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Depression, Anxiety, and  
Related Topics

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An independent academic psychologist, based in England, who has written extensively on different areas of psychology with an emphasis on the critical stance towards traditional ideas.

A complete listing of his writings at <http://psychologywritings.synthasite.com/> and <http://kmbpsychology.jottit.com>.

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# **1. DEPRESSION IN LATER LIFE**

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## **1.1. LATE-LIFE DEPRESSION**

Late-life depression is linked to a number of risk factors - biological (eg: physical illness), psychological (eg: death of spouse), and social (eg: loneliness) - either separate or together. "These risk factors can lead to relapse of depressive symptoms in those with an existing vulnerability, or first onset of the disorder in later life" (Allan and Ebmeier 2013 p302).

Major depressive disorder has a prevalence of 1-5% of community-dwelling older adults, and nearly half of those in long-term care facilities, while up to one-third of community-dwellers have sub-threshold depression (ie: some symptoms but not enough for full diagnosis) (Saracino et al 2016). These figures may be an underestimation as older adults show irritability or withdrawal more than low mood (what Gallo et al (1997) called "depression without sadness"). "Despite its elevated prevalence, depression is not a normal part of ageing", Saracino et al (2016) emphasised.

Lee et al (2012) distinguished three sub-groups of older adults with depression:

- Individuals with high levels of all symptoms
- Those with high levels of some symptoms
- Those with somatic symptoms only (eg: sleep disturbance).

Mora et al(2012) outlined four sub-groups from their study of community-dwellers: low level of symptoms, high level of symptoms, sub-threshold depression with anhedonia, and sub-threshold depression with somatic symptoms.

But is the experience of depression different in older than younger adults? Table 1.1 summarises three studies that have compared the two groups.

Study	Older adults
Gallagher et al (2010)	Less excessive guilt and thoughts that life not worth living
Ellison et al (2012)	Less crying, sadness, fearfulness, being bothered, or feeling that life a failure
Hegeman et al (2012)	More psychomotor agitation, hypochondriasis, and somatic symptoms

Table 1.1 - Three studies comparing depression in older and younger adults.

Depression in later life could be a product of time-to-death (TTD) rather than distance-from-birth, and may "reflect the impact of biological and/or functional deteriorations, which occur specifically during a limited time period preceding - and precipitating - death" (Diegelmann et al 2016 p672). But this should not disguise the heterogeneity of experience, dependent on both proximal factors (eg: recent loss) and distal factors through the lifespan (eg: life history of challenging circumstances) (Diegelmann et al 2016).

Diegelmann et al (2016) analysed data from the English Longitudinal Study of Ageing (ELSA) between 2002 and 2011. This covered over 1200 individuals over 50 years of old.

It was estimated that 31% of the sample "stayed resilient" (ie: "stably-non-depressed"), another 38% were classed as the "rising-from-few" group (ie: mild depression increasing with less TTD), and 22% were "stably-depressed". The remainder were "soaring-from-zero", who showed a sudden rise in depression with short TTD (though the symptoms were never as bad as the "stably-depressed" and "rising-from-few" groups) (table 1.2). There was no evidence of decline in depression with closer TTD.

Group	10 years TTD	1 year TTD
Stably-depressed	5	5
Rising-from-few	2	4
Stably-non-depressed	1	1
Soaring-from-zero	<1	2

(Center for Epidemiologic Studies Depression Scale; CES-D; where a higher score = more depressive symptoms)

(Data taken from Diegelmann et al 2016 figure 3 p680)

Table 1.2 - Approximate mean depression scores at ten years and one year TTD.

Pharmacotherapy (ie: drug treatment) is the most common response to depression generally, but there are particular considerations for older sufferers, including (Allan and Ebmeier 2013):

i) Age-related physiological changes that influence the processing of the drug in the body.

ii) Co-morbidity of physical conditions.

iii) Polypharmacy risk - ie: interaction with drugs for other conditions.

iv) Drug side-effect profile - eg: venlafaxine can increase hypertension, which is unpleasant at any age, but riskier for older adults. Side-effects from all types of anti-depressants are more common in older adults (Allan and Ebmeier 2013).

The alternative is psychological therapy. There are limited studies with older adults, but, of those performed, cognitive-behavioural therapy (CBT) and psychosocial treatment have proved better than no treatment (Allan and Ebmeier 2013).

## **1.2. SOCIAL PARTICIPATION**

Depression is experienced by a number of older adults - eg: 18-37% in 10 European countries in the Survey of Health, Ageing and Retirement in Europe (SHARE) (Castro-Costa et al 2007) - and it is associated with less social participation and activity. For example, loneliness increases the risk of depression (eg: five times more in Japanese over 50s; Kaji et al 2010).

But what is the direction of the relationship? Also there are confounders, like personality. "For example, persons with certain psychological or personality traits may be more likely to engage in social participation and may also exhibit lower levels of depression, which could result in a spurious association between social participation and depression" (Croezen et al 2015 p168).

Croezen et al (2015) tried to control for this in their analysis of data from SHARE. SHARE was begun in 2004-5 with over 30 000 participants aged 50 years and above, and the fourth wave of data collection took place in 2010-11 with over 10 000 of the individuals.

Social participation in each wave was measured by engagement in five activities (eg: voluntary work, religious organisation membership) in the last month (or year). Twelve depressive symptoms were scored as present or absent, and four or above was a diagnosis of depression.

It was found that the level of social participation was associated with number of depressive symptoms, but the strength of the relationship and the direction depended on the type of social participation activity. Participation in religious organisations at one wave was associated with lower depression at a subsequent wave, while the opposite was the case for political or community organisation participation. There was no relationship for participation in voluntary or charity work, and educational or training courses. There were short-term benefits only for participation in sports or social clubs (ie: no relationship across different waves of data collection).

The researchers were not able to control for all variables, like motivation for participation (eg: joining religious organisation after death of loved one).

### **1.3. CO-RESIDENCE**

The pattern in Western countries during the second half of the 20th century was more older people living alone, particularly for women, as adult children set up separate households, but this trend is showing signs of changing in the 21st century with unmarried children staying longer or moving back into the parental home (co-residence) (Courtin and Avendano 2016).

Using data from the Survey of Health, Ageing and Retirement in Europe (SHARE), Courtin and Avendano (2016) reported that older parents' mental health benefited from co-residence. SHARE is a longitudinal study began in 2004 of adults aged 50 years and above in seventeen European countries, who are interviewed every two years.

Overall, around 40% of the over 50 000 participants lived with an adult child. Concentrating on depressive symptoms, which were measured on a standard 12-point scale, co-resident older adults had a significantly lower number of symptoms than non-co-residents.

Studies in other parts of the world have produced mixed results - co-residence increases depressive symptoms for older parents in Singapore, South Korea, China and Israel, but reduces the symptoms for widowed women in South Korea, for example (Courtin and Avendano 2016). Courtin and Avendano (2016) commented that "the experience of co-residence may be fundamentally different for older parents in European and Asian countries, potentially leading to different effects on their mental health" (p147).

Aranda (2015), however, found no difference in Nordic and Western European countries ("Protestant" tradition countries), but a decrease in depressive symptoms in southern European countries ("Catholic" tradition countries).

Points to note about the studies:

- "Co-resident" can include those living in the same household as well as children living in the same building;
- Little detailed information about motives for co-residence;
- Little information on quality of relationships or level of support for parents provided by co-resident adult children.

#### **1.4. CANCER**

Cancer is a risk for depression in older adults, and depression, in turn, is associated with larger hospital stays and higher mortality in cancer patients (Saracino et al 2016). Saracino et al (2016) explored "the unique factors of depression in older adults with cancer" in a literature review of ninety relevant articles.

There are overlapping symptoms between the two conditions - eg: weight loss, fatigue - and this hinders diagnosis of depression.

In terms of studies of depressed and non-depressed cancer patients, the former reported more insomnia, pain, anorexia, and fatigue, for instance, in a Taiwanese study (Chen and Chang 2004).

Another type of study is to compare depressed individuals with or without cancer. Moorey and Steiner (2007), for example, found more somatic symptoms of depression among cancer sufferers, but no difference in affective symptoms (eg: sadness) or motivational symptoms (eg: hopelessness). On the positive side, the cancer sufferers had less guilt and feelings of worthlessness. But, in this study, "no systematic procedure was utilised to diagnose individuals as 'depressed' and hence, the equivalence of the two groups is unclear" (Saracino et al 2016 p1235).

Saracino et al (2016) noted symptoms of depression in cancer patients that the DSM criteria of depression place less importance on or ignore - eg: social withdrawal, brooding, not participating in treatment despite being able to do so, and "psychic anxiety" (worry).

Cancer impacts on life in many ways, including the economic circumstances of the individual and their family. Mehnert (2011) reported a variable rate of return to work after treatment among cancer survivors from 24% to 94% in a review of sixty-four studies. In terms of income, reductions of about one-third two years after



diagnosis in studies in New Zealand, Ireland and Canada (Zajacova et al 2015). However, the studies used convenience samples of survivors (Zajacova et al 2015).

In a large-scale study, Zajacova et al (2015) used data from the US Panel Study of Income Dynamics (PSID), which covers over 17 000 individuals since 1968. The researchers concentrated on the period 1999 to 2009, and on 1406 individuals diagnosed with cancer. Relative to non-cancer individuals, the group with cancer had a decline in employment and earnings from two years before to two years after diagnosis. The probability of employment fell by 10% in the five years after diagnosis, and earnings from employment dropped by 40% for two years after diagnosis. "The observed effects were primarily driven by losses among survivors who were men. For women who were diagnosed with cancer, the losses largely were not statistically significant. This sex difference may be a result of the lower overall labour-market participation of women, which would attenuate the average effects of cancer. It is also possible that the economic impacts may be greater for men if they suffer from types of cancer or treatments that have greater effects on their ability to work or if their jobs are more physically demanding and less compatible with the rigors of treatment" (Zajacova et al 2015 p4431).

### **1.5. JOINT REPLACEMENT**

Scott et al (2016) reported on total joint replacement (TJR) of the hip or knee and depression and anxiety. Ongoing depression and anxiety (ie: before and after surgery) had a negative impact on surgical recovery (eg: higher rate of mortality in year after operation; greater medication use).

Nickinson et al (2009), for example, found clinically significant levels of depression in 50% of TJR patients two to four days post-operation, but this declined very quickly to 5% at hospital discharge. Other studies have reported up to one-quarter of patients had depression one year post-surgery, while the level of anxiety ranged from 8 to 85% (Scott et al 2016).

Scott et al (2016) performed a meta-analysis on TJR and depression and anxiety in the over 50s using articles from 1980 to 2014, of which twenty-six studies were relevant. The mean prevalence rate of depression was 22% pre-surgery and at three months post-operation, and 13% at one year post-surgery. There were not enough studies to calculate the means for anxiety.

There were small, but significant, decreases in depression and anxiety in the year after surgery, "although it is unclear whether this was uniform across all persons" (Scott et al 2016 p1250).

As with any meta-analysis the quality of studies included were key. Scott et al (2016) noted that:

- i) Only one study had a control group.
- ii) Many studies did not distinguish the severity of depression before the operation.
- iii) Some studies included patients undergoing revision TJR (ie: further surgery), which makes them different to first-time surgery patients.
- iv) Different measures were used to assess depression and anxiety.
- v) There were not enough details to establish the variables that influence pre-operation depression and anxiety (eg: pain, co-morbidity).

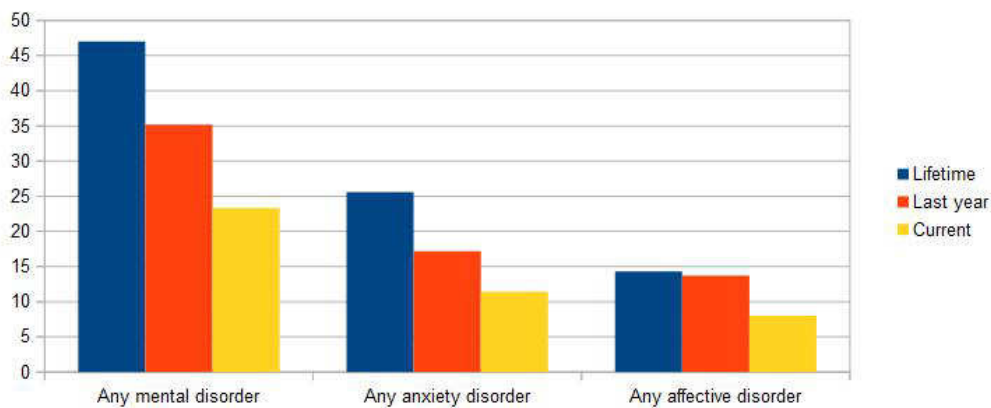
#### **1.6. OTHER MENTAL DISORDERS**

A few studies have looked at the prevalence of mental disorders other than depression in over 65s - including 1% for current schizophrenia and up to 7% for anxiety disorders in Western Europe (Volkert et al 2013), and nearly 20% for somatoform disorders in a small Norwegian study (Leiknes et al 2007).

Where studies found quite different rates, "some authors have argued that older people may have developed coping strategies over the course of their lives that enable them to manage their mental health better than younger people, whereas others have attributed the heterogeneity of the findings to a lack of feasible and age-sensitive standardised and structured instruments for diagnosing mental disorders in elderly people. Older adults with health problems may also deny symptoms when asked to complete lengthy assessments" (Andreas et al 2017 p125).

Andreas et al (2017) reported data from the MentDis\_ICF65+ study which included over 3100 65-84 year-olds from areas in Italy, Spain, England, Germany, Switzerland, and Israel. Mental disorders were diagnosed with an adapted age-sensitive clinical interview tool based on DSM-IV criteria.

Overall, 47% of respondents had experienced a mental disorder in their lifetime, and 35% in the last year. Current prevalence was 23% (figure 1.1). Anxiety disorders were most reported, followed by affective disorders, with differences between countries (eg: lowest one-year prevalence in Italy).



(Data from Andreas et al 2017 tables 2 and 3 p127, and table 4 p128)

Figure 1.1 - Prevalence of selected mental disorders (%).

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## **2. BURDEN OF DEPRESSIVE DISORDERS**

- 2.1. Global burden of disease
- 2.2. Unemployment
- 2.3. Trainee doctors
- 2.4. New treatments and ideas
  - 2.4.1. Augmentation of anti-depressants
- 2.5. Bipolar disorder
- 2.6. Appendix 2A - Predicting response to anti-depressants
- 2.7. References

### **2.1. GLOBAL BURDEN OF DISEASE**

Global Burden of Disease (GBD) studies have been carried out in 1990 (Murray and Lopez 1996), 2000 (Mathers et al 2002), and 2010 (Murray et al 2012). They used the concept of disability adjusted life years (DALYs), where 1 DALY "represents the loss of a healthy year of life and aggregates the years of life lived with disability (YLD) with the years of life lost due to premature mortality (YLL)" (Ferrari et al 2013) <sup>1</sup>.

The GBD 1990 calculated that depressive disorders were the fourth disease burden behind lower respiratory infections, diarrhoeal diseases, and conditions arising during the perinatal period, and equivalent to 3.7% of all DALYs. In GBD 2000 depressive disorders accounted for 4.3% of all DALYs, and were the third leading burden after lower respiratory infections, and diarrhoeal diseases (Ferrari et al 2013).

The GBD 2010 refined the categories of depressive disorders among its inclusion of 291 diseases and injuries across 187 countries. In total in 2010, there were 2.5 billion DALYs calculated, and depressive disorders accounted for 3% of those. That is 2.5% for major depressive disorder (MDD), which is ranked 11th, and 0.5% for dysthymia as 51st leading cause of global DALYs (Ferrari et al 2013) <sup>2</sup>.

There were variations around the world (figure 2.1) <sup>3</sup>.

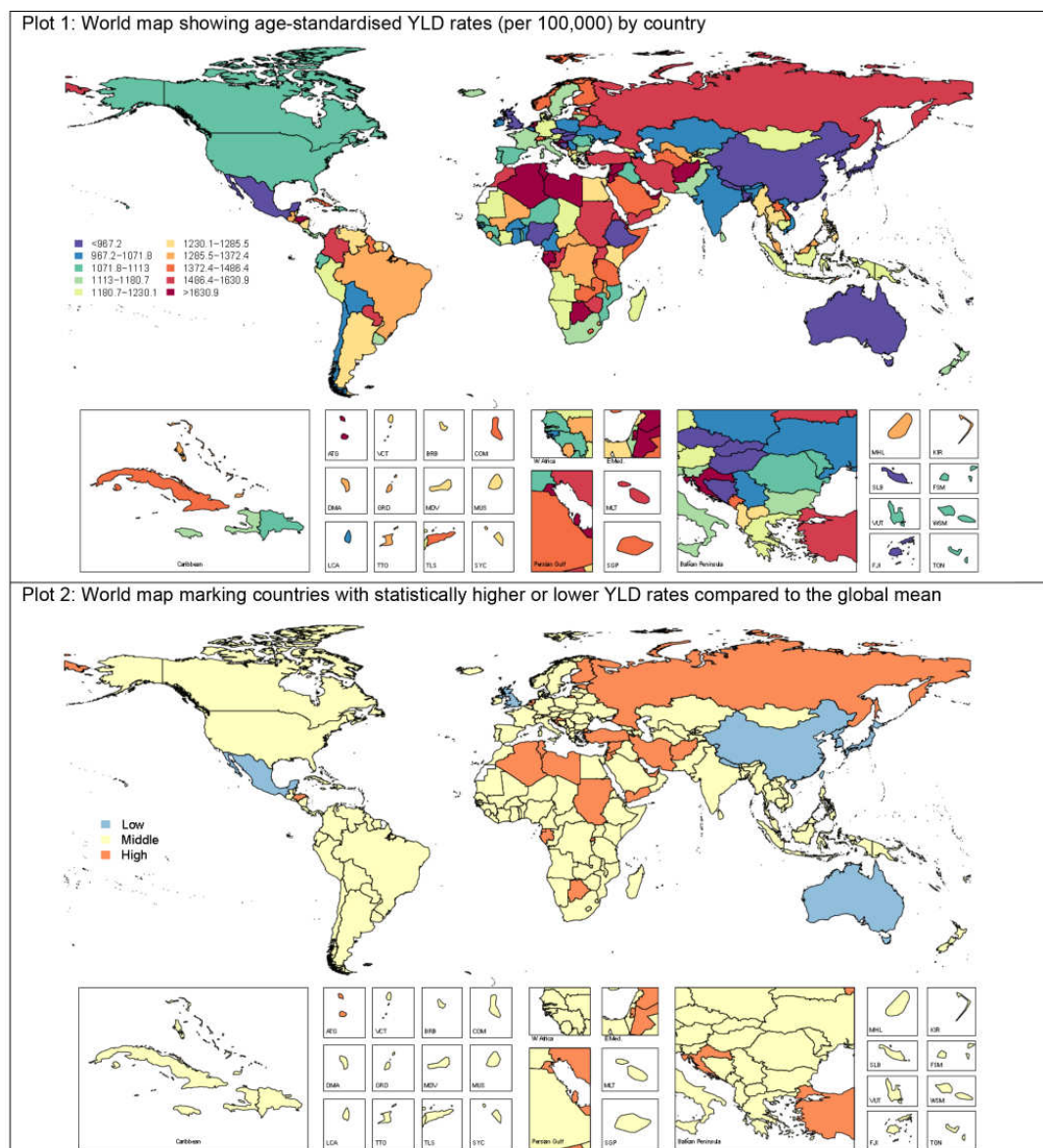
Ferrari et al (2013) noted: "Contrary to recent literature on the topic, our findings suggest that the epidemiology of both MDD and dysthymia remained

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<sup>1</sup> YLLs are calculated as the number of deaths due to the given disorder at a particular age times the standardised life expectancy at that age (Ferrari et al 2013).

<sup>2</sup> Mental disorders generally account for 7.4% of global disease burden, and nearly 20% in the European Union (Kekic et al 2016).

<sup>3</sup> In a retrospective study of medical records for the period 2005 to 2010 in a medical college hospital in one area of south India, Celine and Antony (2014) found that mood disorders were most common. For most mental disorders, female patients were significantly more than males with the exception of psychoactive substance use.



(Source: Ferrari et al 2013 figure 3)

Figure 2.1 - YLD rates (per 100 000) by country for depressive disorders in 2010.

relatively stable over time. There was a slight decrease in the prevalence rate of MDD between 1990 and 2010 but this was too small to allow for any explicit interpretation" (p7).

Thornicroft et al (2017) found that only a minority of sufferers with MDD are treated. They used analysed data from the World Mental Health Survey covering twenty-one countries and over 50 000 respondents with DSM-IV-diagnosed MDD. The following details were found:

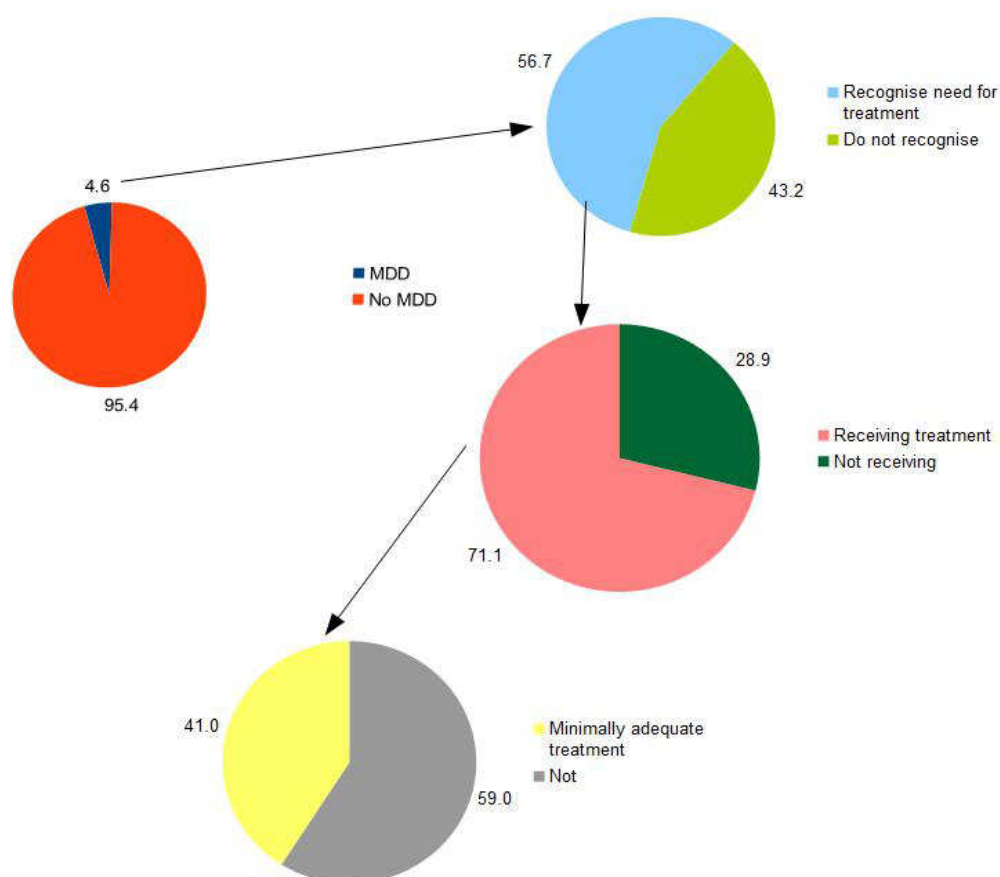
i) 12-month prevalence - Overall, 4.6% of respondents were diagnosed for the last year, with the

figure being 5.2% in high-income countries (eg: USA), and 3.2% in low-/lower-middle-income countries (eg: Romania).

ii) Recognition of need for treatment - Just over half (57%) of the individuals with MDD recognised that they needed treatment, with the figure being 65% in high-income countries and 35% in low-/lower-middle-income countries.

iii) "Contact coverage" - Of those recognising the need for treatment, around seven in ten made at least one visit to a treatment provider (which included traditional healers).

iv) "Effectiveness coverage" - Of those seeking treatment, around 40% received "minimally adequate treatment" (defined as more than one month of medication and at least four visits to a doctor, or at least eight sessions with a "therapist" (including spiritual advisor); Wang et al 2007) (figure 2.2).



