Palombi
BIOTECH MEDICAL PHARMACEUTICAL

SUBMISSION

THE HUMAN RIGHTS COMMISSION INQUIRY INTO ~~INTENTIONAL~~ SELF-HARM AND SUICIDAL BEHAVIOUR IN CHILDREN

Executive Summary

As a result of the dramatic increase in the use of psychotropic medicines in the treatment of depression, it is very likely that a child born since 1985 who experience's suicidal ideation, attempt's suicide or commit's suicide, will be under the influence of one or more psychotropic medicines at the time. Therefore, the true causation of children self-harming is a matter that is open to question. It is not, as is suggested by Beyondblue, simply because a child is depressed that they are at a high risk of self-harm. It may well be, as this submission argues, that the underlying cause of the relevant act is the psychotropic medication itself.

This submission argues that an important and relevant contributor to child self-harming behaviour is the current mainstream medical practise that invariably leads to the 'off-label' prescribing of psychotropic medicines to children in the treatment of 'depression'. Of course, there are other factors at play. This submission does not suggest that these other factors are irrelevant or trivial, but it does argue that psychotropic medications as currently prescribed to children is a significant factor.

The death of a child causes immeasurable trauma in families and in communities. If that death is considered intentional, the reverberations of the act are more keenly felt. Every family member and friend feels the burden of guilt, the feeling that they might have prevented only… if?

But what if a child cannot be held accountable for an act of self-harm? That even the notion of 'intentionality' is a false attribution to give to a child.

There is always a confluence of events that lead to the tragedy of suicide. This submission will closely examine the role that psychotropic drugs have in exposing children to a greater risk of self harming behaviours, including violent acts towards themselves and others.

While the age of 18 is an accepted threshold for the purposes of distinguishing a child from an adult for legal purposes, it is not always an accurate threshold biologically. This is especially true in relation to the development and maturing of the human brain from child to adult.

The legal system rules that a person becomes culpable for crimes when they turn 18. However, it is also established in the scientific annals that the frontal lobe, the part of the human brain where judgement is determined, continues developing beyond the age of 18. These truisms make the legal and the neurological definitions of an 'adult' at odds with one another.

To examine the causes of suicide in the young, this inquiry must examine this intersection between the legal and the medical definitions in order to sensitively and accurately address the contributing factors and effectively gather data to disprove or prove hypotheses about the causes of harm to children.

Additionally, 'intentional self harm' and 'suicidal behaviour' are defined very differently by various stakeholders (researchers, medical practitioners, community organisations and legislators). In order to pin down the causes of these phenomena, this submission will establish the constructs and limitations of these definitions as they apply to children in their stages of physiological and legal development.

Drawing these arguments together, this submission states that any child who self harms does so unintentionally, but at the same time, the child's action is not accidental. The cause cannot be attributed to the child's intention at the time of the act because the cause lies beyond the child itself.

Abandoning the misnomer of 'intentionality' of a child, we can more clearly examine the causes of a child's death by their own hand.

This submission also argues that indirect actions, such as risk-taking behaviour of driving cars at high speed, is to be considered a form of 'self-harming' behaviour as such acts can result in incarceration or institutionalisation or death.

This submission argues that there are many contributing factors to a child self harming, but one of the most important areas to be examined is the psychotropic medication prescribed by Australian medical practitioners for the treatment of 'depression' (sadness, distress, worries and anxieties).

There is also a disparate collection of data on self harm and suicide. The goal posts for data collection keep changing, and no one regulatory body is able to clearly illuminate the successes or failures of various suicide prevention policies. For example, suicide rates in children shot up

dramatically in the latter half of the twentieth century, with the suicide rate of children under 15 nearly doubling in the period of 1960-1969 to 1990-99. Conversely there are claims that the rates of child suicides have broadly decreased over the last ten years, but this has happened within different data collection regimens.

The current mainstream pharmaco-psychiatric practice in Australia, although increasingly nuanced to promote multifactorial and biopsychosocial approach to the cause of depression, still subscribes to the 'chemical imbalance' theory. However, while there is no empirical evidence proving that the chemical imbalance theory is valid, a recent study of Australian public perceptions of the cause of depression found that 88.1% of respondents "perceived a chemical imbalance to be a likely cause of depression".

Subcategories of psychotropic drugs - antidepressants and antipsychotics - are increasingly and alarmingly prescribed to children, even while there is evidence to suggest that most of these drugs increase the incidents of suicide by children.

Psychotropic product guidelines indicate that there are insufficient safety and efficacy data provided to the Therapeutic Goods Administration (TGA) for the manufacturers of these medicines to recommend them for the treatment of children.

Medicines are approved for market by the TGA based on broad safety and efficacy guidelines. But the really close examination of the efficacy of a medicine happens when a pharmaceutical company applies to have the medicine included in the Pharmaceutical Benefits Scheme (PBS). The PBS further restricts most antidepressants for use only in serious disorders like major depressive disorder, or for obsessive compulsive disorder.

Ten years ago warnings that all antidepressants, were the subject of an advisory issued by the TGA warning that they were actually increasing suicidality in children rather than decreasing it.

Even so, there is a growing body of evidence that they are being prescribed to children at increasing rates, and most often by the family general practitioner – one survey found that GPs were prescribing 86% of all antidepressant scripts in Australia. The same survey found that the GPs were frequently prescribing antidepressants for managing mild depression, rather than the "major depressive disorder" diagnosis required for the PBS subsidy.

Data sourced through Freedom of Information disclosure logs shows that in the five years from 2007 to 2011, nearly 600,000 prescriptions for antidepressant medicines were processed through the PBS for children under 17; in that same period, antidepressant use for the age group increased by 27%.

For antipsychotics, the rise in prescriptions is even more alarming. While the numbers are smaller than antidepressants, the increase of antipsychotic prescriptions in the comparable period and age group is 108%.

This evidence demonstrably shows that the Australian medical practitioners have been writing prescriptions through the PBS, a practise of questionable legality, at increasing levels in the absence of any reliable, empirically-based evidence, clinical data, experience or information about the efficacy of these medicines in children and, most importantly, against the recommendations of the medicines' manufacturers in the product information sheets and the TGA.

This submission examines the contrasts and contradictions between the PBS and TGA warnings and regulations with the advice given by the Royal Australian and New Zealand College of Psychiatrists (RANCP). The College has broadly supported the prescription of antidepressants to children off-label since the first warnings about the links between SSRIs and increased suicidality were distributed in Australia.

This dichotomy has been repeated in the last decade with adjustments being made to their recommendations, but with the underlying message that it is still acceptable to prescribe antidepressants to children. This submission makes the case that this is unacceptable.

Introduction

This submission is about persons *under 18* (children) who self-harm, idealise suicide, attempt or commit suicide (the relevant acts) whilst under the influence of psychotropic medications that are:

i) **approved** for use in Australia by the *Therapeutic Goods Administration* (TGA);
ii) **listed** on the *Pharmaceutical Benefits Scheme* (PBS);
iii) **prescribed** by Australian medical practitioners; and,
iv) **dispensed** by Australian pharmacists at pharmacies and hospitals.

The definition of 'child' and the age limit to the scope of this Inquiry

The Inquiry limits the scope to persons under 18. This is consistent with the definition of 'child' in the *Children (Criminal Proceedings) Act 1987* (NSW), namely, "a person who is under the age of 18 years". Within the category of 'children' are 'young children' in the 0 to 12 age range and 'adolescents' in the 13 to 17 age range. The term 'young people' will not be used in this submission since this Inquiry is limited to children. The term 'young people' is ambiguous and superfluous.

Accepting the age limit of this Inquiry, this submission points out that whilst the age of 18, known as the 'age of majority', is today an accepted threshold for the purposes of distinguishing a child from an adult for legal purposes, it is not necessarily the most accurate threshold for medical purposes. Most countries set the age of majority at 18. The arbitrary nature of this threshold is historical and legal.[1]

> "Age-based policies are not exceptional; policies are frequently enacted in the face of contradictory or nonexistent empirical support. Although neuroscience has been called upon to determine adulthood, there is little empirical evidence to support age 18, the current legal age of majority, as an accurate marker of adult capacities."
> Johnson, S.B, Blum, R.W., and Giedd, J.N. (2009): 'Adolescent Maturity and the Brain: The Promise and Pitfalls of Neuroscience Research in Adolescent Health Policy', *Journal of Adolescent Health*, 45(3) 216-221.

In the United States, in some States, the age of majority is 21 years (although the voting age is 18). Until 1972 the age of majority in Australia was also 21. However, it is recognised, increasingly so as more information about the biological differences between the children and adults becomes available, that it is not necessarily the case that a person, even at 24, is an adult biologically. This is particularly important in the field of psychology and psychiatry because the

[1] Johnson, S.B, Blum, R.W., and Giedd, J.N. (2009): 'Adolescent Maturity and the Brain: The Promise and Pitfalls of Neuroscience Research in Adolescent Health Policy', *Journal of Adolescent Health*, 45(3), 216-221.

frontal lobe, the part of the human brain that pertains to judgement, continues developing well beyond the age of 18.[2]

There are also relevant ethnic and genetic differences that impact upon the ability of any person,[3] let alone a child,[4] to deal with psychotropic medicines.[5] This is now well accepted by the medical community, and is, increasingly, an issue for consideration in the field of pharmcokinetics.[6] Indeed, it is also recognised by the medical community that gender differences[7] are also relevant to individual responses to psychotropic medicines.[8]

By limiting the Terms of Reference to persons under the age of majority, i.e., children as defined by law, the Commission imposes a limitation that makes little sense from a medical perspective. As a result relevant and material information (including medical data) must be excluded merely because of the Commission's adherence to an artificial and legal construct - the age of majority.

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[2] Fuster, J.M. (2002), 'Frontal lobe and cognitive development', 31(3-5), *Journal of Neurocytology*, 373-385; Johnson, S.B, Blum, R.W., and Giedd, J.N. (2009): 'Adolescent Maturity and the Brain: The Promise and Pitfalls of Neuroscience Research in Adolescent Health Policy', *Journal of Adolescent Health*, 45(3), 216-221; Donald T. Struss, Robert T. Knight (Eds) (2013), *Principles of Frontal Lobe Function*, (Oxford University Press).

[3] Bradford, L.D., (2002), 'CYP2D6 allele frequency in European, Caucasians, Asians, Africans and their descendants', *Pharmacogenomics*, 3 (2), 229-243; Howard, L.A., Sellers, E.M., and Tyndale, R.F. (2002), 'The role of pharmcogenetically-variable cytochrome P450 enzymes in drug abuse and dependence', *Pharmacogenomics*, 3 (2), 185-199; Scrodo, M.G., and Spina, E., (2002), 'Cytochrome P450 polymorpisms and response to antipsychotic therapy', *Pharmacogenomics*, 3 (2), 201-218; Kirchheiner, J., Nickchen, K., Bauer, M., Wong, M-L., Licinio, J., Roots, I., and Brockmoller, J., (2004), 'Pharmacogenetics of antidepressants and antipsychotics: the contribution of allelic variations to the phenotype of drug response', *Molecular Psychiatry*, 9, 442-473; Zanger, U.M. and Schwab. M. (2013) Cytochrome P450 enzymes in drug metabolism: Regulation of gene expression, enzyme activities, and impact of genetic variation', 38 (1), *Pharmacology & Therapeutics*, 103-141.

[4] Vitiello, B., Correll, C., van Zwieten-Boot, B., Zuddas, A., Parellada. M., and Arango, C (2009) 'Antipsychotics in children and adolescents: Increasing use, evidence for efficacy and safety concerns', *European Neuropsychopharmacology*, 19, 629-635; Vitiello, B., Chapter A7 'Principles in Using Psychotropic Medication in Children and Adolescents' in J.M. Rey (Ed) IACAPAP Textbook of Child and Adolescent Mental Health (http://iacapap.org/wp-content/uploads/A.7-PSYCHOPHARMACOLOGY-072012.pdf).

[5] Piatkov, I., Jones, T. and McLean, M., (2012), 'Cases of Adverse Reaction to Psychotropic Drugs and Possible Association with Pharmacogenetics', *Journal of Personalized Medicine*, 2, 149-157; Dinama, O., Warren, A.M., Kulkarni, J. (2014), 'The Role of Pharmacogenomic testing in psychiatry: Real World Examples', *Australian and New Zealand Journal of Psychiatry*, 0004867413520050;

[6] Scheuplein, R., Chamley, G. and Dourson, M. (2002) 'Differential Sensitivity of Children and Adults to Chemical Toxicity: I, Biological Basis, 35(3), *Regulatory Toxicology and Pharmacology,* 429-447.

[7] Gleiter, C.H., and Gundert-Remy, U., (1996) 'Gender differences in pharmacokinetics', *European Journal of Drug Metabolism and Pharmacokinetics*, 21 (2), 123-128; Beierle, I, Meibohm, B., and Derendorf, H. (1999) 'Gender differences in pharmacokinetics and pharmacodynamics', *International Journal of Clinical Pharmacology and Therapeutics*, 37 (11), 529-547; Anderson, G.D., (2008) 'Gender differences in pharmacological response', *International Review of Neurobiology*, 83, 1-10.

[8] Marazziti D., Baroni, S., Picchetti, M., Carlini, M, Falaschi, V., Lomardi A. and Dell'Osso, L. (2013) 'Pharmacokinetics and pharmacodynamics of psychotropic drugs-Effect of sex', *CNS Spectrums*, 18(3), 118-127.

The use of the word 'intentional' as a qualifier

The Commission's *Call For Submissions* and *Terms of Reference* direct the Inquiry to instances of "intentional self-harm and suicidal behaviour" committed by children. However, the word 'intentional' is otiose for three reasons.

First, in the context of this Inquiry the word 'intentional' means the doing, by a child, of any of the relevant acts *on purpose, deliberately or with intent*. The word assumes that children have a sufficient level of understanding, at the time of the relevant act, that they have the capacity for forming an intent to perform the act upon themselves (without the assistance of others). While it might be possible to conclude that a child has committed a relevant act upon themselves, whether they did so intentionally is another matter.

It is to be noted that Commonwealth, State and Territory criminal laws uniformly provide that a child under the age of 10 is incapable of committing a criminal offence[9] and that a child aged between 10 and 14 has the benefit of a rebuttal presumption provided by the defence of infancy.[10] What this means is that a child under 15 is deemed to be incapable of understanding whether their behaviour is wrong. Culpability cannot attach to the acts of children under 10 and may only attach to the acts of children over 10 and under 15 if, and only if, the legal presumption is rebutted. If the same rationale is applied beyond criminal law, then children under 15 are accepted by society to be legally incapable of forming an intent in respect to the performance of any relevant act.

