (WGS) testing at a highly subsidised rate on Medicare, or free of charge, in order to save valuable time, which can be used to initiate the appropriate, personalised therapies and treatments. The results are to be retained on the proposed National Autism Register and de-identifiable for research purposes.

[ToR j] The adequacy of funding for research into autism

Current funding for basic autism research is inadequate. Given the rapidly rising economic cost and social impact of autism, there is an

urgent need for a significant uplift in the level of funding for research into its causes.

A funding plan for biological autism research worth at least $60 million/year, or $300 million over five years, is recommended.(see Recommendation 11). The social benefits arising from such research include:

- earlier diagnosis than presently possible using only psychological evaluation
- better, tailored treatments and therapies
- reduced social impact on families eg less stress, more work opportunities, more holidays, more free time, etc

The economic benefit includes flattening the curve of expenditure on health, care, education, housing, and employment which currently is estimated to be costing approximately $26.5-29.7 billion/year. $60 million/year represents just 0.2% of the average cost of $28 billion/year.

Projects Requiring Funding

I. The CRC Autism Biobank should be given an expanded role. All those formally diagnosed with ASD should be registered on the above proposed National Autism Register, and be offered the opportunity to provide biological samples so that a full analysis of an individual's biological status can be obtained as early as possible, and appropriate treatment/interventions recommended. The de-identified specimens should also be retained for further examination by researchers looking for other potential biomarkers.

II. The application of computational and statistical analysis to these data to produce an Autism Matrix will speed up the discovery of the causes of autism, and thus enable researchers to suggest the most appropriate treatments to various sub-sets of autism.

III. The same services should be offered to all those who have been diagnosed with Prader-Willi syndrome, Angelman Syndrome, and Williams Syndrome. The prevalence of these (so-called orphan) conditions is so much lower than that for autism being 1/15,000, 1/15,000-20,000, 1/10,000 respectively and all patients, parents, researchers would benefit from this proposal.

IV. All those diagnosed with ASD, or suspected of having ASD, should be offered Whole Genome Sequence (WGS) testing at a highly subsidised rate on Medicare, or, preferably free of charge, in order to save valuable time which can be used to initiate the appropriate, personalised therapies and treatments. Large scale testing will bring the cost of WGS testing down, and result in savings later in a person's life journey. As most parents with children on the spectrum have very limited income, the supply of biological test specimens as well as their analysis, interpretation, and discussion of the results with the parents, or individuals, should be free of charge, or generously covered by Medicare to encourage participation. Any follow-up pathology considered necessary over, say, the following five years should also be included in such a scheme.

V. A small number of GPs have been collecting very detailed analyses of biological specimens from their ASD patients over many years. This is a valuable resource, and it is recommended that a task force be established to find a way of bringing the relevant GPs and researchers together for the common good.

OVERALL OBJECTIVE

The terms of reference require the committee to focus its attention on productive and meaningful ways to improve services and support for autistic people in the areas of education, healthcare, employment, housing, justice and rights.

This submission is focused on the following Terms of Reference (ToR)

- a) Current approaches and barriers to consistent, timely and best practice autism diagnosis
- b) the prevalence of autism in Australia
- e) the demand for and adequacy of Commonwealth, state and local government services to meet the needs of autistic people at all life stages
- g) the social and economic cost of failing to provide adequate and appropriate services, including to support key life stage transitions of autistic people
- h) the development of a National Autism Strategy and its interaction with the next phase of the National Disability Strategy
- j) the adequacy of funding for research into autism

Definition of autism and some typical characteristics

Autism (ASD) was first described by psychiatrist Leo Kanner in 1943, and since then has been considered almost exclusively as a psychiatric phenomenon. As such it was diagnosed and managed primarily by psychiatrists and psychologists, though since around the turn of the century, others, such as paediatricians, speech and occupational therapists, have become involved.

People with ASD tend to have communication deficits, such as responding inappropriately in conversations, misreading nonverbal interactions, or having difficulty building friendships appropriate to their age. In addition, they may be overly dependent on routines, highly sensitive to changes in their environment, or intensely focused on inappropriate items (1).

Put simply, the two characteristics defining autism are:

1. Social communication deficits

2. Restricted interests and repetitive behaviours

There are three distinct levels within the diagnosis as follows:

- Level 1 Requiring support
- Level 2 Requiring substantial support
- Level 3 Requiring very substantial support

[The International Classification of Diseases, ICD-11 has a similar definition].

According to the Helping Children with Autism (HCWA) autism should be diagnosed by "a multidisciplinary team usually includes a paediatrician or child psychiatrist, a psychologist and a speech pathologist. It might also include other professionals like an occupational therapist. These professionals might want to see you and your child several times. (2)

ASD affects more boys than girls by approximately 3.5:1, and often occurs with a number of other conditions (co-morbidities), such as ADHD (37-78%)(**3**), intellectual disability (ID), epilepsy (about 25-30%), erratic sleep patterns (50-80%), gastrointestinal problems (9-70%), allergies, food sensitivity/eating disorders, poor muscle

1 American Psychiatric Association Diagnostic and Statistical Manual 5 (DSM-5) (2013)

2 https://raisingchildren.net.au/autism/learning-about-asd/assessment-diagnosis/asd-diagnosis (Website)

3 https://www.researchgate.net/publ cation/305846193_ (2016)

tone, language disorders, lack of eye contact, anxiety, and many others.(**4**)

ASD is generally considered a chronic, life-long, condition, though its manifestations may change with age. e.g. A 2019 Minnesota (USA) study examined the cumulative incidence of clinically diagnosed depression, anxiety, and bipolar disorder through early adulthood in individuals with ASD. The estimates of cumulative incidence by 30 years of age were 7.3% for bipolar disorder, 54.1% for depression, and 50.0% for anxiety, compared with referents, 0.9%, 28.9%, and 22.2% respectively.(**5**)

[ToR a] Discussion

Diagnosis Consistency

The Cooperative Research Centre for Autism (CRCA) has published a major document on the need for diagnostic consistency, and how to achieve it, as a result of perceived and actual inconsistent diagnostic methodology being used around the country. Full details are available in the National Guideline for the Assessment and Diagnosis of Autism Spectrum Disorders.(**6**) (NGADASD)

Diagnosis Timeliness

In Australia diagnosis using the current NGADASD is generally not considered possible before a child is about two years old, and girls tend to be diagnosed later than boys. In some cases e.g. for those with Asperger's (formerly a subset of autism in DSM-IV), this may not occur until they become teenagers. Some people may even reach mature adulthood before receiving a diagnosis.

