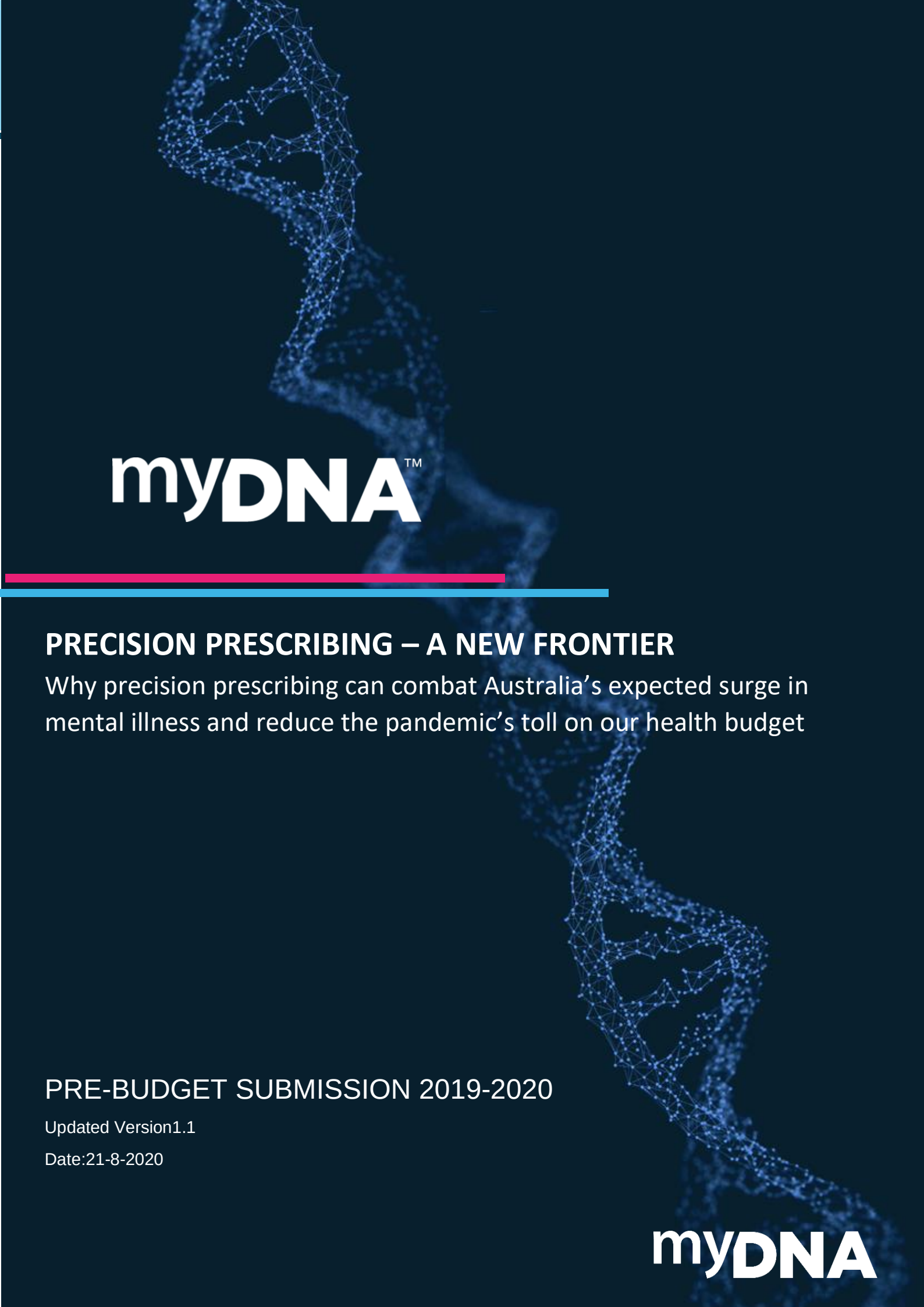


PRECISION PRESCRIBING – A NEW FRONTIER

Why precision prescribing can combat Australia's expected surge in mental illness and reduce the pandemic's toll on our health budget

PRE-BUDGET SUBMISSION 2019-2020

Updated Version1.1

Date:21-8-2020

CONTENTS

1 FOREWORD

The role of precision prescribing to combat our shocking mental health crisis

Social isolation, familial and community disconnection, shock job loss and health fears creates the perfect storm for a person already vulnerable to mental illness to start to spiral.