Secondly, children over 15 and "suffering from a mental impairment" at the time of the act are deemed by law "not criminally responsible."[11] The defence, of course, also applies to adults. *Mental impairment* includes "mental illness" and "a severe personality disorder".[12] It follows, that if the same rationale is applied beyond criminal law, then children over 15 are deemed incapable of forming an *intent* leading to the performance of an act of a relevant act if, at the time they performed the act they were *mentally impaired*. Mental impairment can be temporary. And may apply if a child is under the influence of certain substances, including psychotropic medications, at the time of the relevant act.

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[9] Crimes Act 1914, s4M; Criminal Code Act 1995, s7.1 (Cwth); Children (Criminal Proceedings) Act 1987 (NSW) s.5; Criminal Code 2002, s25 (ACT); Children and Young Persons Act 1989, s127 (Vic); Criminal Code 1899, s29(1) (Qld); Young Offenders Act 1993, s5 (SA); Criminal Code 1924, s18(1) (Tas); Criminal Code Act Compilation Act 1913, s29 (WA); Criminal Code Act, s38(1) (NT).

[10] Crimes Act 1914, s4N; Criminal Code Act 1995, s7.2 (Cwth); Children (Criminal Proceedings) Act 1987 (NSW) s.3; Criminal Code 2002, s26 (ACT); Common law *doli incapax* (Vic); Criminal Code 1899, s29(2) (Qld); Common law *doli incapax* (SA); Criminal Code 1924, s18(2) (Tas); Criminal Code Act Compilation Act 1913, s29 (WA); Criminal Code Act, s38(2) (NT).

[11] For example, Criminal Code Act 1995, s7.3 (Cwth).

[12] For example Criminal Code Act 1995, s7.3(8) and (9) (Cwth).

Thirdly, the word 'intentional' is also problematic from a religious perspective since its meaning draws a nexus between a child's state of mind, the act performed by that child and the commission of what is regarded in the Jewish, Islamic and Christian religions to be a sin. That nexus necessarily implies that children are capable of understanding the consequences of their actions and that they knowingly and deliberately commit a sin. This is particularly unfair to children under 15, not to mention the distress it causes the parents of the child who may be devout, since it imputes *blame* and that, in turn, makes the act sinful. Indeed, it is equally unfair in respect to a child 15 and over that performs such an act whilst *mentally impaired*. Clearly, the word 'intentional' in the context of a religion or faith involves the making of a moral judgement which, respectfully, is abhorrent in the circumstances under consideration.

If the Inquiry's Terms of Reference is understood literally, the scope of the Inquiry excludes any self-harm perpetrated by children on themselves under 15 years and any perpetrated by children 15 and over who were *mentally impaired* at the time of the act.

This submission doubts whether this is what was intended by the Commission given that there are references in the Issue section of the *Call for Submissions* referring to children as young as five.

Consequently, this submission has been prepared on the basis that the use of the word 'intentional' as a qualifier is an oversight. The submission, therefore, includes any act of self-harm, suicidal ideation, attempted suicide or completed suicide perpetrated by any child on themselves (i.e., without the assistance of another person). It is assumed, for the reasons given, that any child does so unintentionally but, at the same time, the child's action is not accidental. In other words, the relevant act is carried out by the child on itself and without the aid of another person, but whatever it is that motivates the child to do so, the cause cannot be attributed to the child's intention at the time of the act. The true cause of the self destructive behaviour, therefore, lies beyond the child itself.

The definition of 'self-harm'

There appears to be no universally recognised definition of the term 'self-harm' in Australia. The Inquiry's *Terms of Reference* contains no definition.

According to Lifeline "people define self-harm in lots of different ways." Comparing the Lifeline, Beyondblue, Headspace and Mindframe webpages it can readily be seen that this is a correct statement.

Lifeline advises visitors to its webpage that: "… self-harm is defined as someone *deliberately* hurting themselves *without wanting to die*". It provides examples such as "cutting the skin with sharp objects, taking an overdose of medication or drinking poison, burning the skin, hitting the body with fists or another object, punching walls or other objects, scratching or picking the skin, resulting in bleeding or welts and pulling out hairs."

Beyondblue defines it by reference to how a person is feeling. It advises visitors to its webpage that: "Sometimes it can feel like *life is just too hard and problems can seem overwhelming*. It's important to sort out the underlying problem - whether it is anxiety, depression or something else. If you are hurting yourself or thinking about suicide …".

Headspace advises visitors to its webpage that: "… self-harm refers to people *deliberately* hurting or mutilating their bodies *without necessarily wanting to die*." Examples are provided and include "cutting part of the body, commonly the arms, wrists, or thighs" or "[t]aking overdoses of prescribed drugs or other substances that cause harm" and " [u]sing cigarettes or lighters to burn the skin". Interestingly, also *included is 'risk taking' behaviour* that "can lead to harm, such as train surfing, driving cars at high speed, illegal drug use, or deliberately unsafe sex."

Mindframe advises visitors to its webpage that the "issue" is "complex". It accepts that there is "no 'universal definition' of self-harm and additionally, there are diverse views concerning the reasons or risk factors for self-harming behaviours". Self-harm "refers to the behaviour of *deliberately* causing oneself pain or injury." Examples "can include, but *is not limited* to, biting, burning or cutting, overdose on prescription or illegal drugs, binge eating or starvation, alcohol or drug abuse, or repeatedly placing oneself in dangerous situations."[13]

Apart from Beyondblue, which addresses its webpage visitor in the first person and by reference to how that person is feeling, the commonalities in the definition of 'self-harm' between Lifeline, Headspace and Mindframe is: *deliberate action*. Lifeline and Headspace also qualify the term by the phrase: "without wanting to die" (Lifeline) with Headspace adding the word "necessarily". Furthermore, Headspace and Mindframe include behaviour that involves risk-taking, and not merely, as Lifeline does, by reference to the direct action such as bodily mutilation or other physical force directed and applied only to their bodies.

For the following reasons, this submission argues that each of the definitions, including Beyondblue's first person approach, is suboptimal particularly where children are concerned.

First, blame and culpability are inappropriate for the reasons already given. The word 'deliberately' means the same as 'intentionally'. It is unfair for children under 15, and for children over 15 who are *mentally impaired,* at the time of the relevant act to be considered, directly or indirectly, culpable. Beyondblue's approach, on the other hand, is careful not to apportion blame, ascribe intent, or accuse the person visiting its webpage of deliberately "hurting" themselves or having thoughts "about suicide." Beyondblue's approach makes sense. It is unhelpful for a person that is already distressed to also be accused of blameworthy conduct, particularly in the case of a child under 15 or a child 15 or over that is mentally impaired as they are unlikely to be able to understand or make sense of the thoughts they are having or the actions they are (or are thinking of) performing.

[13] Emphasis added.

Secondly, distinguishing 'self-harm' from suicidal behaviour, which is another form of self-harm, by reference to the terms, "not wanting to die" (Lifeline) or "not *necessarily* wanting to die" (Headspace), makes little sense when their own examples for 'self-harm' include: "taking an overdose of medication or drinking poison" (Lifeline) or "[t]aking overdoses of prescribed drugs or other substances that cause harm" (Headspace). Clearly, an 'overdose' is a euphemism for attempted suicide or completed suicide, both, obviously contraindications for life. As is "drinking poison". By contrast Mindframe, which does not use the phrase "wanting to die" as a point of distinction, includes "overdose on prescription or illegal drugs" as an example of 'self-harm'. What this analysis suggests is that the distinction between behaviour that is 'self-harming' and 'suicide' by qualifying the former with the qualification of "not wanting to die" is meaningless. This submission suggests that there are degrees of self-harming behaviour. Attempted suicide and suicide are simply a form of self-harming behaviour, which is the accepted position of the Australian Institute of Health and Welfare.[14]

Thirdly, while Lifeline and Beyondblue define self-harming behaviour by reference to harmful acts performed directly upon the body by the person concerned, Mindframe and Headspace go further and include 'risk taking' behaviour such as "driving cars at high speed" or having "unsafe sex" (Headspace) and "binge eating or starvation" or "repeatedly placing oneself in dangerous situations" (Mindframe). This seems to make good sense for the reason that self-harming behaviour that results in injury or death can manifest itself in both direct and indirect ways. It is submitted, therefore, that if indirect behaviour, such as "driving cars at high speed", is to be considered to be a form of 'self-harming' behaviour, then so should any behaviour that has the effect of causing harm to the person concerned regardless of whether the harm is physical or otherwise or direct or indirect. For instance, behaviour that results in a child losing their freedom through incarceration or institutionalisation is self-harming. As should be behaviour towards other people that may lead to the loss of their freedom. For example, a child that carries out a violent act on another person by assaulting, seriously injuring or killing that person, is self-harming themselves at a number of levels. It is self-harming because it may result, if not in criminal proceedings (if the child is 10 and over) and entering the youth justice system,[15] in the loss of the child's freedom (through hospitalisation or institutionalisation through statutory child protection).[16] It will also have a negative impact on their reputation (even as adults in extreme cases). And it will have a negative effect on the child's key familial relationships and friendships as the child is deprived of the love and support that comes from daily interactions with family

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[14] Trends in hospitalised injury, Australia 1999-00 to 2010-11, Australian Institute of Health and Welfare, Injury research and Statistics Series No 86 at Chapter 10 Intentional Self Harm: "This chapter includes suicide and attempts to suicide, as well as cases where persons have intentionally hurt themselves, but not necessarily with the intention of suicide - for example, acts of self-mutilation. This chapter does not include cases where the intent was unspecified, unstated or could not be determined."

[15] Australia's Welfare Report 2013, Chapter 4, page 181: http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129544558

[16] Ibid, at p 175.

and friends. Moreover, self-harming behaviour need not be manifested through physical means, but may include behaviour that has become known as cyber-bullying. Children that participate in such behaviour may cause other children to either attempt or commit suicide. The Australian Government has recently established the cybersmart programme in an attempt to raise awareness of the dangers and unacceptability of such behaviour.

In summary, it is suggested that there is no point in distinguishing between behaviour that is self-harming on the one hand, and suicidal ideation, attempted suicide or suicide on the other. Moreover, it is submitted that all forms of self-harming behaviour, direct and indirect, physical or otherwise, including antisocial, violent, dangerous or reckless behaviour causing harm to other persons, should be included in the definition of 'self-harming' behaviour. Finally, the intention or deliberateness of the child performing any act of self-harm should not be considered as relevant. It matters little what the child's intention is. What matters is the nature of the child's self-harming behaviour and, critically, identifying its underlying and true cause.

The Ambiguities of the Available Statistics

This submission agrees with the statement in the *Call for Submissions* that the "available data [in regard to suicide] … is poor and does not provide a comprehensive picture." At the same time, and for the reasons expressed in the preceding section, the available data and analysis of that data should not be limited to "children … that *intentionally* self-harm." In any event, for the reasons expressed earlier and summarised below, it is fair to conclude that these data under report self-harming events (including suicide and attempted suicide). More problematic is that they do not attribute cause to anything other than the intent of the individuals concerned. This is a major flaw particularly where children under 15 (and those 15 and over that are 'mentally impaired' at the time of the relevant event) are concerned.

Suicide

The Australian Bureau of Statistics (ABS) provides only scant suicide data when it comes to children.[17] Other data for children is provided by the Australian Government's Department of Health[18], but is not much more informative.

According to the Department, the rate of suicide in children under 15 has nearly doubled (92%), from a rate of 0.12/100,000 in 1960-69 to a rate of 0.23/100,000 in 1990-99. During the same 40 year period the corresponding suicide rate increased in the United States by 194%, in Canada by 240% and in New Zealand by 646%. The highest increase was recorded by Ireland with

[17] ABS 3303.0 - Causes of Death, Australia, 2012 at Table 5.1 and Table 5.2: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2012~Main%20Features~Age~10010

[18] Suicide rates in childhood (under 15 years of age), Australian Department of Health: http://www.health.gov.au/internet/publications/publishing.nsf/Content/mental-pubs-i-intsui-toc~mental-pubs-i-intsui-tre~mental-pubs-i-intsui-tre-chi

3,900%. The only countries to record decreases were England and Wales by 20%, Germany by 20% and Hungary by 34%.

Unfortunately, these data have very limited interpretive value since there is no universal agreement as to how to attribute cause of death, by an act of suicide, to a child. To be sure, it might be assumed that these data include cases where the cause of death was self inflicted by the child, but there are no ABS data on the underlying causes of this ultimate self-destructive and violent act, so it is impossible to know, from the ABS statistics, whether the suicides were 'intentional' or not and, more relevantly, what motivated or drove these children to suicide. Furthermore, to impute intention to suicide in the case of children is problematic for the reasons already explained.

Despite the shortcomings, the Department states: "the rate of suicide among the youngest age group has more than doubled since 1960. A similar trend can be observed among both males and females." This is clearly a disturbing trend. The seriousness of the situation demands some analysis, however unreliable these data.

Self-Harming

As discussed earlier, the main source of statistics for acts of self-harm in Australia is the Australian Government's Australian Institute of Health and Welfare. The Department's latest report is T*rends in Hospitalised Injury, Australia 1999-00 to 2010-11*.[19] Unfortunately, there are a number of problems with these data used in the Report. First, these data do not distinguish between acts of self-harm and suicide or attempted suicide, obviously overlapping with the ABS statistics of 'intentional' suicides. It is therefore impossible to separate from these data, 'self-harming' events from suicide and attempted suicide (which is actually another form of self-harm). Secondly, these data include only cases "where persons have *intentionally* hurt themselves" which, in the case of children under 15 and those 15 and over that are 'mentally impaired' at the time, means that most of these events are, by definition, excluded.[20] Thirdly, expressly excluded from these data are cases "where the intent was unspecified, unstated or could not be determined,"[21] so we do not know how many self-harming events involving children have actually occurred. It is fair to assume, therefore, that these data seriously under report self-harming events involving children. Fourthly, these data draw on ABS statistics using

[19] Op cit, 14.

[20] Ibid, p93.

[21] Ibid.

the classification ICD-10-AM X60-X84 (essentially the same as the ABS statistics on suicide which are expressly limited to cases of "intentional self-harm").[22]

As a result the submission's concerns, already expressed in respect of suicides and attempted suicides, are applicable here.

The Terms of Reference

1. Why children … engage in ~~intentional~~ self harm (including suicidal behaviour)?

The question posed by the Inquiry's Terms of Reference is a *non sequitur*. By law a child under 15 (or a child over 15 that is mentally impaired at the time of the act) cannot form an intent in respect to the doing of an act of self-harm. If a child does self harm, the appropriate question to ask is why? And it must be asked without seeking to apportion blame or impute purpose or intent on the child that performs the act on themselves without the direct involvement of another person (in other words, by their own hands). It is also wrong as a matter of law to infer deliberateness on the child, because the word means: "done consciously and intentionally."

As tragic as is an act of self-harm, such as a suicide or attempted suicide, it is clear from the available ABS and Departmental data that we have a problem in Australia with children self-harming. This submission suggests that these data are, for the reasons already expressed, seriously **under-recording the size of that problem**. Unfortunately, the criteria used to record such data effectively means that no one is able to use any of these data to form a reliable and definitive opinion on what are, or are not, the environmental or biological triggers for such events and what policies, practices or measures are effective and efficient mitigators for such events.