(Data from Thornicroft et al 2017 table 1 p121)

Figure 2.2 - Percentage of respondents diagnosed with MDD, recognising need for treatment, receiving it, and to minimally adequate standard.

Around 1 in 5 individuals with MDD in high-income countries received "minimally adequate treatment", but this was 1 in 27 in low-/lower-middle-income countries.

The data were self-reports of symptoms, and treatment received, and the surveys varied slightly between countries. Treatment providers were wide-ranging, including psychiatrists, doctors, social workers, counsellors, religious or spiritual advisors, and "any other type of healer".

## **2.2 UNEMPLOYMENT**

Unemployment and depression and other mental health problems go together more than among the employed. "This may be caused by selection of those with health problems into unemployment or by causal negative health effects of job loss and unemployment. Previous studies including meta-analyses have found support for both mechanisms. On the one hand pre-existing mental ill health is associated with an increased risk of unemployment and a lower likelihood of re-employment. On the other hand unemployment is followed by poorer and re-employment by improved mental health outcomes" (Leinonen et al 2017 p2).

A longer period of unemployment and/or recurrent episodes of joblessness are also relevant, though there are differences between groups (eg: worse outcomes for men) (Leinonen et al 2017).

But depression has also been found among individuals working at organisations that are involved in major downsizing (eg: Sweden; Magnusson Hanson et al 2016). "The effects of unemployment on mental ill health may thus be largely related to overall experiences of job insecurity and less to the particular status of actually being without a job" (Leinonen et al 2017 p2).

Leinonen et al (2017) explored the relationship between unemployment, re-employment, and anti-depressant use using Finnish data. For the period 1995 to 2009, 28 000 individuals who experienced unemployment were compared to over 124 000 employed ones. Six groups were distinguished for analysis purposes:

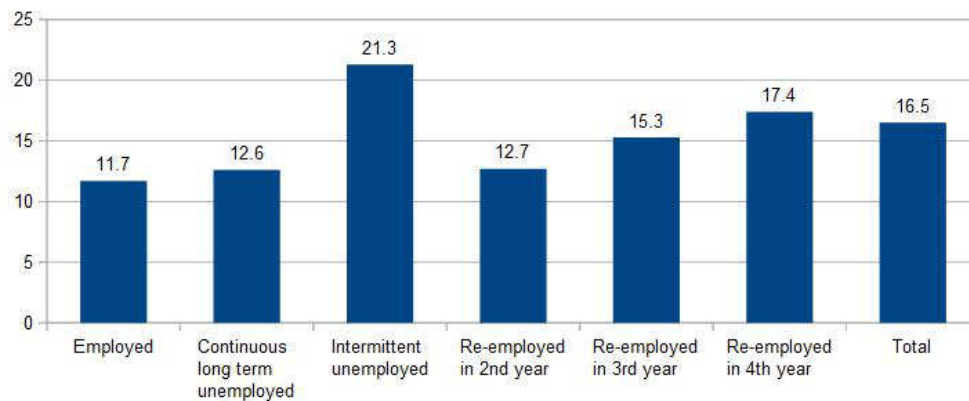
- Continuously long term unemployed (for four years)
- Intermittently unemployed over four years
- Unemployed in one year and then re-employed
- Unemployed in two years and then re-employed
- Unemployed in three years and then re-employed
- Employed continuously (over a four year period) (reference group).

"Unemployment" was defined as having more than one



month without employment. Anti-depressant use was standardised as defined daily doses (DDD).

Overall, 17% of unemployed individuals had anti-depressant medication compared to 12% of the employed. Anti-depressant use was more common among intermittently unemployed (21.3%) than the continuously long term unemployed (12.6%) (figures 2.3 and 2.4) <sup>4</sup>.



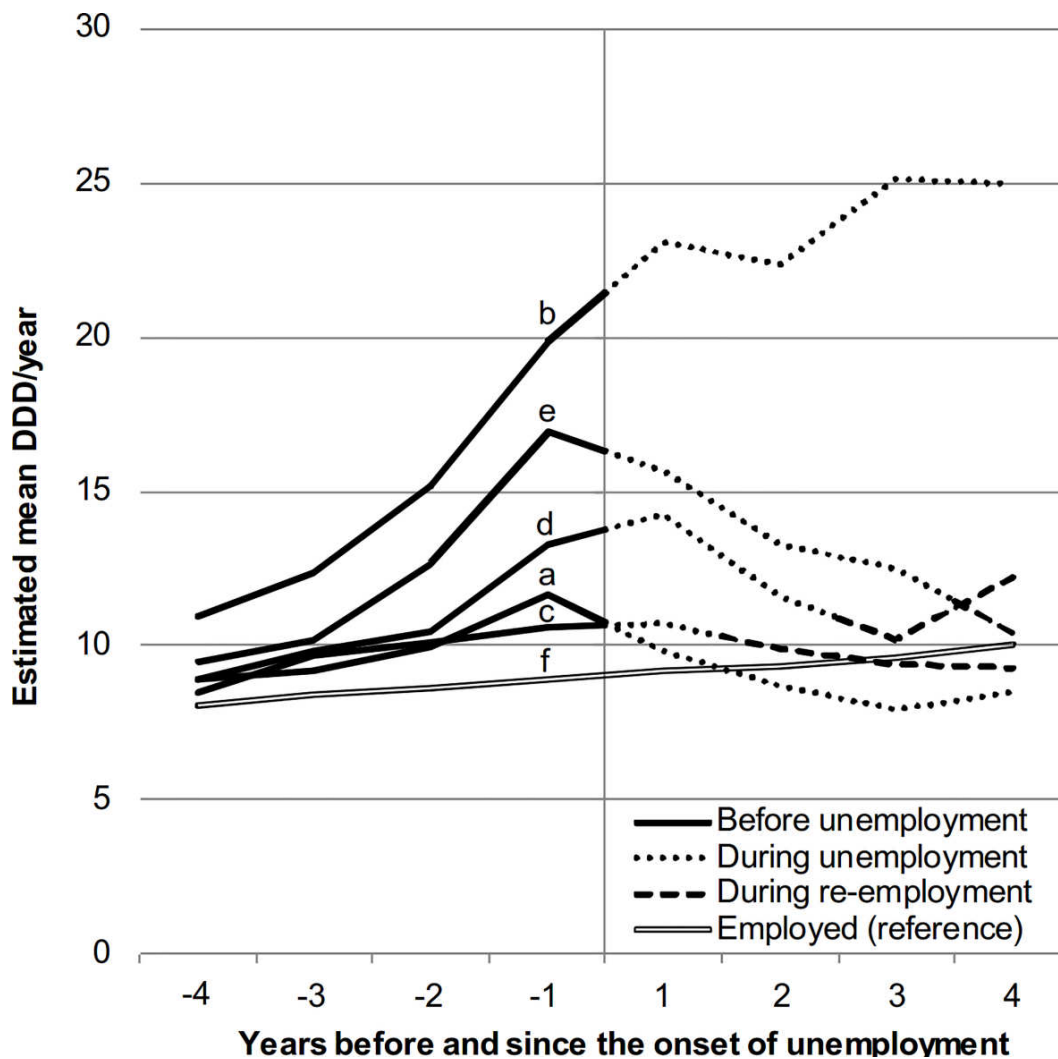
(Data from Leinonen et al 2017 table 2)

Figure 2.3 - Percentages taking anti-depressant medication based on unemployment and employment.

In terms of the direction of the relationship between depression and unemployment, Leinonen et al (2017) summed up thus: "The findings indicate that depressive morbidity is more likely to be followed by unemployment than vice versa. Morbidity increases in the years leading to unemployment, particularly in cases of intermittent episodes or long duration before eventual re-employment. By way of exception, such health decline is not particularly strong for those eventually becoming continuously long-term unemployed over several years. Nevertheless, all of the unemployed groups have poorer mental health already before becoming exposed. Even though in Finland employees are not allowed to be dismissed on health grounds, those with poorer health may be among the first to be made redundant and have poorer employment opportunities after termination of temporary contracts. We found that the observed increases in depressive morbidity mostly restrict to the time before unemployment. Even though morbidity continues to increase

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<sup>4</sup> Leinonen et al (2017) commented that "the observed decline in antidepressant medication among the continuously long-term unemployed is likely to be partly explained by under-treatment of depression as a result of financial difficulties, lack of motivation due to poor chances of re-employment or other disadvantages related to prolonged exclusion from employment" (p11)..



(Estimated mean DDD/year among those with (a) continuous long-term unemployment, (b) intermittent unemployment, (c) reemployment in the second (d) third or (e) fourth year since the year of onset, as well as (f) the employed reference group. Adjusted for age, gender, education, living arrangements, and calendar year)

(Source: Leinonen et al 2017 figure 2)

Figure 2.4 - Trajectories of anti-depressant use before and after onset of unemployment.

since transition to intermittent unemployment, this happens at a slower pace than in the preceding years, therefore more likely to reflect continuance of an already declining trend in mental health than a negative outcome triggered by unemployment" (p9).

The researchers considered the following methodological issues with their study:

- + Nationally representative sample.
- + Longitudinal data.

+ Multiple measures of depression and employment over time.

- Lack of exact dates for period of unemployment. "Those who had several months of both unemployment and employment in a particular calendar year were defined as unemployed. As a result, the reported decline in medication during unemployment may have partly taken place while already transitioned to re-employment, because this may have begun in the preceding calendar year" (Leinonen et al 2017 p11).

- Having anti-depressant use as the measure of depression. For example, it misses individuals with depression who did not seek treatment, as well as income differences in the population as individuals have to pay partly for medication in Finland (Leinonen et al 2017).

- No details of diagnoses. Anti-depressants can be prescribed for sleep problems, chronic pain, and anxiety.

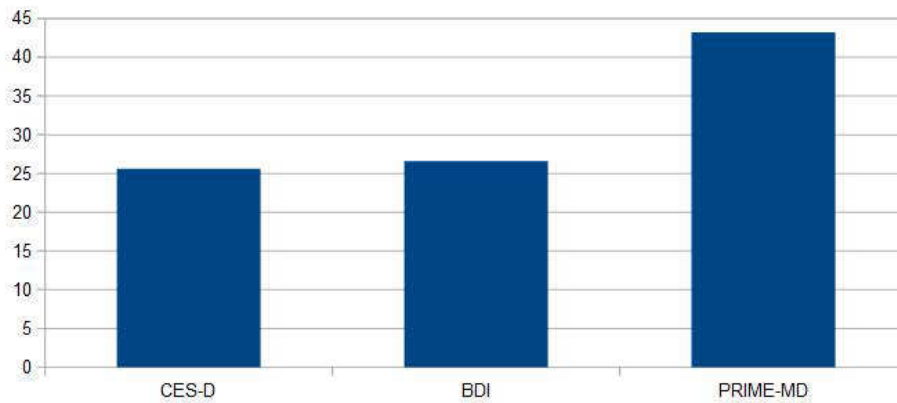
### **2.3. TRAINEE DOCTORS**

Rates of depression vary between different occupational groups. For example, Mata et al (2015) reported an average of 29% (range 21-43%) from 54 studies on trainee doctors (resident physicians) (n = 17 560). This meta-analysis covered articles published between 1963 and 2015.

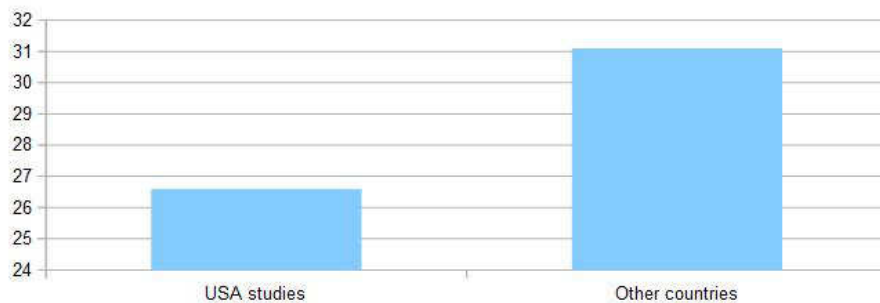
The included studies varied on methodology, including:

- Design - cross-sectional or longitudinal (figure 2.5c);
- Place of study - majority in North America (figure 2.5b);
- Sample - trainees from multiple or single specialities, interns or resident physicians;
- Size of sample - media 141;
- Measure of depressive symptoms - various self-reported questionnaires (figure 2.5a) or structured diagnostic interview.

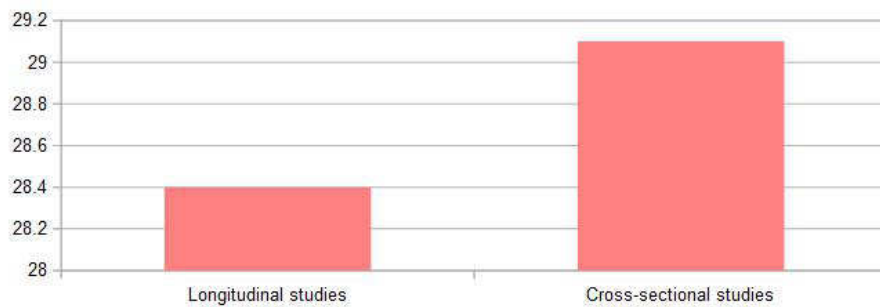
All studies showed an increase in depressive symptoms from baseline (mean increase 16%). Lower quality methodological studies produced higher depression estimates (eg: less representative participation population; less valid measure of depression) (figure 2.6).



(a) Three selected self-reported questionnaires



(b) Country of study

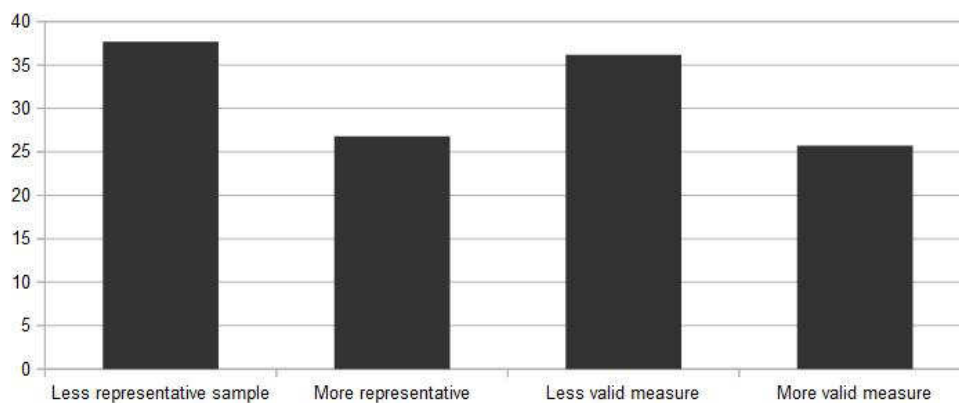


(c) Study design

(CES-D = Center for Epidemiologic Studies Depression Scale; BDI = Beck Depression Inventory; PRIME-MD = Primary Care Evaluation of Mental Disorders questionnaire)

(Data from Mata et al 2015 figures 3 and 4 p2379)

Figure 2.5 - Variations in prevalence of depressive symptoms.



(Data from Mata et al 2015 figure 5 p2380)

Figure - Prevalence of depressive symptoms based on two differences in quality of methodology of studies.

## 2.4. NEW TREATMENTS AND IDEAS

Among the new ideas about depression is that zinc deficiency plays a part <sup>5</sup> <sup>6</sup>, and that zinc supplements could be a treatment (Rodriguez 2015). Zinc in the brain is particularly linked to glutamatergic neurons which increase brain activity and neuroplasticity (Rodriguez 2015) <sup>7</sup>.

Swardfager et al's (2013) meta-analysis of seventeen studies found that individuals with depression had an average of 14% less zinc in their blood than controls. While Vashum et al (2014) found that individuals with the highest zinc intake in their diet were 30-50% less likely to be depressed than individuals with the lowest intake. There is also a negative correlation between blood zinc concentrations and the severity of depression, as well as links to depression in pregnant women (ante-natal and post-natal) (Prakesh et al 2015).

In terms of the benefits of zinc supplements, Solati et al (2015) reported a double-blind, randomised, placebo-controlled trial over a three-month period. Zinc supplements are beneficial for individuals with depression and a high risk of zinc deficiency (eg: vegetarians, alcoholics), but supplements can cause complications if overdone (Rodriguez 2015) <sup>8</sup>.

<sup>5</sup> Rats given a zinc-deficient diet also showed anxiety-like behaviour (Prakesh et al 2015).

<sup>6</sup> Low magnesium intake could also be a risk for depression (eg: Winther et al 2015 - rats fed magnesium-deficient diet).

<sup>7</sup> Zinc is the second most abundant metal in living organisms after iron, and the human body contains 2-3 gm (with high concentrations in the limbic system in the brain). It is involved in growth, cell function, and wound healing, for instance (Prakesh et al 2015).

<sup>8</sup> Individuals will respond differently to supplements as they do to medications (appendix 2A).

Among new treatments for depression, a form of cognitive-behavioural therapy called behavioural-activation (BA) therapy concentrates on changing behaviour. Individuals are encouraged to spend more time doing behaviour that is rewarding because "patients' negative thoughts and avoidance worsen in the absence of satisfying activities. This keeps them trapped in a cycle of misery and dysfunction" (Hellerstein 2016 p26).

Dimidjian et al (2006) found that 241 depressed individuals benefited as much from BA as anti-depressants in a RCT, while Hellerstein et al (2015) reported that 69% of sixteen individuals with major depression could restart work.

#### **2.4.1. Augmentation of Anti-Depressants**

Around 10-33% of depression sufferers "do not obtain an optimum outcome after both first-line and second-line treatment, often described as treatment-resistant depression" (McAllister-Williams et al 2016 p117). One possibility is anti-depressant augmentation. This can be the use of another drug at the same time, which targets other physiological changes. For example, hypothalamic-pituitary-adrenal (HPA) axis abnormalities may be involved in mood disorders <sup>9</sup> (eg: hypercortisolic - too much cortisol), and so a cortisol synthesis inhibitor could be beneficial (McAllister-Williams et al 2016).

An example of this type of drug, which has been tried, is metyrapone <sup>10</sup>. Jahn et al (2004), for example, reported its benefits in a 3-5-week study in Germany.

The Anti-glucocorticoid augmentation of anti-Depressants in Depression (ADD) study (McAllister-Williams et al 2013) followed up at 21 weeks later. Participants in three areas of northern England suffering from MDD and taking serotonin-based anti-depressants were given metyrapone twice daily for 21 days. Of 165 individuals randomly allocated to the drug or control groups, 46 in the drug group and 58 in the placebo group completed the study (ie: data collected at Week 24 - three weeks of drug/placebo plus 21 weeks follow-up). The primary outcome measure was the Montgomery-Asberg

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<sup>9</sup> "Unfortunately, the concept of HPA axis dysregulation in depression is at least as opaque as the now belittled Oedipus complex of Freud or the trendy trauma concepts of various psychiatric disorders... At the moment, researchers are looking at cortisol and HPA axis dysregulation like other scientists are looking at amyloid plaques — not knowing what they actually mean" (Jahn 2016 p92 and p93).

<sup>10</sup> "Metyrapone might act through a combination of mechanisms. It can change neurosteroid concentrations and might restore the diurnal variation of occupation of mineralocorticoid receptors and glucocorticoid receptors in neurons by blocking the 11-oxoreductase activity of the enzyme 11- $\beta$ -hydroxysteroid dehydrogenase type 1 either directly or indirectly by increased formation of endogenous inhibitors (eg: progesterone derivatives), which could accelerate the upregulation of 5HT1A receptors essential for the action of serotonergic anti-depressants" (Jahn 2016 p92).

Depression Rating Scale (MADRS) score (Montgomery and Asberg 1979) (collected at baseline, and Weeks 3, 8, 16 and 24). "Treatment response" was defined as at least a 50% reduction in baseline MADRS score.

The addition of metyrapone to anti-depressants was not found to be beneficial as the difference between the drug and placebo groups was not significant.

The researchers speculated about the negative findings as due to "the nature of the patients studied,... or their relative absence of HPA axis dysfunction. Chronic depression has been shown to be associated with normal HPA axis function. The initial hypercortisolaemia of depression might normalise with time in patients who continue to have symptoms; hence, normal cortisol concentrations might be a result or a cause of chronic treatment-resistant depression" (McAllister-Williams et al 2016 p125). There were differences compared to the participants studied by Jahn et al 2004) (table 2.1) - in particular the patients in the ADD study had "clinical characteristics that are associated with worse outcomes" (McAllister-Williams et al 2016).

<u>Jahn et al (2004)</u>	<u>McAllister-Williams et al (2016)</u>
63 in-patients	165 out-patients
Germany	North-east and north-west England, and West Yorkshire
Treatment-resistant not criteria	Treatment-resistant and inclusion criteria

Different serotonin-based anti-depressants used by participants

Table 2.1 - Key differences in participants between the two studies of metyrapone.