New modelling by the Brain and Mind Centre confirms our worst fears. This terrible pandemic may see more deaths by suicide than by the virus itself. Our suicide rate is likely to surge by more than 25% and even higher still for younger Australians.

We believe this submission will add a new, and vitally important, dimension (and solution) in the fight against such a shocking tidal wave of suicide and depression.

Mental illness is a condition that does not care about who it hits or when or what the socio-economic circumstances are for that person but for young people, the impact on them, their families and their future, can be particularly devastating.

MyDNA has developed a clear and research-driven plan to protect our most vulnerable from self-harm at a time when they are already facing unimaginable emotional and financial stress and uncertainty.

It is a sad fact that even the most experienced specialist or GP must employ a level of guess work when recommending which anti-depressant treatment will work the first time. Studies show, 50% of the time, it will take three or more attempts of prescribing yet another medicine before the right treatment finally settles for that patient. This is because, when it comes to mental health, our genes run interference with how we react to medication.

For someone struggling with severe mental illness, this time to get it right can stretch to months and the consequences of inaccurate prescribing, and potentially poor compliance, can be devastating for them and their families, and for those forced in isolation or who have lost their job; the compounding harm can quickly multiply.

But we know we have a solution. As leading geneticists, pharmacologists and pharmacists, we have researched and developed a new way of determining the best antidepressant treatment for a patient – any patient - suffering any type of mental health disorder.

Now, we have a genetic test that can reveal how an individual process a medication. Known as Pharmacogenomics, this test is converted into vital knowledge for a doctor, who can now be absolutely assured that the medication they prescribe is personalised and accurate – the first time.

I have had many years' experience providing genetic counselling and applying genetic tests to improve health. I started to develop pharmacogenomic testing as a very

practical way to apply genetics to health and have been providing pharmacogenomics as a pathology service for the last 10 years.

This type of test is now used by Australia's leading pathology services providing such tests for doctors and support services in pharmacies across the country. We have built the network to educate GPs, pharmacists and the public. The challenge now is in application. Sadly, it is often not used in the current treatment of mental health disorders.

Amid fears that pandemic could spawn a 'generational mental health crisis', pharmacogenomics and with it, precision prescribing, have an important role to play in protecting those Australians struggling with mental health.

Never before is this needed than now.

Precision prescribing is not in the distant future. It is available now and we believe there is considerable compelling evidence to demonstrate that it must be at the forefront of a GP's prescribing decision making when it comes to treating mental illness.

We know the return on investment back to the patient, their family, their community and the nation at large is incredibly significant. For every dollar spent by the government on subsidising these tests for people with mental health problems, we know the savings are 120 to 1.

Numerous peer-reviewed studies and trials show that genetic testing can reduce the suicide rate as well as expediating a patient's recovery, through the accurate choice of medication.

In particular, pharmacogenomic testing has been shown to deliver significant health budget savings by keeping patients out of emergency departments and public hospital beds and by reducing medicine wastage, as patients abandon wrongly prescribed treatments.

This is a large-scale public health initiative that will have a profound and immediate impact. It is strongly aligned with the Minister for Health's mental health and preventive health agenda. Indeed, we believe myDNA can help mitigate the pending mental health crisis whilst providing much needed relief, by more than $1 billion a year, to an overwhelmed health budget.

We commit this proposal for your urgent consideration and we and look forward to continuing to help support the recovery of all Australians struggling with mental health illnesses.

Yours Sincerely

Leslie Sheffield MB.BS, MSc, FRACP, APP
Consultant Clinical Geneticist
Medical Director and Founder of MyDNA Life Australia

2 EXECUTIVE SUMMARY

As the number of Australians, struggling with their mental health, is expected to surge to unprecedented levels, it is imperative that we treat depression more effectively.

There is a simple step we can now offer these patients to help them onto a speedier recovery to good health. We can personalise their medications to accurately match their genes.

This evidence-based innovation is called a pharmacogenomic test. It effectively removes the blindfold from the doctor.