The submission argues that the reliance on these data, particularly with regard to the numbers of suicides of boys 15 or above and young men between the ages of 18 and 24, by those who seek to show that mainstream psychiatric treatment as currently practiced in Australia is working to reduce the incidence of self-harm is misplaced. These current and available data are unreliable except to show that self-harming does happen and that it happens more frequently than these data record. As to how much more, we simply do not know. As to what are the triggers, we simply do not know. As to what can be done to effectively and efficiently mitigate these events, we simply do not know.

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[22] Ibid, p94. "According to inclusion notes in CD-10-AM, cases should be assigned codes in the range X60-X84 if they were purposely self-inflicted poisoning or injury, suicide or attempted suicide. Determining whether an injury is due to intentional self-harm is not always straightforward. Cases may appear to be intentional self-harm, but inconclusiveness of available information may preclude them from being coded as such. … Some patients may choose not to disclose that their injuries resulted from intentional self-harm … In very young children, ascertaining whether an injury was due to intentional self-harm can be difficult and may involve a parent or care giver's perception of the intent. Ability to form an intention to inflict self-harm and to understand the implications of doing so requires a degree of maturation that is absent in infancy and early childhood. The age at which self-inflicted acts can be interpreted as intentional self-harm is not well defined and is the subject of debate. Such sources of uncertainty about the assignment of intent limit the certainty of any estimates of intentional self-harm based on routine hospital data."

This submission argues that a contributing factor to the self-harming by children is psychotropic medication prescribed by Australian medical practitioners for the treatment of 'depression'[23] (sadness, distress, worries and anxieties).

It is the truth that there is no proven biological cause for depression.[24]

It is the truth that there is no proven biological cause for schizophrenia.[25]

It is the truth that there is no proven biological cause for bipolar disorder.[26]

It is the truth that there is no proven biological cause for attention deficit hyperactivity disorder.[27]

It is the truth that there is no proven biological cause for any mental behavioural disorder[28] defined in the DSM-V[29] or ICD-10[30] other than substance and medication induced disorders.

It is the truth that current mainstream pharmaco-psychiatric practice in Australia, although increasingly promoting a multifactorial and biopsychosocial approach to the cause of depression, subscribes to the chemical imbalance theory.[31] Indeed, the most recent study (2013) of Australian public perceptions of the cause of depression found that 88.1% of respondents "perceived a chemical imbalance in the brain to be a likely cause of depression"

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[23] Allan V. Horwitz and Wakefield, James C. (2007) *The loss of sadness: How psychiatry transformed normal sorrow into depressive disorder* (Oxford University Press, New York, NY).

[24] Paul Gilbert, (1992), 'Depression: The Evolution of Powerlessness' (Lawrence Erlbaum, East Sussex, U.K.) pp 23-24.

[25] "The cause of schizophrenia remains unknown, but it is generally assumed that it has an organic basis." Christopher D. Firth, (1992), *The Cognitive Neuropsychology of Schizophrenia*, (Lawrence Erlbaum, East Sussex, U.K.) p 4.

[26] "There is no single, proven cause of bipolar disorder, but research suggests that it is the result of abnormalities in the way some nerve cells in the brain function or communicate." Kahn, D.A., Ruth Ross, M.A., Printz, D.J., and Sachs, G.S., (2000), 'Treatment of Bipolar Disorder: A Guide for Patients and Families', National Depressive and Manic-Depressive Association, Medication Treatment of Bipolar Disorder.

[27] "The etiology [sic] of ADHD is not known but recent studies suggest both a strong genetic link as well as environmental factors such as history of preterm delivery and perhaps, maternal smoking during pregnancy." Rowland, A.S., Lesesne, C.A., and Abramowitz, A.J., (2002), 'The epidemiology of attention-deficit/hyperactivity disorder (ADHD): A public health view', *Mental Retardation and Developmental Disabilities Reviews*, 8 (3), 162-170.

[28] Whitaker, R.B., (2008), 'Reality Check: What Science Has to Tell Us About Psychiatric Drugs and Their Long-Term Effects', *Journal of College Student Psychotherapy,* 21 (3-4), 97-123.

[29] Diagnostic and Statistical Manual of Mental Disorders (Series 5).

[30] International Classification of Diseases (Series 10).

[31] The chemical imbalance theory was put forward by Joseph Schildkraut in 1965. The theory claims low levels of norepinephrine is linked to 'depression'. Subsequently, a similar association was made between serotonin levels and 'depression'. Lacasse J.R. and Leo, J., (2008) 'Serotonin and Depression: A Disconnect between the Advertisements and the Scientific Literature', *PLoS Medicine*, 2(12): e392, 1211-1216; Pilkington, P.D., Reavley, N.J., and Jorm, A.F., (2013), 'The Australian public's beliefs about the causes of depression: Associated factors and changes over 16 years', *Journal of Affective Disorders*, 150, 356-362.

and 83.4% thought that in regard to "depression with suicidal ideation."[32] One of the explanations proffered by the authors of the study was:

> "The pharmaceutical industry in particular has promoted the idea that depression is caused by a chemical imbalance that can be corrected through the use of antidepressants."
> Pilkington, P.D., Reavley, N.J., and Jorm, A.F., (2013), 'The Australian public's beliefs about the causes of depression: Associated factors and changes over 16 years', *Journal of Affective Disorders*, 150, 356-362.

Another was the public's education through "the public health messages promoted by awareness organisations such as *beyondblue*",[33] which while emphasising a "biopsychosocial explanation for depression",[34] continues to promote the chemical imbalance theory.

Similar public perceptions have been found to exist elsewhere.

> "Biomedical causal explanations of depressions, principally the "chemical imbalance" theory, have been vigorously promoted in recent decades to reduce public stigma and facilitate pharmacotherapy. As a result, the chemical imbalance theory has become the dominant cultural understanding of depression in the United States."
> Kemp, J.J., Lickel, J.L., and Deacon, B.J. (2014), 'Effects of a chemical imbalance causal explanation on individuals' perceptions of their depressive symptoms', *Behaviour Research and Therapy*, 56, 47-52.

However, it is the truth that there is no empirical evidence proving that the chemical imbalance theory is valid.[35]

> " … there is no credible evidence that mental disorders are caused by chemical imbalances, or that medicines work by correcting such imbalances."
> Deacon B.J., (2013), 'The biomedical model of mental disorder: A critical analysis of its validity, utility, and effects on psychotherapy', *Clinical Psychology Review*, 33, 846-861.

Regrettably, the rigid adherence by mainstream psychiatry to the chemical imbalance theory inevitably means that psychotropic medications approved by drug regulators, such as the Food and Drug Administration (FDA) in the United States and the Therapeutics Goods Administration (TGA) in Australia, for the treatment for serious or specific forms of mental disorders, such as schizophrenia, are being prescribed by Australian medical practitioners to children for the treatment of 'depression' in Australia. And it is also happening in other countries.

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[32] Pilkington, P.D., Reavley, N.J., and Jorm, A.F., (2013), 'The Australian public's beliefs about the causes of depression: Associated factors and changes over 16 years', *Journal of Affective Disorders*, 150, 356-362, 359.

[33] Ibid.

[34] Ibid.

[35] Smith, D.C., (1999), 'The Limits of Biological Psychiatry', *Journal of the American Academy of Psychoanalysis*, 27, 671-680; Deacon B.J., (2013), 'The biomedical model of mental disorder: A critical analysis of its validity, utility, and effects on psychotherapy', *Clinical Psychology Review*, 33, 846-861.

The prescribing of medicines in Australia

Before a medicine can be legally promoted and sold in Australia it must first be approved by the TGA. However, before a TGA approved medicine can be dispensed by a pharmacist *under the PBS* it must be listed on the PBS Schedule.

It is not illegal for an Australian medical practitioner to prescribe a medicine that has been approved by the TGA for a specific indication (e.g., schizophrenia in adults) for an indication that has not been approved by the TGA (e.g., depression in children). This practise is called 'off-label' prescribing. It is, however, illegal for a medicine to be made available under the Pharmaceutical Benefits Scheme (PBS), namely, as a 'pharmaceutical benefit', to a person for an indication that has not been approved by the Pharmaceutical Benefits Advisory Council (PBAC) and listed in the PBS Schedule.[36] This is because medicines listed on the PBS are subsidised by the Commonwealth through the PBS. When a patient has a pharmacist fill a prescription for a medicine that is listed on the PBS, the patient only pays a set fee. This fee is less than the actual cost of the medicine, which is paid by the Commonwealth. As a result, when a medical practitioner writes a prescription for medicine for the treatment of an unapproved PBS indiction, the patient is not entitled to receive a PBS benefit in respect to that medicine.

The Commonwealth keeps records of the number of prescriptions and the cost of these prescriptions, so it is possible to obtain information from the Department of Health Services about the prescribing of any medicine listed on the PBS Schedule.

There is, therefore, a very important distinction between a non-PBS, or 'private', prescription and a PBS prescription for a medicine (first approved by the TGA so it can be promoted and sold in Australia) and subsequently listed the PBS (so it can be made available as a 'pharmaceutical benefit' under the PBS). In other words, an Australian medical practitioner is permitted to write a prescription for a TGA-approved medicine for the treatment of a non-TGA-approved indication, however, the patient may only have that prescription filled by an Australian pharmacist and receive a *pharmaceutical benefit* if the medicine is to be used in the treatment of a PBS-approved indication.[37]

This is a crucial distinction in the case of psychotropic medicines and children for the reasons that are about to be explained.

Psychotropic medicines and their prescribing to children for the treatment of depression

In this submission the following psychotropic medicines, all approved by the TGA and all listed on the PBS Schedule, will be considered. There are other psychotropic medications but these

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[36] National Health Act 1953 s.105(b): "A person shall not: … (b) obtain a pharmaceutical benefit to which the person is not entitled;"

[37] Ibid.

have been excluded from consideration due to the need for brevity. The psychotropic medicines under consideration (original trade mark name: generic name) are:

1. **Abilify** (aripiprazole)
2. **Aropax** (paroxetine)
3. **Cipramil** (citalopram)
4. **Efexor-XR** (venlafaxine)
5. **Lexapro** (escitalopram)
6. **Luvox** (fluoxamine)
7. **Pristiq** (desvenlafaxine)
8. **Prozac** (fluoxetine)
9. **Risperdal** (risperidone)
10. **Seroquel** (quetiapine)
11. **Zoloft** (sertraline)
12. **Zyprexa** (olanzapine)

The following table lists each of these medicines and provides information that is consistent with the Consumer Medication Information Sheet (CMI) as approved by the TGA. The CMI is contained in the medicine's packaging. It provides the patient with information about the medicine, including known adverse side effects and other relevant information about the medicine and its administration.

Table 1 - Consumer Medication Information Sheet

Original Trade Mark	Type	TGA Approved Indication	Recommended for Children?
Abilify	Antipsychotic	schizophrenia	NO
Aropax	Antidepressant	depression	NO
Cipramil	Antidepressant	depression	NO
Efexor-XR	Antidepressant	depression	NO
Lexapro	Antidepressant	depression	NO
Luvox	Antidepressant	depression, obsessive compulsive disorder	NO (depression) NO (OCD under 8)
Pristiq	Antidepressant	depression	NO
Prozac	Antidepressant	depression, obsessive compulsive disorder, premenstrual dysphoric disorder	NO
Risperdal	Antipsychotic	schizophrenia, bipolar 1 disorder, disruptive behaviours, autism	NO (schizophrenia under 15) NO (disruptive behaviours under 5) YES Autism
Seroquel	Antipsychotic	schizophrenia, bipolar disorder	NO (schizophrenia under 13) NO (mania under 10)
Zoloft	Antidepressant	depression, obsessive compulsive disorder, premenstrual dysphoric disorder	NO (OCD under 6)
Zyprexa	Antipsychotic	schizophrenia	NO

As Table 1 shows, in the case of eight of the 12 medicines the approved CMI for the product absolutely does not recommend the medicine for in children for any indications. Only four permit prescribing to children and even then, are limited to specific age groups. The only absolute exception is **Risperdal** (risperidone) for autism (but as is apparent in Table 2 on the next page, this medicine was not listed on the PBS for this use). The explanations in the CMIs for excluding children include:

"[the name of the medicine] is not recommended for use in children under the age of 18 years as there is not enough information on its effects in this age group." or

"The use of [the name of the medicine] is not recommended to treat depression in children and adolescents under 18, as the drug has not been shown to be effective in this age group and there are possible unwanted effects." or

"Do not give [the name of the medicine] to a child or adolescent. There is no experience with its use in children or adolescents under 18 years old." or

"Do not give [the name of the medicine] to a child or adolescents under 18 years of age. The safety and effectiveness of [name of medicine] in this age groups have not been established." or

"[the name of the medicine] is used to treat depression in adults only. It is not recommended for treatment of this condition in children and adolescents as the safety and effectiveness of this medicine, when used for depression in this age group, have not been established." or

"[the name of the medicine] is not recommended for use in children and adolescents under 18 years of age." or

"[the name of the medicine] cannot be recommended for use in children with schizophrenia under 15 years at the present time as there is little experience with the product in this group." or

"Do not give [the name of the medicine] to children or adolescents unless recommended by your doctor. The effects of [the name of the medicine] have only been studied in children aged between 10 and 17 years with mania and in children aged between 13 and 17 years with schizophrenia. There is not enough information on its effects in children to recommend its use in other age groups or for other conditions."

The CMIs, for the most part, indicate that there is insufficient safety and efficacy data provided to the TGA for it to permit the sponsors of these medicines to recommend the use of these medicines for the treatment of children.

In Table 2 on the next page, the medicines are listed against the PBS Schedule Approvals. These differ in important respects from the TGA approvals particularly in regard to depression. The PBS

approvals are restricted to 'major depressive disorders'. The point being, that the relevant medicines are not approved for 'depression'.

There is further evidence that the prescription of these drugs off-label is often occurring in the offices of general practitioners (GPs). GPs refer patients to psychologists and psychiatrists, as required, but they are also the main prescribers of psychiatric drugs - well beyond the volumes of the smaller population of psychiatrists. An extensive survey of GPs' prescribing revealed that they were writing 86% of all antidepressant scripts in Australia.

The same survey showed that they were frequently prescribing antidepressants for the management of 'chronic mild depression'. This is significant as antidepressants are listed on the PBS for 'major depressive disorders' and the prescription of them for less serious disorders is risky for the patient, considering the side effect profile.