4 https://www.frontiersin.org/articles/10.3389/fpsyt.2018.00751/full (2019)
5 https://jamanetwork.com/journals/jamapediatrics/article-abstract/2755414 (2019)
6 https://www.adcet.edu.au/resource/9929/a-national-guideline-for-the-assessment-and-diagnosis-of-autism-spectrum-disorder-in-australia/#:~:text=The%20Gu deline%20aims%20to%20create,receive%20the%20optimal%20clinical%20care. (2018)

Obtaining a formal diagnosis in Australia is difficult. The whole process, from the time a parent suspects something is not quite right with their child, to getting a referral and booking meetings with the two or more specialists, to obtain an assessment and subsequent diagnosis, is very time consuming and frustrating for many parents. In fact it has been described as a "diagnostic odyssey" (**7**) This is particularly the case for those living in country areas, where the numbers of such specialists are much lower than in the cities. It is thought that a proportion of Aboriginal and Torres Strait Islander communities (**8**) children remain undiagnosed.

An unpublished 2009 survey (**9**) of over 200 Australian parents showed that the delay between a parent's suspicion of their child having autism, and actually getting a diagnosis was approximately two years. The main reason for this was health professional reassurances that there was nothing wrong with their child, and that “the delay is normal and nothing to worry about”. Such comments accounted for just under 50% of the delays. Nearly 20% of parents were told their child was too young for assessment, and a further ~20% of the delays were due to not being able to get to see a psychologist for a diagnosis earlier. In 2016, the average age of autism diagnosis in Australia was four years old, while fewer than 3 per cent of children with autism were diagnosed before the age of two (**10**).

In that same year, a free smartphone app was launched that empowers parents and caregivers to identify autism earlier, and more accurately than ever before. The app helps detect signs of autism in babies as young as 12 months, which will give more children with the condition the chance to receive life-altering early intervention. It was designed by Salesforce, based on research

7 https://bmcpediatr.biomedcentral.com/art cles/10.1186/s12887-019-1888-6 (2020)

8 https://www.mq.edu.au/__data/assets/pdf_file/0011/928208/FINAL-REPORT-We-Look-After-Our-Mob_SCREEN.pdf (2019)

9 Unpublished Parent Survey Report (2009)

10 https://www.abc.net.au/news/2016-02-14/autism-app-asdetect-helping-parents-detect-signs/7163902#:~:text=The%20average%20age%20of%20autism,before%20the%20age%20of%20two. (2016)

carried out by Dr Josephine Barbaro of La Trobe University's Olga Tennison Autism Research Centre (OTARC)9.

In 2018 this was followed up by the Victorian Government announced an $11.1 million training program, to be run by OTARC for all Maternal and Child Health Nurses (MCHN), to help them recognise the early signs of autism (**11)**.

Despite these advances, according to Dr Barbaro, the average age of diagnosis is still substantially later, at around 4 to 5 years of age.

(ToR a) Recommendation 1

Autism is not just in the head. It is a whole of body condition. As discussed in [ToR j], it usually occurs with one or more co-morbidities, such as gastrointestinal problems, allergies, poor sleep patterns and many other symptoms. As such, all those studying to become health professionals should be given sufficient education and training to recognise the behavioural aspects of autism, as well as its accompanying physical health co-morbidities. This training should also be made available to the ATSI and CALD communities, as it is suspected that a proportion of newcomers to Australia may not be familiar with the many presentations of autism behaviour and accompanying co-morbidities.

Further discussion on diagnosis and the prospect of using biomarkers, as well as the benefits of DNA testing can be found under [ToR j] and in the Appendices A, B, and C.

[ToR b] Discussion

The prevalence of autism in Australia is published on a three year basis by the Australian Bureau of Statistics (ABS) under item 4430.0 - Disability, Ageing and Carers (SDAC), and the data for the period 2003-2018 may be summarised as shown.

11 https://otr.anmfvic.asn.au/art cles/mch-nurses-to-train-in-early-identification-of-autism (2018)

Table 1

Year	Number	% Increase
2003	34,200	-
2006	No data	-
2009	64,600	+88.9
2012	115,400	+78.6
2015	164,000	+42.1
2018	205,200	+25.1

Note 1 'Autism' and 'autism spectrum disorders' are used to denote conditions including autism spectrum disorder, Asperger's Syndrome, Pervasive Developmental Disorder – Not Otherwise Specified, Rett Syndrome and Childhood Disintegrative Disorder. Descriptions of these disorders can be found in the Diagnostics and Statistics Manual of Mental Disorders (DSM) IV-TR and the DSM 5.

Note 2 The data for 2003 -2012 were collected on the basis of DSM-IV-TR. The data for 2015 and 2018 refer to DSM-5

The epidemiology of autism in Australia has always been fraught with difficulty as there is no national register. This may be demonstrated by examining the two following examples:

- as shown above, in 2018 there were 205,200 Australians with autism, a 25.1% increase from the 164,000 with the condition in 2015.
- males were 3.5 times more likely than females to have the condition, with prevalence rates of 1.3% and 0.4% respectively (**12**).

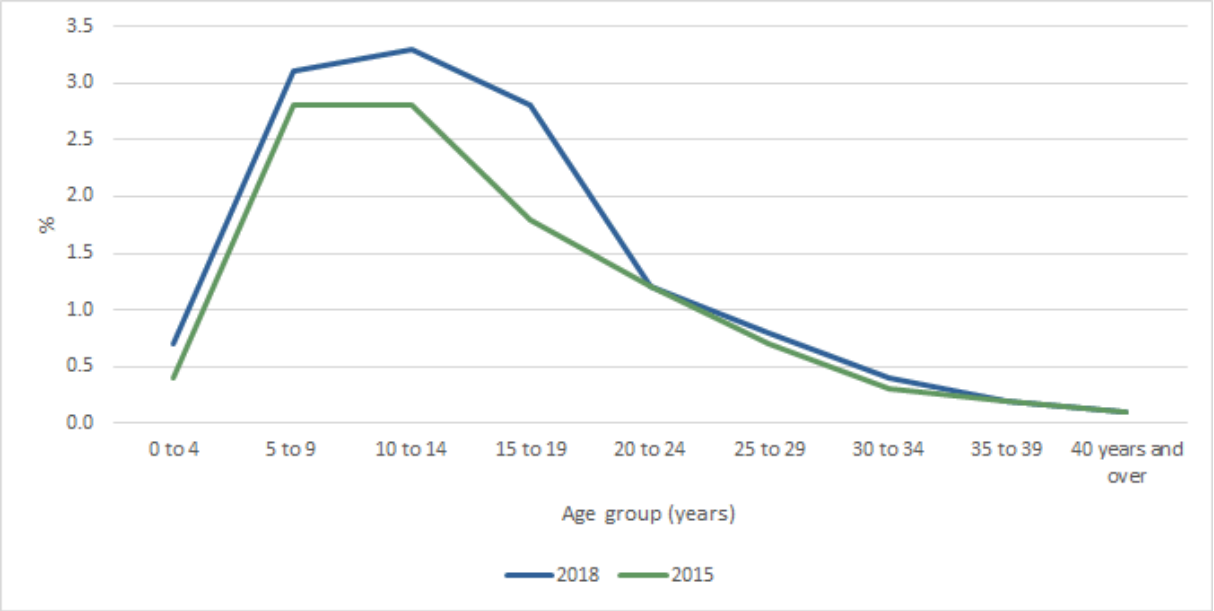
In the same year, Autism Spectrum Australia (Aspect, a major support organisation based in NSW) revised its autism prevalence rates from 1 in 100 to an estimated 1 in 70 people in Australia on the autism spectrum. That is an estimated 40% increase or around 353,880 people - approximately 1.4 % of the population.(**13**)