Currently many doctors choose a medication with the hope that the patient will have the average response, but individuals respond differently. Knowing an individual's gene-medication response would reduce the amount and length of treatment required. Pharmacogenomic testing has been shown to be clinically effective in randomized studies and very cost effective.

> **If 30% of Australians on Jobseeker, with depression, were offered a pharmacogenomic test, it will deliver cost benefit savings of $1 billion per annum in healthcare costs and productivity.**

Major Depressive Disorder is a common cause of illness in adults and young Australians. Depression not only causes ill health and increases the suicide rate, it has major negative effects on participation in the work force and education. It does not just affect the sufferer, but also their family and friends.

Depression is mostly treated with antidepressant drugs, but less than 50% of the time the first drug tried does not work, or worse, produces serious side effects that may stop the person continuing the medications whilst costing the community increased hospitalisation.

Sometimes it precipitates suicidal ideation or the young person committing suicide. Pharmacogenomic testing helps the doctor choose appropriate medication for an individual thus minimising adverse effects. The individual benefits as does the community.

There are four major pathology services offering pharmacogenomic testing. The proposed $10.5 million expenditure would reduce suffering, it would reduce the suicide rate and speed up the return of the individual to full productivity at the same time as currently saving $1 billion dollars for the Government per year.

For this proposal we ask the government to purchase 85,000 DNA test kits and make them available to people on jobseeker who need them.

3 THE PROBLEM

Even before the COVID-19 pandemic and the predicted surge in mental illness and suicides; too many Australians (one in five) have been struggling with their mental health.

Now, the pandemic is predicted to trigger an additional 1500 suicide-related deaths every year over the next five years, resulting in a 'generational mental health crisis'

1 POOR COMPLIANCE

Poor compliance to medications results in suicide, a common cause of death.

Unfortunately, standard antidepressant therapy does not provide recovery in a significant number of people.

A recently published large trial (N = 3,671), conducted across 41 sites over 7 years, found that only 40% of participants with major depressive disorder achieved recovery after acute first line antidepressant treatment.(1) 20% of participants had not recovered after two years of treatment, and at least 10% of participants were found to be unresponsive to treatment despite multiple treatments over time.(2)

Current patient response to antidepressant treatments are not predictable and often it is the prescriber's experience and medicine side effect profiles that govern the choice of antidepressant given to the patient. SSRIs are the 1st line of treatment for depression and have shown a response rate of only 60-70%. Tricyclic Antidepressants on the other hand have a response rate of 50-80% only.

There has also been an annual average increase of 6.1% in the estimated number of mental health-related GP encounters recorded since 2010-11.

It was found that depression was the most common mental health condition managed by GPs which equated to 32.8% of mental health related GP visits.

Compounding the problem that the medications being prescribed are ineffective, is that the most common management of mental health-related problems was for the GP to prescribe, supply or recommend medication 61.6% of the time as first line treatment.(3-8) Pharmacogenomic testing has been shown in clinical trials in psychiatry to reduce unnecessary drug-related adverse reactions.(9)

2 COST OF INEFFECTIVE ANTIDEPRESSANTS

Improving the quality and safety use of antidepressant treatment will positively lead to better utilisation of health funds.

Before the pandemic hit; it was estimated that approximately $458 million is spent each year on antidepressants.(10) This amount is expected to surge along with the increased number of Australians who will struggle with their mental health or have their mental illness further exacerbated.

The spiralling costs of antidepressants can be reduced if we can ensure every patient can have a simple pharmacogenomic test to eliminate the repeated trials of different antidepressants.

Research shows it takes mostly three attempts to get the medication right. In this time, patients' mental health can spiral.

Taxpayers funds are wasted on discarded medication, more GP and specialist visits, potential hospitalisation and the impacts on productivity.

The further pressures of self-isolation, physical distancing, economic and health worries will intensify this negative impact on the health budget.

It is in the interests of the patient and the taxpayers to ensure precision prescribing is used to help health professionals choose the right antidepressant for the right patient and avoiding the devastating trial and error approach.

4 THE SOLUTION

Pharmacogenomic testing has the benefit of providing guidance on the prescription of medicines throughout the patient's lifetime.