"The GP survey clearly implies that antidepressants are frequently utilized for the management of 'chronic mild depression'…the survey data suggest prescribing is often inconsistent with the PBS listing for the 'major depressive disorders'. It is not possible to determine from these data whether this is inappropriate clinical practice."
McManus, P. Mant, A., Mitchell, P., Britt, H. and Dudley, J., (2003) 'Use of Antidepressants by General Practitioners and Psychiatrists in Australia', *Australia and New Zealand Journal of Psychiatry*, 37:184-189

Table 2 - PBS Schedule

Original Trade Mark	Type	PBS Schedule Listing	Recommended for Children?
Abilify	Antipsychotic	schizophrenia	NO
Aropax	Antidepressant	major depressive disorders, obsessive-compulsive disorder, panic disorder	NO
Cipramil	Antidepressant	major depressive disorders	NO
Efexor-XR	Antidepressant	major depressive disorders	NO
Lexapro	Antidepressant	major depressive disorders	NO
Luvox	Antidepressant	major depressive disorders, obsessive compulsive disorder	NO (depression) NO (OCD under 8)
Pristiq	Antidepressant	major depressive disorders	NO
Prozac	Antidepressant	major depressive disorders, obsessive compulsive disorder	NO
Risperdal	Antipsychotic	schizophrenia, adjunctive therapy for acute mania associated with bipolar I disorder	NO (schizophrenia under 15) NO (acute mania)
Seroquel	Antipsychotic	schizophrenia, monotherapy for acute mania associated with bipolar I disorder, maintenance treatment of bipolar I disorder	NO (schizophrenia under 13) NO (mania under 10)
Zoloft	Antidepressant	major depressive disorders	NO
Zyprexa	Antipsychotic	schizophrenia, maintenance treatment of bipolar I disorder	NO

Tables 1 and 2 conclusively show that none of these 12 psychotropic medicines are approved for use in the treatment of 'depression' in children. As for the four antipsychotic medicines that do permit limited prescribing, two are absolutely not recommended for children for the

treatment of schizophrenia, and two are restricted to children 13 and over, and 15 and over, respectively for the treatment of schizophrenia. In this regard it should be noted, apart from schizophrenia being an uncommon disorder in children[38], that there is considerable controversy among psychiatrists over the diagnosis of schizophrenia in children.[39]

Despite this lack of regulatory approval, information obtained from the Department of Human Services under Freedom of Information (FOI) Request Id 2011/CO09395, shows that in the 2007 to 2011 period 578,753 prescriptions for antidepressant medicines were processed through the PBS to children under 17. The actual number for children is higher but unfortunately the information for 17 is included in the 17 to 21 age group. Interestingly, the number of prescriptions for antidepressant medicines processed under the PBS for this age category was 1,281,729.

Table 3 - No of PBS prescriptions

Class of Medicine	Age range	2007	2008	2009	2010	2011	TOTAL
Antidepressant	**0-16**	102,370	105,513	113,440	127,549	129,871	**578,743**
Antidepressant	**17-21**	218,928	232,657	253,835	287,064	289,245	**1,281,729**
Antipsychotic	**0-16**	32,874	48,906	56,704	64,014	68,431	**270,929**
Antipsychotic	**17-21**	56,372	66,246	71,346	78,815	81,809	**354,588**

From Table 3 it can be seen that the number of prescriptions for antidepressant medicines in the 0-16 age group rose from 102,370 in 2007 to 129,871 in 2011, an increase of 27% in five years. However, for antipsychotics the increase, from 32,874 to 68,431, is 108%.

This evidence demonstrably shows that Australian medical practitioners have been writing prescriptions for children through the PBS, a practise of questionable legality, at increasing levels in the absence of any reliable empirically based evidence, clinical data, experience or information about the efficacy of these medicines in children and, most importantly, against the recommendations of the medicines' manufacturers in the product information sheets and the TGA.

[38] "Schizophrenia in subjects younger than 13 is defined as very-early-onset schizophrenia, and its prevalence is estimated at 1 in 10000, while early-onset schizophrenia occurs between 13 and 17 years, and its prevalence is about 0.5%." Masi, G. and Liboni, F., (2011) 'Management of Schizophrenia in Children and Adolescents', *Drugs*, 71 (2), 179-208.

[39] Helmut Remschmidt (Ed) (2001), *Schizophrenia in children and adolescents,* (Cambridge University Press, Cambridge UK)

Indeed, this situation is difficult to comprehend given that in 2004 medicines regulators around the world began warning against the prescribing of a class of psychotropic medicines, known as Selective Serotonin Reuptake Inhibitors (SSRIs), to children. Six of the eight antidepressant medicines in Tables 1 and 2 are SSRIs (Aropax, Cipramil, Lexapro, Luvox, Prozac and Zoloft).

The Medicines Regulator Advisories: a reaction to information indicating increased suicide risks

The first of the class of SSRI psychotropic medicines was approved for marketing in the United States in 1988. This was **Prozac (fluoxetine)**. Within a decade four more SSRIs had been approved in the United States. The same was happening in Australia. Indeed, it was a global phenomenon. With the advent of these new atypical antidepressants, the original and older tricyclic antidepressants which were introduced in the mid-50s, were fast losing favour with the medical profession. The prescribing shift away from tricyclic antidepressants and to atypical antidepressants was significant.[40] The consequences, however, were not apparent in1998.

"The psychotropic medication visits of children and adolescents (younger than 18 years) increased significantly from 1.10 million in 1985 to 3.73 million visits in 1993 and 1994; as a proportion of all psychotropic medication visits, they increased from 3.4% to 8.2%, respectively. … The increase in psychotropic medication visits by children and adolescents can be accounted for by the increase in these visits to primary care physicians."

What is relevant to this Inquiry is the link between the increase in prescribing of antidepressants to children from the late-80s and through the 90s and increasing child suicides in the 1990s.

"The large growth in antidepressant visits can be entirely accounted for by the use of SSRIs. Antidepressant drug visits increased across all physician classes. The distribution of those visits, however, changed in important ways. In 1985, primary care physicians provided 47.5% of all antidepressant drug visits, the most of all physician specialities. In 1993 and 1994, psychiatrists provided almost 44% of all antidepressant drug visits, with the primary care providing 41%. In addition, a larger proportion of antidepressant drug visits to psychiatrists involved the use of SSRIs than either primary care of other physicians."
Pincus, A.P., Tanielian, T.L., Marcus, S.C., Olfson, M., Zarin, D.A., Thompson, J., and Magno Zito, J., (1998), 'Prescribing Trends in Psychotropic Medications', *JAMA*, 279 (7), 526-531.

Apart from the changing prescribing patterns that are directly attributable to SSRIs, there was another important change.

"Overall visits for depression to psychiatrists also doubled. … The proportion of psychiatric visits for depression that included a prescription of a psychopharmacological agent increased from 53.5% to 70.9%."
Pincus, A.P., Tanielian, T.L., Marcus, S.C., Olfson, M., Zarin, D.A., Thompson, J., and Magno Zito, J., (1998), 'Prescribing Trends in Psychotropic Medications', *JAMA*, 279 (7), 526-531.

In other words, SSRIs were being increasingly prescribed by psychiatrists to an increasing population of people diagnosed with 'depression'. Without being unnecessarily cynical, it is

[40] Pincus, A.P., Tanielian, T.L., Marcus, S.C., Olfson, M., Zarin, D.A., Thompson, J., and Magno Zito, J., (1998), 'Prescribing Trends in Psychotropic Medications', *JAMA*, 279 (7), 526-531.

undoubtedly the case that the movement of patients away from primary care physicians to psychiatrists also meant that psychiatrist incomes were rising proportionally. The other notable beneficiary of the change in prescribing patterns were the manufacturers of antidepressants, particularly, in the SSRI class.

"The availability of new SSRIs, beginning with fluoxetine [Prozac] in 1988, sertraline [Zoloft] in 1991, and paroxetine [Aropax] in 1992, has had an enormous impact on the prescription of psychopharmacological agents. Virtually all the substantial increase in psychotropic drug prescriptions can be accounted for by the use of these medications."
Pincus, A.P., Tanielian, T.L., Marcus, S.C., Olfson, M., Zarin, D.A., Thompson, J., and Magno Zito, J., (1998), 'Prescribing Trends in Psychotropic Medications', *JAMA*, 279 (7), 526-531.

The study to which this submission refers to above was published in 1998. The limit of its analysis was 1994. There is no equivalent study available for Australian conditions, however, it is likely that similar shifts in prescribing patterns along and patient movements were occurring in Australia and in other developed countries.

By 2003, however, concerns were being raised about the extraordinary rise in suicide rates during the previous decade. It must be remembered that there is a lag of some 18 months before realtime events become data. Therefore, it would not have been until 2001-2 that the events of 1998-9 were available in statistical form.

"Despite the lack of FDA approval and methodologic flaws in existing pediatric SSRI trials, by the close of the century, the use of SSRIs in the paediatric population neared the same level of use as in the adult population. Because no non-SSRI medications [tricyclic antidepressants] showed effectiveness in children and adolescents with depression, providers within psychiatry and primary care were generally willing to prescribe SSRIs to children and adolescents during the 1990s."
Michell, A.M., Davies, M.A., Cassesse C., and Curran, R., (2014), 'Antidepressant Use in Children, Adolescents, and Young Adults: 10 Years After the Food and Drug Administration Black Box Warning', *Journal for Nurse Practitioners*, 10 (3), 149-156.

The significant rise in the prescribing of atypical antidepressants to children, unfortunately happen to coincide with an unprecedented increase in suicides in children, with a few exceptions, across the developing world.

The United Kingdom

The first country to react was the United Kingdom in 2003. The SSRI under the parliamentary spotlight was paroxetine [Aropax in Australia, Paxil in the United States and Seroxat in the United Kingdom]. In June 2003 the Committee of Safety in Medicines (CSM) was the first to warn about paroxetine. In September 2003 this warning was extended to venlafaxine (which is a SNRI, not an SSRI). In December 2003 this warning was extended to all SSRI and SRNI antidepressants after the Committee had completed its review of suicide statistics in children. The Committee then established the Expert Group on the Safety of SSRIs. The Expert Group delivered its report in December 2004.

"Based on the work of the Group, CSM issued advice on the use of SSRIs in the paediatric population in June, September and December 2003. In summary, that advice was that the balance of risks and benefits for the treatment of depressive illness in under-18s is judged to be unfavourable for paroxetine (Seroxat), venlafaxine (Efexor), sertraline (Lustral), citalopram (Cipramil), escitalopram (Cipralex) and mirtazapine (Zispin). It is not possible to assess the balance of risks and benefits for fluvoxamine (Faverin) due to the absence of paediatric clinical trial data. Only fluoxetine (Prozac) has been shown in clinical trials to be effective in treating depressive illness in children and adolescents, although it is possible that, in common with the other SSRIs, it is associated with a small increased risk of self-harm and suicidal thoughts. Overall, the balance of risks and benefits for fluoxetine in the treatment of depressive illness in under-18s is judged to be favourable."

The Committee's green light for **Prozac** (fluoxetine) was controversial at the time[41] and remains so today, a decade later.[42] The findings on Prozac were based on a series of studies[43] that were funded by Eli Lilly, **Prozac's** manufacturer. And it would seem the FDA's green light, discussed below, was also influential on the Committee.

The United States

The second country to react was the United States. On 2 January 2004 the U.S. Department of Health and Human Services's, Food and Drug Administration (FDA), called a meeting of its Psychopharmacology Drugs Advisory Committee and Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee.[44] The meeting took place on 2 February 2004. The FDA's response was swift. On 22 March 2004 the FDA issued its first advisory.

"Today the Food and Drug Administration (FDA) asked manufacturers of the following antidepressant drugs to include in their labeling a Warning statement that recommends close observation of adult and paediatric patients treated with these agents for worsening depression or the emergence of suicidality. The drugs that are the focus of this new Warning are: Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvox (fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and Remeron (mirtazapine)."

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[41] Sparks, J.A., and Duncan, B.L., (2004), 'The Ethics and Science of Medicating Children', *Ethical Human Psychology and Psychiatry*, 6 (1), 25-39.

[42] Peter C Gotzsche (2013), *Deadly Medicines and Organised Crime*, (Radcliffe Publishing, London, New York)

[43] Geller, D.A., Hoog, S.L., Heiligenstein, J.H., Ricardi, R.K., Tamura, R., Kluszynski, S., Jacobson, J.G., (2001), 'Fluoxetine Treatment for Obsessive-Compulsive Disorder in Children and Adolescents: A Placebo-Controlled Clinical Trial', *Journal of the American Academy of Child & Adolescent Psychiatry*, 40 (7), 773-779; Emslie, G.J., Heiligenstein, J.H., Wagner, K.D., Hoog, S.L., Ernest, D.E., Brown, E., Nilsson, M., and Jacobson, J.G., (2002), 'Fluoxetine for Acute Treatment of Depression in Children and Adolescents: A Placebo-Controlled, Randomized Clinical Trial', *Journal of the American Academy of Child & Adolescent Psychiatry*, 41 (10), 1205-1215; Liebowitz, M.R., Turner, S.M., Piacentini, J., Beidel, D.C., Clarvit, S.R., Davies, S.O., Graae, F., Jaffer, M., Lin, S., Sallee, F.R., Schmidt, A.B., and Simpson, H.B., (2002),'Fluoxetine in Children and Adolescents with OCD: A Placebo-Controlled Trial', *Journal of the American Academy of Child & Adolescent Psychiatry*, 41 (12), 1431-1438.

[44] Memorandum from Dr Susan Cummins to Dr Thomas P. Laughren dated 2 January 2004.

What followed next was the FDA's decision to issue a Black Box Warning all five SSRIs and four SNRI antidepressant medicines on 15 October 2004. Prozac was excluded.

> "In letters issued today, FDA directed the manufacturers of all antidepressant medications to add a "black box" warning that describes the increased risk of suicidality in children and adolescents given antidepressant medications and notes what uses the drugs have been approved or not approved for in these patients. FDA's letters to the manufacturers also discuss other labeling changes designed to include additional information about pediatric studies of these drugs. These labeling changes are applicable to the entire category of antidepressant medications because the currently available data are not adequate to exclude any single medication from the increased risk of suicidality."

A little under a year later, on 30 June 2005, the FDA issued a further advisory regarding antidepressants and suicidality, only it was directed to adults. On 2 May 2007 the FDA issued an updated advisory regarding antidepressant use in children, adolescents and adults. This advisory remains in operation today.

One of the unexpected consequences for GlaxoSmithKline (GSK), the manufacturer of Aropax (Paxil in the United States and Seroxat in the United Kingdom), was the decision by New York's Attorney-General, Mr Eliot Spitzer to prosecute GSK on the ground of fraud for "withholding negative information and misrepresenting data on prescribing its antidepressant Paxil to children."

Australia

News of the FDA's action reached Australia quickly. On 25 March 2004 the ABC's National Radio programme, 'The World Today', ran the story: "TGA considers placing health warnings on anti-depressants." Dr Bill Lyndon, a psychiatrist, speaking on behalf of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) responded.