12 https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4430.0Main+Features102018 (2018)

13 https://www.autismspectrum.org.au/news/autism-prevalence-rate-up-by-an-estimated-40-to-1-in-70-people-11-07-2018?gclid=Cj0KCQjwz4z3BRCgARIsAES_OVej-Wv3zRzPKKeSE1IzW3fweaahzI6XNkUy7u3j-U_XWSrbhyH9B38aAhgPEALw_wcB (Website)

The ABS regularly provides a lot more detail than the bald numbers shown in the above table. For instance, the reports usually include a graph of prevalence with age, as shown below for 2018:

Prevalence of autism, by age – 2015 and 2018



Source(s): ABS Survey of Disability, Ageing and Carers: Summary of Findings 2018

The apparent change in prevalence with time is explained by the ABS as follows:

The design of the SDAC may also influence the observed drop in autism prevalence as people age. The first stage of the SDAC interview, in which it is identified whether there is a person with disability living in the household, is asked of the first responsible adult with whom the interviewer makes contact. In instances where a child is living at home with their parents, it is more common for a parent to provide the responses to these questions. However, when people are in their late teens and start moving out of home, they will be more likely to answer these questions for themselves, and this may affect their propensity to identify as living with autism, although the exact level of this impact is unknown.

There are other factors that may also be impacting on the change in prevalence with age. People may learn coping strategies as they mature and no longer feel they are restricted in any of the areas of limitation considered in the SDAC. Similarly, intervention therapies may effectively remediate the challenges of autism for some, allowing them to function without experiencing limitations in their everyday activities.

It is also possible that people are less likely to identify a child as having autism as they get older because there is some sensitivity around the issue, either for the person or for the other family members.

It is clear that the reasons for the apparent change, which has been consistent over the years, both in Australia and abroad, are speculative, and more research needs to be done to find out the real reasons. The ABS does provide another possible reason relating to a higher mortality rate, based on a research paper by Hwang et al, but this is unlikely to explain such a large drop in numbers. (See later under [ToR i]).

It is also worth noting that May et al. reported that milder cases of ASD are being diagnosed in Australia, resulting in one of the highest reported prevalence rates in the world (**14**).

Autism in Aboriginal and Torres Strait Islanders (ATSI)

With regard to the ATSI community, the Helping Children with Autism (HCWA) scheme identified 1,500 children (ie ~0.2% of an estimated total ATSI population of 700,000 as having ASD. They represented 4.7% of the 32,199 children accessing the scheme. By comparison the remaining 95.3%, or 30,068, represent ~0.12% of the total non-ATSI population of 24.3 million and 8.5% of the non-ATSI ASD population. The researchers (Lilley et al.) state that "the absence of research on autism in Aboriginal and Torres Strait Islander communities is concerning." Certainly the apparent discrepancies in prevalence and services provided requires investigation.

[ToR b] Recommendation 2

A National Autism Register needs to be established in order to collect real time information, and in order to obtain an understanding of the longitudinal development of autism with age.

14 https://pubmed.ncbi.nlm.nih.gov/32124539/ (2020)

[ToR b] Recommendation 3

A concerted effort needs to be made to ensure that the ATSI community is well served with health professionals able to assess and diagnose autism.

[ToR e] Discussion

When the Productivity Commission reported on the proposed NDIS in 2011 it cited data from the SDAC 2009 showing only 53,530 people with Autism/Aspergers (cf data in Table 1). A full analysis of the effectiveness of the NDIS with regard to those on the autism spectrum was released in June 2018. (**15)**

In brief, ASD was found to be the largest primary disability category with approximately 68,000 with an approved plan. (29% of active participants had a primary disability of ASD). This is an apparent increase of 27% in the space of about 9 years, and further increases can be expected. Some of the increase may be due to population increase (13.7% over this period), but this does not explain the difference.

Clearly, reliance on the ABS/SDAC data, which tends to lag by about two years, is not a satisfactory basis on which to formulate government policy regarding the services expected to be required by the ASD community in 5,10, or 20+ years' time.

A recent private request to have autism listed on the 2021 Census form was rejected, though changes to the form will allow collection of data concerning other long term health conditions such as arthritis, asthma, cancer, dementia, diabetes, heart disease, kidney disease, lung conditions, stroke and mental health conditions (**16**). Given the prevalence rates of dementia (1.8%) (**17**), kidney

15 https://data.ndis.gov.au/reports-and-analyses/outcomes-participants-autism-spectrum-disorder (2018)
16 https://www.abs.gov.au/websitedbs/D3310114.nsf/Home/2021+Census+review+of+topics (2020)
17 https://www.dementia.org.au/information/statistics/prevalence-data (Website)

disease (1%) (**18**) and stroke (1.7%) (**19)** are similar to that of autism, (1-1.4%), it is difficult to understand the logic behind this decision, especially as the three conditions mentioned tend to occur in mid-life, compared with autism, which usually appears within 2-3 years of birth.

[ToR e] Recommendation 4

A National Register of all people with ASD needs to be established in order to provide sufficient services for the ASD, now and in the future. This Register needs to be established in real time, as soon as people receive an official diagnosis. Their development over the years can be followed, at say, 5 year intervals, so that such requirements can be refined with their age, and take into account the impact of any medical treatments which may have an impact on their needs. These longitudinal data will provide much needed information about their social, educational, employment, and housing needs, as well as a record of their changing abilities. It will also contribute to better forecasting of NDIS funding needs. A similar project, relating only to medical incidents, is already being developed in the UK, linking the National Down Syndrome Cytogenetic Register to Hospital Episode Statistics (**20)**.