The past decade has seen scientific advances in the area of pharmacogenomics (PGx) providing clinicians with the ability to match drugs to individual patients based on their genetic profile. PGx is the study of genetic variations that influence how an individual respond to drugs.

In depression, not only does pharmacogenomics help select a particular antidepressant for a patient but also help detect potential adverse effects and consequently reduce the risk of premature discontinuation of antidepressants due to reduced compliance.

There are many practitioners that believe pharmacogenomics can provide guidance to optimise the antidepressant treatment for individual patients. (4-9) Pharmacogenomic testing has been shown in clinical trials in psychiatry to reduce unnecessary drug-related adverse reactions.(10)

Starting in October 2019, **UnitedHealthcare, the largest private health insurer in the USA** announced the cover of PGx tests designed to predict a patient's response to mental health medications. UnitedHealthcare has covered the use of PGx testing to guide therapy decisions for antidepressants as a proven and medically necessary test. **The Royal College of Pathologists Australia (RCPA)** have also recently published a position statement support the use of PGx testing in several clinical areas including depression.

> **Our vision is that every Australian should have access to subsidised PGx testing when prescribed an antidepressant in line with healthcare trends in the USA.**
>
> **In an effort to improve the treatment and management of depression as well as reduce the suicide rate in young Australian adults we put forward our 3-point plan below which describes the strategy to overcome existing barriers and ensure widespread adoption of PGx testing.**

1 Impact - Fast-track finding the right medication and double the success rate of antidepressant therapy

We must counter the expected surge in our suicide rate and human and economic toll by this mental health crisis. To do this; medication adherence needs to be optimised.

PGx has been recently shown by Bousman et al who reviewed 5 randomised controlled trials (RCTs) evaluating the benefit of PGx guided antidepressant therapy vs treatment as usual concluded that patients who received PGx guided therapy were 1.7 more times likely to achieve symptom remission.

In addition, approximately 50% of patients do not respond to their first line antidepressant therapy and therefore our goal is to double the success rate amongst young depressed Australians receiving antidepressant therapy.

In summary, PGx testing has far reaching impacts:

- Saving lives
- Improve depression treatment outcomes via more targeted approach to prescribing of medications
- Enormous economic benefit by saving the precious health dollar

2 Reach - National access via traditional pathology tests at a subsidised cost.

Over the last 10 years myDNA has invested over $20M through private and government grants to establish the foundation in Australia to deliver a national program through general practice, pharmacy and private pathology.

Testing is now available via myDNA, as well as the 3 largest pathology providers in Australia: Healius, Australian Clinical Labs and Sonic pathology.

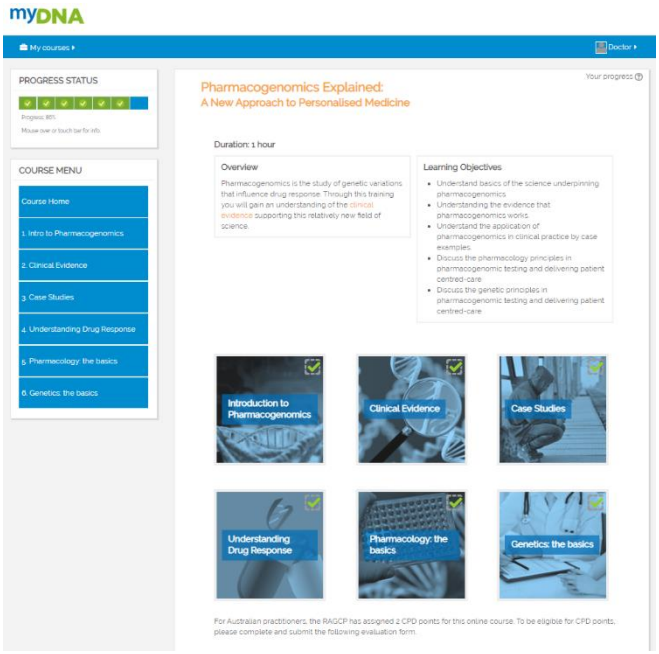
In an effort to make this testing available to all young Australians, in particular, we need to reduce the cost barrier to improve access to this life saving test.

myDNA is proposing for the government to subsidise the cost of this test as per cost section below.