> "When these sorts of concerns are raised it is important for all authorities, including people like the College of Psychiatrists, as well as the TGA, all of us need to seriously look at these concerns and appraise them. But we also need to be careful not to throw out very important drugs that save a lot of lives on the basis of as yet unsubstantiated claims or unproven claims."
> Dr Bill Lyndon, The World Today, 25 March 2004.

But even before that report went to air, the RANZCP had already been consulted by the TGA's Adverse Drug Reactions Advisory Committee (ADRAC). On 11 March 2004, eleven days sooner than the FDA issued its first warning on 22 March 2004, the TGA issued its own advisory. The TGA confirmed that expert advice had been obtained from both the RANZCP and the Royal Australasian College of Physicians Division of Paediatrics and Child Health. And consistent with Dr Lyndon's approach, the TGA did not do what the FDA was about to do. Instead, the TGA explained that "ADRAC considers that the current data are not conclusive regarding the efficacy and safety of SSRIs in MDD [Major Depressive Disorder] in children and adolescents." On the

basis of that statement, rather than advise against the prescribing of certain antidepressants to children, the TGA simply warned:

> "… that "[a]ny SSRI use in children and adolescents with MDD should be undertaken only within the context of comprehensive management of the patient, as outlined in the NHMRC Clinical Practice Guidelines for Depression in Young People (1997)." It also noted that "the current Australian Product Information for paroxetine and venlafaxine recommends against their use in children and adolescents."

The response was directed only to MDD - not 'depression'.[45] This is a significant difference to the FDA. Psychiatrists would know that MDD is a specific form of 'depression', one that "requires a distinct change of mood, characterised by sadness or irritability and accompanied by at least several psychophysiological changes, such as disturbances in sleep, appetite, or sexual desire; constipation; loss of the ability to experience pleasure in work or with friends; crying; suicidal thoughts; slowing of speech and action … [that] must last a minimum of 2 weeks and interfere considerably with work and family relations."[46] In other words, MDD is a specific and severe form of 'depression'.[47]

The U.K. Committee's report, while referencing MDD to children, explained that expressly excluding or restricting use of antidepressants to treat MDD in children "to specialist use" was "not among the available regulatory responses" since no licences had been "granted for the use of SSRIs in children and adolescents with MDD" and the concern was, if they were to do so, that their actions could be mistaken interpreted as "authorising the use of the product in a group for which there was no licensed indiction."[48]

Another important point of difference is the TGA's reference back to the NHMRC's guidelines entitled '*Depression in young people'* issued in 1997, one year before the peak of child suicides, in 1998 is based on "evidence available in 1996". [49]

The RANZCP's response, based on what Dr Lyndon described as "unsubstantiated claims", was a clear statement to the effect that the RANZCP was not prepared to criticise the prescribing of antidepressants to children. On the other hand, an expert committee in the United Kingdom and two expert committees, both part of the FDA, that had examined the available evidence were, apparently, convinced about the reliability of the 'claims'. Clearly, there was some apparent disconnect between psychiatrists in the two hemispheres on this point. The question is why?

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[45] Belmaker, R.H., and Agam, G., (2008), 'Major Depressive Disorder', *New England Journal of Medicine*, 358, 55-68.

[46] Ibid. [Emphasis added]

[47] NHMRC Clinical Practice Guidelines *Depression in young people*, March 1997, p 3. "Major depressive disorder: a sad mood with four or more other depressive symptoms (see below) for at least two weeks duration."

[48] Report of the CSM Expert Working Group on the Safety of SSRI Antidepressants, p 62.

[49] Op cit 47, p 25.

One possible answer appears to be centred around the RANZCP's Guidelines for the Treatment of Depression, published in summary form in March 2003, about a year earlier.[50] The principal authors of this paper, Profs Ellis and Hickie, both recipients of funding from Eli Lilly, **Prozac's** manufacturer (although not disclosed in the paper), failed to mention the word 'children' once. Indeed, there was no discussion in their paper about any adverse side-effects of antidepressants. And throughout the paper they made constant references to SSRIs or SNRIs for use in the treatment of 'depression' of any form and in respect to any person, child or adult.

Given its already stated position on the treatment of 'depression', it would seem that the RANZCP's answer, in part, was to distinguish between 'depression' and MDD in its response to the concerns raised internationally over a practise which its Treatment Guidelines expressly promoted but which, now, was the subject of scrutiny and review by medicines regulators in the United Kingdom and the United States.

There is, however, another more plausible explanation. It is about the practise of prescribing 'off-label' but doing so lawfully under the PBS. While it is not illegal for a medical practitioner to prescribe a medicine for a purpose, or indication, that is not approved, or licensed, by the TGA for that purpose, it is illegal for a medicine so prescribed to be subsidised by the PBS when that indication is not listed on the PBS.[51] Tables 1 and 2 show, in respect of 12 psychotropic medicines approved by the TGA and listed on the PBS, that there are important differences. For example, **Aropax** (paroxetine), **Cipramil** (citalopram), **Efexor-XR** (venlafaxine), **Lexapro** (escitalopram), **Luvox** (fluoxamine), **Pristiq** (desvenlafaxine), **Prozac** (fluoxetine) and **Zoloft** (olanzapine) are licensed by the TGA for 'depression' (Table 1). Luvox, Prozac and Zoloft are also licensed for other mental disorders. However, the PBS Schedule for these psychotropic medicines narrows the scope of approval from 'depression' to MDD (Table 2), which, as we know is a specific and severe form of 'depression' that is very rare in children. Given that the RANZCP was well aware of this important distinction, it could not be seen to countenance an illegal practise. It had no choice but to limit its response to MDD, since the prescribing of any of the above mentioned psychotropic medicines under the PBS was an implicit admission of illegality. In any event, none of these medicines were recommended for the treatment of 'depression' in children by the manufacturers, and arguably, none were licensed by the TGA for such a purpose.

Subsequently, in June 2004 the RANZCP released the 'Australian and New Zealand clinical guidelines for the treatment of depression'.[52] The paper's lead authors were, once again, Profs Ellis and Hickie, who, on this occasion, disclosed their financial affiliations to Eli Lilly, Pfizer,

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[50] Ellis, P.M., Hickie, I.B., and Smith, D.A.R., (2003), 'Summary of guidelines for the treatment of depression', *Australasian Psychiatry*, 11 (1), 34-38.

[51] National Health Act 1953 s.105(b): "A person shall not: … (b) obtain a pharmaceutical benefit to which the person is not entitled;"

[52] Ellis, P., Hickie, I., and the CPG Team for Depression (2004), 'Australian and New Zealand clinical practice guidelines for the treatment of depression', *Australian and New Zealand Journal of Psychiatry*, 38 (6), 389-407.

Wyeth and Bristol-Myers Squibb. They also referred to 'children' on three occasions. In the course of the discussion, the authors advised that 'depression' "does occur in children but more often in teenagers." Moreover, 'depression' "affects boys and girls equally until the age of 15, after which it is more common in girls" and that "from ages 11-18 the rate increases from 0.5% to 3.4% for **a major depressive episode** and from 0.9% to 3.2% for **dysthymic disorder.**" Crucially, given the TGA's advisory of 11 March 2004 reference to MDD, the authors confirm that: "Most major depression begins in the late 20s." In other words, while children do get 'depressed',[53] MDD occurs mostly in adults. According to Beyondblue's Clinical Practice Guidelines (2011) "around 4%" of Australian children have experienced MDD or dysthymia.

This is a significant admission by the RANZCP, particularly since in the United Kingdom, as confirmed in the UK Expert Committee Report: "licences have not been granted for the use of SSRIs in children and adolescents with MDD".[54] In other words, the treatment of MDD in children with antidepressants was not approved by the U.K.'s medicines regulator.

On 17 June 2004 the TGA issued an updated advisory on the subject. Once again, the focus of the advisory was on the treatment of MDD.

"It should be noted that none of the SSRIs is approved for the treatment of MDD in children or adolescents in Australia, but these drugs are being used for this purpose. Two SSRIs (fluvoxamine and sertraline) are approved in Australia for the treatment of obsessive-compulsive disorder (OCD) in children and adolescents."

It is clear from these documents that in neither the United Kingdom or Australia were antidepressant medicines approved, or licensed, for the treatment of MDD, let alone for 'depression', in children. So why, as noted by the TGA, were antidepressants being prescribed for such a purpose by RANZCP members and other medical practitioners?

An answer can be found in the UK Expert Committee Report.

"Although evidence-based medicine relies on the availability of high quality trial evidence, it was acknowledged that doctors often have to make treatment decisions in the absence of such conclusive evidence and will, particularly in specialist settings, prescribe medicines that have not been licensed for a particular use. Therefore, the law allows doctors freedom to prescribe in the contraindicated population if they consider, from their knowledge and experience, it to be in the best interests of the patient. It remains possible that SSRIs and the related antidepressants may be effective in the treatment of depressive illness in some children, but the currently available evidence does not identify the population which may benefit."[55]

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[53] The prevalence of depression in children is 0.9%. Table 4.1, p 33, The Mental Health of Children and Adolescents in Great Britain, U.K. Office of National Statistics (2000)

[54] Report of the CSM Expert Working Group on the Safety of SSRI Antidepressants, p 62.

[55] Ibid.

Of course, the Report was written in the context of the law in the United Kingdom. In Australia, however, the law is not the same because of the distinction between the permission to prescribe 'off-label', which is legal, and the *National Health Act 1953,* the principal statute governing the operation of the PBS, that makes it an offence to receive a 'pharmaceutical benefit' for which one is "not entitled". Aiding and abetting the commission of that offence is also an illegal act. Whether the RANZCP's members are aware of this important distinction is a matter of conjecture. This submission makes no statement, nor draws any adverse inference, in this regard.

Nevertheless, the Australian medical profession, apparently with the imprimatur of the TGA, justifies the prescribing of psychotropic medicines for unlicensed and unapproved purposes, not on the basis of "evidence-based medicine" but on the basis of their "knowledge and experience".

If this is so, then, respectfully, what is the point of requiring any medicine to be subject to the approval of a medicines regulator if the approval of a medicine for one purpose is permissive of that medicine being used for a totally different purpose simply because a medical practitioner is of the opinion that it should be?

It would seem to be the case that as of June 2004 it mattered not that a manufacturer recommended against the prescribing of a psychotropic medicine for the treatment of depression in children. It mattered not that the TGA had not approved, or licensed, the use of antidepressants for the treatment of depression in children. And it mattered not that it was illegal for an antidepressant medicine to be provided under the PBS for the treatment of depression in children. As far as the RANZCP and the TGA was concerned, so long as a medical practitioner was of the opinion that such a medicine should be prescribed to a child, then evidence-based medicine and the law could be ignored.

This is particularly concerning given that both the lead authors of the RANZCP's Treatment Guidelines for the Treatment of Depression were financially affiliated with Eli Lilly, the manufacturer of **Prozac**.

Some Australian psychiatrists become alarmed at the RANZCP Treatment Guidelines

A number of Australian psychiatrists were alarmed by the RANZCP's Treatment Guidelines. One of these is Prof Gordon Parker, then Scientia Professor of Psychiatry (and Executive Director of the 'Black Dog Institute') at the University of New South Wales. Prof Parker's concerns were raised in an article published[56] in the *Australian and New Zealand Journal of Psychiatry*, the same journal that published the RANZCP's Treatment Guidelines.

"Despite RCTs [randomised controlled trials] of treatments for 'major depression' generating the largest evidential database existing in psychiatry, their intrinsic limitations are not widely

[56] Parker, G., (2004), 'Evaluating Treatments for Mood Disorders: Time for the Evidence to Get Real', *Australian and New Zealand Journal of Psychiatry,* 38 (6), 408-414.

appreciated. Most RCTs are designed to determine whether a treatment is 'efficacious', safe and tolerated, information that is required by licensing authorities. Such efficacy data is (at best) of some potential use to clinicians, but quite inappropriate 'evidence' for shaping clinical guidelines when its validity is suspect. " [Emphasis added]
Parker, G., (2004), 'Evaluating Treatments for Mood Disorders: Time for the Evidence to Get Real', *Australian and New Zealand Journal of Psychiatry,* 38 (6), 408-414.

Prof Parker not only criticised the RANZCP's Treatment Guidelines because of their focus on randomised controlled trials as a "single reality", but also because the data obtained from such trials had been misinterpreted. More specifically he was concerned that the data did not establish the efficacy of antidepressants.

"In English law, decisions can be reached on the basis of how the evidence might be interpreted by the 'man on the Clapham bus'. If such 'evidence' (both the overviews and the two recent large individual trials) of antidepressants were presented to the Clapham bus traveller, his interpretation would be that antidepressants are not distinctly superior to placebo therapies or, more worryingly, that they act as placebos." [Emphasis added]
Parker, G., (2004), 'Evaluating Treatments for Mood Disorders: Time for the Evidence to Get Real', *Australian and New Zealand Journal of Psychiatry,* 38 (6), 408-414.

He was also critical of the prescriptiveness of the Guidelines, which appeared "to be above challenge."

"But poor science is poor science. In describing the general process, the authors state that one of the 'quality features' of the RANZCP guidelines is 'systematic review', involving comprehensive review of 'randomized controlled trials of predefined quality', summarized 'through meta analysis', which together with other evidence and expert opinions, is 'critical for the formulation of clinical recommendations but also to allow the evidence to "speak for itself " '. This could allow a process where whatever level I evidence is poured into the top of the funnel comes out the spout untrammelled and preserved or where the guideline teams might judge – as I do here – that the level I evidence is a nonsense, and quietly insert their views and those of other experts to produce guidelines. It would be of interest if the authors of the RANZCP depression guidelines were to detail which option they selected."
Parker, G., (2004), 'Evaluating Treatments for Mood Disorders: Time for the Evidence to Get Real', *Australian and New Zealand Journal of Psychiatry,* 38 (6), 408-414.

Finally, Prof Parker raised the issue of the influence of the pharmaceutical industry over the psychiatric medical profession by reference to a review undertaken by the late Prof Howard Meltzer, Professor of Health Medicine, University of Leicester, of a clinical study that showed that "a new NK1 inhibitor was no better than placebo as an antidepressant."

"Meltzer suggested that 'in aggregate, our field would appear to have a lot of problems in its scientific basis, ethics, and independence from the pharmaceutical industry', and concluded that 'much of the negative news represents the result of not taking all available information into account and a lack of understanding of the importance of specific features of the illnesses in question'."
Parker, G., (2004), 'Evaluating Treatments for Mood Disorders: Time for the Evidence to Get Real', *Australian and New Zealand Journal of Psychiatry,* 38 (6), 408-414.

Prof Parker was critical of the profession's strict adherence to a "single reality" and proposed a more holistic approach to the evaluation of medicines, including that clinical experience of psychiatrists with their patients be incorporated, because randomised clinical trials, in his opinion, are not, in themselves, reliable indicators of the efficacy and safety of psychotropic medicines.