CBT is an effective treatment in the short-term for depression, even for individuals who have not responded to anti-depressants, but it is not clear about the long-term benefits (eg: 5 years later) (Wiles et al 2016). Depression is a relapsing condition, so long-term effectiveness is important.

Wiles et al (2016) reported the long-term data from the CoBaT trial (Wiles et al 2013) <sup>11</sup>, which recruited adults in three UK areas (Bristol, Exeter and Glasgow). Half of the 469 participants were randomly assigned to receive 12-18 sessions of CBT on top of their anti-depressants. Self-reports of depressive symptoms were

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<sup>11</sup> Information at <http://www.thecobaltstudy.ac.uk/>.

collected at six and twelve months, and 3-5 years later (average 40 months). The group receiving CBT had lower depressive symptom scores than the usual care (control) group at all measurement points, and they were less likely to be taking anti-depressants at the long-term follow-up.

Uher and Pavlova (2016) drew this conclusion: "Although anti-depressant drugs and brain stimulation treatments are effective only as long as the treatment is continued, CBT provides long-term benefits without continued treatment or booster sessions, which is probably because the participants learn skills that they continue practising after the treatment stops. Consequently, discontinued CBT might be as effective as continued treatment with anti-depressant medication and more effective than anti-depressant medication that is discontinued" (p95).

However, many participants on the trial, despite the CBT and anti-depressants, were still scored in the moderately depressed range (Uher and Pavlova 2016).

Three key methodological issues about the CoBaLT study can be highlighted:

i) The response rate at long-term follow-up was 59% of original participants. Wiles et al (2016) admitted: "Limited resources meant that the long-term follow-up data were collected by postal questionnaire rather than self-completion of a questionnaire at a face-to-face appointment with a researcher (as at the 6 and 12 month follow-ups). This difference probably affected the response rate achieved..." (p142).

ii) The same measures used throughout - eg: main outcome measure was the Beck Depression Inventory (BDI-II) (Beck et al 1996). Self-report data was validated with patients' notes.

iii) Most participants in the intervention group did not receive CBT after the trial sessions, so little "contamination".

## **2.5. BIPOLAR DISORDER**

Individuals with bipolar disorder (BD) often have metabolic disorders, like obesity or type 2 diabetes, while those with a longer duration of the illness have a more sensitive immune system (Mansur et al 2016).

Adipokines (eg: leptin), which are involved in the regulation of appetite and food intake, are also different in individuals with BD. Mansur et al (2016) compared fifty-nine patients with BD at an outpatients clinic in Sao Paulo, Brazil, with twenty-eight healthy



controls. There was no difference between the patients and the controls in levels of adipokines in the blood, but there was a difference among the individuals with BD. Those with low levels of adipokines had more mood episodes, and more depressive symptoms than BD patients with high levels of the cell signalling protein secreted by adipose tissue. The findings were correlational only.

Bauer et al (2016) performed a systematic review of studies of lifestyle interventions to help overweight and obese adults with BD. Only six studies were found up to June 2015.

Lifestyle interventions included healthy diet and more exercise, and the studies showed such interventions "targeting diet, physical activity, self-motivation, and beliefs surrounding wellbeing are feasible and efficacious in individuals with BD" (Bauer et al 2016 p5). For example, Frank et al (2015) used a "lifestyle coach" to help the individuals with BD develop and maintain behaviour changes in sleep pattern, food intake, and overall functioning. After six months, there was a decrease in weight.

Bauer et al (2016) summarised a number of issues about lifestyle interventions for individuals with BD with weight problems:

i) It is not clear about "the mechanisms underlying the establishment of maladaptive routines and disruption of dietary habits and physical activity in BD patients and whether they are the same or differ from those in the general population" (Bauer et al 2016 p5).

ii) Initiating and maintaining physical activity was less successful, and that may be "due to the focus of the health professionals on the health benefits of exercise rather than on the individuals' value of the benefits of physical activity" (Bauer et al 2016 p5).

iii) Long-term changes to lifestyle involve a multi-disciplinary team, including lifestyle coaches, dieticians and fitness trainers, which is expensive.

iv) Are individual- or group-based programmes better?

"While a group can provide encouragement, helpful information and non-judgmental support, some individuals may feel intimidated and overwhelmed as they would compare themselves to their peers and feel they are not able to change their lifestyles. A group setting also leaves less room to work on individual goals, especially if these are quite different (eg: decreasing sedentary behaviour versus eating more healthy)" (Bauer et al 2016 p5).

v) Are group-based programmes more effective with only individuals with BD (homogeneous groups) or mixed with non-BD participants (heterogeneous groups)? The former "promotes social cohesion and increases feelings of safety because participants share the same mental illness", while heterogeneous groups help "individuals realise that concerns about health and lifestyle are struggles of all people in all circumstances. This realisation may help individuals to focus on their commitment to make changes to their lives" (Bauer et al 2016 p5).

Martin (2007) took a different approach to bipolar disorder (manic depression) pointing out that to understand mania requires to understand "what people do with 'mania' and why they do it" (p9), along the lines of understanding the meaning of a word in a foreign language. For example, her interviewees in California saw "manic depression as tantamount for a career in Hollywood, so common was it known to be in the entertainment industry and so necessary did its manic qualities seem for success in that field" (pp31-32).

Martin (2007) expanded on her approach: "I want to propose that 'the human condition' might include both mania and depression within it. I have been guided by this analogy: consider manic depression to be a hand with a pointing finger. We might want to know about the physical properties of the hand, its muscles, tendons, bones, and how they enable the finger to point. Without those physical structures and relationships, no finger could point. But while the structures are necessary for pointing, they are not sufficient to understand what a pointing finger means. The pointing finger is a gesture that takes its cultural meaning from its use in a particular social context. By looking at mania and depression as 'gestures', my aim is to move toward a social theory of irrationality" (p29).

## **2.6. APPENDIX 2A - PREDICTING RESPONSE TO ANTI-DEPRESSANTS**

Cipriani et al's (2016) meta-analysis found that thirteen of fourteen anti-depressants were not effective for major depressive disorder in children and adolescents. Fluoxetine (eg: "Prozac") was the most effective, but the researchers lamented the lack of data generally (Wilson 2016).

The chemical imbalance explanation of depression, advocated by pharmaceutical companies, has been challenged. "Anti-depressants do change how we feel, in a way that some find helpful and others don't. But that doesn't mean they are correcting a chemical imbalance. Many people find alcohol helps them relax, but that's not

because it's correcting an alcohol deficiency in their brain" (Wilson 2016 p21).

Individuals vary in their responsiveness to medications. In the case of anti-depressants, high peripheral inflammation is associated with less improvement in symptoms. It is suggested that high levels of inflammation prevent anti-depressants from working because of interference with the same biological processes (eg: monoamine and tryptophan) (Cattaneo et al 2016).

Cattaneo et al (2016) reported the presence of certain molecules related to the immune system in the blood (ie: biomarkers) predicted responsiveness to anti-depressants. The data came from the Genome-Based Therapeutic Drugs for Depression (GENDEP) study<sup>12</sup>, which is an open-label comparison of two anti-depressants (nortriptyline and escitalopram) with over 800 adults in European countries with unipolar depression. The participants were randomised to one of the drugs for twelve weeks.

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<sup>12</sup> <http://gendep.iop.kcl.ac.uk/>.

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### **3. SUICIDE AND TRAUMATIC BRAIN INJURY**

Traumatic brain injury (TBI) is a risk factor for later suicide <sup>13</sup>. Only a small proportion of cases of concussion <sup>14</sup>, for instance, have severe symptoms (ie: resulting in hospital admission) <sup>15</sup>, which has been linked to later depression, and suicide, especially among military personnel (appendix 3A) and repetitive TBIs. It is unclear whether mild concussion is a risk factor for suicide (Fralick et al 2016) <sup>16 17</sup>.

Studies are usually quite small because of the limited number of TBI patients (eg: 55 patients; Wilson et al 1994). One exception is Teasdale and Engberg's (2001) study using data from a Danish population register of admissions to hospital for the period 1979-1993 (ie: over 167 000 individuals with TBI). These individuals were divided into concussion <sup>18</sup>, cranial fracture, and cerebral haemorrhage/lesion. Before the end of the study period in 1993, 895 of these patients had died of suicide.

Individuals with a TBI were 2-4 times more likely to die from suicide than the general population. This converts to an absolute increase of 1% over a fifteen-year period (Teasdale and Engberg 2001). TBI patients with substance misuse had an even greater risk (figure 3.1). Teasdale and Engberg (2001) observed: "Perhaps the most striking finding has been the increased rate of suicides among patients who have had no more than a concussion, leading typically to only a single day in hospital for observation, or a cranial fracture with no identified cerebral lesion" (p439).

This study was dependent on the correct recording of TBI in hospital records, and the accurate reporting of suicide as the cause of death. In the former case, the researchers estimated that about 10% of TBIs were coded incorrectly, and in relation to suicides, certain deaths - "for example, from drug overdoses, drowning, and falls

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<sup>13</sup> The suggestion is that TBI seems to lead to executive dysfunction, and this plays a role in suicide (Brenner et al 2011).

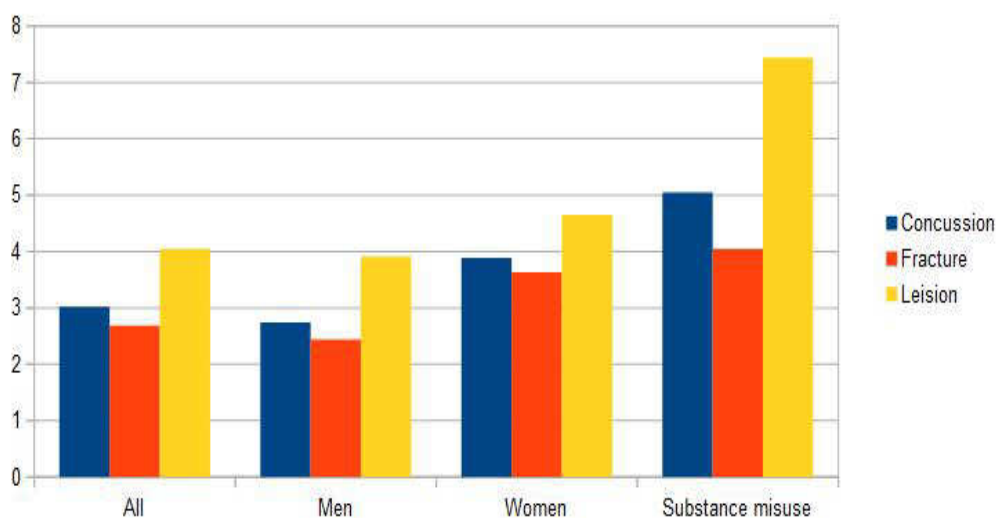
<sup>14</sup> The American Academy of Neurology defined concussion as a "pathophysiologic disturbance in neurologic function characterized by clinical symptoms induced by biomechanical forces, occurring with or without loss of consciousness. Standard structural neuroimaging is normal, and symptoms typically resolve over time" (quoted in Radakrishnan et al 2016).

<sup>15</sup> Around 10-20% of concussion cases do not resolve within a week, and post-concussive symptoms can last for months (known as post-concussive syndrome) (Radharkrishnan et al 2016).

<sup>16</sup> Concussion and mild TBI are often used interchangeably (Radharkrishnan et al 2016).

<sup>17</sup> The symptoms of concussion include headache, dizziness, nausea, feeling as if in a mental fog, increased irritability (Radharkrishnan et al 2016).

<sup>18</sup> Concussion is the most common TBI with the equivalent of 1 per 1000 adults in the USA annually (Fralick et al 2016).



(Data from Teasdale and Engberg 2001 tables 2 and 4 p438)

Figure 3.1 - Selected standardised mortality rates for suicide after TBI, where the general population equals one.

from high places - could have been erroneously recorded as accidental deaths" (Teasdale and Engberg 2001 p439). Possible causes of suicide, like unemployment, were not explored.

Fralick et al (2016) investigated whether there was a difference in the risk of suicide based on the day of the week of the concussion - in particular, recreational injury (weekends) versus occupational injury (weekdays). A cohort of adults diagnosed with concussion in Ontario, Canada, were studied between 1992 and 2012. The health care services database was used for details of hospital admissions, and official death certificates for cause of death.

In total, there were over 230 000 participants, and 667 suicide deaths. Those individuals receiving concussion on a weekday were the majority of suicides, with a suicide risk three times the general population. Weekend concussions, however, were four times the risk of the general population. Other risk factors for suicide included prior suicide attempt, prior mental health problems, low socio-economic status, and being male.

In another Canadian study, Richard et al (2015) confirmed a higher risk of suicide for TBI but during childhood and adolescence. Data from the Quebec Health Insurance Board were used for all under 17s who received medical treatment in 1987 (ie: 135 703 children and

adolescents). This cohort were followed until 2008. There were 428 suicides. The risk of suicide as an adult was greater with TBI than no TBI. The risk increased with age (ie: higher for TBI in adulthood than childhood). Other risk factors for suicide included repeated TBIs, particularly in adolescence and adulthood, and prior mental health problems.

This study depended on secondary data, where there is always a risk of misclassification errors:

a) Coroners and cause of death - Lesage et al (1994) checked on classifications of death from suicide or road traffic accident by interviewing relatives at length, and found little misclassification in the Quebec coroner's database.

b) TBI information based on physicians' billing data and not medical records - However, Kostylova et al (2005) confirmed this as a valid source of TBI information. Billing data were found to have 81% agreement with the Canadian Hospitals Injury Research and Prevention Programme, which is a computerised record of childhood injuries in emergency rooms, for a sample of over 3000 children in hospital in Montreal.

Looking at death after TBI from any cause, Harrison-Felix et al (2009) found that such individuals were three times more likely to die from suicide than the general population. But over twenty times more likely than the general population to die from seizures, for example. This was based on a cohort of 1678 adults surviving one year after a TBI between 1961 and 2002 at a specialist TBI and spinal cord injury hospital in the USA. The general population comparison data used was US national information.

## **EPILEPSY**

Suicide <sup>19</sup>, attempted suicide, and suicidal ideation has been reported as higher among individuals with epilepsy than without, and the relationship could be bidirectional (Hesdorffer et al 2016). Hesdorffer et al (2006) suggested that there may be a common underlying factor between suicidal behaviour and epilepsy (eg: serotonin and glutamate neurotransmitters; stress).

Hesdorffer et al (2016) found support for this argument using data from the UK Clinical Practice Research Datalink (CPRD), which covered thirteen million individuals between 1987 and 2013. It was a case-control

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<sup>19</sup> The risk for completed suicide is nearly forty times greater with prior suicide attempt, while epilepsy increases the risk five-fold (Harris and Barraclough 1998).



study. Individuals with epilepsy were the cases (n = 14 059), and four matched controls for each were selected (n = 56 184). The date of diagnosis of epilepsy, and of first suicide attempt were collected.

It was found that 278 cases (and 434 controls) attempted suicide in the time before diagnosis of epilepsy. This works out as over twice as greater risk of attempted suicide with epilepsy than without.

### **APPENDIX 3A - MILITARY PERSONNEL**

Brenner et al (2011) analysed data from the US Veterans Health Administration (VHA) for 2001-6. This covered around 50 000 cases of TBI (out of 7.8 million users) and 105 deaths by suicide of them (out of a total of 11 384 suicides by veterans). TBI was divided into three categories as used by Teasdale and Engberg (2001).

Those individuals who had experience a TBI were significantly more likely to die by suicide than individuals not receiving a TBI:

- 1.5 times more (unadjusted ratio);
- 2.00 times more (controlling for patient demographics - eg: age, sex);
- 1.55 times more (controlling for demographics and psychiatric diagnosis).

In terms of concussion/cranial fracture, the following increased risks of suicide were calculated:

- 1.88 (unadjusted);
- 2.60 (controlled for demographics);
- 1.98 (controlled for demographics and diagnosis) (figure 3.2).

Overall, TBI was "an independent influence on suicide risk separate from other mental health conditions" (Brenner et al 2011 p262).

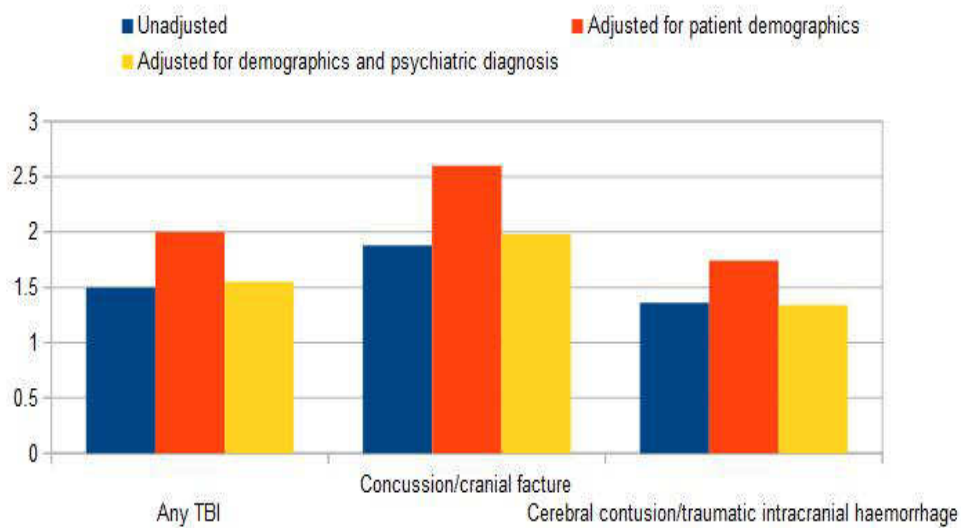


Figure 3.2 - Increased risk of suicide based on TBI, where 1.00 is risk with no TBI.

#### Key limitations of the study:

- Retrospective data.
- Risk of misinformation about TBI in patient records.
- Missed cases not seen by VHA.
- Information missed because not in patient records (eg: psychiatric problems).
- Limited details about effect of severity of TBI.
- Some control variables not included in analysis (eg: level of pain).
- Dependent on accuracy of screening procedures by VHA.
- Use of ICD-9 codes for classifying type of TBI (WHO 1977), but ICD-10 codes for mental disorders (WHO 2004).

Military veterans are a high risk group for suicide generally, with twice as many suicides in the USA than non-veterans (Anestis and Capron 2016).

Generally, the majority of suicide attempts do not end in death, except where firearms are used (80-95% end in death) (Anestis and Capron 2016). In the USA, suicide is five times more likely in the homes of gun owners (Simon 2007). Certain veterans are more likely to be gun

owners, even keeping a loaded firearm by the bed (Freeman et al 1994). Diminished fear of death/bodily harm and heightened pain tolerance are characteristics of such individuals (Joiner 2005). But are these characteristics a product of military training or does the military attract individuals with such characteristics (Anestis and Capron 2016)?

Whichever, "a picture of elevated military suicide risk driven largely by ready access to and comfort with firearms and a propensity to use firearms in suicide attempts, ultimately resulting in a heightened suicide rate and a higher percentage of lethal attempts within military samples" (Anestis and Capron 2016 pp30-31).

Anestis and Capron (2016) explored publicly available data in the USA on state-wide suicide rates, veteran populations, and firearms legislation. The number of veterans per 100 000 in a US state was significantly positively correlated with (i) the state-wide overall suicide rate ( $r = +0.68$ ;  $p < 0.01$ ), (ii) the firearms suicide rate ( $r = +0.70$ ;  $p < 0.01$ ), and (iii) the proportion of suicides resulting from firearms ( $r = +0.61$ ;  $p < 0.01$ ). Altogether, "the association between veteran population and overall suicide rate was largely explained by the elevated proportion of suicides by firearms in states with higher veteran populations" (Anestis and Capron 2016 p30).

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## **4. ANXIETY DISORDERS**

- 4.1. Details
- 4.2. Overgeneralisation of anxiety
- 4.3. Obsessive compulsive disorder
- 4.4. Appendix 4A - Neuroimaging
  - 4.4.1. Emerging technologies
- 4.5. References

### **4.1. DETAILS**

Anxiety Disorders (ADs) include "excess worry, hyperarousal, and fear that is counter-productive and debilitating" (Remes et al 2016 p1).

Remes et al (2016) undertook a review of reviews on the prevalence of ADs among adults. Forty-eight relevant reviews (up to May 2015) were found.

The following information was established about ADs:

- i) The overall prevalence varied from 4 to 25%. But "reviews produced inflated prevalence estimates with the use of less robust methodologies" (Remes et al 2016 p8).
- ii) The prevalence was similar between 1990 and 2010. Remes et al (2016) noted: "A sharp rise in younger people over time was noted, but changing age and population structures were hypothesised to be the drivers of this" (p3).
- iii) Differences around the world - lowest in East Asia and highest in North America and the "Arab world".
- iv) Twice as many women suffered as men.
- v) Younger individuals (under 35) suffered more.
- vi) Specific phobia and generalised anxiety disorder (GAD) were the most common ADs and panic disorder the least common.
- vii) ADs were common with bipolar disorder.
- viii) ADs were associated with addiction, and chronic physical diseases (table 4.1). Also "anxiety symptoms tended to persist post-disease if present before disease onset" (Remes et al 2016 p8).

The researchers noted the "need for further studies on the prevalence of anxiety disorders in the context of: personality disorders; Indigenous cultures in Canada, the United States, New Zealand, and Australia; African,

DISEASE	FINDING
Cardiovascular disease	Eg: "Individuals with non-cardiac or non-specific chest pain presenting to emergency departments, particularly women and those who are younger, appear to be disproportionately affected by anxiety" (Remes et al 2016 p5).
Cancer	Varying from 15-23% of cancer patients, but over 70% of those in the later stages of the disease.
Respiratory disease	Between 23 - 75%.
Diabetes	Significantly higher than non-diabetic individuals for both ADs and sub-threshold symptoms.
Other	Eg: much higher among polycystic ovary syndrome sufferers.

Table 4.1 - Anxiety Disorders and chronic physical diseases.

Middle Eastern, Eastern European, Asian and South American countries; and marginalised populations, such as injection drug users, street youth, and sex workers" (p9).

### 3.2. OVERGENERALISATION OF ANXIETY

When individuals experience a particular stimulus that leads to an aversive outcome, an appropriate response of avoidance is learned. Stimulus generalisation is where the same response occurs to stimuli similar to the original. But how far to generalise? Laufer et al (2016) referred to a "better safe than sorry" approach (ie: wider generalisation) because "a miss (incorrectly identifying the dangerous stimulus as a safe one) is more costly than a false alarm (incorrectly identifying a safe stimulus as the conditioned one)" (p713).