3 Education - Upskill healthcare practitioners

Education and upskilling our healthcare providers on the clinical utility of PGx testing is key to how we make PGx available to all young people Australians. myDNA and Healius have developed an RACGP approved online education module to educate GPs and other healthcare providers on the use of pharmacogenomics in the clinic.

These modules provide an overview of the science that underpins PGx, provides case studies to illustrate the clinical application in mental health and overview of the current evidence as described in the international PGx clinical guidelines (CPIC and DPWG).



RACGP

Our solution would be to make this type of education available to all healthcare practitioners nationally through a traditional government program.

The following is a case study showcasing the power of precision prescribing and the life changing impact on a young boy's life.

Web address: https://youtu.be/klJs9dmlFyY

5

FINANCIALS

Cost savings of $1B per annum could be realised through improved treatment of depression in young Australians.

Over the last 10 years, myDNA has invested over $20M through private and government grants to establish the foundation in Australia to deliver a national program through general practice, pharmacy and private pathology.

As part of our submission, we are asking for a $10.5M per annum to fund the subsidy of PGx testing targeted towards Australians suffering from depression who have lost their jobs. **The funding will be used to realise cost savings of $1B per annum** through improved treatment of depression in young Australians.

There are several US-based cost benefit studies for the use of pharmacogenomic testing in depression. Using figures from a recent study by Benitez et al(11) and adjusting for the Australian solution described in the below table, **a net benefit of $12,000 per patient** per annum could be realised. These savings were derived from avoiding hospitalisations, medication wastage, and other medical complications.

More than1.3 million Australians are on jobseeker with expectations this could rise to 1.7million in September of which 1 in 5 (or 340,000) could experience depression. It would be reasonable to assume that about 25% or 85,000 of these young people each year will be referred for a PGx test to guide their antidepressant therapy by their treating doctor.

For this proposal we ask the government to purchase 85,000 DNA test kits and make them available to people on jobseeker who need them.

The cost involved in subsidising the test is broken into 3 areas:

1. **Cost of the test**
   Currently patients pay out of pocket AU$197 for a PGx test in Australia compared to approximately US$2000 for a PGx test in the US. Our proposal here in Australia is for the government to subsidise the test by only having to pay the at cost amount of AU$100 which is 50% less than what the patient is currently paying.

2. **Cost of education**
   The cost allocated is to expand on the current myDNA education program and develop additional modules to ensure a successful rollout of PGx testing. It also covers the cost to ensure accessibility and promotion of the online educating system.

3. **Cost of protocols**
   There will be additional costs associated with establishing the governance and protocols around this service and to ensure access to adequate skills to support

the program such as clinical geneticists, clinical pharmacologists and pharmacists.

Total costs:

The key components for funding this proposal include:

ITEM	ITEM COST
Pathology testing (PGx multigene test)	
85,000 tests @ $100 per test	$8.5M
Education of healthcare providers	
Provision of online education and educational sessions nationally	$1.4M
Administration	
Program support and delivery	$0.6M
Total Cost	$10.5M

Net savings to government:

The total cost saving that could be realised in this proposal is $1 Billion per annum.

ITEM	TOTAL
Total cost	$10.5M
Cost savings (85,000 tests @ $12,000 saving per patient)	$1B
Net savings to government	**$1 Billion per annum**

6 SUMMARY OF BENEFITS

a. BENEFIT TO PATIENTS AND FAMILIES.

Pharmacogenomics can improve the health of patients by matching the right medication and dose to the right patient.

It helps do this ahead of time so that when a person is prescribed a medication, their doctor is informed of which medication will work best for that person.

There are many benefits to the patient that can be realised here: safer medications, improved treatment response, reduced risk of side effects and toxicity, reduce time away from work due to illness and reduced hospitalisation rates due to ineffective treatment or adverse drug reactions.

Families can also benefit from having family members that are better cared for and treated. In the area of mental health, patients are often having to trial a number of antidepressants before they respond to their pharmacological treatment.

b. BENEFIT TO TAXPAYERS/GOVERNMENT

This proposal would result in considerable savings to the government and the community by reducing the amount of trial and error in the treatment of depression in young Australians. It would reduce the suicide rate and prevent considerable suffering.