[ToR g] Discussion

Economic Cost of Failing to Provide Adequate and Appropriate Services

An estimate of the economic cost of autism in Australia was provided to the Productivity Commission by Synergies Economic

18 https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/4364.0.55.001~2017-18~Main%20Features~Kidney%20disease~65#:~:text=In%202017%2D18%2C%201.0%25,the%20prevalence%20increasing%20w th%20age. (2018)

19 https://www.aihw.gov.au/getmedia/56bb591f-6c56-4397-b928-8de6872e2cdd/aihw-aus-221-chapter-3-7.pdf.aspx#:~:text=The%20estimated%20prevalence%20of%20stroke,events%E2%80%94around%20100%20every%20day. (2018)

20 https://ijpds.org/article/view/480/404 (2018)

Consulting in 2013. (**21**) This cost-benefit framework estimated the economic benefit of early intervention focusing on five key areas – education, employment, living independence, healthcare, and quality of life. It concluded there was a Benefit Cost Ratio (BCR) of between 4.1 and 11.3. It goes on to say "an accurate estimate for the population wide benefit of early intervention is currently constrained by the absence of a robust evidence base on the long-term benefits of early intervention. Research that focuses on building this evidence base will assist in the more robust application of the framework". And "The key issue is how early intervention actually alters the lifetime trajectory for a child with autism, from when they enter school all the way through their adult life. The evidence of this is currently limited".

Overall, the report suggested annual total costs, including burden of disease, of between $8.1 billion (low prevalence) and $11.2 billion (high prevalence), with a mid-point of $9.7 billion. This equates to an average annual cost of approximately $87,000 (in 2010 dollars) per person with ASD. The most significant cost components were:

- the burden of disease (**22**)
- employment
- informal care.

Direct costs i.e. healthcare, social services and education represented about 12% of the total costs. A number of costs were not included in this study due to a lack of data, such as the cost of alternative therapies and early intervention programs; costs associated with co-morbid conditions; unemployment/underemployment; additional living support services, and the costs of family breakdown.

21 https://www.pc.gov.au/__data/assets/pdf_file/0004/215266/sub0032-ndis-costs-attachmenta.pdf (2013)
22 https://www.aihw.gov.au/reports-data/health-cond tions-disability-deaths/burden-of-disease/glossary

The quantified impact of a disease or injury on a population using the disability-adjusted life years (DALY^) measure.

^ (DALY) A measure of healthy life lost, either through premature death or living with disability due to illness or injury.

At $87,000 per person, per year, and assuming a figure of approximately 250,000 (1% of the population) the annual cost would be $21.75bn in 2010 dollars, or $26.5bn in 2020 dollars (**23**). This figure could be even higher ($29.7bn) based on 280,000 (the average of the 2018 SDAC data in Table 1: 205,200, and the ASPECT figure of 353,880).

Given the continued growth in numbers diagnosed, it is essential to reduce the abovementioned costs by providing earlier diagnosis, which will enable early intervention to be started in the crucial early years of existence. This will enable autistic people to lead more productive and fufilling lives than would otherwise be the case.

In 2019 a detailed review of the economic costs of autism was published (**24)** covering the following areas:

- medical and healthcare service costs,
- therapeutic costs,
- (special) education costs,
- costs of production loss for adults with ASD,
- costs of informal care and lost productivity for family/caregivers
- costs of accommodation, respite care, and out-of-pocket expenses.

At the individual level, obtaining a diagnosis can be a very costly exercise e.g. A full psychological evaluation can cost around $1500, then there are additional charges for the paediatrician, and maybe a

23 https://www.in2013dollars.com/australia/inflation/2010?amount=21.75
24 https://link.springer.com/article/10.1007/s10803-019-04014-z (2019)

psychiatric charge on top costs on top. (**25)** These costs may be only partially offset with Medicare, HCWA, and/or private health insurance, though it is suspected that families with autistic children are less likely to be able to afford such health insurance, due to limited parental work opportunities if the child/children is/are severely affected.

Outside the scope of the HCWA# (which applies to children up to the age of 7), there are usually many additional costs for ongoing medications, speech and/or occupational therapy which may not be covered by the NDIS, and which may be only partially covered by Medicare.

#The HCWA is being phased out 31 March 2021, and funding will then be provided by the NDIS.

[ToR g] Recommendation 5

The Productivity Commission should revisit the above exercise every five or ten years using the data to be collected through the previously proposed National Autism Register.

Social Impact

The impact of autism on families cannot be underestimated. The lives of families are irrevocably changed from the day of diagnosis. The impact on aspects of family lives include financial, emotional and mental health of parents, marital relationships, physical health of family members, sibling relationships as well as relationships with extended family, friends and neighbours.

This can be seen in the following table based on the previously quoted SDAC and Aspect figures for 2018 under [ToR b]

Table 2

25 https://outsidethesquarepsychology.com.au/attachments/Outside_the_square_ASD_DX.pdf (2016)

People with ASD	Parents	Grandparents	Siblings (estimated 1:0.8)^	Total	% Population
205,200	410,400	820,800	164,160	1,600,560	6.4
205,200	410,400	410,400#	164,160	1,190,160	4.8
353,880	707,760	1,415,520	283,104	2,760,264	11.0
353,880	707,760	707,760#	283,104	2,052,504	8.2

^ Average number of children per family (2016) (**26**)

based on only one set of grandparents being involved

The % population averages of the above data (SDAC+ Aspect), with only one set of grandparents, or both sets involved, are 6.5 and 8.7% respectively.

These data suggest that having one autistic child impacts approximately 6.5-8.7% of the Australian population, just within the immediate family. The impact on the family's ability to have normal social relationships with their local community also needs to be considered.

NB The SDAC does not offer any information on the frequency of multiplex autism families, ie those with more than one ASD child/person. Such data would be automatically collected by the proposed National Autism Register. Even allowing for such families, it is estimated autism most probably affects at least 5% of the nation, directly and indirectly, and no doubt exists in every electorate. More precisely, taking the average numbers (SDAC + Aspect) for just parents and one set of grandparents from above table, (Total 1,18160) these people represent 6.75% of the electoral role of 16,540849, as at 31 March 2020. (**27**)

While anecdotally having an autistic child gives rise to a higher chance of separation or divorce, there is very little evidence to support this effect. Two studies from the USA come to opposite

26 https://quickstats.censusdata.abs.gov.au/census_serv ces/getproduct/census/2016/quickstat/036 (2016)

27 https://www.aec.gov.au/enrolling_to_vote/enrolment_stats/ (2020)

conclusions in this regard (**28)** (**29**). There appears to have been little similar research in Australia.

Inadequate provision of appropriate services on the journey through school can result in contact with the justice system. The present justice system in Australia lacks adequate services for those on the spectrum having to negotiate their way through it, and who are incarcerated. (**30**)

A UK study (**31**) into the important role of education keeping children out of the justice system indicates major problems in this area, and no doubt a similar situation applies in Australia.