Individuals with Generalised Anxiety Disorder (GAD) show an overgeneralisation, where "stimuli that are only somewhat similar to the original stimulus would still elicit increased anxiety in affected individuals. In an unsafe environment full of complex stimuli where the original stimulus is still dangerous, this is an extreme but rational strategy" (Laufer et al 2016 p713). This is a "choice bias" (Hartley and Phelps 2012).

An alternative possibility is that anxious individuals perceive the stimulus differently after the association with an aversive outcome is learned. Laufer et al (2016) found that this "compromised perception" leads to overgeneralisation.

Their participants were twenty-eight individuals with GAD and sixteen healthy controls in Israel. In the

learning phase of the experiment, participants were played three different tones in random order (300, 500, and 700 Hz). One tone was associated with a positive outcome, and the participants would gain money if they pressed a button after hearing it. Another tone had a negative outcome, and the participants would lose money if they did not press another button within 2.5 seconds<sup>20</sup>. The third tone had no outcome, and was the control. The participants learned which tone was which by trial and error over 63 trials (ie: 21 for each tone).

The generalisation phase of the experiment involved tones that were similar to the originals by varying degrees (3%, 10% and 20% variation). These were included inbetween the originals. The positive and negative outcomes of the originals remained, and the pressing of a different button was required when a new tone was played. The new tones did not lead to monetary gain or loss. There were 128 trials, of which 96 tones were new. The correct recognition of the new tones was scored.

The optimal behaviour is an "as-narrow-as-possible generalisation around both original tones" (Laufer et al 2016) (ie: do not press gain or loss button in response to new tone).

GAD participants had a wider generalisation than controls around the loss tone (ie: press loss button in response to new tones that were 10% and 20% different to the original). For example, about half the GAD group responded to a new tone that was 20% different to the original loss tone as if it was a loss compared to about one-fifth of controls.

The GAD participants also showed a wider generalisation around the gain tone, but not to the neutral tone.

Laufer et al (2016) concluded: "These findings support the notion that anxiety patients overgeneralise due to altered perception of the stimulus and therefore do so even in a safe context when the original stimulus is no longer dangerous and even when the generalisation harms them. We further hypothesised that there should be evidence for altered neural representations that are formed during conditioning" (p714).

To confirm this hypothesis, a sub-set of participants performed the experiment in a functional magnetic resonance imaging (fMRI) scanner (appendix 4A), and there were differences in brain activity between GAD and control participants (eg: in the amygdala). Laufer et al (2016) felt that "affective stimuli shape early sensory representations during conditioning, and these

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<sup>20</sup> This type of learning is based on classical conditioning, and it has been argued that specific phobias, for example, develop this way. For instance, being scared by a particular dog as a child leads to fear of dogs as an adult.

altered representations later result in less discrimination between the conditioned stimulus and new safe stimuli" (p718).

Laufer et al (2016) did not rule out the possibility that individuals with anxiety overgeneralise their anxiety response to stimuli similar to the original negative stimulus because of choice bias and perceptual changes.

#### **4.3. OBSESSIVE COMPULSIVE DISORDER**

Knowing when stimuli in the environment are dangerous is an important survival skill, and so is knowing when stimuli are non-threatening or when previously threatening stimuli are now safe. Individuals with obsessive compulsive disorder (OCD) may be poorer at the latter, according to a study by Apergis-Schoute et al (2017).

The ventromedial prefrontal cortex (vmPFC) is the key brain area involved here - playing "a multi-faceted role in integrating affective evaluative processes while mediating flexible behaviour and is implicated in fear learning and anxiety-related disorders. Prefrontal inflexibility in OCD suggests rigidity in threat estimation alongside a persistent urge to perform compulsive behaviours..." (Apergis-Schoute et al 2017 p3216).

Forty-three individuals with OCD and 35 matched healthy controls in the UK were involved in the study using a threat reversal paradigm. Participants were shown pictures of faces, and one expression (eg: anger) was paired with a mild electric shock while another expression (eg: smile) was not. As this association was learned, participants showed an anticipation of a shock or not depending on the face shown. Then the pairing was reversed, and participants received a shock with the smiling face but not the angry one. The healthy controls came to anticipate the shock with the smiling face because they had "updated" their learning, but the OCD sufferers did not. Based on neuroimaging, the hyperactivation of the vmPFC in the OCD group seemed to be the reason (ie: an impairment in "safety signalling" by vmPFC) (Apergis-Schoute et al 2017).

#### **4.4. APPENDIX 4A - NEUROIMAGING**

Neuroimaging technology has improved in the last few years to such a point that there are those who see the possibility "to render the activities of the working mind visible in the living brain" (Rose 2016). For example, Haynes et al (2007) asked participants in a scanner to decide if they would subtract or add two number presented



a few seconds later. In nearly two-thirds of cases, the researchers correctly predicted the choice based on brain activity pattern in the medial prefrontal cortex (Rose 2016).

Such experiments and others lead to headlines in the popular press about "mind-reading", and fears about the future are voiced. Rose (2016) commented:

Both utopian and dystopian speculations are based on extrapolations from limited experiments in very artificial situations which bear little relevance to how beliefs, intentions, desires and the like are manifested, experienced, communicated and regulated in the everyday world. Claims about mind reading in the popular media undoubtedly entail familiar mishmashes of technology, software, epistemology, ontology, expectations, ethics and politics. And when the speculations of neuroethicists, the exaggerations of neuroscientists, the imaginations of science fiction, and the aspirations of our military researchers coincide, a heady mix of unreality usually results. Practical applications of these brain-reading technologies are most likely merely to add to the multiple other low-tech - and perhaps less fascinating - tools that are already used for these purposes for children, asylum seekers, job seekers, benefit seekers and many others. Perhaps the most interesting questions are less technical than political - not "can we read the mind", but why, in particular practices, do some want to read some minds, and why do some dream that new neurotechnologies will make this possible? (p158).

At a more mundane level, Rose (2016) pointed out a number of general problems with neuroimaging:

i) They need "incredibly sophisticated computer packages" to turn the "data from voxels in a three-dimensional space into simulated images" (Rose 2016).

ii) The search for the localisation of a behaviour in an area of the brain ignores "the complex circuitry of the human brain and the fact that any mental function entails, and depends upon, activity in multiple regions and circuits of the human brain and its integral connections with inputs from the wider nervous system" (Rose 2016 p148).

fMRI uses blood oxygenation level-dependent (BOLD) signals as a "surrogate measure of neuronal activity" (Hall et al 2016). The principle is that active neurons require oxygenated blood and the flow can be recorded, along with the used (deoxygenated) blood.

Hall et al (2016) advised caution about interrupting BOLD signals. They stated: "To fully understand the physiological basis of the BOLD signal, and therefore be able to optimise experimental design and interpretation, we need a complete understanding of the processes that generate it at the molecular, cellular, vascular and voxel level. While..., we are still some way from this

complete understanding..." (p7).

iii) The limited knowledge about the physiology of the brain - "we actually have almost no idea of the appropriate scale to image mental function - at the cellular level, at the level of specific circuits, at the level of the whole brain, at the level of the whole nervous system" (Rose 2016 p148).

iv) Scanners have low ecological validity. In other words, it is highly unrealistic to study the activities of the brain in social behaviour while an individual is alone in the constrained situation of the machine.

Neuroimaging involves a one-off snapshot of the brain, and it is assumed that this is representative of the individual's daily brain functioning, but conditions fluctuate over time (Hadhazy 2016). One response is repeated measuring as in the "MyConnectome project" which aims to examine one brain in great detail. The project is focused upon its founder, Russell Poldrack, who had two brain scans per week over eighteen months in 2012-14, along with giving regular blood samples and keeping details records of food and exercise, for example (Hadhazy 2016).

#### **4.4.1. Emerging Technologies**

Williams (2005) noted how emerging technologies (ETs) can be presented as utopian or dystopian depending on proponents or opponents of the change, but he questioned "such 'linear' conceptions of innovation pathways and 'impacts', pointing to the unpredictability of technical and social outcomes of earlier innovations" (p3). Furthermore, contemporary discourse about ETs "seems to be an attempt to look further into the future and map the technical and social outcomes in greater detail than previously, which can make these futures appear as largely determinate and imminent; as if the future is already assured; already here. Attempts at foresight are thus foreshortened; the future is compressed into the present" (Williams 2005 p4) <sup>21</sup>.

This idea of "compressed foresight" is part of the desire to resolve debates between proponents and opponents of ETs, and part of "increasing effort to anticipate the future and map the technical and social outcomes in a higher level of detail than previously" (Williams 2005 p5). Thus, "the gap between imagined and actual futures is foreshortened; our attempts at

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<sup>21</sup> Paul-Choudhury (2016) referred to "exponentialism" - "the belief not only that what is happening will keep happening, but that it will happen ever faster".

foresight, at anticipation of the future, are thus compacted and compressed" (Williams 2005 p5). Similarly, Brown (2003) argued that "technology hype mobilises the future into the present" (Williams 2005).

Williams (2005) noted also "the reified treatment of emerging technologies - as though these were broadly homogeneous entities with finite technical properties and socio-economic implications - rather than diverse and heterogeneous bundles of capabilities" (p6).

But, surely, ETs throughout history have always had proponents and opponents. What is different today is that ETs "are seen as crucial for wealth creation - indeed economic survival - in a competitive global knowledge economy, that will transform health and the quality of life" (Williams 2005 p8). While, at the same time, public concerns over potential undesired consequences of their developments "have come to the fore" (Williams 2005). So, "advance in science and technology is both imperative and vulnerable" (Williams 2005 p8).

O'Neil (2016) highlighted that decision-making algorithms are "based on choices made by fallible human beings", and though designed with the best intentions, "encoded human prejudice, misunderstanding and bias into the software systems..." (p51). For example, decisions to give a loan are based on mathematical scores which include area of residence/postcode. Alternatively, credit reports are used with the inbuilt assumption that individuals who are not in debt are responsible people, thereby ignoring circumstances that cause debt outside the individual's control. O'Neil (2016) coined the phrase "weapons of math destruction" for the decision-making algorithms.

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## **5. MENTAL ILLNESS AND URBAN LIFE: BIOLOGY AND SOCIOLOGY**

- 5.1. Urban life and mental health
- 5.2. Recent studies on urban life
- 5.3. Appendix 5A - Epigenetics
- 5.4. Appendix 5B - Local biologies
- 5.5. References

### **5.1. URBAN LIFE AND MENTAL HEALTH**

A link between urban living and poor mental health was formally observed as early as the late nineteenth century in the Connecticut Hospital for the Insane, where Burr (1903) noted a 20-30% higher rate of urbanites in the institution. In terms of national statistics, the US Government calculated a rate of 86 per 100 000 for city-dwellers as "insane and feeble-minded in institutions" in 1914 compared to 41 for countryfolk (Fitzgerald et al 2016a). It was felt that the abnormality of urban life was the cause. "This attention to insanity in the city was thus not only a concern with epidemiology but arose from a religious, ethical and social commitment to understanding the deleterious relationship between modern society and mental health" (Fitzgerald et al 2016a p143).

Cities were also the home of immigrants, and of particular immigrants to the USA. As one official, at the end of the nineteenth century, warned of being overrun of hordes of "degraded" immigrants from southern and eastern Europe (Fitzgerald et al 2016a). This is a version of the "urban drift" theory, which sees the mentally ill as attracted to urban areas, as opposed to something about urban life than causes mental illness ("social causation" theory).

Faris and Dunham (1939) saw a geography of mental disorders in a city which "decrease from the centre to the periphery of the city, in more or less the same pattern as 'poverty, unemployment, juvenile delinquency, adult crime, suicide, family desertion'" (Fitzgerald et al 2016a p144).

Furthermore, "paranoid schizophrenia [associates] with percentage of hotel residents and lodgers; catatonic schizophrenia with percentage of foreign-born and Negroes; manic-depressive psychosis with median monthly rentals; alcoholic psychoses with per cent of population on relief; dementia paralytica with distribution of vice resorts... senile psychoses with percentage of home ownership; senile psychoses combined with arteriosclerosis with percentage of population on relief and with per cent of population of native white parentage" (Faris and Dunham 1939 quoted in Fitzgerald et al 2016a pp144-145).

The explanation that Faris and Dunham provided was a combination of biological and social: "the human mind is built on, and is never independent of, a physiological base... [However] the mind... is [also] a product of a process of social interaction. Mentality, abilities, behaviour, are all achievements of the person, developed in a history of long interaction with his surroundings, both physical and social" (Faris and Dunham 1939 quoted in Fitzgerald et al 2016a p145). In many senses, this is a combination of the social drift and social causation ideas. Subsequent researchers, however, have wanted to distinguish between the ideas, and so dismissed Faris and Dunham's work. So, "the possibilities identified by those like Faris and Dunham - that psychiatric illness, through its association with urban life, poverty, racism and marginalisation, might become the meeting-ground for a constitutive relation between the sociological and life sciences - faded away" (Fitzgerald et al 2016a p148).

More recently, Lederbogen et al (2011) argued that individuals who live in cities and/or were raised in them have "distinctive neurological responses to a stressful stimulus" (Fitzgerald et al 2016b). In other words, "'the city' has been narrated and theorised as a torrent of stress-inducing stimulation (visual, auditory, affective) - with the urban dweller, in her turn, understood as the fretful recipient of its hectic, and often pathological, energy" (Fitzgerald et al 2016b p222). Abbott (2012) wondered "if city living was somehow making the brain more susceptible to mental-health conditions" (quoted in Fitzgerald et al 2016b).

Fitzgerald et al (2016b) coined the term "Neuropolis" to describe the city as "a matrix of transactions between urban life and the always-developing, malleable brains of urban citizens" (p223) <sup>22</sup>.

The belief that urban life is "unhealthy" is confirmed by recent studies that compare brain activity in the city and in the country. For example, Aspinall et al (2013) got participants to wear portable EEG headsets as they walked through urban areas of Edinburgh and outside the city. The EEG readings and the self-reports showed less arousal outside the city.

In terms of explanations, by the twenty-first century with the development of epigenetics (appendix 5A), sociologists and biologists can "bury the hatchet" (Editorial 2012). Epigenetics is the idea that genes will be influenced by environmental factors. Stress, in

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<sup>22</sup> In terms of modern urbanity as different to the past, McKibben (2010) referred to "a sort of Earth 2.0", while Graham and Marvin (2001) argued that the "modern infrastructural ideal" is "increasingly under threat" (Jackson 2014 p222).

particular, is "the gateway" for this process (Fitzgerald et al 2016a). For example, Galea et al (2001) found that physically assaulted Detroit residents had a particular gene expression which led to post-traumatic stress disorder (PTSD) and depression. Thus, "different aspects of the urban environment are distinctly and variably linked to brain structure, function, and hence phenotype" (Galea 2011 quoted in Fitzgerald et al 2016a).

Combining biological and sociological understandings, Fassin (2009) coined the term "life-as-such" to describe "life as the course of events which occurs from birth to death, which can be shortened by political or structural violence, which can be prolonged by health and social policies, which gives place to cultural interpretations and moral decisions, which may be told or written - life which is lived through a body (not only through cells) and as a society (not only as species)" (Fassin 2009 quoted in Fitzgerald et al 2016a p152). Fitzgerald et al (2016a) referred to a "bioeconomy of urban experience" (ie: "the relations between capital, biology, and mental distress") to capture the complexity of lived experience in the city and the interaction of biological and environmental/social factors there.

Fitzgerald et al (2016a) pointed out: "It has become a cliché to ask 'how does experience - of stress, violence, loneliness, etc - get 'under the skin?' ". Such a question, while welcome for new forms of enquiry into the embodied consequences of inequality, exclusion, racism and trauma, none the less poses the biological/social distinction too sharply - it misses the 'intra-actions' through which vital forms of life are not shaped by a binary split, but actually inhere in the complex of organism and milieu" (p153).

Another point to bear in mind is that there is "the city and the city" (Mieville 2011). In other words, there are differences between cities, as well as within them, which limit generalisations. This could give "local biologies" (Lock 2001) (appendix 5B), where "biological differences might produce a very different kind of subjective experience - which would, in turn, shift the way that local worlds are both made and made sense of" (Fitzgerald et al 2016a pp155-156).

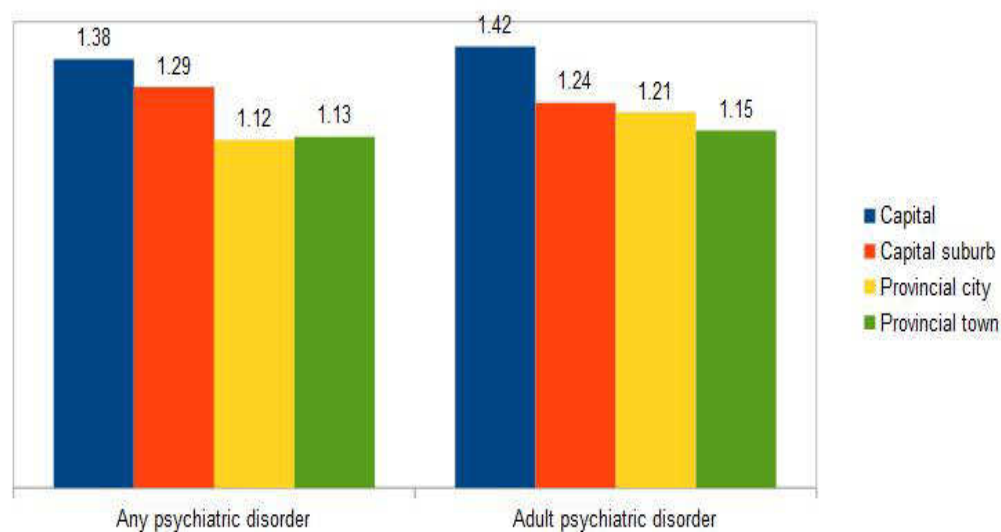
## **5.2. RECENT STUDIES ON URBAN LIFE**

Based on a population-based cohort of everyone born in Denmark between 1955 and 2006, Vassos et al (2016) found greater likelihood of mental illness among individuals born in urban than rural areas (figure 5.1).

For the 2.9 million individuals, place of birth was established from the Danish Civil Registration System, while details of use of psychiatric facilities/services

between 1995 and 2012 came from the Danish Psychiatric Central Research Register. The degree of urbanisation was categorised as capital (Copenhagen), capital suburb, provincial city, provincial town, or rural area.

The authors listed possible explanations for the findings, including differences in service utilisation and availability, diet, stress, lifestyle, family-level factors, infections, complications during pregnancy, quality of housing, fear of crime, and social participation (Vassos et al 2016).



(Data from Vassos et al 2016 table 2 p437)

Figure 5.1 - Relative risk of psychiatric disorders (where born in a rural area = 1).

Peen et al's (2010) meta-analysis found that urban dwellers were about 20% more likely to develop anxiety disorders and twice that for mood disorders than rural dwellers.

So, improving access to green spaces in the city may be the solution. Alcock et al (2014), for example, found that individuals moving within urban areas to areas with more green spaces were happier (than those moving to areas with less green spaces), and this persisted for at least three years after the move. The improvement in mental health, however, was quite small (Gilbert 2016).

Cohen-Cline et al (2015) isolated genetic variation by studying twins. Twins with access to green space had less depressive symptoms than co-twins without the access.

In terms of health, the ease with which individuals can walk around an urban area is important. More walkable



areas are associated with lower childhood obesity and lower body mass index in older adults (DeWeerd 2016). But more walking in the city increases the exposure to air pollution (eg: James et al 2015; women in the Nurses' Health Study in the USA).

Stress has been found to be detrimental to health through the effects of physiological processes in the stress response on the immune system. For example, HIV progresses faster in stressed gay men, or children from poorer backgrounds have higher rates of asthma, or long-term unemployed men die earlier than those employed (Maxmen 2016). More than that, "psychological stress among the urban poor is distinct from that of those who live in rural areas, perhaps because income disparity is not as obvious" (Maxmen 2016 p59).

### **5.3. APPENDIX 5A - EPIGENETICS**

Epigenetics is "the study of modifications in gene expression brought about by mechanisms other than changes in DNA itself. The most researched aspect of epigenetic marking is known as DNA methylation, involving the addition of a methyl group, a so-called chemical cap, to part of a DNA molecule, thus preventing the expression of a gene or genes" (Lock 2015 p151).

Interest in epigenetic mechanisms that regulate genes in the brain smacks of "a new round of somatic determinism" (Lock 2015). The "contribution of environments – social and environmental – to human development, health, and illness are not denied by epigeneticists, but there is a distinct danger that the molecular endpoints that these variables bring about, and very little else, may well receive undue attention" (Lock 2015 p154).

Epigenetics in relation to the foetal environment is seen in the case of pregnant women in the "Dutch Hunger Winter" (famine in the Netherlands in 1944-45) (eg: Heijmans et al 2008). Children born just after (ie: the mother pregnant during the famine) had disproportionately high levels of conditions like diabetes in later life. Despite being nourished themselves during pregnancy, their children "inherited similar health problems thought to be incited by epigenetic effects" (Lock 2015).

Women born during severe food deprivation in the first trimester of their pregnancy had an increased risk of hospitalisation for adult schizophrenia, but not men (Susser and Lin 1992).

This "environmental epigenetics" (Lock 2015) produces an "embedded body" – "heavily impregnated by its own past and by the social and material environment within which it dwells. It is a body that is imprinted by

evolutionary and transgenerational time, by 'early-life', and a body that is highly susceptible to changes in its social and material environment" (Niewohner 2011 quoted in Lock 2015). What this means for researchers following this idea is that "events of significance in people's lives are researched and documented, to some extent standardised, and then systematically examined for associations with bodily epigenetic changes" (Lock 2015 p160).

Sen et al (2015) found that the high blood lead levels of 35 pregnant women in Detroit could affect the DNA methylation of the offspring such that the next generation would be affected (ie: the women's grandchildren). The lead in the blood would alter the foetal germ cells, and this is how the consequences of the lead pollution is passed on to the next generation.

#### **5.4. APPENDIX 5B - LOCAL BIOLOGIES**

Lock and Kaufert (2001) used menopause around the world as an example of "local biologies". The medical view of the menopause has emphasised its pathology with the subsequent increased risk of certain illnesses, like heart disease and osteoporosis. But using research from Japan, Canada and the USA, Lock and Kaufert (2001) questioned "the notion of a universal menopause by showing that both the symptoms reported at menopause and the post-menopause disease profiles vary from one study population to the next. For most of the symptoms commonly associated with menopause in the medical literature, rates are much lower for Japanese women than for women in the United States and Canada, although they are comparable to rates reported from studies in Thailand and China. Mortality and morbidity data from these same societies are used to show that post-menopausal women are also not equally at risk for heart disease, breast cancer, or osteoporosis" (p494).