The RANZCP responds - in defence of evidence-based medicine

The RANZCP's response was authored by Profs Ellis and Hickie and Dr Smith.[57] Interestingly, given the practise of prescribing psychotropic to children 'off-label' was approved by the RANZCP, which by definition is not evidence-based medicine, the authors "make no apology for utilising an evidence-based approach to this project, reflecting international and National Health and Medical Research Council (NHMRC) practice." The inconsistency is immediately apparent.

The RANZCP was, nonetheless, caught in a pincer movement between evidence-based medicine, which until 2002 seemingly supported the use of antidepressants in children, and the evidence-based medicine since 2002 that seemingly did not. The RANZCP ultimately sided with the former using off-labelling as the mechanism in which to deploy its collective decision. And in the process suppressed the potential and looming dangers that such an election posed for Australian children and the ramifications for their families.

One year before the UK Expert Committee was established, in 2002, three Australian psychiatrists and RANZCP members, Dr Raphael Chan, Prof Joseph Rey and Prof Philip Hazell, published a paper in the *Medical Journal of Australia*.[58] The paper called for the NHMRC practice guidelines for the treatment of depression in "young people" to be updated. Their argument was that much had happened in the field of psychiatry since 1997, when the guidelines were first published. The authors referred to four peer-reviewed papers that supported the use of antidepressants in children. Two of these paper supported the use of **Prozac** (fluoxetine). One supported the use of **Aropax** (paroxetine). All three papers discussed 'randomised clinical trials' funded by the manufacturers of the respective antidepressants. The final paper was a review of antidepressants in adults that made a very brief reference to the Prozac trials. They recommended the update include the following:

"SSRIs, particularly fluoxetine and paroxetine, should also be considered as a first-line treatment."

Incidentally, Prof Hazell had a financial affiliation to Pfizer, the manufacturer of **Zoloft** (sertraline).

[57] Ellis, P.M., Hickie, I.B. and Smith, D.R., (2004), 'Evidence-based guidelines: response to Professor Gordon Parker's critique', 38, *Australian and New Zealand Journal of Psychiatry*, 891-895.

[58] Chan, R.T.W., Rey, J.M., and Hazell, P.L., (2002), 'Clinical practice guidelines for depression in young people: are the treatment recommendations outdated?', *Medical Journal of Australia*, 177, 440-443.

Absent from the paper was a reference to an important paper published in 1999 co-authored by Prof David Healy.[59] Prof Healy was concerned that a link between Prozac and suicidality, was being "denied on the basis that RCTs [randomised clinical trials] are the only means to demonstrate cause and effect."[60] He was particularly critical of the manner in which randomised clinical trials are designed.

"However, the use of RCTs by pharmaceutical companies is largely determined by registration requirements for evidence of some treatment effect. The patients recruited to such studies are samples of convenience, which need not represent either the general population or any vulnerable population within in it. These trials are not designed to answer the question of whether the drug on occasion can trigger an emergence of suicidality. To date, there have been no such trials. A meta-analysis of studies conducted for other purposes, using instruments that were never designed to settle this question is no substitute, given experimental indications showing patients and observers may fail to rate even intense newly emergent drug-induced suicidality (Healy and Farquhar, 1998). Quite simply, beneficial effects on suicidality in a majority of depressed patients do not outrule drug induced problems anymore than a reduction of pertussis induced brain damage outrules vaccine induced injuries."
Healy, D., Langmaak, C., and Savage, M., (1999) 'Suicide in the course of the treatment of depression', *Journal of Psychopharmacology*, 13 (1), 94-99.

By June 2004, however, there was no denying the fact that the concerns Prof Healy foreshadowed in his 1999 paper were coming to pass.

Nonetheless, the RANZCP was not prepared to concede the point. While Profs Ellis, Hickie and Dr Smith acknowledged that the "correct subdivision of depression remains controversial", they relied on there being "clear agreement" on differing kinds of severe depression in support of the approach taken in the Guidelines. Dismissing Prof Parker's criticism that randomised clinical trials "tend to recruit subjects who are more prone to respond" and "exclude people with significant comorbidity", the authors fell back on the American Psychiatric Association and British Association of Psychopharmacology guidelines that showed "based on careful selection of quality studies, … antidepressants are superior to placebo."

A third TGA (ADRAC) Advisory in 2004

On 15 October 2004 the TGA issued a further advisory entitled: "Use of SSRI antidepressants in children and adolescents".

"None of the SSRIs, and indeed no antidepressant, is currently approved in Australia for the treatment of MDD in children and adolescents (persons aged less than 18 years). Fluoxetine, but none of the other SSRIs, is approved in the US for MDD in young people without a specified lower age limit. Two of the SSRIs, fluvoxamine and sertraline, are approved in Australia for children and adolescents with obsessive compulsive disorder (OCD)."

[59] Healy, D., Langmaak, C., and Savage, M., (1999) 'Suicide in the course of the treatment of depression', *Journal of Psychopharmacology*, 13 (1), 94-99.

[60] Ibid, p 95.

The significant change from the previous advisory issued in June was that "no antidepressant", not just SSRIs, were not approved for the treatment of MDD in children. Another significant change change was an admission, in line with the concerns raised by both Profs Parker and Healy, that there were problems with the design of clinical trials.

"In general clinical trials of SSRIs in children and adolescents have excluded severely depressed patients and have not adequately monitored participants for self-harm or suicide-related events. Other non-SSRI antidepressants have been subjected to even less scrutiny, and may be inefficacious and also associated with suicidality, as well as having other undesirable effects such as the toxicity in overdose of the tricyclics."

Most importantly, the TGA changed the primary recommendation to include "other psychiatric conditions" in addition to MDD and distanced itself from the NHMRC by deleting reference to the NHMRC's guidelines for the treatment of depression in children issued in 1997. It replaced the recommendation with the need for all children prescribed with an antidepressant to managed "only within the context of comprehensive management of the patient" which should "include careful monitoring for the emergence of suicidal ideation and behaviour …". Finally, it recommended that:

"Prescribers should be aware that the marketers of fluvoxamine and sertraline (indicated for OCD) advise against use in children and adolescents with MDD, and of citalopram, escitalopram, paroxetine, venlafaxine and fluoxetine warn or caution against use in patients aged less than 18 years for any indication."

Respectfully, this advisory contained a series of mixed messages that simply made little sense in the context of the TGA (ADRAC) acknowledging that:

(a) antidepressant clinical trials were of questionable reliability;

(b) no antidepressant had been approved for the treatment of any psychiatric condition in any children other than **Luvox** (fluvoxamine) and **Zoloft** (sertraline) for obsessive compulsive disorder;

(c) no antidepressant had been recommended by the manufacturer for the treatment of any psychiatric condition in children; and,

(d) suicidal ideation or behaviour and self-harm in children and adolescents treated with an SSRI antidepressant could be a reasonably foreseeable reaction to the medication.

And yet, "any use of SSRIs in children and adolescents" could be used if "undertaken … within the context of comprehensive management of the patient."

Developments in the United States

The People of the State of New York v GlaxoSmithKline

On 2 June 2004 the Attorney General for the State of New York, Mr Eliot Spitzer, sued GlaxoSmithKline (GSK) alleging it had:

" … engaged in repeated and persistent fraud by misrepresenting, concealing and otherwise failing to disclose to physicians information in its control concerning the safety and effectiveness of its antidepressant medication paroxetine HCL ("paroxetine") in treating children and adolescents with Major Depressive Disorder ("MDD")."

The Complaint confirmed that:

"Paroxetine has not been approved for any condition or illness in children or adolescents".

And that:

"New York, like other states, permits physicians to prescribe FDA-approved drugs for conditions or diseases for which FDA approval has not been obtained when, through the exercise of independent professional judgment, the physician determines the drug in question is an appropriate treatment for an individual patient. This practice is referred to as "off-label" use, and prescribing paroxetine for children and adolescents is an off-label use"

In short, the situation in the State of New York, putting to one side the matter of the PBS that is exclusively an Australian institution and that is governed under the *National Health Act 1953*, was the same in Australia. Medical practitioners rely on information provided by medicine manufacturers in making decisions about whether or not to prescribe medicines to patients. Clearly, it is in the interests of medicine manufacturers that they do prescribe medicines. However, it was alleged that GSK had only "disclosed publicly" positive information "about the paediatric use of paroxetine", while it "withheld and concealed negative information concerning the safety and effectiveness of the drug as a treatment for paediatric MDD."

The most damning allegation was that GSK claimed to its sales representatives that:

"Paxil demonstrates REMARKABLE Efficacy and Safety in the treatment of adolescent depression."

And the relevant clinical study simply "did not demonstrate remarkable efficacy and safety in treating adolescent depression." Indeed, on 10 June 2003, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) concluded that:

" … its analyses of GSK's studies suggested the risk of self-harm and potential suicidal behaviour of youngsters with MDD was between 1.5 and 3.2 times greater for the paroxetine group that for placebo."

The GSK sales representatives had, nonetheless, proceeded to misrepresent the study results to medical practitioners, and, remarkably, continued doing so.

"But a spokeswoman for Glaxo said "we did publicly communicate" the results of other studies in various forums, including medical conventions and letters to physicians. "There are many, many studies each year," said Mary Anne Rhyne. "It's impractical to believe that every company in the industry will be able to publish from every study." Paxil has not been approved by the U.S. Food and Drug Administration for pediatric use and Ms. Rhyne said Glaxo has never

> promoted it for such use. She said all of Glaxo's data on the drug were made available to the FDA and other regulatory agencies."[61]

And right up until the matter was finally resolved with the U.S. Department of Justice on 2 July 2012 GSK remained unrepentant. In the Department's media release it was confirmed that GSK would plead guilty to criminal charges and "pay $3 billion to resolve its criminal and civil liability arising from the company's unlawful promotion of certain prescription drugs …".

This is the largest health care fraud settlement in U.S. legal history.

Incidentally, **Aropax** (paroxetine) is one of the two psychotropic medicine that Dr Raphael Chan, Prof Joseph Rey and Prof Philip Hazell[62] suggested justified this recommendation in 2002:

> "SSRIs, particularly fluoxetine and paroxetine, should also be considered as a first-line treatment."

In addition to its most successful prosecution of GSK, the US Department of Justice successfully prosecuted **Bristol-Myers Squibb** in 2007 for its off-label promotion of **Abilify** (aripiprazole) for use in children, Eli Lilly in 2009 for its off-label promotion of **Zyprexa** (olanzapine) for use in children and Astra Zeneca in 2010 for its off-label promotion of **Seroquel** (quetiapine) for use in children.

Further developments in Australia

In the meantime the Australian subsidiary of GSK was not investigated nor charged nor prosecuted in regard to the promotion of **Aropax** (paroxetine) in Australia. It is almost as if the instructions given to GSK sales representatives in the United States were quarantined and never disseminated around the world to subsidiaries in other countries. It is suggested this is a most unlikely scenario.

Indeed, it is unlikely that the Department of Health, the TGA and ADRAC would have done anything had it not been for Dr Yolande Lucire, a Sydney-based psychiatrist. Dr Lucire wrote to Prof John Horvarth, the Chief Medical Officer, in June 2004. On 6 July 2004 Prof Horvarth replied that he had consulted with Dr McEwen (TGA) and "understand from him that a number of your concerns have been considered …". Dr Lucire also wrote to Ms Jane Halton, then Secretary of Health and Ageing, on 28 October 2004 explaining that "SSRIs induced suicide [is] at an average rate of 200 per 100,000 treated (at single dose)." Ms Halton replied on 19 November 2004 confirming that it was "a very important issue and the Department is carefully monitoring the situation." Unfortunately, it was not until Dr Lucire wrote again to Ms Halton on 30 January 2008, reminding her of the "database [of] some two hundred admissions of suicidality"

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[61] Martinez, B., (3 June 2004), 'Spitzer Charges Glaxo Concealed Paxil Data', *Wall Street Journal*.

[62] Chan, R.T.W., Rey, J.M., and Hazell, P.L., (2002), 'Clinical practice guidelines for depression in young people: are the treatment recommendations outdated?', *Medical Journal of Australia*, 177, 440-443.

that Dr Lucire had already provided her Department (ADRAC) in 2004, that a decision was made to investigate. Ms Halton eventually replied to Dr Lucire on 7 September 2008 advising her:

"In order to address your ongoing concerns, the TGA recently established a special expert advisory panel, comprising independent psychiatrists and epidemiologists, to consider and comment on the case reports that you have provided. The panel will also review the relevant literature and determine the degree to which the adverse effects that you have documented are currently reflected in the literature and the various Product Information documents. The panel is expected to report by the end of the year and I will write to you again when I have received its findings."

The Report of the Psychiatric Drug Safety Expert Advisory Panel

"In August 2008 the TGA established an independent panel of psychiatrists and epidemiologists to undertake a specific review of selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotic medicines. The panel, known as the Psychiatric Drug Safety Expert Advisory Panel (PDSEAP) was tasked with undertaking a detailed review of the safety of these particular psychiatric medications. The PDSEAP has now completed its work and its report is being made public."

Unfortunately, the 103 page Report devoted only half a page to "High Risk Populations: Children and Adolescents".[63] This section consisted of a cursory, perfunctory, review of carefully selected literature that was essentially inconclusive. The Report contained no recommendations relevant to children.

Interestingly, one of the panelists was Prof Wayne Hall. Prof Hall was the co-author of paper with Prof Hickie (financially affiliated with Eli Lilly, manufacturer of **Prozac** (fluoxetine)) published in 2003 in the *British Medical Journal*.[64] The paper sought to explain trends in suicides in the 1990s, but specifically excluded children younger than 15, limiting its analysis to ABS data for the age groups starting with the 15-24 group. The authors, nevertheless, made an interesting finding:

"We found a steep increase in antidepressant prescribing in Australia from 1991 to 2000, which, unlike in earlier studies, was not accompanied by a decline in overall rates of suicides because there was a large increase in suicide in young people over the same period."

This is a significant finding that the expert panelists failed to refer to in their Report. Instead, the section in the Report dealing with children and adolescents is identical, word for word, with what Prof Hall and co-author Ms Jayne Hall wrote in a later paper published in 2006.[65] It would seem reasonable to conclude that the expert panel simply chose to ignore Profs Hall and Hickie's earlier finding, possibly because it was inconsistent with the position that the panelists preferred

[63] The Report of the Psychiatric Drug Safety Expert Advisory Panel, p 29.

[64] Hall., W.D., Mant, A., Mitchell, P.B., Rendle, V.A., Hickie, I.B., and McManus, P., (2003),'Association between antidepressant prescribing and suicide in Australia, 1991-2000: trend analysis', 326, *British Medical Journal,* 1008.