Pharmacogenomics is a relatively new way of testing how the body processes specific drugs and has recently been shown to be clinically effective in treating

depression in 7 randomized controlled trials and in several cost benefit studies and there are several more in progress.(5, 12-17)

For example:

i) Greden et al(17) showed there was an improvement in response and more remission of depression in the group that had treatment guided by pharmacogenomics than those randomised to treatment as usual.

ii) Bousman et al(18) reviewed 5 of these studies in a meta-analysis and concluded that patients who had pharmacogenomic guided therapy were 1.7 more times likely to achieve symptom remission than individuals who had treatment without pharmacogenomic testing.

Several of these randomized controlled trials assessed cost benefit.

i) One US based study was of a home health agency and showed that the use of pharmacogenomics reduced the rate of re-admissions to hospital by 52% and also reduced the rate of emergency department visits by 42%. Costing this using Medicare average costs of readmission resulted in a savings of USD$4382 per patient over 60 days.(11)

ii) Also, in the USA, Maciel et al(19) modelled the effect of pharmacogenomic testing for patients treated with depression. They found a savings of USD$3962 annually per patient for pharmacogenomic- guided medication management.

iii) Groessl et al(20) modelled the results of the randomised controlled trail of Bradley(16) and found for moderate to severe major depressive disorder pharmacogenetic-guided treatment increased the quality adjusted life years(QALY) and resulted in a saving of US$2918 in direct medical costs and $1690 in indirect costs 10. This savings is considerably more as the test cost was assumed to be US$2000 and not AUS$99.

iv) There are several more cost effectiveness studies demonstrating the cost-effectiveness of the treatment of depression using pharmacogenomics.(21-23)

7

ABOUT myDNA

MyDNA Life is an Australian company at the forefront of providing simple DNA testing and subsequent analysis of patient's test results ("personalized medicine").

MyDNA is the Australian Leader in applying pharmacogenomic tests in clinical practice. It does this through its own laboratory (Genseq Labs) and provides the pathology interpretation to 2 other pathology companies. The testing enables doctors and patients in Hospitals and Private Medical Practice to greatly improve their quality of life by the use of a personally tailored medication program based on their unique DNA profile.

What is pharmacogenomics?

Various factors have been traditionally considered by doctors for determining dose and drug type, such as age, body size, liver and kidney function and the taking of other drugs.

Now we know that an individual's genetic make-up can also affect how the body processes drugs. The most evidence for this is specifically for gene changes (variants) that influence drug metabolism. The study of variations of DNA in genes and how these changes affect drug response is called pharmacogenomics. Many drugs are processed (metabolised) from one chemical entity to another and the speed and ability to do this can affect the drug response. Testing these variants has become the mainstay of pharmacogenomics and represents an important additional factor, other than the traditional ones described above, that reflects individual variation in drug response.

The literature has been growing rapidly in this field over the last 10 years. Recently a high-profile review was published that summarised international best practice recommendations for the application of pharmacogenomics in everyday drug use. This review concluded there were 20 genes and 80 medications that had actionable recommendations in the literature for different genetic variation results.(24)

myDNA Life seeks to provide the link between genetic results and these recommendations and is making this available to be used in practice as an important new way to understand individual variation in drug response and the occurrence of adverse effects.