The samples were 1255 Japanese women, 7802 from Massachusetts (USA), and 1307 from Manitoba (Canada), all aged 45-55 years old. They varied significantly on the prevalence of fourteen of sixteen symptoms common to menopause (eg: hot flushes, sleep problems, headaches).

Lock and Kaufer (2001) concluded that "the end of menstruation should not be conceptualised as an invariant biological transformation, that local biologies are at work, and that it is appropriate to think of biology and culture as in a continuous feedback relationship of ongoing exchange, in which both are subject to variation" (p503).

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## **6. OPIOID TREATMENT FOR SUICIDAL THOUGHTS**

It is estimated that up to 70% of sufferers of major depressive disorder do not respond to initial treatment. Some of these individuals benefit from switching to another treatment, but many remain with the symptoms (Fava et al 2016). Thus, the search for new and effective treatments, particularly drugs. There is interest about the opioid (painkiller) buprenorphine.

For example, Yovell et al (2016) gave low doses of buprenorphine to forty individuals in Israel with high suicide motivation, and forty such individuals received a placebo. The opioid group showed immediate reductions in their suicidal thoughts (ie: in first week), and there were also benefits at the end of the one month trial <sup>23</sup>.

A larger study by Fava et al (2016) used a randomised, double-blind, placebo-controlled design with a two-stage sequential parallel comparison element with 142 depressed patients at 31 sites in the USA (figure 6.1). In stage 1, participants received four weeks of combined opioids buprenorphine and samidorphan at daily low or high dose, or a placebo. Placebo-responders were studied separately, and stage 2 was the same as stage 1.

The low dose participants improved significantly more than the placebo group, and the high dose group improved non-significantly (figure 6.2) <sup>24</sup>. Fava et al (2016) commented: "Although there was evidence in both dosage groups of anti-depressant activity, greater and statistically significant treatment effects were observed in the [low] dosage group. Although an inverse or U-shaped dose response is not uncommon for psychiatric medications, the specific reason for this observed dose response is uncertain. A potential explanation may relate to adverse events" (p506).

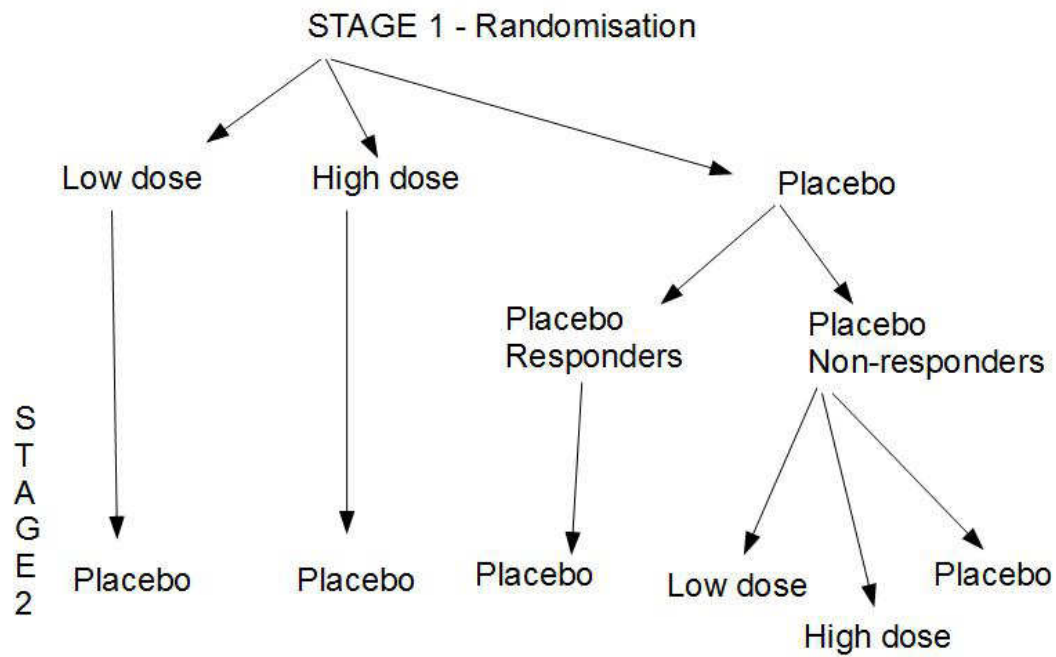
Chen et al (2011) felt that the method used by Fava et al (2016) identified more placebo responders, and increased the chance of finding a difference between the drug and placebo groups.

The exact mechanism of the drug is not known, though it acts on different opioid receptors in the brain (Locklear 2016).

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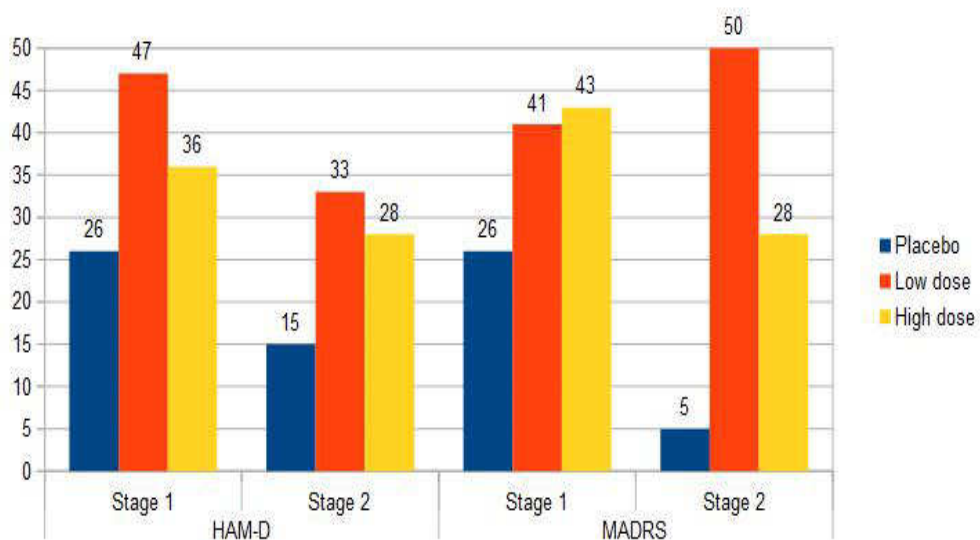
<sup>23</sup> Two interesting observations have been made about suicide (Shute 2016):i) Suicide is time-limited - eg: two-thirds of survivors of suicide attempts had started planning it less than an hour beforehand (Shute 2016).ii) Survivors do not necessarily try again - eg: Seiden (1978) found that 90% of individuals who were stopped from jumping off the Golden Gate Bridge in San Francisco between 1937 and 1971 died a natural death.

<sup>24</sup> The overall effect size for the low dose was 0.50-0.54, which compares to 0.35-0.48 for atypical anti-psychotics (Fava et al 2016).



(Based on Fava et al 2016 figure 1 p502)

Figure 6.1 - Design of Fava et al (2016).



(HAM-D = Hamilton Depression Rating Scale; reduction of  $\geq 50\%$  from baseline.  
MADRS = Montgomery-Asberg Depression Rating Scale; reduction of  $\geq 50\%$  from baseline)

Figure 6.2 - Percentage of participants responding based on two measures of depression.

Kosten (2016) raised a concern about buprenorphine - it has "abuse liability and the potential to produce opioid dependence in opioid-naive patients, particularly when used at low intra-nasal doses" (p446). This fear of abuse could lead to depot implant, but this is a challenge because "a surgical insertion of a buprenorphine implant is not a typical psychiatric practice, and furthermore, removal of the implant is required several months later, after the buprenorphine in it is exhausted. Removal of these implants has been technically difficult because of potential breakage of its packaging on attempted removal. Leaving the non-dissolving packaging in the patient is not possible, since it can become a site for infection and abscess formation" (Kosten 2016 p447).

Furthermore, Kosten (2016) noted about the illegal and abusive aspects, "the implants will contain a large amount (about 300 mg) of liquid buprenorphine that can be injected, snorted, or otherwise abused by simply removing it from the implant" (p447).

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## **7. BIOPSYCHIATRY**

- 7.1. Crises in psychiatry
- 7.2. Global psychiatry
- 7.3. Diagnosis
- 7.4. Power of psychiatry
- 7.5. "Science fictions"
- 7.6. Self-management of depressions
- 7.7. Appendix 7A - Pharmaceutical industry
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### **7.1. CRISES IN PSYCHIATRY**

Rose (2016) described psychiatry as having a "threefold crisis":

i) Of diagnostic systems - Despite the many updates of DSM, up to the current DSM5 in 2013, there was not "a single clinically validated biomarker for any psychiatry disorder", and "there was no clear boundary of ill and well, there were no simple genetic disorders, similar symptomology could arise from different biology, similar biology could lead to different symptomatology" (Rose 2016 p96). This is leading to the search in the brain for the means of diagnosis of mental disorders rather than depending on observable symptoms as in DSM. "But this belief in the neural foundation of such disorders is an unproven hypothesis" (Rose 2016 p96).

ii) Of its explanatory models - It has proved difficult "to identify the disordered brain circuits that are hypothesised to underpin or sub-serve the specific anomalies in cognition, affect or volition that characterise the experience of mental health problems..." (Rose 2016 p96).

iii) Of its therapeutic capacities - In the USA in 2010, for example, about one in seven men and a quarter of women were prescribed psychiatric drugs (Rose 2016), yet the underlying basis for their use (eg: neurotransmitter theory) is questioned.

Concentrating on anti-depressants, Rose (2016) observed that "few now believe in the basic explanatory form of neurotransmitter hypothesis of mental disorder, let alone the dream of specificity - that each psychiatric disorder could be linked to a specific anomaly related to one - or a small number - of dopamine, serotonin, glutamate or any of the many dozens



of neurotransmitters that have now been identified. If the drugs work – and that remains an open question for many persons and many conditions, especially those forms of mild to moderate distress that are the conditions most treated by such drugs – they almost certainly do not work in this way" (p97). This leads to "the paradox – more and more people are taking the drugs, especially for relatively minor problems of mental health – while the hypothesis on which they are based is no longer viable" (Rose 2016 p97).

Rose (2016) offered some solutions to the crises in psychiatry. Firstly, to realise that "a disorder – even a 'mental disorder' – is a disorder of a whole person (not just a brain) – a living organism shaped by time and development from conception, and always in transaction with a social and environmental setting" (p97). This also means that "brain" and "body" are inseparable. And finally, "an organism is not merely a sum of parts that can be isolated and experimented on in the purified space of the laboratory, then simply extrapolated to the whole as it lives in the wild world of real existence" (Rose 2016 p98).

In relation to genetic explanations, Rose (2016) concluded: "We need to think of gene sequences, not as an inherited programme that merely reveals itself, but as they activate and de-activate, methylate and demethylate over the course of development, and always in relation to their milieu" (pp98–99).

## 7.2. GLOBAL PSYCHIATRY

Behague (2016) noted concerns among psychiatrists in Brazil, for instance, about the "emerging globalisation<sup>25</sup> of 'Anglophone biopsychiatry'... canonised in diagnostic manuals and backed by industry. Many worried that chronic medication-use can hinder substantive improvements in a patient's emotional state and become a mere 'therapeutic lid' that keeps the conditions accounting for mental strife under wraps, simmering but still wounding" (p134)

<sup>26</sup>.

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<sup>25</sup> "Globalisation may be thought of initially as the widening, deepening and speeding up of worldwide interconnectedness in all aspects of contemporary life" (Held et al 1999). Globalisation includes interconnectedness of production globally, the rise of trans-national corporations, and the "McDonaldisation" (Ritzer 1993) of society (Deacon 2007). The diverse reactions to globalisation can be seen in political positions like "neoliberalism", which embraces free-market globalisation, through to "localisation", which seeks a return to local production, usually in a sustainable way (Held and McGraw 2002).

<sup>26</sup> Talking about the "prevention paradox", Rose (1992) stated that there can "a conflict... between the collective interest, which requires community-wide change, and that of many of the individuals concerned, who could well consider that their prospect of benefit was negligible" (quoted in Verweij 1998 p56).

From her fieldwork in southern Brazil, Behague (2016) distinguished "two main kinds of 'adolescences' within which two kinds of pharmaceutical use evolved".

i) Medication as "a temporary vehicle to personal betterment", usually among the upper-middle class, based on the assumption that "the end of adolescence would also bring a reduction in distress" (Behague 2016).

ii) For youths from lower socio-economic groups medication use became chronic, like the "pharmaceutical lid".

However, Behague (2016) preferred to explain this process, not through "the globalisation of biopsychiatry", but in "how contemporary clinical enactments of adolescence animate - and potentially transform - historic problematics relating to education, employment, politics, classism, feminism, livelihood, inequity, parenting, kinship, and upward mobility" (p150). In other words, it is more of a local process, and is "not at all similar to the kind of pharmaceuticalisation (appendix 7A) that is propelled by neurobiological framings of adolescence and broader theories of the 'chemical brain' as has been the case in the United States" (Behague 2016 p137).

The line between legal and illegal drugs can be blurred, as well as a drug itself being both of these. De Zordo (2016) used the example of misoprostol in Brazil, where it is used legally in hospitals in obstetric procedures, and purchased illegally to self-induce abortion. Though the drug is safer in the latter use than traditional methods, misoprostol still carries risks in the wrong dose and without medical guidance.

Commenting on the illegal use of misoprostol by low-income women, De Zordo (2016) reported a negative attitude by doctors towards such women. Misoprostol was "labelled as the 'easy solution' chosen by young, low-income women, who are stigmatised for their 'irresponsible' sexual behaviour and limited use of contraception that only women, not men, are considered to be responsible for" (De Zordo 2016 p30).

De Zordo (2016) went on:

The most conservative gynaecologists that I interviewed distinguished between different kinds of birth control techniques and women at the same time. In their opinion, middle and upper class women use contraception more effectively and avoid unwanted pregnancies and illegal, unsafe procedures. On the contrary, their 'irresponsible', low-income female patients at public hospitals used misoprostol 'as a contraceptive' and then sought post-abortion medical help, making public maternity services collapse. These 'bad patients' should be punished because they could have used other legal pills (hormonal pills and the morning-after pill). Only a minority of physicians,

those in favour of the legalisation of abortion, as well as social workers, mentioned the deep gender and social inequalities that make contraception difficult and much more accessible to middle and upper class women at private clinics, which also provide illegal, but safe abortion (p31).

Da Matta (1997 quoted in De Zordo 2016) distinguished between "sub-citizens" and "super-citizens" in social divisions in society. De Zordo (2016) said: "Physicians distinguish their poor patients as 'sub-citizens' depending on the black market, backstreet abortion and public post-abortion care services, from their private patients. The latter are 'super-citizens' who are 'above the law' and can easily access the private health market providing the best medical services and techniques, including safe abortion" (p31).

De Zordo (2016) referred to "a globalised double (reproductive) citizen regime", which is "achieved by creating a distinction between women who can legally and safely (and freely, in many countries where abortion is legal) access to this drug and low-income women who cannot. This is either due to the illegal status of abortion or because of their irregular/illegal status as migrants in countries where abortion is legal" (pp31-32).

### 7.3. DIAGNOSIS

"The question of whether or not psychiatrists are able to 'carve nature at its joints', to understand the 'natural' causes of disorders, has long been a preoccupation of both the psychiatric field and its critics" (Decoteau and Sweet 2016 pp414-415).

Talking generally about medicine, but applicable to mental problems, Rosenberg (2002) observed that the "modern history of diagnosis" <sup>27</sup> is inextricably related to disease specificity <sup>28</sup>, to the notion that diseases can and should be thought of as entities existing outside the unique manifestations of illness in particular men and women <sup>29</sup>. During the past century especially, diagnosis,

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<sup>27</sup> The general "disease classification system" (DCS), as Lowy (2011) called it, is based on three historical developments in medicine: "the elaboration of the concept of specificity of diseases, the wide diffusion of new paper technologies and administrative practices, and the use of statistics to define normal values for a population" (Lowy 2011 p300).

<sup>28</sup> "A diagnosis - that is, a statement of the patients' 'real' complaint - provides an interpretation of symptoms, describes the patients' likely future(s), and, in present-day medicine, often determines which specialists they consult, how they are treated, and which tests and therapies will be reimbursed by a national or a private health insurance. Diagnosis thus homogenises medical practices" (Lowy 2011 p301).

<sup>29</sup> "Classification has sometimes been presented as an autonomous way of knowing" (Lowy 2011 p299).

prognosis, and treatment have been linked ever more tightly to specific, agreed-upon disease categories, in both concept and everyday practice" (p237)<sup>30 31</sup>. This process has become "increasingly technical, specialised and bureaucratised" (Rosenberg 2002)<sup>32</sup>.

Numbers, scores, and quantitative data are important in this process. There is "the bureaucratic need for numbers that legitimate and trigger a sequence of additional diagnostic, therapeutic, and administrative actions", but in doing so, "obscures the very constructedness of those numbers" (Rosenberg 2002 pp249-250).

The socially constructed nature of numbers and categories is seen when "official definitions" change<sup>33</sup>. In 1999, for instance, the National Institutes of Health in the USA redefined overweight as a body mass index (BMI) above 25, down from 27 previously (Rosenberg 2002). Overnight an individual with a BMI of 26 become overweight. The "New York Times", at the time, saw "excess body fat increasingly being viewed as a disease" allowing room for the "pharmaceutical fix" (Rosenberg 2002).

Rosenberg (2002) summed up: "In the act of diagnosis, the patient is necessarily objectified and recreated into a structure of linked pathological concepts and institutionalised social power. Once diagnosed, that bureaucratic and technically alienated disease-defined self now exists in bureaucratic space, a simulacrum thriving in a nurturing environment of aggregated data, software, bureaucratic procedures, and seemingly objective treatment plans" (p257). But, he stated: "We are never illness or disease but, rather, always their sum in the world of day-to-day experience. Illness and disease are not closed systems but mutually constitutive and continuously interacting worlds" (Rosenberg 2002 p258).

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<sup>30</sup> Zola (1972) observed that "while it is probably true that individuals are no longer directly condemned for being sick, it does seem that much of this condemnation is merely displaced. Though his immoral character is not demonstrated in his having a disease, it becomes evident in what he does about it" (quoted in Verweij 1998 p76).

<sup>31</sup> Medicalisation refers to "the emergence of medical definitions for previously non-medical problems" (Conrad 1992 quoted in Verweij 1998). "Concerning preventive medicine, the term 'medicalisation' refers to the process that medical terms are used for 'new' areas: human behaviour, properties, events, and problems which used to be part of normal human life. The practical consequence of this conceptual process is that (healthy) persons tend to adjust their life and life-style according to medical information, advice and procedures" (Verweij 1998 p103).

<sup>32</sup> "Diagnosis gives meaning to symptoms and suffering of patients; it places a particular case or condition, more or less formally, in contemporary DCS; and thus it helps organise medical and public health activities" (Lowy 2011 p300).

<sup>33</sup> Responding to the critical position on mental illness, Storr (1997) stated that there are "a number of persons in any society who are, and should be, regarded as mentally ill and who may, unfortunately, require confinement against their will, at any rate temporarily" (p298).

The National Institute of Mental Health (NIMH) (representing "biological psychiatry") in the USA has argued for a "biological 'replacement'" to the American Psychiatric Association's (APA) ("diagnostic psychiatry") official DSM criteria, and "diagnostic psychiatry is represented as something of an 'incompetent butcher', while biological psychiatry claims the image of skilled surgeon" (Decoteau and Sweet 2016 p415).

"Since its inception, powerful factions in the field of psychiatry have presumed that biological dysfunction anchored mental health diagnoses, and yet the precise location and function of this biological cause has remained elusive... Each time that psychiatric research fails to secure the biological basis for mental disorders, leaders reinvent the field anew - typically in the image of greater biological scientificity (Decoteau and Sweet 2016 p415). Decoteau and Sweet (2016) described this behaviour as an attempt to conceal the social nature of diagnosis of mental illness with "a fantasy of biological cause". Traditionally, US psychiatry has had "three central blocs of influence", argued Pilgrim (2014) - social psychiatry, biological psychiatry, and psychoanalysis - but "biological psychiatry has been ascendant since the 1970s" (Decoteau and Sweet 2016).

Analysing newspaper, magazine, psychiatric and blog articles, and books about the development of DSM-5, along with the APA and NIMH websites, Decoteau and Sweet (2016) distinguished two debates - "the increasing biologisation of psychiatry as a field and the over-medicalisation of everyday life" (p418). "Biologisation" is seen in phrases like "psychiatry as a medical field".

The problem is that "biological psychiatry does not have 'slam dunks' like diabetes [Greenberg 2013]", and that "neuroscientific evidence for psychiatric disorders is 'fragmentary' and 'not ready for prime time' (Casey et al 2013)" (Decoteau and Sweet 2016 pp425-426).

#### **7.4. POWER OF PSYCHIATRY**

Talking about the "medicalisation of modern living", Moncrieff (1997) commented critically: "Variation in mood is a characteristically human way of responding to circumstances but unhappiness has become taboo in the late twentieth century, perhaps because it undermines the image that society wishes to project. Medicalisation diminishes the legitimacy of grief and discontent, and therefore reduces the repertoire of acceptable human responses to events and denies people the opportunity to indulge their feelings. At the same time it diverts attention away from the political and environmental factors that can make modern life so difficult and distressing. It may be no coincidence that the concept of depression has reached its present peak of popularity in

western societies reeling from two decades of increased unemployment and the marginalisation of a substantial section of the population" (p67).

Emphasising the social control inherent in psychiatry, Moncrieff (1997) stated that the "medical model of mental illness has facilitated the move towards greater restriction, by cloaking it under the mantle of treatment. This process of medicalisation of deviant behaviour conceals complex political issues about the tolerance of diversity, the control of disruptive behaviour and the management of dependency. It enables a society that professes liberal values and individualism to impose and re-inforce conformity. It disguises the economics of a system in which human labour is valued only for the profit it can generate, marginalising all those who are not fit or not willing to be so exploited" (p70).

Diniz and Brito (2016) used the case study of a woman (Zefinha) confined to forensic hospitals in Brazil for nearly forty years to discuss the "psychiatric authority over confinement". At eighteen years old, Zefinha was imprisoned for assaulting a neighbour, then she was transferred to a forensic hospital. The researchers noted that "the expert evaluation changes with time, even though her insanity keeps categorised as paranoid schizophrenia. The evaluation changes not in terms of the diagnosis or the numbers from the manual for the international classification of diseases, but in terms of the conclusion about the need to segregate Zefinha from the world. It is not the medicine of classification that is altered, but the medicine of the reasons for internment" (Diniz and Brito 2016 p14).