[65] Hall., W.D., and Lucke, J., (2006), 'How have the selective serotonin reuptake inhibitor antidepressants affected suicide mortality?', *Australian and New Zealand Journal of Psychiatry,* 40, 941-950, pp 946-7.

to take on the issue, and one that was completely consistent with Prof Hall's later paper. It seems nothing, according to the expert panelists, in three years between 2006 and 2009, had changed. That is not, as will be discussed in the next section, the case. Much had changed. Apart from the US Department of Justice's investigation and prosecution of several pharmaceutical companies that continued to encourage the prescribing of psychotropic medicines to children, children continued to self-harm whilst being under the influence of antidepressant medicines.

Beyondblue's Clinical Practice Guidelines (2011)

The *Depression in Adolescents and Young Adults Guidelines* was approved by the NHMRC on 11 February 2011. The approval is valid for a period of five years. It is the very latest in clinical guidelines applicable to children in the treatment of depression in Australia. This is the information that is presented on the issue of SSRIs and suicidal ideation:

SSRIs and suicidal thinking

• RCTs (Keller et al 2001; March et al 2004; Berard et al 2006; Donnelly et al 2006; von Knorring et al 2006) and analyses of data on nearly 2,200 children and adolescents taking SSRIs collected by the US Food and Drug Administration (FDA) (Stone & Jones 2006) found a statistically significant increase in suicidal thinking/behaviour. Further exploration of the FDA dataset (Hammad et al 2006) corroborated this association. There were no completed suicides in the study populations.

• The results of the FDA review (Stone & Jones 2006) also show a trend towards antidepressants (SSRIs and new generation antidepressants) increasing the rate of suicidal thinking or behaviour among young adults aged 19 to 24 years.[66]

Health authority recommendations

Different countries have adopted different regulatory responses to findings on the safety and efficacy of antidepressants in children and young people.

• UK health authorities have advised doctors to avoid SSRIs for the treatment of depression in children and young people, except fluoxetine.

• US health authorities have recommended that for individuals up to 24 years of age 'black-box' warnings about the increased risk of suicidality be included on medication prescribing and patient information leaflets.

In Australia, the Adverse Drug Reactions Advisory Committee (ADRAC) has issued a statement noting that while SSRIs are commonly prescribed for young people with depression, none has been approved for this purpose in Australia (although fluoxetine, fluvoxamine and sertraline have been approved for treating obsessive-compulsive disorder in this age group). ADRAC has also advised that prescribers in Australia should note that the marketers of SSRIs warn, or caution against the use of SSRIs for depression in people aged less than 18 years. While not preventing their use, ADRAC advised that the use of SSRIs in young people should only occur in the context of a comprehensive management plan for the patient, which includes careful monitoring for the development of suicidal thinking or behaviours. ADRAC also noted that patients already being treated with an SSRI should not have their medication ceased abruptly.[67]

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[66] Beyondblue Clinical Practice Guidelines for Depression in Children and Young Adults (2011), p 55.

[67] Ibid, 56-57.

It would seem, however, that psychotropic medicines, despite the fact that they are not approved for the purpose, have been and continue to be prescribed for the treatment of depression in children in Australia. (Table 3)

Case Studies

These four case studies are true stories of children (their names are fictitious) who were prescribed with psychotropic medicines by Australian medical practitioners for the treatment of 'depression'. One has been included even though he had just turned 18 because the events leading to the treatment of his depression commenced when he was a child and because, at the time of the events recorded in his case study, he was still a child.

The first contact they had with these medications occurred without a diagnosis of a serious mental disorder. This is significant, because as has already been established, these medicines are not recommended for use in children by the manufacturers and the TGA, nor are they listed for such use on the PBS, for the treatment of 'depression'.

In some cases the children were diagnosed with schizophrenia and other mental disorders *after* they had already been medicated, which raises the obvious question about the validity of the original diagnosis. The decision to medicate a child according to the TGA must involve the close monitoring of that child for any adverse side-effects including suicidal ideation. Moreover, the side-effects can be very severe, especially for a child, and do mimic symptoms that are consistent with schizophrenia. For example, side-effects listed for **Zoloft** (sertraline) include agitation, nervousness, anxiety, frightening dreams, abnormal thinking, teeth grinding, loss of appetite, impaired concentration, thoughts of suicide or attempting suicide or self harm.[68] These are symptomatic of schizophrenia, major depressive disorder, bipolar and other mental disorders. The question is, was the child schizophrenic (or another serious mental disorder) before or after the medication was commenced?

When their first psychotropic medicine was prescribed, each of the them were facing some sort of life problem which had made them unhappy and unsettled like bullying, sexual abuse or the breakup of a relationship.

All attempted suicide. One succeeded.

[68] Ibid, Heading: Side Effects

Child One

Self-harming behaviour: suicidal ideation, attempted suicides, cutting, dieting.

Age at first psychotropic medicine: 15

Reason for medical visit: Bullying and a bad sexual experience.

Child 1 was an excellent student in primary school and was awarded a scholarship to an exclusive private high school. When she started at her new school, she was bullied, and while some of the bullies were expelled for their behaviour, some girls remained and continued to harass Child 1. When she was in her mid-teens, Child 1 had a bad sexual experience with a boy who was a close family friend, which triggered a family crisis. Thoughts of suicide started entered her head and she began to cut herself, but did not attempt suicide.

She was first prescribed **Zoloft** (sertraline) at 15. Her medical practitioner, a local GP, then added **Risperdal** (risperidone), an antipsychotic, to Child One's treatment after two months. Both of these were prescribed to her 'off-label' as **Zoloft** (sertraline) is not recommended for children under 18 unless they've been diagnosed with obsessive compulsive disorder[69] and **Risperdal** (risperidone), should only be given to schizophrenic patients – and Child 1 had not been diagnosed with either. Child 1 was depressed. She was not schizophrenic, nor was she an obsessive compulsive.

Subsequently Child 1 became extremely suicidal and was hospitalised as a result. In hospital she was was prescribed a cocktail of psychotropic medicines consisting of **Zoloft** (sertraline), **Risperdal** (risperidone), **Avanza** (mirtazapine) and then eventually **Prozac** (fluoxetine).

During this time the intensity of her death wishes varied. On a bad day she had an impulse to suicide every hour, on other days, two or three times a day.

'I saw myself hanging, jumping in front of a car, off a building, electrocuting myself…'
Child 1

During stays in hospital, Child 1 met anorexic patients, and then became obsessed with dieting like them. She stopped taking her antidepressant medicines but remained on **Zyprexa** (olanzapine), an antipsychotic. Child 1 said that this made her feel she both lethargic and fat (antipsychotics are well known to slow metabolism). She then took an overdose of 80 paracetamol tablets. Child 1 survived.

She was eventually given medical advice to withdraw slowly from all of the medication and she recovered. She was 16 by this time. Child 1's case is an example of how psychotropic medications intensify depression, not reduce its symptoms. It is also an example of what happens between child and doctor.

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[69]Ibid

Child Two

Self-harming behaviour: Committed suicide

Age at first psychotropic medicine: 18

Reason for medical visit: Chest infection.

Child 2, , an 18-year-old university student, had a lingering respiratory infection so he booked an appointment to visit his family GP. Child 2 also told the GP that he had recently broken up with his girlfriend and was not sleeping well. The GP gave him a sample packet of **Lexapro** (escitalopram) and told him to take 10 milligrams daily. The GP also prescribed him an antibiotic for his chest infection.

Child 2 went home and started taking **Lexapro**, but not the antibiotic. In the first 24 hours of taking the drug, his mother described Child 2 as "playful", but his condition deteriorated soon after.

By the fourth day of taking the **Lexapro**, he was restless and kept saying: "I've got to go. I've got to go."

Child Two's mother said he seemed "robotic" but then would become agitated and start crying. He could not articulate what he needed and did not talk of suicide. Child 2 left his house. His mother who thought he was just going for a drive. He drove to a nearby hardware store, bought a rope and hanged himself.

He went to his GP for a chest infection. Yes, he was depressed. But within a week of taking **Lexapro** he was dead.

Child 3

Self-harming behaviour: Numerous attempted suicides, cutting herself, hallucinations and violent ideations.

Age at first psychotropic medicine: 14

Reason for medical visit: Relief from trauma due to sexual abuse in Year 7

Child Three's parents divorced when she was a year old. She lived predominantly with her mother, a nurse, and her father remained in her life.

When she reached high school, Child 3 was sexually abused but told a psychiatrist later that she repressed the memories of it and tried to get on with her schooling. She was good at sport

but didn't like school in general and started associating with a bad crowd and experimenting with cannabis, alcohol and cigarettes –alienating her from the rest of her classmates.

Child 3's memories of sexual abuse came back in Year 9. She was depressed. At 14 she was prescribed **Aropax** (paroxetine) by her GP.

Subsequently, she was diagnosed with bi-polar disorder and schizophrenia. She was then a cocktail of antidepressants, antipsychotics and ADHD drugs.

She recalls anxiety, agitation, frustration, panic attacks but other memories are hazy. She had dreams which were both violent and hostile.

"I used to have this dream where I tried to kill everyone in the school and kill myself."
Child 3

She attempted suicide by hanging. She dreamt about suicide by gun. She cut her legs and arms for over a year. She overdosed on one of her ADHD medications.

She was admitted to psychiatric hospitals at least half a dozen times and was physically restrained numerous times for violence towards others and herself. Her parents took her out of school and took time off work to care for her. She felt awful and sleepy and became hostile.

Her father was distressed at seeing her tied up to a bed in hospital. He was also sent a bill for a security guard by the hospital, which he refused to pay. One doctor said to Child Three's father "She is seriously toxic" and then refused to give her father any more information.

Child Three had visual hallucinations of "a little blue guy who walked on walls". She says she only had the visions while on her cocktail of medications.

Child Three was eventually seen by a medical practitioner who disagreed with the original diagnosis of schizophrenia. She was slowly taken off all the antipsychotics and ADHD medicines. She remained on antidepressants. She is recovering.

Child Four

Self-harming behaviour: Attempted suicide, violent ideation, assault

Age at first psychotropic medicine: 14

Reason for medical visit: Relief from trauma due to childhood sexual abuse

From the age of 8 to 14 a family member sexually abused Child 4, but when she told her family, they did not believe her and instead sent her to a psychiatrist. Child 4 was depressed.

Child 4 was prescribed **Prozac** (fluoxetine). Immediately she started experiencing violent suicidal and homicidal feelings. Her behaviour became erratic and she assaulted a complete stranger at a bus stop and was placed in juvenile detention.

Three public sector hospitalisations did not relieve her condition. Her behaviour worsened and she started using cocaine.

After a medical practitioner suspected Child 4's medications were possibly causing her more harm than good, they were slowly withdrawn and the manias and side-effects ceased.

After a miscarriage she was prescribed various painkillers, an antipsychotic and benzodiazepines. This induce mania (including erotomania and drug use). Then the drug craving, substance misuse, gambling mania coalesced and she got out went out of control.

She again recovered when imprisoned. Following a stillbirth in prison (and attendant medications), she had a relapse, grieved, pleaded for help and was again given **Prozac** (fluoxetine).

She continues a pattern of medication and withdrawal and is currently in prison. Because she has been repeatedly put on medication since 14 her brain may have been irreparably damaged.

Self-Harming behaviour and the link to 'depression' as the main cause - where is the evidence?

According to Beyondblue's *Clinical Guidelines for the Treatment of Depression in Children and Young Adults:*

"The strongest risk factor for suicide are mental health disorders, particularly depression. In 2005, 14% of all suicide deaths were of young people, and suicide accounted for one-fifth of all deaths of young people. Suicide rates increased with age for both males and females: from 1 death per 100,000 young people aged 12 to 14 years to 5 per 100,000 15 to 17 year olds and 13 per 100,000 18 to 24 year olds."[70]

This statement clearly suggests that 'depression' is the leading cause of children self-harming (which is defined to include suicide attempts and suicides). The truth is far more complicated. And one of the reasons it is, is that since the introduction of SSRI antidepressants and atypical antipsychotics in the late 1980s, the prescribing of these medications to children for the treatment of depression (and other mental disorders) has skyrocketed around the developed world.[71]

"The psychotropic medication visits of children and adolescents (younger than 18 years) increased significantly from 1.10 million in 1985 to 3.73 million visits in 1993 and 1994."

And this trend has not abated, as the Pharmaceutical Benefits Advisory Committee's Report, released in May 2014 shows:

"In the 0–19 year age group, the three most commonly used antipsychotics were risperidone, quetiapine and olanzapine. Two periods of time are compared to examine

[70] Beyondblue Clinical Practice Guidelines for Depression in Children and Young Adults (2011), p 2.

[71] Pincus, A.P., Tanielian, T.L., Marcus, S.C., Olfson, M., Zarin, D.A., Thompson, J., and Magno Zito, J., (1998), 'Prescribing Trends in Psychotropic Medications', *JAMA*, 279 (7), 526-531.

change in utilisation for the most popular medicines using the population standardised numbers of patients in 2008 and 2011 (Figure 4). Between 2008 and 2011 there was a large increase in the use of quetiapine, with the number of patients in the 0–19 year age group who were supplied the drug more than doubling (an increase of 138%). Risperidone use also increased in all age groups across this age category (+46%)."
PBAC Report: Antipsychotics in children and adolescents (February 2013), p 9

As a result of the dramatic increase in the use of these medicines in the treatment of depression, it is very likely that a child born since 1985 who experience's suicidal ideation, attempt's suicide or commit's suicide, will be under the influence of one or more psychotropic medicines at the time. Therefore, the true causation of children self-harming is a matter that is open to question. It is not, as is suggested by Beyondblue, simply because a child is depressed that they are at a high risk of self-harm. It may well be, as this submission argues, that the underlying cause of the relevant act is the psychotropic medication itself.

This submission argues that an important and relevant contributor to child self-harming behaviour is, in fact, the current mainstream medical practise that invariably leads to the 'off-label' prescribing of psychotropic medicines to children in the treatment of 'depression'. Of course, there are other factors at play. This submission does not suggest that these other factors are irrelevant or trivial, but it does argue that psychotropic medications as currently prescribed to children is a significant factor.

It is regrettable that despite the overwhelming evidence of there being a serious problem involving children, for more than a decade the RANZCP, the TGA and the various State and Federal Departments of Health have not acted decisively to stop the off-label, and illegal (if the PBS is involved), prescribing of psychotropic medicines to children. Indeed, it would appear as if they have countenanced the practise through the various TGA advisories. The failure of the TGA and the Departments of Health to appreciate the conflicts of interest that have influenced some key medical opinion leaders, funded primarily by the Australian taxpayer (but who also receive funding from pharmaceutical companies), to overlook or minimise the real risks of this erroneous practise for reasons unknown. They have enabled those same 'independent' experts to undermine the role of the TGA, which should be to protect the Australian people, particularly, children from medicines that have not been demonstrated, through independent-based empirical evidence, to be safe and efficacious in the context of the prescribed purpose.[72] The nomenclature of 'depression' and the fuzzy logic that has overemphasised a link between 'depression' and self-harming behaviour is also partially responsible for the regulatory failure.