7 REFERENCES

1. Rush AJ. STAR*D: what have we learned? Am J Psychiatry. 2007;164(2):201-4.
2. Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiatry. 2006;163(11):1905-17.
3. Binder EB, Holsboer F. Pharmacogenomics and antidepressant drugs. Ann Med. 2006;38(2):82-94.
4. Horstmann S, Binder EB. Pharmacogenomics of antidepressant drugs. Pharmacol Ther. 2009;124(1):57-73.
5. Singh AB. Improved Antidepressant Remission in Major Depression via a Pharmacokinetic Pathway Polygene Pharmacogenetic Report. Clin Psychopharmacol Neurosci. 2015;13(2):150-6.
6. Perlis RH. Pharmacogenomic testing and personalized treatment of depression. Clin Chem. 2014;60(1):53-9.
7. Licinio J, Wong ML. Pharmacogenomics of antidepressant treatment effects. Dialogues Clin Neurosci. 2011;13(1):63-71.
8. Fabbri C, Serretti A. Pharmacogenetics of major depressive disorder: top genes and pathways toward clinical applications. Curr Psychiatry Rep. 2015;17(7):50.
9. Fagerness J, Fonseca E, Hess GP, Scott R, Gardner KR, Koffler M, et al. Pharmacogenetic-guided psychiatric intervention associated with increased adherence and cost savings. Am J Manag Care. 2014;20(5):e146-56.
10. Deloitte Economics - Australian Centre for Health Research. Improving the Quality Use of Medicines in Australia. Realising the Potential of Pharmacogenomics 2008. [cited 2019 Dec 20]. http://www.globalaccesspartners.org/Improving_the_Quality_Use_of_Medicines_in_Australia.pdf].
11. Benitez j CC, Scott D. Use of combinatoriaL pharmacogenomics guidance in treating psychiatric disorders; financial impact on a health plan 2018.pdf. Per Med. 2018;15(6):481-94.
12. Winner JG, Carhart JM, Altar CA, Allen JD, Dechairo BM. A prospective, randomized, double-blind study assessing the clinical impact of integrated pharmacogenomic testing for major depressive disorder. Discov Med. 2013;16(89):219-27.
13. Perez V, Salavert A, Espadaler J, Tuson M, Saiz-Ruiz J, Saez-Navarro C, et al. Efficacy of prospective pharmacogenetic testing in the treatment of major depressive disorder: results of a randomized, double-blind clinical trial. BMC Psychiatry. 2017;17(1):250.
14. Elliott LS, Henderson JC, Neradilek MB, Moyer NA, Ashcraft KC, Thirumaran RK. Clinical impact of pharmacogenetic profiling with a clinical decision support tool in polypharmacy home health patients: A prospective pilot randomized controlled trial. PLoS One. 2017;12(2):e0170905.
15. Saldivar JS, Taylor D, Sugarman EA, Cullors A, Garces JA, Oades K, et al. Initial assessment of the benefits of implementing pharmacogenetics into the medical management of patients in a long-term care facility. Pharmgenomics Pers Med. 2016;9:1-6.
16. Bradley P, Shiekh M, Mehra V, Vrbicky K, Layle S, Olson MC, et al. Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. J Psychiatr Res. 2017;96:100-7.
17. Greden JF, Parikh SV, Rothschild AJ, Thase ME, Dunlop BW, DeBattista C, et al. Impact of pharmacogenomics on clinical outcomes in major depressive disorder in the GUIDED trial: A large, patient- and rater-blinded, randomized, controlled study. J Psychiatr Res. 2019;111:59-67.

18. Bousman CA, Arandjelovic K, Mancuso SG, Eyre HA, Dunlop BW. Pharmacogenetic tests and depressive symptom remission: a meta-analysis of randomized controlled trials. Pharmacogenomics. 2018;20(1):37-47.
19. Maciel A, Cullors A, Lukowiak AA, Garces J. Estimating cost savings of pharmacogenetic testing for depression in real-world clinical settings. Neuropsychiatr Dis Treat. 2018;14:225-30.
20. EJ G, Tally SR, Hillery N, Maciel A, Garces J. Cost effectiveness of a pharmacogenetic test to guide treatment for major Depressive disorder. Journal of managed care and specialty pharmacy. 2018;24(8):726.
21. Perlis RH, Patrick A, Smoller JW, Wang PS. When is pharmacogenetic testing for antidepressant response ready for the clinic? A cost-effectiveness analysis based on data from the STAR*D study. Neuropsychopharmacology. 2009;34(10):2227-36.
22. Sugarman EA, Cullors A, Centeno J, Taylor D. Contribution of Pharmacogenetic Testing to Modeled Medication Change Recommendations in a Long-Term Care Population with Polypharmacy. Drugs Aging. 2016;33(12):929-36.
23. Winner J, Allen JD, Altar CA, Spahic-Mihajlovic A. Psychiatric pharmacogenomics predicts health resource utilization of outpatients with anxiety and depression. Transl Psychiatry. 2013;3:e242.
24. Relling MV, Evans WE. Pharmacogenomics in the clinic. Nature. 2015;526(7573):343-50.