The psychiatric reports <sup>34</sup> could be divided into three time frames - "abnormality" (first seven years), "danger" (next twenty-one years), and "abandonment" (subsequently) (Diniz and Brito 2016).

## **7.5. "SCIENCE FICTIONS"**

Bioethical discussions are usually about new developments and the future implications, but sometimes there are concerns about "anticipated scientific discoveries" or "science fictions" (Emmerich 2016). One example is the idea that the current knowledge on the neurochemistry and neuroscience of "love" will lead to "love drugs" (or "perhaps more accurately, 'pair-bond behaviours'"; Emmerich 2016).

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<sup>34</sup> Michel Foucault described psychiatric reports as "privileged judicial statements that include statutory presumptions of truth", and the psychiatrist as "an arbiter 'on the question of the reality or non-reality of madness'" (quoted in Diniz and Brito 2016 p5).

Earp et al (2015), for example, wondered "whether it is ethical to pursue research into love and to develop love-related neurotechnologies if one consequence of doing so will be its medicalisation" (Emmerich 2016 p110). Emmerich (2016) argued that this view ignored that "medicalisation is a sociological process, [and] the medicalisation of love will contribute to the ongoing socio-cultural development of love, marriage and intimacy" (p110). For him, medicalisation is intertwined with the processes of:

- Biomedicalisation - social processes seen through the lens of "techno-science" <sup>35</sup>;
- Therapeuticisation - social experiences as "susceptible to some therapeutic intervention" <sup>36</sup>;
- Moralisation - moral judgments and normative values are attributed to health behaviours, say.

#### **7.6. SELF-MANAGEMENT OF DEPRESSION**

Brijnath and Antoniades (2016) observed: "'Self-management' is now ubiquitous in government policies and strategies, health promotion campaigns and patient intervention programmes across most of the Western world... The term refers to medical, behavioural, role and emotional management, the end result of which is better management of the self and of one's disease rather than cure" (p1). By learning problem-solving and decision-making skills, for instance, the upshot is a "health-literate, empowered patient" (Brijnath and Antoniades 2016). But self-management programmes ignore wider factors like cultural norms, health and social care provision, and family support.

The popularity of self-management for health providers and authorities has been linked to neo-liberal ideas - eg: social problems like unemployment and poverty

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<sup>35</sup> "Rather than being focused on restoring a patient to good health via interventions that purport to cure illness and disease – as is largely the case with medicalisation – biomedicalisation involves extending the jurisdiction of medicine to cover the promotion and governance of health ... As such, biomedicalisation's concerns reorientate our understanding of health to encompass what Downing(2011) calls biohealth. While health is the antithesis of sickness, illness or being unwell, biohealth has no antithesis; it is not restricted to our present state but encompasses our uncertain futures including 'risk factors' and 'lifestyle'. As far as biohealth is concerned we are all sick or, rather, we could always act to provide ourselves with a healthier future" (Emmerich 2016 p115).

<sup>36</sup> Rose (1991) called it "the social consequences of psychology": "The nature of human 'being' - our subjectivity - has been fundamentally reconfigured by psy-sciences" (Emmerich 2016 p116). Illouz (2008) talked of a "therapeutic ethos" as the self, relationships, and love are subject to the discourses of therapy. She noted that now the "skills required for a good marriage are equivalent to the skills required to conduct business or even international diplomatic negotiations" (quoted in Emmerich 2016).

are attributed to the individual as a problem of "self-care" (Lemke 2001). "Self-management in practice often means a stronger reliance on individual self-sufficiency and pro-market forces, matched by a concomitant drop in government funding for social and care services" (Brijnath and Antoniadou 2016 p1).

The State retreats to "govern at a distance" (Rose and Miller 1992). The neo-liberal idea of responsibility, which is presented with other ideas like choice and empowerment, can lead to blame (Rose 1996) <sup>37</sup>.

Brijnath and Antoniadou (2016) explored these neo-liberal ideas as applied to depression in a study of individuals living with the condition in Australia. Interviews were conducted with fifty-eight Indian-Australian and White-Australian volunteers in Melbourne.

A number of respondents talked about their depression with reference to self-control and management. For example, "Susan" said: "I've sort of taken control of my life now. I'm not letting the depression run me. I'm sort of running my depression" (p4). While "Anand" commented: "If you have to get out from the struggle, you have to do it yourself... you help yourself. The people are there, but that's only for the temporary sort of support" (p4).

This was reinforced by unrewarding encounters with health professionals and services, and/or the feeling that too much reliance on them was a sign of failure. In the first case, "Olivia" referred to having to wait "half an hour" on hold on an emergency telephone support line. In terms of dependence, "Melissa" admitted: "My psychiatrist, I just, I do not know, I have tried, I have tried to not go and have not been very successful... I rely on her a lot which I do not think is health... I just do not think it is healthy to have such a reliance on someone" (pp4-5).

"Adam's" experience sums up the self-management ethos as his psychiatrist gave him medication: "Look if it [antidepressants] works, it works but you'll have side effects. You just have to balance it up and you know it's up to you" (p5). However, self-managing individuals

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<sup>37</sup> Rose (1996) distinguished certain features of "community psychiatry" (ie: the closure of large psychiatric hospitals and provision of mental health care in the community) that mesh with neo-liberal ideas:

- i) An emphasis on personal responsibility, choice and empowerment which locates the mental health problem as an individual problem;
- ii) The involvement of non-mental health agencies in the care of mental health (eg: housing, employment);
- iii) The importance of accountability, and consequently blame - "The greatest burdens falling on those most unable to shoulder them. When failure results, this can only be understood as a reflection of individual merit or effort e to seek to explain it any other way is further evidence of one's own moral and practical deficits" (Peacock et al 2014 quoted in Brijnath and Antoniadou 2016).



adjusted their drug dosage, and used other means to control their symptoms (eg: alcohol). For example, "Michael" admitted: "I would drink just to sleep".

"Karen" showed the internalisation of blame when the medication did not help: "My fault. Sometimes I get a little bit slack with my medication" (p6).

Brijnath and Antoniades (2016) noted that the participants "neither talked about their right to state services nor about familial, social nor work reforms; despite conditions of inequity, they perceived that change needed to occur only within them for their depression to improve. To that extent, Indian- and Anglo-Australian participants appeared to have become neo-liberal patients, releasing the government from its responsibilities and allowing it to govern at a distance. They had absorbed, enacted and responded to the current rationalities and techniques of care within community psychiatry by emphasising personal responsibility, self-directing their help-seeking and treatments and blaming themselves when they failed to achieve their desired outcome" (p6).

Brijnath and Antoniades (2016) ended with a damning statement: "there is a disconnect between the policy rhetoric of self-management, how it is operationalised within the mental health system and what patient's ultimately articulate as their understandings and practices of self-management. Such a disconnect creates conditions for risky health practices and poor health outcomes. Few would consider self-medicating with alcohol and other drugs, adjusting prescription dosages without the input of a qualified health professional or reducing interactions with health services as optimal practices for people grappling with depression. Instead such practices highlight that the operationalisation of self-management within a neo-liberal context without giving sufficient acknowledgement to the importance of a therapeutic relationship, a reciprocal bond, a feeling of being cared for, may ultimately do more harm than good to human health" (p7).

## **7.7. APPENDIX 7A - PHARMACEUTICAL INDUSTRY**

Pharmaceutical companies cannot be promoted medicines off-label (ie: "for a non-authorized indication or in a non-authorized form, strength or dosage") in the European Union (Vilhelmsson et al 2016). However, off-label prescribing by physicians is permitted (Vilhelmsson et al 2016).

Kesselheim et al (2011) outlined three types of off-label promotion:

- i) Expansion to unapproved diseases;
- ii) Expansion to unapproved variations of the approved diseases;
- iii) Expansion to unapproved dosing regimens.

The reason that off-label is forbidden is that "promotion of pharmaceuticals whose effectiveness and safety has not been confirmed may entail serious risks to patients and unjustified cost to the health care system. Moreover, off-label promotion may challenge the integrity of the medicines regulatory system by undermining the authority of regulators and discourage companies from conducting trials for new medicines or indications" (Vilhelmsson et al 2016 p2) <sup>38</sup>.

Analysis of forty-one pharmaceutical industry whistle-blower complaints (Kesselheim et al 2011) (table 7.1) found that some off-label marketing/promotion practices are difficult to detect. For example, at educational events for doctors, there can be a blurring of the line between scientific presentation of data and promotion, while it is difficult to regulate a private meeting between a physician and a pharmaceutical company sales representation. Whistle-blowers are important as the "discovery of the least visible activity will depend on reports from those with direct knowledge of it" (Vilhelmsson et al 2016 p14).

In the UK, self-regulation of off-label promotion is done by the Association of the British Pharmaceutical Industry (ABPI) under the Prescription Medicines Code of Practice Authority (PMCPA).

Vilhelmsson et al (2016) analysed the PMCPA rulings on off-label promotion between 2003 and 2012. There were seventy-four cases <sup>39</sup>, of which 57% were initiated after complaints from rival companies and 22% from health professionals.

Half the cases were expansion to unapproved variations of the approved disease (eg: Rebif approved for a sub-group of multiple sclerosis (MS) patients and promoted for all). Just over one-third of cases were expansion to unapproved disease (eg: Fostair approved for

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<sup>38</sup> Martin (2007) recounted this story of meeting a sales representative of a pharmaceutical company in Iceland in 2003: "I asked the representatives at one booth why they had come to Iceland, with its small population and lack of direct-to-consumer (DTC) advertising. The reps explained that they expected Iceland to be the first European country to permit DTC advertising. They were there to make connections with fledgling patient support organizations for depression and other conditions, and to support them financially as they have done in the United States" (pp13-14).

<sup>39</sup> Involving 43 companies and 65 drugs, and half of the companies were repeat violators (Vilhelmsson et al 2016).

- Analysis of 41 publicly-available whistle-blower complaints of off-label marketing against pharmaceutical companies in the USA between 1996 and 2010. This was eighteen cases filed under the False Claims Act, and involving fifty-five whistle-blowers, of which the majority were pharmaceutical sales representatives (70%).
- Types of off-label marketing - unapproved diseases (35/41), variations of unapproved disease (22/41), unapproved dosage (14/41).
- Off-label marketing covered four groups:
  - i) Prescriber-related - eg: direct financial incentives to doctors.
  - ii) Business-related/internal practices - eg: direct orders within company to conceal activities.
  - iii) Payer-related - eg: falsification of billing codes to health insurance companies.
  - iv) Consumer-related - eg: funding of consumer organisations.
- Kesselheim et al (2011) noted: "Some of the practices we identified have been highlighted in anecdotal reports and are relatively well known. Others have received little or no attention, such as pharmaceutical marketing representatives working directly with physicians and their office managers to circumvent reimbursement restrictions set by government payers and other insurers. Nearly a quarter of the whistle-blowers alleged that pharmaceutical sales representatives were given access to patients' confidential medical records at physicians' offices for the purposes of trolling for prospective targets for illegal direct-to-consumer promotion of off-label uses" (p6).

Table 7.1 - Kesselheim et al (2011).

asthma use, but promoted for chronic pulmonary disease (COPD)). The categories of ruling were not mutually exclusive, and one-third of cases were expansion to unapproved dosing regimens (eg: Innohep was promoted for long-term use with cancer patients when it was approved for short-term use only) (Vilhelmsson et al 2016).

Ten of the 74 cases were ruled as serious misconduct, including "failures to comply with an undertaking previously given, cases involving especially aggressive marketing, marketing posing a risk to patient safety, and marketing of a prescription-only drug to the public" (Vilhelmsson et al 2016).

Off-label promotion, in all but two cases, was aimed at prescribers (usually with print materials - eg: glossy advertisement in the "British Medical Journal"). The two exceptions included information on a patient group website. This is different to the USA where direct-to-consumer marketing is allowed, and pharmaceutical companies also target health insurance companies (Vilhelmsson et al 2016).

In concluding, the effectiveness of self-regulation was questioned by the researchers: "We estimated that companies over the study period jointly paid around

£260,000 (€360,000) to the PMCPA for off-label promotion. Administrative charges in the UK do not reflect the seriousness of company breaches, nor are they designed to harm corporations financially. In fact, charges for violations are typically less than a company would pay for a single print advertisement. It is highly unlikely, then, that PMCPA charges serve any kind of deterrent function. According to the PMCPA, the most important sanction available to the UK self-regulatory body to discourage violations is, rather, adverse publicity... However, it is unclear whether this publicity poses a significant reputational risk to companies (Vilhelmsson et al 2016 p15).

### 7.7.1. Self-Diagnosis

Ebeling (2011) focused on self-diagnosis, which "increasingly exists within a cultural context where disease is commercialised and diagnosis is pharmaceutically shaped" (p825). Diagnosis generally is a social phenomenon, sometimes contested, embedded within a medical relationship, that includes power, control and "contending interests" (Ebeling 2011). Direct-to-consumer (DTC) advertising is one of the "contending interests" as the patient is marketed <sup>40</sup> a "branded affliction" (Ebeling 2011) <sup>41</sup> <sup>42</sup>.

Ebeling (2011) argued that marketing strategies to encourage self-diagnosis is based around patients presented as consumers who have the power to choose the (brand of) drug they want <sup>43</sup> <sup>44</sup>. She concentrated on the marketing of an anti-depressant and a birth control pill as treatments for pre-menstrual dysphoric disorder (PMDD) <sup>45</sup>. Self-diagnosis of PMDD was encourage via a checklist on a website, for example. "The power to 'brand' a

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<sup>40</sup> So important is marketing within pharmaceutical companies that promotional planning has been observed with basic compounds before clinical testing and years away from regulatory approval (Fugh-Berman and Dodgson 2008).

<sup>41</sup> For example, Mintzes et al (2003) reported that individuals exposed to DTC advertising were twice as likely to request a brand-name drug from a doctor than those not exposed.

<sup>42</sup> DTC spending by pharmaceutical companies was estimated at over 2 billion dollars in the USA in the first half of 2009, while Americans spend twice as much as individuals in other developed countries on prescription drugs (Ebeling 2011).

<sup>43</sup> "Pharmaceutical marketing claims of patient empowerment through self-diagnosis are made within a broader context of disease marketing (Dyer 2006). Drug marketers recognise that in order to foster a conducive marketplace for their medications, the promotion of indications and symptoms is far more profitable than selling a cure; if symptoms are universal enough, virtually anyone can be rendered a patient in need of treatment (Healy 1997). Through the creation and expansion of new disease categories, based on symptoms by those who are also developing treatments, pharmaceutical companies trade on the mutability of diagnosis..." (Ebeling 2011 p827).

<sup>44</sup> Donohue (2006) showed how advertising is presented by pharmaceutical companies as a tool of empowerment for patients rather than a means to increase their sales.

<sup>45</sup> Classed as a "depressive disorder not otherwise specified" in DSM-IV.

disease early in the drug development process is essential to the branding of treatments, the patented drugs that pharmaceutical companies seek to protect from competitors, and to ensure high revenues for their brand-name pills. In order to brand a disease, pharmaceutical marketing often exerts influence over diagnostic categories by the outright construction of new disease states..." (Ebeling 2011 p826).

The symptoms on the checklist of the pharmaceutical company-supported website were vague, but ultimately led to a self-diagnosis of "something wrong", which has the name PMDD. For example, one item asked about mood swings in a day that include suddenly feeling tearful or sad or having feelings easily hurt, but there was no option for "mood swings where a woman feels say, joyfulness, hopefulness, blissfulness or exuberance" (Ebeling 2011 p830). The website "serves as a pathologising checklist for women's emotional and bodily experience of menstruation through its construction of the experience to fit the PMDD diagnostic category, it is also a standardization instrument to categorise what is biologically normal and what is not" (Ebeling 2011 p830).

### **7.7.2. Clinical Trials**

The integrity of clinical trials is being challenged. Goldacre (2016) noted "growing concern about systematic structural flaws that undermine the integrity of published data: selective publication <sup>46</sup>, inadequate descriptions of study methods that block efforts at replication, and data dredging through undisclosed use of multiple analytical strategies" (p7). Data-dredging goes with outcome-switching (ie: switching from pre-specified outcomes which may not be significant to other outcomes that are more favourable, but without explaining the rationale for doing so).

Allison et al (2016) raised concerns about errors <sup>47</sup> in published scientific papers and their experiences of getting corrections:

- i) Journal editors are slow to respond;
- ii) Journals are unclear about where to send

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<sup>46</sup> Only about one-third of clinical trials completed in 2007-10 at leading Us medical institutions were published within two years of finishing (Chen et al 2016).

<sup>47</sup> Common statistical errors include miscalculation of effect size in meta-analysis, and "the DNS error". This is where two separate groups are significantly different to baseline and so it is assumed that the two groups must be significantly different to each other. "Rather than comparing 'differences in nominal significance' (the DNS error) differences between groups must be compared directly" (Allison et al 2016 p28).

"expressions of concern";

iii) When errors are acknowledged, journals can be reluctant to retract articles;

iv) Journals charged authors for publishing letters about errors in previous articles;

v) Authors vary in their willingness to provide raw data for re-analysis;

vi) Informal "expressions of concern" (eg: online comments) are ignored.

Talking generally about academic articles in the PubMed database (which covers all articles related to medicine and health), the number of studies added in 2014 was 27 times that of 1991 (Ioannides et al 2016). This is in part due to increase citations by researchers, and academic articles as marketing tools (Nature 2016).

"Adaptive pathways" (AP) is an idea proposed by the pharmaceutical industry that would "skip several steps designed to protect patients from unsafe and ineffective drugs, allowing new drugs for 'unmet medical needs' to be launched on the market faster, on the basis of fewer data" (Davis et al 2016 p265). The European Medicines Agency (EMA) has embraced the idea, originally the brainchild of NEWDIGS (New Drug Development Paradigms) at the Massachusetts Institute of Technology ("an industry funded think tank"; Davis et al 2016).

AP could "increase uncertainty about the benefit-harm balance of new drugs but claims that such uncertainty is ethically defensible where patients have unmet needs and that the uncertainty would progressively reduce as additional 'confirmatory' data are collected in the post-marketing period" (Davis et al 2016 p265).

AP could mean smaller and/or shorter clinical trials, and/or with highly selected patient groups, and no final phase testing (known as phase III). But, Davis et al (2016) warned, "nearly half of all investigational drugs that successfully complete phase II studies fall in phase III, mostly because of lack of safety or efficacy" (p266). They also stated: "confirmatory studies are often slow to complete, and drugs with uncertain benefit-harm profiles may be prescribed to patients for many years, sometimes even until patent protection expires" (Davis et al 2016 p266).

There has been a concern that clinical trials in low- and middle-income countries by sponsors from high-income countries could be exploiting participants, primarily through testing without consent. But participants in high-income countries, who have limited

or no access to healthcare services <sup>48</sup>, could be exploited despite giving their consent to participate - ie: "being exposed to the risks and burdens of clinical trials without realising the benefits that result from them" (Dal-Re et al 2016 p857).

Ways to overcome this problem include additional healthcare by the sponsors (eg: extended follow-up), or provide the new drug at a subsidised price through non-governmental organisations (Dal-Re et al 2016). "In some cases, research participants who are poor and lack access to health care may benefit more from non-health-related benefits, such as education and training, or social services. In cases where the participants belong to a defined community, community programmes, such as health promotion efforts, could be implemented through health workers or non-governmental organisations" (Dal-Re et al 2016 p861).

On the other hand, such benefits "might unduly induce them to enrol in research. Undue inducement occurs when the benefits offered to potential research participants are so large that they lead individuals to enrol in trials that are clearly contrary to their interests. Recognising this, the most effective response to concerns regarding undue inducement is to ensure that the level of additional benefits offered to participants is commensurate with the risks and burdens posed by the trial" (Dal-Re et al 2016 p861).

### **7.7.3. Adverse Events**

Adverse events (AEs) are "harmful or undesirable outcomes that occur during or after the use of a drug or intervention but are not necessarily caused by it" (Golder et al 2016). Serious AEs are rare, but it is important that they are known about. There is concern, however, that AEs in published studies are the tip of the iceberg compared to unpublished studies - ie: "publication bias or selective omission of outcomes data, whereby negative results are less likely to be published than positive results" (Golder et al 2016).

Golder et al (2016), worryingly, found that "a lower number of side effects are generally reported in published than unpublished studies, and a wider range of named side effects are reported in unpublished than published studies". The researchers performed a systematic review of published articles on AEs of health care interventions using fifteen databases, and unpublished data through "any other avenue", including personal and industry contacts, regulatory websites, and

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<sup>48</sup> For example, individuals without health insurance in the USA, or irregular or undocumented migrants in Europe (Dal-Re et al 2016).

the "grey literature" (published, but not peer reviewed).

The median percentage of published sources with AEs information was 46%, but it was 95% for corresponding (matched) unpublished documents <sup>49</sup>. Overall, the percentages were 43% for all published studies and 83% for all unpublished documents.

Two studies were found that compared specific types of AEs in published and unpublished sources. One of them found that over 90% of fatal AEs in one pharmaceutical company's trial reports were not fully listed in published information.

Golder et al (2016) stated: "We identified serious concerns about the substantial amount of unpublished adverse events data that may be difficult to access or 'hidden' from health care workers and members of the public. Incomplete reporting of adverse events within published studies was a consistent finding across all the methodological evaluations that we reviewed". They went on: "It is not clear if the differences stemmed from slips in attention and errors, or whether the peer review process led to changes in the data analysis. Journal editors and readers of systematic reviews should be aware that a tendency to overestimate benefit and underestimate harm in published papers can potentially result in misleading conclusions and recommendations" (Golder et al 2016).

Commenting on the move to human clinical trials of drugs, Kimmelman and Federico (2017) warned: "Commercial interests cannot be trusted to ensure that human trials are launched only when the case for clinical potential is robust" (p26). In some cases, poorly designed and conducted animal studies, unrealistic conditions, and modest effects often precede human trials (Kimmelman and Federico 2017).

Leaving aside the risk to participants in human trials, "trials of ineffective therapies place burdens on society. Drug development is costly, in terms of money and people. Patients, healthy volunteers and experts involved in testing a dud treatment are not available for more promising ones. Expenses wasted on ineffective therapies and uninformative trials result in higher drug prices" (Kimmelman and Federico 2017 p26).