"Could it be a case of the old belief or assumption "you must be out of your mind to kill yourself" that has somehow become accepted? The notion that suicide is caused by depression is so strongly established in the mindset that even educated health professionals refuse to question the evidence and thus try to fit every suicide into this model. "
Shahtahmasebi, S., (2013), 'Examining the claim that 80-90% of suicide cases had depression', Frontiers in Public Health, 1, 1-2.

[72] Healy, D., (2006), 'Did regulators fail over selective serotonin reuptake inhibitors?', *British Journal of Medicine*, 333, 92-95.

If 'depression' is the cause of self-harming behaviour in children, is it not appropriate to try and understand the various environmental factors that make children depressed?

"Mood disorder, especially in combination with non affective comorbidity, like conduct disorder and substance abuse, was found to be a substantial contributor to suicidal risk. A previous attempt is a very strong and independent predictor of a future attempt, particularly with continued suicidal ideation or depression. Suicidal ideation is more likely to progress to suicidal behavior in the face of alcohol or substance abuse. Suicidal tendencies run in families, as do depression, aggression, and alcohol and substance abuse. Family adversity, such as neglect or abuse, is a powerful independent antecedent of psychopathology and suicidal behavior. Suicidal youth are more attracted to death and less able to generate alternatives to suicide when faced with stress. Suicidal behavior is associated with other health risk behaviors (e.g., having unprotected sex, binge drinking), and family cohesion, parental supervision, and perceived self-efficacy are protective against these intercorrelated risk behaviors."
Brent, D.A., (2011), 'Preventing Youth Suicide: Time to Ask How', Journal of the American Academy of Child and Adolescent Psychiatry, 50 (8), 738-739.

In 1992 Dr Fergusson and Mr Lynskey co-authored a paper published in the *Journal of the American Academy of Child and Adolescent Psychiatry*.[73] Their paper examined a cohort of New Zealand children who had attempted suicide. While the authors found that 90% of the cohort had, by 16 years, at least one mental disorder, the results also showed that they "came from socially disadvantaged or dysfunctional family circumstances characterized by economic disadvantages, parental substance abuse or offending, marital conflict and instability, compromised child-rearing, and high residential mobility." Their suggested remedy was not, however, to prescribe antidepressants.

"The finding of relatively strong common pathways linking childhood and family circumstances to later adjustment and suicide risks may have a number of implications for the design of prevention strategies to reduce risks of suicidal behaviors in adolescence. In particular, the findings of the present analysis strongly reinforce a number of recommendations made by Garland and Zigler (1993) in their review of adolescent suicidal behaviors and prevention methods. Specifically, Garland and Zigler suggest that an important component of primary prevention of adolescent suicide involves the development of family support programs to address the needs of high-risk families and their offspring. They describe these programs in the following ways. "These programs seek to empower families by improving their ability to cope with the debilitating stresses facing families today such as poverty, single parenthood, geographic mobility, substance use and adolescent pregnancy" (p. 177)" [Emphasis added]
Fergusson., D.M., and Lynskey, M.T., (1992), 'Childhood Circumstances, Adolescent Adjustment, and Suicide Attempts in a New Zealand Birth Cohort', *Journal of the American Academy of Child and Adolescent Psychiatry*, 34 (5), 612-622.

[73] Fergusson., D.M., and Lynskey, M.T., (1992), 'Childhood Circumstances, Adolescent Adjustment, and Suicide Attempts in a New Zealand Birth Cohort', *Journal of the American Academy of Child and Adolescent Psychiatry*, 34 (5), 612-622.

Australian Statistics, Self-Harming Behaviour and Psychotropic Medicines

The available ABS suicide statistics are a very poor evidentiary tool for the reasons discussed earlier. However, since they are the only statistics available it is necessary to include them in this submission. Table 4 on page 46 contains ABS data for a 20 year period,1993 to 2012 for all age groups commencing with 0-14 and thereafter in 5 year increments from 15-19 through to 75-79. Above 79 is open. For each year and age group is the number of 'intentional' suicides. The averages for 20 years, and then for 10 years, 1993-2002 and 2003-2012, are provided in the columns at the end of the table. The final column shows the percent change between the 1993-2002 and 2003-2012 periods. The green arrow indicates a decrease. The red arrow indicates an increase.

Each of the datum is highlighted by the colours blue, green or red. The colour blue indicates that the datum is equal to the 10 year average for the respective 10 year period. The colour green indicates that the datum is less than that average. The colour red indicates that it is greater than that average.

The primary analysis is in the 0-14 and 15-19 age groups. The other age groups are provided nonetheless.

The Table provides data for males, females and males and females combined.

The Table shows that in the case of both males and females the numbers of 'intentional' suicides in the 0-14 age group have averaged 6 for males and 4 for females in both 10 year periods. In terms of number of suicides the highest recorded for males is 10 in 1999. For females the highest recorded is 9 in 2011. In the 15-19 age group the averages vary significantly. In males the 10 year average is 106 in the 1993-2002 period and 77 in the 2003-2012 period. This is a decrease of 27.4%. In females the averages are 28 and 32 respectively. This is an increase of 14.3%.

The Table also shows, by way of colour coding, that the number of suicides above the respective 10 year average for males is grouped in the 1993-2002 period, with the highest number of suicides recorded, 121, in 1997. In all but 2000, the number of suicides is higher than the average. However, in the 2002-2012 period, all but one year, 2010 (91), are below the respective 10 year average. In the case of females, the pattern is very different. There are two groupings of red in both decades. In the 1993-2002 period the highest number of suicides recorded is 41 in 2000, but there are two years, 1997 (33) and 1998 (35), where the number of suicides are above average. In the 2003-2012 another grouping is evident in 2011 (36) and 2012 (59). The sudden jump from 36 in 2011 to 59 in 2012 is significant (64% increase).

Analysis

0-14 age group

The data in Table 4 suggests that there is virtually no change over a period of 20 years in the number of 'intentional' suicides. Although the numbers are low in comparison with the other age groups, clearly this is a significant finding. However, it is also apparent from the colour coding that between 1996 and 2000 for both males and females, but particularly with males, that there were above average numbers of suicides. What is also noteworthy is that for both males and females there are significant periods in the 2003-2012 period where the number of suicides are above the average. This is for the 2004-2008 period for males and 2010-2012 period for females.

15-19 age group

The data in Table 4 suggests that there are significant differences between males and female patterns of suicide between the first and second 10 year periods. The concentration of red in the 1993-2002 period suggests that there was a serious and consistent cause or causes of above average suicides for males. Whatever the cause or causes, in the 2003-2012 period, there is a noticeable fall in the numbers of male suicides below the average. However, for females the situation is not as clear. Indeed, the number of suicides appear to have fallen in 2001-2003, 2005-2006 and 2008-2010, but spikes in 2004, 2006 and 2011-12, with a very significant spike in 2012.

It is not possible to provide any explanation for these data, however, it would appear that there is no correlation of patterns of suicides between males and females, and while there has been a reduction in the number of male suicides in the 15-19 age category in 2003-2012, there has been an increase in the number of females in that same period. This suggests that there is no one clear cause and effect in this age category.

	Reference year																				20 yr	10 yr av	10 yr av	% Change
	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	average	1993-2002	2003-2012	10 yr av
Age group (years)	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.	no.				
Males																								
0-14	4	4	6	7	8	6	10	8	6	4	6	7	7	7	8	8	0	8	7	6	6	6	6	NIL
15-19	111	122	98	114	121	116	97	89	95	97	89	53	67	81	84	73	77	91	81	70	91	106	77	27.4%
20-24	234	252	252	237	295	248	212	174	181	164	162	143	166	149	150	155	133	135	160	144	187	225	150	33.3%
25-29	200	205	236	236	294	314	272	235	226	214	180	172	156	124	160	165	167	144	175	168	202	243	161	33.8%
30-34	206	209	239	229	246	277	235	240	260	229	227	221	207	153	181	189	169	173	168	180	212	237	187	21.1%
35-39	152	174	220	234	215	273	224	234	240	222	185	174	167	185	209	207	201	229	171	196	206	219	192	12.3%
40-44	134	180	162	179	216	206	203	210	207	209	197	208	204	167	167	212	195	221	185	204	193	191	196	2.6%
45-49	154	150	154	151	153	167	165	152	171	159	187	131	177	193	164	198	197	224	196	204	172	158	187	18.3%
50-54	93	120	116	115	141	147	147	139	140	143	112	126	138	141	147	148	162	164	149	181	138	130	147	13.1%
55-59	84	91	108	93	97	88	102	80	101	84	88	89	93	115	107	130	119	136	130	139	104	93	115	23.7%
60-64	86	82	69	88	80	75	74	66	74	74	66	78	68	81	93	88	117	115	101	107	84	77	91	18.2%
65-69	74	76	63	68	77	87	63	56	63	64	63	71	47	56	61	82	64	62	82	78	68	69	67	2.9%
70-74	61	65	54	68	69	49	77	64	64	51	65	64	49	57	44	57	49	58	52	69	59	62	56	9.7%
75-79 (or over 75)	94	100	96	112	131	97	121	113	107	103	109	123	111	114	124	121	135	154	146	155	118	107	129	20.6%
All ages	**1,687**	**1,830**	**1,873**	**1,931**	**2,143**	**2,150**	**2,002**	**1,860**	**1,935**	**1,817**	**1,737**	**1,661**	**1,658**	**1,624**	**1,699**	**1,833**	**1,785**	**1,914**	**1,803**	**1,901**	**1,842**	**1,923**	**1,762**	**8.4%**
Females																								
0-14	1	3	0	7	7	2	8	1	5	4	7	1	3	1	4	3	3	5	9	8	4	4	4	NIL
15-19	19	17	29	26	33	35	27	41	25	27	24	32	24	29	32	25	28	26	36	59	30	28	32	14.3%
20-24	36	40	55	30	60	47	44	34	38	29	25	37	33	39	34	35	38	55	57	51	41	41	40	2.4%
25-29	38	43	49	49	59	56	55	57	55	47	41	30	43	35	41	37	50	51	41	41	46	51	41	19.6%
30-34	40	42	50	47	56	53	61	49	53	56	70	48	36	39	49	53	53	47	44	52	50	51	49	3.9%
35-39	53	55	50	65	64	77	48	67	65	48	57	41	51	55	52	63	57	59	59	64	58	59	56	5.1%
40-44	27	44	54	45	58	58	56	65	53	74	45	50	43	57	59	52	49	54	65	69	54	53	54	1.9%
45-49	43	38	48	50	45	33	57	34	49	51	57	51	46	37	53	56	48	64	57	48	48	45	52	15.6%
50-54	28	30	41	38	51	39	40	33	57	43	36	38	39	46	55	60	67	55	48	69	46	40	51	27.5%
55-59	19	23	31	21	32	30	20	29	28	35	37	24	25	43	46	39	48	45	51	44	34	27	40	48.2%
60-64	18	24	19	19	24	23	22	22	20	21	22	17	25	30	38	21	32	30	26	38	25	21	28	33.3%
65-69	20	14	23	15	25	20	17	20	13	15	20	17	20	19	19	16	22	15	17	21	18	18	19	5.6%
70-74	19	18	14	23	22	21	12	21	20	15	13	12	18	23	15	21	14	16	22	19	18	19	17	10.5%
75-79 (or over 75)	33	37	32	27	41	39	23	30	38	38	23	39	38	41	33	27	43	44	44	51	36	34	38	11.8%
All ages	**394**	**428**	**495**	**462**	**577**	**533**	**490**	**503**	**519**	**503**	**477**	**437**	**444**	**494**	**530**	**508**	**552**	**566**	**577**	**634**	**506**	**490**	**522**	**6.5%**
Persons																								
0-14	5	7	6	14	15	8	18	9	11	8	13	8	10	8	12	11	3	13	16	14	10	10	10	NIL
15-19	130	139	127	140	154	151	124	130	120	124	113	85	91	110	116	98	105	117	117	129	121	134	108	19.4%
20-24	270	292	307	267	355	295	256	208	219	193	187	180	199	188	184	190	171	190	217	195	228	266	190	28.6%
25-29	238	248	285	285	353	370	327	292	281	261	221	202	199	159	201	202	217	195	216	209	248	294	202	31.3%
30-34	246	251	289	276	302	330	296	289	313	285	297	269	243	192	230	242	222	220	212	232	262	288	236	18.1%
35-39	205	229	270	299	279	350	272	301	305	270	242	215	218	240	261	270	258	288	230	260	263	278	248	10.8%
40-44	161	224	216	224	280	264	259	275	260	283	242	258	247	224	226	264	244	275	250	273	247	244	250	2.5%
45-49	197	188	202	201	198	200	222	186	210	210	244	182	223	230	217	254	245	288	253	252	220	201	239	18.9%
50-54	121	150	157	153	192	187	187	172	197	186	148	164	177	187	202	208	229	219	197	250	184	170	198	16.5%
55-59	103	114	139	114	129	118	122	109	129	119	125	113	118	158	153	169	167	181	181	183	137	120	155	29.2%
60-64	104	106	88	107	104	98	96	88	94	95	88	95	93	111	131	109	149	145	127	145	109	98	119	21.4%
65-69	94	90	86	83	102	107	80	76	76	79	83	88	67	75	80	98	86	77	99	99	86	87	85	2.3%
70-74	80	83	68	91	91	70	89	85	84	66	78	76	67	80	59	78	63	74	74	88	77	81	74	8.6%
75-79 (or over 75)	127	137	128	139	172	136	144	143	145	141	162	162	149	155	157	148	178	198	190	206	156	141	171	21.3%
All ages	**2,081**	**2,258**	**2,368**	**2,393**	**2,720**	**2,683**	**2,492**	**2,363**	**2,454**	**2,320**	**2,214**	**2,098**	**2,102**	**2,118**	**2,229**	**2,341**	**2,337**	**2,480**	**2,380**	**2,535**	**2,348**	**2,413**	**2,283**	**5.4%**

Recommendations

- Establish a comprehensive database on suicide deaths and incidents of self harm. There should be one regulatory body responsible for collection that has systems in place for cooperation with police, coroners, and health services to collect the data. Data should include:

  - History of patient treatment in the lead up to self-harm, including therapies, hospitalisations, medications prescribed, diagnoses of mental disorders, interventions, interactions with community services. *NOTE: This will need to include follow up interviews with patients' families, pharmacists and medical practitioners*.

  - Blood test results determining the presence of drugs in the patient's system including prescription drugs or illicit drugs.

  - Genetic testing and racial profile of patient (in order to determine if there are any physiological indicators for self-harm, suicide, and adverse reaction to medications).

  - Detailed categorisation of the self-harm, with inclusion of self-harming behaviours like dangerous driving and violent acts.

- An Inquiry into medical practitioners' prescribing of psychotropic drugs off-label and in disregard of manufacturer's recommendations.

- A Royal Commission investigating the authorising, regulation and marketing of psychotropic medicines in Australia.

DATE: 2 June 2014

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