NB The very limited research carried out overseas, appears to indicate that the ASD prison population may be very small. A 2006 study carried out in the UK into offending and other law-breaking by 25 people with "high functioning" ASD/Asperger Syndrome indicated that the rate of law-breaking, including offending, was very low. The participants with a diagnosis of an ASD were significantly ($p<0.01$) less likely to report that they had engaged in illicit drug-taking; in contrast, they were significantly more likely ($p<0.05$) to report activities which could be categorised as 'criminal damage'. Moreover, they tended to have a greater history of violent behaviours. (**32**)

[ToR g] Recommendation 6

Further research should be carried out on the social impact, especially on parents and siblings, of having an autistic child through longitudinal studies.

28 https://link.springer.com/article/10.1007%2Fs10803-011-1269-y (2011)
29 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2928572/ (2010)
30 https://www.emerald.com/insight/content/doi/10.1108/IJPH-11-2017-0051/full/html (2019)

31 https://theconversation.com/too-many-children-with-autism-are-let-down-by-schools-and-end-up-in-prison-107376 (2019)
32 https://www.tandfonline.com/doi/full/10.1080/14789940600589464?src=recsys

[ToR g] Recommendation 7

Further research is needed to investigate the proportion of those in prison with autism, with the aim of providing appropriate health checks and therapies.

Suicide in adults with autism

There have been a number of reports on the link between autism and suicide, or attempted suicide in recent years.

In a UK study (**33**) a retrospective analysis of clinical survey data from adults newly diagnosed with Asperger's syndrome (a subset of autism) was carried out at a specialist diagnostic clinic in England between 2004, and 2013. 243 (66%) of 367 respondents self-reported suicidal ideation, 127 (35%) of 365 respondents self-reported plans or attempts at suicide, and 116 (31%) of 368 respondents self-reported depression.

Another recent study by Hwang et al in Australia (**34**) discusses the higher rate of mortality in people with ASD. Mortality rates for those on the autism spectrum were 2.06 times that of the general population. Concurrent ID, epilepsy, mental health conditions, and chronic physical health conditions were associated with a higher risk of death for those on the spectrum. "Nervous system and sense disorders" and "injury and poisoning" were the top-ranked causes.

A study made by Kirby et al. used existing surveillance data in the state of Utah, USA (population approx 3 million), to determine incidence of suicide among individuals with ASD over a 20-year period, and to characterize those who died. Females with ASD were over three times as likely to die from suicide as females without

33 https://pubmed.ncbi.nlm.nih.gov/26360578/ (2014)

34 https://onlinelibrary.wiley.com/doi/full/10.1002/aur.2086 (2019)

ASD. Young people with ASD were at over twice the risk of suicide than young people without ASD.

It is interesting to note that in Australia, the male:female ratio of all suicides is approx 3:1 ref ie similar to the male:female autism ratio. (**35**)

At present nobody knows how many of the approximately 3000 suicides per year in Australia are associated with autism. During the three month Covid 19 lockdown, people felt a very strong need for human to human contact. It was a temporary event, with a known end in sight, compared with the life-long loneliness and helplessness experienced by some on the spectrum.

Clearly, health is a key factor in the quality of life of individuals with autism, and it is incumbent on governments to be able to offer a health service which is capable of providing the appropriate support.

In passing, it is interesting to note that Professor Patrick McGorry was recently reported by the ABC (May 7) (**36**) as saying there is a need for a National Register of all suicides.

[ToR g] Recommendation 8

The proposed National Autism Register of children born with autism in Australia, should also be used to keep a record of attempted suicides, actual suicides and deaths from other causes. It is anticipated that it will eventually be able to help identify people at a higher risk of early mortality when combined with medical data.

Contact with the justice system could also be recorded for research purposes.

35 https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2018~Main%20Features~Intentional%20self-harm,%20key%20characteristics~3 (2018)

36 https://www.abc.net.au/news/2020-05-07/national-suicide-register-needed-coronavirus-surge/12208668 (2020)

[ToR i] Discussion

A National Autism Register

Western Australia has had an autism register for all those on the spectrum since 1999. It was created with the purpose of knowing how many children are diagnosed in WA each year and increasing knowledge of ASD. (**37)**

Some of the uses of the Autism Register include:

- Research (using its own data, and for linking interested families with current projects).
- Understanding characteristics that are shared across everyone with a diagnosis
- Help in planning for appropriate services, including health, education and disability.

The Register collects simple demographic and diagnostic information such as:

- Date of birth, gender, primary language at home
- Diagnostic criteria used
- Diagnostic methods
- IQ (verbal and non-verbal) and/or developmental abilities
- Other cognitive assessments
- Co-morbidity (the presence of other conditions)
- Language assessments
- Adaptive behaviour

It is difficult to understand why a National Autism Register has not be established with exactly the same eminently sensible objectives.

37 https://autism.telethonkids.org.au/autismregister/ (Website)

It should also be used to collect data on those born overseas who subsequently receive a diagnosis of autism.

[ToR i] Recommendation 9

The key element for establishing a National Autism Strategy is to have a National Autism Register as a single source of reliable information for use by all levels of government.

[ToR i] Recommendation 10

All those diagnosed with ASD, or suspected of ASD, should be offered Whole Genome Sequence (WGS) testing at a highly subsidised rate on Medicare, or free of charge, in order to save valuable time, which can be used to initiate the appropriate, personalised therapies and treatments. The results are to be retained on the proposed National Register and de-identifiable for research purposes. This large scale testing will bring the cost down and result in savings later in a person's life journey.

Additional elements which need to be included in the strategy are discussed and recommended under [ToR j].

[ToR j] Discussion

Background Briefing

Over the last 20 years or so, much progress has been made, primarily in the USA, in understanding the genetics and biochemistry of autism, partly as a result of the discovery of the full DNA sequence in the Human Genome Project completed in 2003, and partly because of advances in laboratory diagnostic equipment. These developments have encouraged research into the aetiology of autism (and many other so-called mental conditions). Already hundreds of millions of dollars have been expended on investigating the aetiology of autism in the USA where it is now affecting 1 in 54

children (**38**). This research will eventually lead to earlier diagnosis than is presently possible, and better treatments, resulting in better outcomes, not only for the child, but also for the family and the wider community. Consequently, there has been a worldwide gradual interest in trying to unravel the causes of autism, especially as Governments watch its rapid rise in apparent prevalence and increasing economic cost. Given its heterogeneous nature, this is a long term project, similar to the research into the aetiology of cancer, which has been the subject of many billions of dollars since the 1960s.