Kimmelman and Federico (2017) proposed three questions to ask in helping in the move from animal to human testing of drugs:

a) What is likelihood that this drug will prove

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<sup>49</sup> Matched documents are where there is a published study and unpublished documents on which it was based. Unmatched documents included where there are unpublished documents than are not in published studies.



clinically useful (based on similar drugs and treatments for the focused disease)?

b) If the drug works with humans, what is the likelihood of seeing that in animal studies (based on the applicability of animal models)?

c) If the drug does not work with humans, what is the likelihood of seeing that in animal studies (based on rigour of animal studies)?

#### **7.7.4. Efficacy**

Young (1976) defined efficacy as "the ability to purposively affect the real world in some observable way, to bring about the kinds of results the actors anticipate will be brought about" (quoted in Alford 2017).

The RCT "is designed to isolate for purposes of analysis (to dissolve a whole into parts). But life is lived as a synthesis (a putting together of parts into wholes). Not only do efficacies tend to combine, but the acts of giving/taking medicine and looking to effects are integrated into larger processes of dealing with problems and living life" (Whyte et al 2003 quoted in Schwartz 2017).

Nichter (1992) described RCTs as having "curative efficacy" as opposed to "healing efficacy", which "involves the perception of positive qualitative change in the condition of the afflicted and/or concerned other" (Nichter 1992 quoted in Alford 2017). "While the curative approach frames efficacy as a discrete and static entity, healing efficacy is fluid and shifting, intimately linked to the perceptions and expectations of social actors" (Alford 2017 p244).

Schwartz (2017) argued that RCTs failed to understand healing as processual, or "relational efficacy". In the former case, RCTs have a point in time when "the absence of disease pathology becomes equated with cure", but treatment can be "a series of outcomes over a long period of time" (Schwartz 2017). Waldram (2000) critically observed that "how that point in time is established never seems to be addressed, but this sometimes appears rather opportunistic on the part of researchers" (quoted in Schwartz 2017).

Schwartz (2017) defined "relational efficacy" as "a broader set of social relations that include not only those between patients, providers, families and communities, but also the relations that each of these actors has with the medicine itself" (p239).

For example, Whyte et al (2003) described the medicine given for a child's cough in the Philippines: "Medicines provide women the reassurance that something

can be done about the illness (a sense of agency if you like) and children with the recognition that they are ill and entitled to good care. They also show others in the community that the child is being looked after – obviating judgments of parental negligence. Social and pharmacological efficacies are co-produced in the therapeutic process [...] The 'calming' down of the cough is desirable socially – the sound of the cough signals poor care. It not only irritates the child's lungs, it also irritates others, like fathers and mothers-in-law, potentially leading to social distresses that go beyond the illness condition of the child" (quoted in Schwartz 2017).

This is similar to the "total drug effect" (Helman 2000) – "the total drug effect depends on a number of elements in addition to its pharmacological properties. These are: The attributes of the drug itself (such as taste, shape, colour, name). The attributes of the patient receiving the drug (such as experience, education, personality, socio-cultural background). The attributes of the person prescribing or dispensing the drug (such as personality, professional status or sense of authority). The setting in which the drug is administered – the 'drug situation' (such as a doctor's office, laboratory or social occasion) [...] All of these aspects can play a role in generating the 'meaning response' because they can determine the confidence the patient has in the treatment and the expected outcome" (Helman 2000 quoted in Schwartz 2017).

So, the difference in response between individuals to the same medicine can be due to variations in the mixture of the various elements of the "total drug effect".

Schwartz (2017) concluded that the upshot is that RCTs "should situate studies of efficacy within their proper contexts, rather than in the laboratory" (p241).

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## **8. POST-CONFLICT TRAUMA AND DISASTER RECOVERY**

- 8.1. Introduction
- 8.2. Sri Lanka
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  - 8.3.2. Older people as assets
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### **8.1. INTRODUCTION**

Pedersen et al (2015) summed up the situation about the mental health effects of war (appendix 8A) thus: "The consequences of exposure to intentional violence such as armed conflict and war are compounded by multiple factors. Researchers and practitioners remain divided along a continuum as to the psychopathological effects attributable to the traumatic experience. While some tend to minimise the psychological needs of individuals exposed to traumatic experiences, others assume all of the exposed, including victims and survivors, are in need of psychosocial assistance, including treatment and rehabilitation services" (p15) <sup>50</sup>.

These researchers summarised their review of the literature on the subject under three sets of questions:

1. What are the paradigms supporting the interventions to help reduce the mental health burden of civilians in conflict and post-conflict settings?

The paradigms vary between "trauma-focused intervention" to "wider, more comprehensive psychosocial approaches". The former approach focuses on a simple causality chain between trauma and mental health consequences, while the wider approach includes overall stress and prior conditions, like poverty (Pedersen et al 2015).

2. What are the main gaps in delivering

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<sup>50</sup> Violence experienced by children in humanitarian settings in a particular issue (appendix 8B).

interventions?

Successful delivery of help depends on identifying those in need, and this relies on screening (which can produce "false positives" and "false negatives" <sup>51</sup>).

Successful help also depends on the efficacy of treatment, and there are problems in establishing this. Symptom reduction is the most common measure of success. Pedersen et al (2015) noted that studies have been "most often made with a before and after design for which the reliability of the measures used for symptom reduction is likely to be low (Type II error), and in most cases of such exposure to extreme traumatic experiences, the remission of symptoms may be a long and often unattainable treatment goal" (p16).

Pedersen et al (2015) highlighted that treatments "cannot be separated from the context, the social and cultural realities of the family and the community". This can be linked to the "persistent gap" between local understanding of distress and trauma, and the Western-based category of Post-Traumatic Stress Disorder (PTSD), say.

3. What are the best practices in interventions for civilians in conflict and post-conflict settings?

Pedersen et al (2015) summed up the characteristics of beneficial interventions as having:

- Good screening;
- "an implicit commitment to avoid inflicting further damage, while ensuring minimal disruption of existing (and still sufficient) coping and protective influences" (p18);
- Taking account of local understandings;
- Building on existing resources;
- Promoting empowerment.

## 8.2. SRI LANKA

Jayasuriya et al (2016a) studied the prevalence of anxiety and depression (psychological distress) in the five years after war in Sri Lanka ended in 2009 <sup>52</sup>. Over 18 000 individuals in eighteen of 25 districts were surveyed between February and April 2014. The districts

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<sup>51</sup> False positives are individuals who are diagnosed as ill when not, and false negatives are cases of illness that are diagnosed as healthy.

<sup>52</sup> The Liberation Tigers of Tamil Eelam fighting the central government for a separate Tamil homeland for 26 years, and defeated.

were categorised as conflict zones based on geographical areas of war, and large population displacement.

Around 17% of respondents lived in the severe conflict zone (SCZ), 23% the moderate conflict zone, and the remainder in the minimal conflict zone (MCZ). The three groups were compared in the analysis. particularly the SCZ and MCZ.

Overall, 12% of individuals had symptoms of depression and 14% anxiety, but this varied between 40% and 23% respectively in the SCZ group and 10% and 13% respectively in the MCZ group.

The likelihood of depression was linked to factors like older age (over 50 years old), ethnic minority membership (particularly Tamil), exposure to threat and living in areas of severe conflict, proximity to army camps, and scarcity of food, but not time in a camp for internally displaced persons, loss of job, or proximity to police station. Protective factors were access to healthcare, higher education, and improvements in safety in the community.

Symptoms of anxiety were linked to age, perceived threat, ethnic minority membership, being married, residency in a camp, scarcity of food, and loss of job, but not living in a severe conflict zone or proximity to police station. The only significant protective factor was improvement in community safety.

Siriwardhana and Wickramage (2016) noted a number of methodological issues, including:

i) The classification of districts into severe, moderate and minimal conflict zones based on the level of conflict experienced between January 2008 and May 2009 "fails to recognise the historical, geographical, and contextual complexity of civil conflict and communal violence in Sri Lanka, which stems not only from conflict in the north and east of the country, but also insurgencies and political violence in other parts of the island" (Siriwardhana and Wickramage 2016 p97).

ii) The study was originally designed to gain an understanding of the intentions to migrate and not mental health issues. Thus, Siriwardhana and Wickramage (2016) questioned the conceptual basis to some of the factors (eg: proximity to police station and mental distress).

Jayasuriya et al (2016b) replied that "symbols or environmental triggers can remind conflict-affected populations of past traumas, thereby perpetuating or worsening post-traumatic mental health problems" (p100).

iii) Related to ethics, Siriwardhana and Wickramage (2016) queried: "it would have been helpful to know if and how duty of care was ensured for respondents identified as having serious mental health issues. Beyond



obtaining verbal consent for participation, researchers working with vulnerable communities, especially in post-conflict settings, should ideally take measures to ensure duty of care for those identified through screening methods or those clearly showing signs of mental distress" (pp97-98).

Jayasuriya et al (2016b) pointed out that their national survey was limited in its ability to respond to the needs of individuals. Furthermore, the measure of mental distress was not a diagnostic tool, and the interviewers were trained for this job and were not clinicians (appendix 8C).

### **8.3. OLDER ADULTS**

Variations in life expectancy around the world mean that defining when an individual becomes old is not easy. The United Nations uses sixty years old, but Karunakara and Stevenson (2012) preferred fifty years old.

Older people have high death rates in humanitarian crises<sup>53</sup>, like famine or flood, "partly due to their inherent vulnerability and partly due to services that inadequately deal with their needs often because these are not well identified or understood" (Karunakara and Stevenson 2012). Issues related to vulnerability include mobility and vision problems, which limit standing in queues for food distribution, and carrying heavy food packages, for instance (Karunakara and Stevenson 2012).

On the side of service providers, Karunakara and Stevenson (2012) argued that humanitarian agencies, donors, and international bodies neglect the health and nutritional needs of older people.

#### **8.3.1. Hurricane Katrina**

Oliver-Smith (1996) described a natural disaster as a "crise revelatrice" ("A revealing crisis") as "the fundamental features of society and culture are laid bare in stark relief by the reduction of priorities to basic social, cultural and material necessities" (quoted in Adams et al 2011). "Disasters reveal social vulnerability, with ramifications for adjustment, recovery, and long-term well-being... Community ability to recover varies by geographic location, class, race, ethnicity, gender, and age..., highlighting social inequalities, physical vulnerabilities..., or the trouble with the language of vulnerability... and failures in

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<sup>53</sup> In the South Sudan refugee crisis in 2012, a six-week period of data showed the mortality rate of over 50s to be four times 5-50 year-olds (Karunakara and Stevenson 2012).

social justice" (Adams et al 2011 p249) <sup>54</sup>.

Adams et al (2011) coined the term "ageing disaster" to describe how older adults are disproportionately affected by natural disasters and their aftermath. These researchers concentrated on "Hurricane Katrina" in 2005 in New Orleans with interviews of 163 survivors aged 40 to 98 years old, participant observation, and analysis of media reports.

More older adults died after Katrina in the Greater New Orleans area - eg: 75% of bodies found immediately after were over 60s (who made up 15% of the pre-storm population) (Adams et al 2011). Lack of evacuation facilities, particularly for the infirm elderly, was one factor. The collapse of infrastructure in the post-storm period was another factor (eg: local clinics closed) (Adams et al 2011).

There was a continuation of the disaster (ie: the consequences) over many years that one interviewee summed up as "Katrina never really ended". "The event, Hurricane Katrina, became the open-ended experience, 'Katrina'" (Adams et al 2011 p256).

"Bureaucratic obstacles presented by government and insurance companies lengthened residents' efforts to create normalcy in their world, to rebuild or to move into a partially rebuilt home, and to establish ongoing relationships with medical caregivers where such services were available. For those impacted by the post-hurricane battle for basic survival, the notion that some folks simply 'could not recover' was palpable. They felt that the elderly who died in this initial period did so because of a sense of ultimate defeat - their 'life was over'" (Adams et al 2011 p255).

"William" (77 years old), four years post-storm, described it thus: "Well, see there's two things going on. There's recovery from Katrina and there is the aging process. And it's hard to tell which is which in terms of your emotions" (p257). He then recounted the struggle for compensation and insurance claims, and ended: "...maybe the smartest thing for me to do would be to say, to hell with it. I don't need that extra 10- or 15- or 20-thousand [dollars]" (p257) <sup>55</sup>.

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<sup>54</sup> "Representations of disaster bring into existence new 'preparedness industries' (Lakoff and Collier 2008), paving the way for new, market-driven entrepreneurialism (Klein 2007) and justifying policies of social cleansing and redistribution that favour fiscal growth over social welfare" (Adams et al 2011 pp249-250).

<sup>55</sup> The struggle of residents to deal with the bureaucracy of government grants and insurance claims was described by one resident thus: "Well, it's kind of like a hamster's wheel. You keep spinning, but you are trying to reach the end of your destination in terms of a job, a home, resources, rebuilding, but you are not getting anywhere. You are in that spinning wheel, you know, but you keep trying. You get up and you go to this place, and you go to this place" (Adams 2012 p199). The upshot was that many residents gave up and left. One abandoned house had "Broken Dreams Inside" spray-painted on the front wall (Adams 2012).

But older adults did show resilience. "Nancy" (72 years old), for example, observed that "we had had worse" as she compared her experiences to the death of a child. While "Alice" (65 years old) talked of living through other storms, and "Elvelina" (89 years old) recalled: "As a child, I can remember my mother had nine children and it was very hard. We lived in the country during the Depression. I remember that. I had to live through that" (p259). "Those elderly who did not perish as a result of the flooding, exposure, or illness in the first year post-hurricane were able to focus on 'making the best of it', in part by realising that it was not the first time they had dealt with hardship and adversity. Not surprisingly, the older the person, the more comparative life experiences they were able to bring to the task of adaptation" (Adams et al 2011 pp258-259).

In some ways, middle-aged residents suffered more: "For returning residents in the 'sandwich' generation – those who were burdened with the multiple tasks of rebuilding, finding jobs, and working and caring for children and parents simultaneously – adjustment and attempts to achieve some inner equilibrium were frequently not achieved. Rather, these adults faced multiple challenges with a sense of futility and fear that they would 'break' under the pressure. Those responsible for taking care of others talked at length about weight gain, a return to smoking and drinking, and developing asthma, allergies, high blood pressure, and anxiety disorders. Many middle-aged study participants, both men and women, cried during our interviews – far more frequently than did elderly participants – as they recounted their struggles and current circumstances" (Adams et al 2011 p262).

Adams (2012) highlighted the role of private organisations in recovery in New Orleans: "Humanitarian relief and recovery assistance are now market affairs in which government remains, de facto, involved, but by way of markets organised for profit more than for relief. New Orleans reveals how markets have penetrated into the public sector with real implications for citizens in need. Poverty is turned into a problem of entrepreneurialism, and disasters are turned into market opportunities for profit, while government funding fuels capital accumulation in the corporate sector at the expense of many in communities like New Orleans" (p186).

The public-private partnership is seen in organisations like "HandsOn Network", which involved corporate sponsors, public funding, and volunteers. Adams (2012) stated: "HandsOn offers a glimpse into the ways that market solutions generate large infrastructures of corporate activity that on the one hand redistribute federal aid and corporate profits to a small sector of

the non-profit world. On the other hand, these market solutions also enable corporations to profit on the world of humanitarian, and volunteer, relief work. The arrangement ideally transfers capital from private back to public, but it also enables the use of public funds for private corporate growth in ways that are largely unchecked by public sector legislation or priorities, fuelling not just a free market, but a free-for-all market where profits are allowed even when services are not provided and the labour is largely unpaid" (p206). The merging of charity and business has been called "philanthrocapitalism" (Bishop and Green 2008) <sup>56</sup>.

Adams (2012) recounted the case study of Henry and Gladys Bradlieu, and their battle to gain a grant to rebuild from public funds administered by a private company. Any application for funds required an affidavit from the previous owner to establish the current owner (which was twenty years previously), and property tax records, and fingerprinting and "mug shots" to avoid fraud. After refusal for a grant the second time, Henry had a "massive stroke".

Adams et al (2009) used the term "chronic disaster syndrome" to describe "the cluster of trauma- and post-trauma-related phenomena that are at once individual, social, and political and that are associated with disaster as simultaneously causative and experiential of a chronic condition of distress in relation to displacement" (p616). Individuals suffer from the trauma of the disaster, but also from the society's response to the aftermath.

The researchers quoted the case study of "Sally" (56 years old), still living in temporary accommodation two and a half years after Katrina. Her experience of the storm included eight hours semi-submerged in her flooded house, rescue and transfer to a local school for three days with little water or food, and later evacuation to Houston on a bus with only a bottle of water. The aftermath was experienced as "a sad recognition" of the reality of rebuilding (or not as the case was). "It was hard enough to have lived through the disaster, but what

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<sup>56</sup> Adams (2012) was critical of "philanthrocapitalism": "Using philanthrocapitalism to care for the needy, just like sub-contracting to for-profit companies, can result in the production of a state of chronic disaster for those trying to recover. Life and labour are brought under conditions in which both public and private sector humanitarian relief efforts are beholden to market measures of success. Unpaid labour in the form of volunteers and needy subjects are used to generate profits at the one end of the corporate configuration, while grassroots volunteer groups are forced to scramble and compete for resources from wealthy donors by showing that they too can earn profits on the work of helping others. Despite the ostensible goal of creating downward flows of capital from the corporate sector to the needy public, this arrangement also produces a net upward flow back up to new corporations that make money on charity efforts..." (p208).

was almost more unbearable for residents with whom we spoke was that two and, then, three years later, and despite over \$17 billion in federal aid for rebuilding homes (and over \$109 billion in federal aid for both emergency relief and long-term recovery projects...), New Orleans was still a mess" (Adams et al 2009 p620).

Where neighbourhoods were being rebuilt, the feeling of residents was that "nothing would ever be the same". For example, "Frances" said: "It takes a good deal of endurance and strength. But after three years with so little visible recovery, it wears down and erodes that strength... Life as I knew it is gone" (Adams et al 2009 p621).

Residents often asked, where did the government money pledged for rebuilding go? Among the bureaucratic decisions (good and bad), it was subsequently found that \$136 million "had been fraudulently spent in Katrina-related contracts and that another \$428 million, although not fraudulently invested, has been misappropriated in corporate contracts" (Adams et al 2009 p629).

Klein's (2007) term "disaster capitalism"<sup>57</sup> can be applied to the post-Katrina situation. "The eviction of the poor from New Orleans, the obliteration of a public infrastructure that could care for those evicted, the eventual demolition of their homes, the payment of exorbitant prices to private companies to provide sub-standard trailers as temporary housing, and, finally, the huge contracts awarded to private firms to rebuild former public housing units as mixed-income condominium properties all point to an exemplary study in disaster capitalism..." (Adams et al 2009 p630).

Adams et al (2009) continued: "Rather than seeing these political and economic arrangements of disaster capitalism as ancillary to, or a remedy for, the individual experiences of chronic disaster syndrome, we suggest that they need to be seen as part of the syndrome itself" (p631).

### **8.3.2. Older People as Assets**

In recent years Australia has regularly experienced extreme weather events and natural disasters, including a firestorm in Canberra in 2003, the "Black Saturday" fires in Victoria in 2009 (which killed nearly 200 people), and severe floods in Queensland in 2010 (Howard et al 2017). Howard et al (2017) reported on a research study in rural Australia on the role of older people in preparing for,

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<sup>57</sup> After a shock to a society (eg: natural disaster, war), there is a "blank slate" that allows "government reconstruction programmes to prioritise private-sector contracts over the continued support of public-sector infrastructure" (Adams et al 2009 p630).

responding to and recovering from such events <sup>58</sup>.

The researchers ran seventeen focus group discussions with 111 participants, of which forty-one were aged 65-74 years old, in three rural areas in Australia. Analysis of the transcripts produced three key themes:

i) "Willingness to participate, time and organisation" - The older adults "reported willingness and an availability to plan for, respond to and recover from natural disasters much more often than other groups" (Howard et al 2017 p525).

ii) "Networks, reciprocity and experience" - The older adults reported a sense of responsibility to get involve locally as well as an awareness of their own vulnerability. This can be seen in a quote from a female participant: "If you walk down your street you'd sort of think there's an elderly lady who lives in there on her own and you sort of think. Then a few days - I walk quite a bit - and if I don't see her, I start thinking I hope she's all right. Because that's what you think. Like, I'm in an area now and I'm getting older myself, I didn't even think about it before but now you sort of think well they're on their own and they're elderly. You know as you're walking, you sort of see - and if I don't see them I start thinking I'll have another look tomorrow. Then you see them of course and everything is all right" (p526).

The older adults reported being well prepared for emergencies with stocks of items, like batteries and food. "The level at which older participants planned for natural disasters and actively shared resources with neighbours during past crises was noticeably higher than for other participants overall" (Howard et al 2017 p527).

Past experiences of natural disasters was an important "resource" of the older adults. This was summed up in one woman's experience: "I guess you do learn things. I was on the last train home when the bushfire closed up here, closed the [freeway]... It was the last train to go through. That brought me to the realisation that had we been in a car we could have got caught because it's pretty easy to and I always carry water in the car now. Always carry water because what struck me most was how much water they were giving to the people in the cars" (p527).

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<sup>58</sup> A key idea is that of "social capital" which is "generated and supported through formal and informal networks and connections in societies" (Howard et al 2017). Social capital is seen as beneficial generally for older adults in, for example, protecting against depression, and for better health and wellbeing (Howard et al 2017).

iii) "Participation in local decision making and planning" - The older respondents were the most eager age group to be involved, but they "consistently reported frustration with a perceived mismatch between their motivation, skills, time and engagement, and opportunities to enact their ideas. Older research participants reported feeling disempowered about their access to decision making, and excluded from formal, natural disaster planning processes. Many reported feeling bureaucracy and prescriptive systems were denying them permission to carry out practical preventative measures. For this group, a sense of alienation from decision-making processes in the community left them feeling frustrated and powerless to contribute where they felt they could" (Howard et al 2017 p528).

Howard et al (2017) concluded that their focus groups challenged "the framing of older people as purely vulnerable and 'at risk' in relation to natural disaster preparedness. While it is critical not to minimise the risks and vulnerabilities of all groups in the face of natural disasters, the findings from this study highlight the importance of viewing older people as much more than passive recipients of support when it comes to natural disaster preparedness. The responses of older research participants were consistent with findings from earlier studies in which older people were found to be active community participants and contributors" (p529).

#### **8.4. IMPORTANCE OF SOCIAL NETWORKS**

The psychological effect of the "Great East Japan Earthquake" (GEJE) and associated tsunami on 11th March 2011 has been well studied. The prevalence of psychological distress was estimated at around half of the survivors, but this declined with time (Sone et al 2016).