Australian Research

There are two broad areas of research happening in Australia at the present time. These may be considered as follows:

- Psychological
- Biological

Psychological research

Psychological research has been carried out here (and overseas) since the 1950s/60s, primarily in the area of defining autism, and its early detection - based on autism's behavioural characteristics, as mentioned in [T0R a]. This has lead to further research into improving existing therapies, such as the Early Start Denver Model (ESDM), speech, occupational and physical therapies. Other areas of interest being investigated by OTARC include sleep, anxiety and emotional regulation (**39**)

While these therapies have been used with some considerable success, they have usually been applied only after a child has received a formal diagnosis, which, as mentioned above, can take a considerable time. It is generally agreed that the earlier the

38 https://www.cdc.gov/ncbddd/autism/data.html (2020)
39 https://www.latrobe.edu.au/otarc/researchers/research-themes (Website)

diagnosis, the better chance of "normalising" a child's behaviour and general health, so this delay can affect the degree of success in implementing these interventions. (**40**)

There is also considerable research being carried out by the CRCA in the fields of education, transitions to adulthood, and employment. (See below).

As psychological research will no doubt be covered by other parties, the following section of this submission is focused only on the need for funding biological research funding.

Biological Research

Biological research is focused on understanding the genetics, physiology, and neurodevelopmental aspects which underlie the abovementioned behaviours. It is only in the last twenty years or so that this area of research has been very slowly gathering more interest, mainly in genetics, (**41**) (**42**) environmental issues, (**43**) and gestational vitamin D deficiency. (**44**) Some very limited research has been carried out in Australia to examine possible pharmaceutical treatments, such as oxytocin (**45)** and fluoxetine (**46**) by Guastella et al. and Reddihough et al. respectively.

The inherent heterogeneity of autism is such that unless specific subsets of autism are selected, testing pharmaceuticals using the gold standard of randomised, double blind, cross-over placebo trials (RDBCOPT), tend to result in failure, because of the wide range of behaviours and co-morbidities exhibited by those on the spectrum.

40 https://raisingchildren.net.au/disability/serv ces-support/services/early-intervention (Webs te)
41 https://www.nature.com/articles/s41380-018-0049-x (2018)
42 https://pubmed.ncbi.nlm.nih.gov/22965006/ (2014)
43 NHMRC grants 1117154 Hannan (2017), Ponsonby 1147970 (2018), 1170724 (2020)
44 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5385921/ (2017)
45 https://pubmed.ncbi.nlm.nih.gov/25087908/ (2014)
46 https://pubmed.ncbi.nlm.nih.gov/31638682/ (2019)

Furthermore pharmacological therapies such as methylphenidate (eg Ritalin) risperidone (eg Risperdal) and aripiprazole (eg Abilify), fluoxetine (eg Prozac) have very limited use, owing to their side effects.(**47**) (**48**)

NB Risperidone is the only FDA approved drug for treating autism related irritability.

Funding Biological Research

In the period 2005-2017, the value of research grants relating to autism basic science, mainly from the NHMRC, have amounted to only $22 million averaging $1.7 million/year.(**49**) For a condition, affecting between 205,000 and 350,000 people, costing at least $26.5-29.7 billion/year (and growing), this level of research funding appears to be patently inadequate, even allowing for the $8 million cash and $28 million in kind funding by the CRCA over the period 2013-2019. (**50**)

At the time the establishment of the CRCA was being considered, there were 115,400 people on the spectrum in 2012 (Table1) and Government was committed to funding $31M over 8 years to cover three programs. (**51**)

- Research and development - a better start through better diagnosis
- Enhanced learning and teaching
- Finding a place in society

47 https://www.autism.org/wp-content/uploads/2018/12/ParentRatings2009.pdf (2009)
48 https://www.autism.org/wp-content/uploads/2018/12/aspergers-treatment-ratings.pdf (2009)
49 https://www.researchgate.net/publication/334897881_A_Portfolio_Analysis_of_Autism_Research_Funding_in_Australia_2008-2017 (2019) Also private commun cation w th author Jacquiline den Houting
50 https://www.autismcrc.com.au/sites/default/files/2019-11/Autism%20CRC%20Annual%20Report%202018-19%20-%20Web%20version%20-%2012-11-2019.pdf (2019)
51 CRC Autism Annual Report 2013/14

To date each program has received similar cash funding 1) $8 million 2) $5.5 million 3) $6.8 million. Total $20.3 million.

By comparison, in 2015, the Federal Government provided an additional $200 million for dementia research over five years through the NHMRC National Institute for Dementia Research significantly boosting funding for Australia's dementia research sector to more than $60 million per annum (**52**). In 2018, dementia, affecting over 400,000 people, mostly elderly, was estimated to cost Australia more than $15 billion/year (c.f. above mentioned estimate $26.5-29.7 billion for autism in 2020). The following table compares the two sets of funding with regard to $/person:

Table 3

Autism					
Date	No. Diagnosed (SDAC)	Grant $m (date)	Period (years)	Grant $m/year	Approx, $/person/yr
2012	115,400				
2015	164,000	31 (2014)	8	3.875	~23.6
2018	205,200	-	-	-	18.9
2018	353,880 (est) (Ford/Aspect)	-	-	-	~11.0
Dementia					
2015	400,833 (2016 est) (**53**)	200 (2015)	5	40	99.8

As can be seen, funding for autism research lags well behind that for dementia, being five to ten times less per person diagnosed as the numbers have increased.

[ToR j] Recommendation 11

Focused research expenditure is an essential part of developing a National Autism Strategy. Given the rapidly rising economic cost

52 https://www.dementia.org.au/statistics?gclid=Cj0KCQjw3Nv3BRC8ARIsAPh8hgKWkqYyXKoGg8h1O6rbBOxQciLZ0zt9OlJZKpD3_mF_w7kvKPQ0aFAaAisnEALw_wcB (Website)

53 https://www.dementia.org.au/files/NATIONAL/documents/The-econom c-cost-of-dementia-in-Australia-2016-to-2056.pdf (2017)

and social impact of autism, there is an urgent need for a significant uplift in the level of funding for research into its causes. Using an estimated figure of 280,000 (mid-range between SDAC and Aspect data) for the autism population in 2020, and a figure of at least $108/person (based on the dementia funding of $100+8% inflation since 2015), then a five year funding plan for autism should be worth approximately $30 million/year, or $150 million over the period. This is still well below what is required to build up a sustainable level of research capacity, particularly with regard to understanding the aetiology of autism. A more appropriate figure would be at least twice this amount ie $60 million/year or $300 million over 5 years, given the relative economic cost to society, with preferably 75% to go towards such research.

NB BioAutism Ltd knows that Australia has the scientists to do the research, and has been in contact with many since its foundation eight years ago, but they are frustrated by the lack of funding by the NHMRC, and so drift into other areas of research where they are more likely to win grants. They need to be encouraged to stay in the autism field, secure in the knowledge there will be sustainable funding for the next 5-10 years.

Which research should be funded?

The National Autism Strategy needs to concentrate funding in the following three key areas of biological research for improved, earlier diagnosis and better treatments and health outcomes.

1. BioBanking

In 2013 the CRCA established an autism biobank. (**54**)

"The establishment of this biobank is a valuable international resource incorporating detailed clinical and biological information that will help accelerate the pace of ASD discovery research.

54 https://www.autismcrc.com.au/biobank (Website)

Recruitment into this study has also supported the feasibility of large-scale biological sample collection in children diagnosed with ASD with comprehensive phenotyping across a wide range of ages, intellectual abilities, and levels of adaptive functioning. This biological and clinical resource will be open to data access requests from national and international researchers to support future discovery research that will benefit the autistic community.

The primary group of participants were children with a confirmed diagnosis of ASD, aged between 2 and 17 years, recruited through four sites in Australia. No exclusion criteria regarding language level, cognitive ability, or co-morbid conditions were applied to ensure a representative cohort was recruited. Both biological parents and siblings were invited to participate, along with children without a diagnosis of ASD, and children who had been queried for an ASD diagnosis but did not meet diagnostic criteria." (**55**)

This biobank has already collected a range of biological samples (some 2,900) of blood, urine, stool and hair, mainly from primary school aged children, as well as blood samples from their parents.

Brief details of how these samples may be used to advance the early diagnosis and treatment of autism can be found in Appendices A, B and C.

[ToR j] Recommendation 12

The CRC Autism Biobank should be given an expanded role. All those formally diagnosed with ASD should be registered on the above proposed National Autism Register and be offered the opportunity to provide samples of blood, urine, stool, and hair to it, so that a full analysis of an individual's biological status can be obtained as early as possible, and appropriate treatment/interventions recommended.

55 https://pubmed.ncbi.nlm.nih.gov/30149807/ (2018)

The de-identified specimens should also be retained for further examination by researchers looking for other potential biomarkers.

[ToR j] Recommendation 13

As a rider to Recommendation 12, the same services should be offered to all those who have been diagnosed with Prader-Willi syndrome, Angelman Syndrome, and Williams Syndrome. The prevalence of these (so-called orphan) conditions is so much lower than that for autism being 1/15,000 (**56**), 1/15,000-20,000 (**57**), 1/10,000 (**58)** respectively and all patients, parents, researchers would benefit from this proposal.

[ToR j] Recommendation 14

The heterogeneous nature of autism indicates that large quantities of specimens are required in order to uncover data which is statistically significant. It is therefore recommended that the supply of these test specimens, their analysis, and discussion of the results with the parents or individuals, should be free of charge, or generously covered by Medicare to encourage participation, as most parents with children on the spectrum have very limited income. Any follow-up pathology considered necessary over, say, the following five years should also be included in such a scheme.

2. Producing a biological based autism matrix for early detection

In 2019, the CRCA produced a paper "Characterizing the Interplay Between Autism Spectrum Disorder and Co-morbid Medical Conditions: An Integrative Review" (**59)**

56 https://www.racgp.org.au/afp/2013/januaryfebruary/prader-willi-syndrome/#:~:text=At%20least%20261%20cases%20have,Willi%20Syndrome%20Association%20of%20Australia. (2013)
57 https://www.angelmansyndrome.org/ (Website)
58 https://www.wsfsgv c.org.au/about-williams-syndrome/#:~:text=About%20Williams%20Syndrome%20%7C%20Williams%20Syndrome,Support%20Group%20(Victoria)%20Inc.&text=Williams%20Syndrome%20(or%20Williams%2DBeuren,approximately%201%20in%2010000%20Australians. (Webs te)
59 https://www.frontiersin.org/articles/10.3389/fpsyt.2018.00751/full

It suggested "Future research should aim to systematically examine the interactions between these physiological systems, rather than considering these in isolation, using robust and sensitive biomarkers across an individual's development. A consideration of the overlap between medical conditions and ASD may aid in defining biological subtypes within ASD and in the development of specific targeted interventions". This concept should be taken further by devising an Autism Matrix as follows:

Most autism research to date has concentrated on trying to find biomarkers in which researchers happen to have specialist knowledge. e.g. a genetic researcher will look for gene variants or epigenetic markers, a blood researcher may look for iron or zinc levels, a neuroscientist may look at certain parts of the brain such as brain stem cells, an immunologist may be interested in looking at cytokine levels etc. None of this research is ever considered with reference to particular autism subgroups based on behavioural characteristics (phenotypes).

These data need to be analysed and synthesized in matrices using computational and statistical analysis such that they can produce a program based on say, 5-10 different types of biomarkers which distinguish them from average (referent) values for non-autistic children and adults of different sex and ages. The objective of the program is to produce an accurate forecast of whether a child is likely to be autistic as soon as possible after birth, so that early intervention can be started as soon as possible.

The production of such a matrix will require a large team of highly qualified data analysts, with experience in a wide range of disciplines, such as that lead by Professors Visscher, Wray, and Yang at the Queensland Brain Institute.

3. General Practitioners and Autism

In Australia, many parents are aware of multiple co-morbidities in their ASD children, yet there appears to be have been little, if any, formal research in this area.

Unpublished Australian data from a survey of over 200 parents (**9**) suggests that food sensitivity and fussy eating are common (48% and 71% respectively) in those with ASD, as are diarrhoea and constipation (approx 43% and 37% respectively).

Other findings indicated that

- 64% had poor sleep patterns
- 61% had gross motor delay
- 46% displayed hyperactivity
- 34% had allergies
- 28% had eczema.

There are a number of General Practitioners (GPs) in Australia who have acquired considerable clinical knowledge of hundreds of children and adults on the spectrum, and who already have in their data bases substantial amounts of detailed analyses of specimens such as blood, urine, stool, and hair. Unfortunately this information is not available to researchers who could develop statistical analyses, (as proposed in Project 2 above) which would enable earlier diagnosis than it possible at the present time using the new Guidelines. This valuable resource should not be allowed to go to waste.

[ToR j] Recommendation 15

It is recommended that a task force be established to find a way of bringing the relevant GPs and researchers together for the common good. As in Project 2 above, the application of computational analysis/artificial intelligence to analyse and synthesize all these

data into an Autism Matrix will help speed up the discovery of the causes of autism, and thus enable researchers to suggest the most appropriate treatments and therapies to various sub-sets of autism.

APPENDIX A – GENETIC TESTING

Blood

Blood is a major source of information about the genes (see below), epigenetics, the immune system, antioxidant levels (eg glutathione), essential elements (eg iron, zinc, cobalt, sulphur) and toxic elements, (e.g. arsenic, cadmium, lead, mercury). The heel prick blood test (also known as the Guthrie test), taken as soon as a baby is born, has already been used to investigate potential biomarkers for autism. (**60**)

Genetics

Autism has a high heritability component, though there continues to be some debate as to how important it is. Recent studies show concordance for autism in monozygotic (MZ) twin pairs is typically at least double that in dizygotic (DZ) twin pairs, resulting in high heritability estimates (60%-90%) (**61**) (**62**)

Fragile X syndrome (FXS) is the most common single gene cause of autism, responsible for 2% to 6% of all cases of autism, which is generally accepted as having polygenetic origins. Knowledge of the molecular mechanisms involved in its pathogenesis has facilitated the development of targeted treatments, with the potential to reverse or dramatically improve both behavioural and cognitive deficits. Professor Randi Hagerman, (**63**) an internationally recognized researcher in the field of genetics of ASD, UC Davis,

60 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981185/ (2013)
61 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4724890/ (2015)
62 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5818813/#:~:text=Studies%20have%20found%20that%20autism,)%20to%20be%20about%2090%25. (2017)
63 https://health.ucdavis.edu/team/children/598/randi-hagerman-pediatric-child-development--behavior-autism-neurodevelopmental-disorders-sacramento (Website)

California has clinically recommended that all individuals diagnosed with autism should have the FX DNA test (both PCR and Southern blot) when the aetiology of their autism is not known. (**64**)

Fragile X is just one of a number of genetic variants associated with autism. In fact approximately 1000 genes have been found to date that may have some bearing on its incidence. Some are also associated with Angelman's syndrome, Prader-Willi syndrome, Williams syndrome, and many other conditions.

Further information about autism genetics can be found in a paper by G Bradley Schaefer "Clinical Genetic Aspects of ASD Spectrum Disorders" (**65**) and research by Scheffer et al (Melbourne) "Tracing Autism Traits in Large Multiplex Families to Identify Endophenotypes of the 2 Broader Autism Phenotype" (**66**)

Epigenetics

Epigenetics involves genetic control by factors other than an individual's DNA sequence. Epigenetic changes, which are involved in many normal cellular processes can switch genes on or off, and determine which proteins are transcribed.

In 2015 Melbourne based researchers Loke, Hannan, and Craig reviewed the potential role of epigenetics in the aetiology of autism, the details of which are outside the scope of this document. (**67**) In 2019 a pilot study in Japan by Kimura et al claimed to have found an epigenetic biomarker for adult "high-functioning" ASD (**68**).

64 https://molecularautism.biomedcentral.com/articles/10.1186/2040-2392-1-12 (2010)
65 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4783914/ (2016)
66 https://www.biorxiv.org/content/10.1101/659722v1.full.pdf (2019)
67 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4443738/ (2015)
68 https://www.nature.com/articles/s41598-019-50250-9 (2019)

APPENDIX B - THE BENEFITS OF DNA TESTING

Since 2010 there has been a massive reduction in the cost of DNA testing. In accordance with Prof Hagerman recommendation in Appendix A , all Australians suspected of having, or diagnosed with ASD should be checked for Fragile X, and have a whole genome sequence (WGS) carried out to determine what underlying genetic factors may be contributing to their condition. Interestingly, a bill, HR 4144, "Ending the Diagnostic Odyssey Act" was introduced in the USA in August 2019. (**69**) The bill's aims include providing a more timely diagnosis for children who may have an underlying genetic disease, decreasing costs associated with later diagnoses that result in avoidable testing and treatment, and providing psychological benefits from peace of mind. A paper in JAMA Paediatrics dated 29 June 2020 discusses some of the pros and cons of WGS. (**70**)

In 2017 the ABC reported that a WGS cost A$6,400, which is not covered by Medicare (**71**) and substantially higher than the US$1,000 (approximately A$1,500) offered by Veritas Genetics (USA) in 2016 (**72**).

The ABC report went on to say that the Australian Genomic Healthcare Alliance, is considering a national approach for a proposal to fund genomic testing through Medicare.

It is anticipated that such a test regime will be more than offset by the savings in other expenses ie special education, health care,

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69 https://www.congress.gov/bill/116th-congress/house-bill/4144/text?format=txt (2019)

70 https://jamanetwork.com/journals/jamapediatrics/fullarticle/2767278?guestAccessKey=eb8d90fb-bfeb-44d7-94f2-1266d7894ecc&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jamapediatrics&utm_content=olf&utm_term=062920 (2020)

71 medicare/8632238#:~:text=Testing%20will%20cost%20%246%2C400%20with,treatment%20will%20not%20be%20investigated (2017)

72 https://www.cnbc.com/2019/07/01/for-600-veritas-genetics-sequences-6point4-bill on-letters-of-your-dna.html (2019)

specialised housing, not to mention valuable time wasted as a result of treatments which have not been personalised, and therefore likely to have a lower success rate.

Another benefit of such testing is that it will be a valuable resource for researchers to investigate which genetic variations may contribute to which co-morbidities and behaviours displayed by people with ASD. Such analysis will be of benefit to other researchers looking for the shared origins of ASD, schizophrenia, bipolar disorder, ADHD, major depressive disorder (**73**) and many other conditions associated with autism.

73 https://www.thelancet.com/journals/lancet/art cle/PIIS0140-6736(12)62129-1/fulltext (2013)

APPENDIX C - COMPREHENSIVE PATHOLOGY TESTING

Urine, stool, and hair samples enable valuable information to be obtained. As they are all derived from food ingestion (we are what we eat), they provide an indication of how a person's internal microbiome reacts, thus helping to build an holistic picture of the individual's pathology.

Urine

Urine contains soluble waste products and is a useful source of information about the essential and toxic elements listed above, as well as organic acids, carbohydrate metabolism, energy production (as an indicator of mitochondrial function), indicators of bacterial, yeast, or fungal origin, among others.

Stool

Stool contains a lot of information about intestinal health markers, bacteriology, parasitology, digestion, and inflammation.

Over the last ten years there has been a greater realisation that the gut microbiome has a major influence on both physical and mental health, including the immune system. A study carried out in Arizona University into the effects of faecal matter transfer (FMT) in 18 ASD children resulted in a 50% reduction in autistic traits after two years. (**74**) The authors recommended a double-blind, placebo-controlled trial in the future.

74 https://www.nature.com/articles/s41598-019-42183-0 (2019)

Hair

Essential elements, eg iron, zinc, sulphur; and toxic elements, eg arsenic, cadmium, lead, mercury are absorbed from food and the environment and all found in various parts of the body. Hair is a useful source of information about their absorption over a period of several months (depending on how long the hair has grown) and so it can be a useful biomarker when used in conjunction with other tests.