However, there were individual differences in recovery, including those who did not improve with time. Sone et al (2016) found that social isolation post-GEJE was key here. The researchers analysed data on 959 individuals affected by the disaster collected in June-November 2011 and June-November 2014. Social isolation was determined by the Lubben Social Network Scale (LSNS-6) (Lubben et al 2006), which has six items (eg: "how many relatives do you see or hear from at least once a month?"). Each question was scored from 0 ("none") to 5 ("nine or more"), giving a range of 0-30 for the total score. Scores of 12 or less were classed as socially isolated (ie: equivalent to seeing 2-3 relatives per month). Four groups were distinguished for analysis purposes (table 8.1).

Group (n)	2011	2014
"Remained socially isolated" (143)	isolated	isolated
"Became not socially isolated" (96)	isolated	not
"Remained not socially isolated" (614)	not	not
"Became socially isolated" (106)	not	isolated

Table 8.1 - Four groups of social isolation <sup>59</sup>.

Psychological distress was measured by the six-item K6 questionnaire (Kessler et al 2002). For the last month, the individual rated how often they felt nervous, hopeless, restless or fidgety, so sad that nothing could cheer them up, that everything was an effort, or they were worthless. Each behaviour was scored from 0 ("none of the time") to 4 ("all of the time"), giving a total range of 0-24, and 10 or more was taken as a sign of higher psychological distress (ie: the equivalent of "some of the time for all behaviours"). Sixty-one individuals (6.4%) were classed as having higher psychological distress in 2011 and 2014 ("remained high distress"), 10.6% improved, 8.7% deteriorated, and the remainder were low distress in both years. Overall, the prevalence of psychological distress did not change - 17% in 2011 and 15% in 2014.

High psychological distress at any time was associated with severe economic status, poor self-rated health, and dead or missing family members.

Between 2011 and 2014, there were significant improvements in K 6 scores for "became not socially isolated" and "remained not socially isolated" group members compared to the "remained socially isolated" group (figure 8.1).

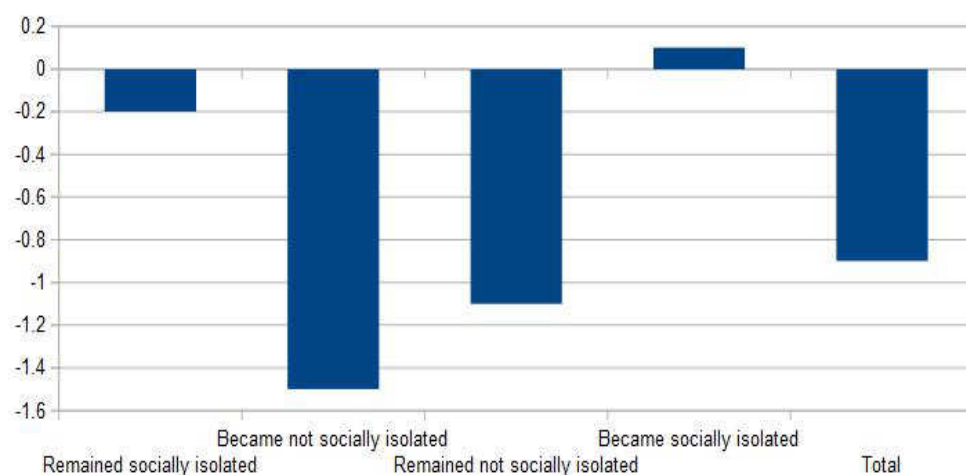
For individuals with low psychological distress in 2011, the "became not socially isolated" and "remained not socially isolated" groups were much less likely to have high psychological distress in 2014 (between one-third and one-fifth). While for individuals with high psychological distress in 2011, the same two groups were much more likely to be low distress in 2014 (two to three times) as compared to the "remained socially isolated" group (table 8.2).

Sone et al (2016) summed up: "Among the people who lived in the disaster area affected by the GEJE, being free from social isolation was associated with

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<sup>59</sup> "Some disaster survivors were required to relocate to temporary housing, and then from temporary housing to disaster restoration housing, and thus their living environment changed over several years" (Sone et al 2016 p100).





(A minus score shows a decline in psychological distress)

(Data from Sone et al 2016 table 3 p99)

Figure 8.1 - Mean change in K6 scores between 2011 and 2014 based on social isolation group.

improvement of psychological distress" (p101).

Note that this study did not have a control group (ie: individuals not affected by the GEJE), and the sample sizes for the different social isolation groups were quite small (Sone et al 2016).

	"Became not socially isolated"	"Remained not socially isolated"
Low psychological distress in 2011 - high psychological distress in 2014	0.21	0.33
High psychological distress in 2011 - low psychological distress in 2014	3.58	2.39

("Remained socially isolated" group = 1.00)

Table 8.2 - Odds ratios of psychological distress in 2014 based on social isolation group.

Hogg et al (2016) looked at the effects of forced relocation after the 2011 Christchurch earthquake in New Zealand. This process involves a number of stressors on top of the experience of the earthquake itself, including loss of home and social networks, and impact of moving into a new neighbourhood and area. While "low socio-

economic groups are more likely to be affected by disaster impacts and relocate due to their higher likelihood of living in hazard prone areas... and less political power to defend their properties" (Hogg et al 2016 p19). On the other hand, individuals who stay in damaged homes face stress over reconstruction as well as the fear of a recurring disaster (Hogg et al 2016).

Hogg et al (2016) used official data to compare mood and anxiety symptoms pre-disaster, and in the first and second years post-disaster. The city was divided into six categories of affectedness, from "no damage" to "severe damage", and individuals were classified as "stayers", "within-city movers", "out-of-city movers", and "returners".

"Stayers" showed lower rates of treatment for mood and anxiety symptoms than "within-city movers" and "returners", but not "out-of-city movers". The likelihood of seeking treatment was nearly three times higher for "returners" than "stayers". "Out-of-city movers" from areas with any damage were more likely to seek treatment than "out-of-city movers" from undamaged areas in the second year after the disaster. Living in an affluent area with minor to moderate damage was a protective factor.

So, overall, moving within the city or temporary relocation were risk factors for receiving treatment for mood and anxiety symptoms compared to staying in Christchurch. "Movers escape the traumatic reminders of the event, but leave their social networks, social support and friends behind, which can result in additional psychological stress and outweigh the effect of living in a less damaged environment" (Hogg et al 2016 p24).

The researchers advised caution about assigning causal relationships between relocation and mood and anxiety symptoms from their data. "As a consequence of data aggregation, it wasn't exactly known in every case, if a treatment happened before or after relocation. Residential location geocoded on a mesh-block level is based on a person's visits to Primary Health Organisations (PHO) and summarised to a quarterly measure leading to uncertainty about the exact time of relocation. This in turn contributed to uncertainty in determining where a person lived, when a treatment has actually happened" (Hogg et al 2016 p25).

Also the New Zealand Ministry of Health data used only records of those seeking treatment. Obviously, individuals who did not seek treatment will be missed.

## **8.5. PTSD AND AMYGDALA**

Threat-related attention bias is increased attention

towards negative emotional stimuli that could be a potential threat. Studies have found this bias among PTSD sufferers as well as the opposite (attention away from threats) (Fonzo et al 2016).

The amygdala is seen to be active with this bias, though, again studies have been contradictory - ie: "both increased and decreased activation to threat and trauma-related stimuli has been observed" (Fonzo et al 2016 p45). Costafreda et al's (2008) meta-analysis found that amygdala reactivity was heightened in response to passive stimuli <sup>60</sup> relative to explicit stimuli <sup>61</sup> in PTSD sufferers. Interaction of the amygdala and areas of the prefrontal cortex seem to be important (Fonzo et al 2016).

The likelihood of experiencing PTSD after a traumatic event has been linked to risk factors, like previous life stressors. In particular, childhood maltreatment (CM) is a "robust risk factor for PTSD", and this could "impact amygdala-prefrontal structure and function" (Fonzo et al 2016).

Fonzo et al (2016) investigated this idea with forty-two PTSD sufferers, of which half self-reported moderate-to-severe CM, and twenty trauma-exposed healthy controls in the USA. Participants were shown a happy or fearful face for 1000 ms, and asked to identify the emotion. On the photograph was the word "fear" or "happy", sometimes in conflict to the facial expression. This was the emotional distractor, and it was expected that individuals with threat-related attention bias would pay more attention to the word "fear", say, than the happy facial expression. This task was performed while in a fMRI scanner.

The PTSD-CM group showed differences in brain activity in part of the prefrontal area compared to the PTSD-only group and the controls. It seems that a history of CM for PTSD sufferers explains the differences in threat-related attention bias and amygdala reactivity found in previous studies of PTSD sufferers.

## **8.6. PTSD AND CARDIOVASCULAR PROBLEMS**

Edmondson and von Kanel (2017) explored the link between PTSD and cardiovascular disease (CVD). After adjustment for other factors, Edmondson et al's (2013) meta-analysis of nine studies, for example, suggested a 53% increased risk for heart attack and deaths among PTSD sufferers as compared to controls (ie: hazard ratio 1.53), while the risk of stroke is over twice as great

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<sup>60</sup> Eg: In a list of words, which includes emotional ones, find names of animals.

<sup>61</sup> Eg: Find the emotional words in a list.

(relative risk 2.36), according to another meta-analysis (Emdin et al 2016).

Much of the data in the studies included in meta-analyses comes from US military veterans (Edmondson and von Kanel 2017). However, in the Nurses' Health Study II, the hazard ratio for CVD was 1.60 for PTSD sufferers (Sumner et al 2015). Using the same sample of 50 000 nurses, Sumner et al (2016) found an increased risk for venous thromboembolism with PTSD.

The next issue is explaining a causal link between PTSD and CVD. A number of mechanisms and factors may be involved (Edmondson and von Kanel 2017), including:

i) Physiological - In PTSD the sufferers' body shows an exaggerated fight or flight response over a long period of time (eg: high heart rate), and the individuals are more sensitive to trauma reminders. "Chronic increases in cardiovascular demand degrade the capacity of the cardiovascular system to support that increased demand. The accumulation of time spent in a state of physiological hyperarousal and intermittent periods of exaggerated physiological reactivity to threat cues is thought to contribute to cardiovascular disease risk through the development of a systemic pro-inflammatory state, and therefore more rapid progression of atherosclerosis, endothelial dysfunction, hypertension, and more pronounced coronary ischaemia under stress" (Edmondson and von Kanel 2017 p323).

There are also changes to the immune system (Edmondson and von Kanel 2017).

ii) Behavioural - An individual with PTSD may have health risk behaviours, like smoking and obesity, which increase the risk of CVD (Edmondson and von Kanel 2017).

From a different point of view, there is PTSD from cardiovascular events (eg: 12% prevalence; Edmondson et al 2012), and this becomes a risk for further cardiovascular problems (Edmondson and von Kanel 2017).

Aiello et al (2016) showed that PTSD produced changes akin to immunological ageing (immunosenescence). Older and younger individuals have differences in their immune system (eg: more late-stage differential memory T cells and fewer naive T cells among older adults; Aiello et al 2016). Put another way, a young individual with PTSD had the immune system of an older adult.

Aiello et al's (2016) data came from the 2008-9 Detroit Neighbourhood Health Study (DNHS), which is a longitudinal study of over 1500 adults in that city. PTSD symptoms were assessed via telephone interviews using a seventeen-item checklist for the lifetime and past year. A blood sample was used to make an assessment of the

immune system.

Of the 85 participants studied, nineteen (22%) had experienced PTSD in their lifetime, and 14 (17%) in the past year. Individuals who had experienced PTSD in either case, compared to the rest of the sample, had immune changes similar to immunosenescence.

## **8.7. APPENDIX 8A - WARS**

Nester (2010) counted 269 wars involving 591 states between 1945 and 1988, with over three-quarters of them being civil wars (Wenzel et al 2015). As well as subsequent and continuing conflicts, there are many occasions for violence-related experiences with the long-term impact on individuals, social networks, economy and society (Wenzel et al 2015).

For example, Zarowsky (2004) described the experiences of Somali refugees in Ethiopia: "emotional distress was about social rupture and injuries and not simply about private suffering. In fact, making a living under such harsh circumstances was a 'recognition of the destruction of much of the fabric of the community at the same time as a refusal to vanish, a collective mourning of both private and collective losses at the same time as a deliberate creation of both history and the possibility of a future through the rhetorical... telling of the story of dispossession to each other, to their children, and to any outsiders who might be made to listen'" (Wenzel et al 2015 p532).

The mental health impact is not just PTSD, but also depression and anxiety, and secondary complications like substance abuse and suicidal ideation (Wenzel et al 2015)<sup>62</sup>.

Wenzel et al (2015) warned that "medicalising the experiences of trauma, and thereby treating survivors of violence as patients, precludes our understanding of how individuals, families, and other social groups actually respond to violence, what their particular complex health and social care needs are, and through what capacities they contribute to the wider communities they belong to" (p531).

Hobfoll et al (2007) outlined five "simple key needs" after mass trauma as a sense of safety, calming, a sense of self- and community efficacy, connectedness, and hope (Wenzel et al 2015).

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<sup>62</sup> For individuals displaced to another country, the "mutual culture 'shock' between host and refugee culture" is often overlooked (Wenzel et al 2015).

## **8.8. APPENDIX 8B - CHILDREN AND VIOLENCE IN HUMANITARIAN EMERGENCIES**

Humanitarian emergencies occur through armed conflict, natural disasters, or political unrest, which can last from days to years. Children in such situations face "multiple forms of harm" (Stark and Landis 2016).

"While awareness of these risks is widespread, efforts to monitor prevalence or trends of violence against children in emergencies are challenging. Large numbers of cases go unreported due to social stigma, lack of appropriate reporting mechanisms, and the fact that violence is often perpetrated by parents, relatives, or close acquaintances, making it particularly difficult for children to come forward" (Stark and Landis 2016 pp125-126).

Stark and Landis (2016) found twenty-two relevant articles published between 1995 and 2014 in their literature review of the subject. Four types of violence towards children were included - physical, sexual, mental, and neglect - though there were various definitions used for them. Overall, the researchers found the picture incomplete, though boys experienced more physical violence and girls sexual violence. Table 8.3 gives an example of one study from Sierra Leone.

- War-related violence in Sierra Leone (14 years old and above).
- Physical violence - beating 7%, torture 2%, gunshot wound 1%, bodily injury 0.9%, amputation 0.2%.
- Sexual violence - 9%.
- Mental violence - abduction 9.3%.

Table 8.3 - Amowitz et al (2002).

It was difficult to know if risk factors for violence against children generally (eg: social norms that condone violence; inadequate economic resources) were applicable to humanitarian emergencies. One possibility was that these risk factors will be exacerbated.

On the other hand, humanitarian emergencies created unique risk factors. "Such risk factors may include the length of time spent in a camp setting or the length of overall displacement; who is accompanying or caring for a child following an emergency; the type of shelter in which children and families are residing; the likelihood of recruitment of children into fighting factions; and a family's access to food rations, to name just a few examples" (Stark and Landis 2016 p134).

## 8.9. APPENDIX 8C - INTERVIEWS USING TEXTING

Reflecting on interviewing via text messaging, Schober et al (2015) concluded that "people interviewed on mobile devices at a time and place that is convenient for them, even when they are multi-tasking, can give more trustworthy and accurate answers than those in more traditional spoken interviews" (p1). The researchers continued that "answers from text interviews, when aggregated across a sample, can tell a different story about a population than answers from voice interviews, potentially altering the policy implications from a survey" (Schober et al 2015 p1).

Traditionally, social surveys were administered face-to-face, or via landline telephones, but in both cases the interviewee was required to be focused on answering the questions. This does not fit with the modern world. "The growing use of smartphones is transforming how people communicate. It is now ordinary for people to interact while they are mobile and multi-tasking, using whatever mode—voice, text messaging, email, video calling, social media—best suits their current purposes. People can no longer be assumed to be at home or in a single place when they are talking on the phone, if they are willing to talk on the phone at all as opposed to texting or using another asynchronous mode of communication. And they may well be doing other things while communicating more than they would have been even a few years ago" (Schober et al 2015 p2) (table 8.4).

Property	Voice	Text
Synchrony	Fully synchronous	Less or asynchronous
Medium	Auditory	Visual
Language	Spoken/heard	Written/read
Conversational structure	Turn-by-turn, with potential for simultaneous speech	Turn-by-turn, rarely but possibly out-of-sequence
Persistence of turn	No	Yes
Persistence of entire conversation	No	Yes, threaded
Social presence of partner	Continuous (auditory) presence	Intermittent evidence from content of texts; no additional evidence between texts
Nonverbal cues of emotional state and intentions	Always present: speech always has pitch and timing	Only present if added by sender through words (e.g., 'LOL'), orthography (e.g., capital letters, punctuation) or emoticons (e.g., 😊)
Character of multitasking	Often simultaneous, especially when hands free, unless other task involves talking	Switching often required between texting and other tasks
Impact of environmental conditions	Potential (auditory) interference from ambient noise	Potential (visual) interference from visual glare
Impact of nearby others	Others may hear speaker's side of conversation; potential audio interference from others' talk	Others unlikely to see conversation on screen, though possible
Required connection to network (cellular or wifi)	Must be continuous	Can be intermittent

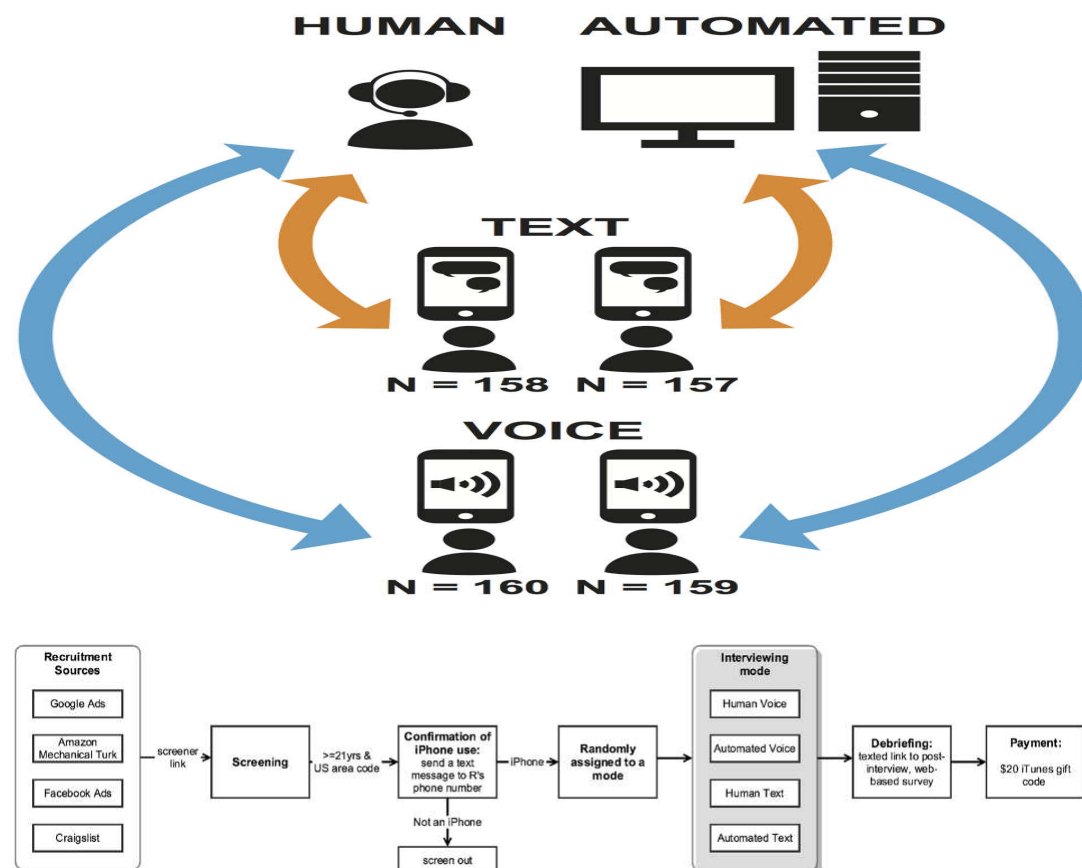
doi:10.1371/journal.pone.0128337.t001

(Source: Schober et al 2015 table 1)

Table 8.4 - Differences between voice and text interviews.

Taking this into account, with the emphasis on accuracy of information collected, Schober et al (2015) designed an experiment using four different modes of interviewing - human telephone interview (human voice condition), human text interview (human text condition), automated telephone interview (automated voice condition), and automated text interview (automated text condition). The two independent variables were thus - human or automated interviewer, and voice or text mode of administration. The outcome measures related to the quality of the data, including disclosure of sensitive information, and truthfulness in answering.

Six hundred and thirty-four iPhone users were successfully recruited via the Internet for this independent groups design experiment (figure 8.2). The same thirty-two questions from major US social surveys were used in each of the four conditions <sup>63</sup>. Fifteen questions required effort to response to test for conscientiousness in answering the survey, and fifteen questions asked about sensitive issues with socially desirable options available.



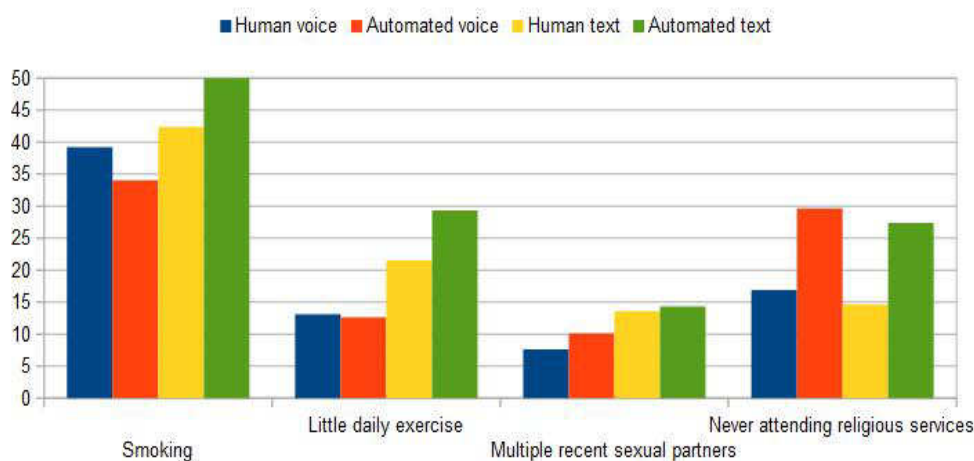
(Source: Schober et al 2015 figures 1 and 2)

Figure 8.2 - Design of experiment.

<sup>63</sup> Copy of questionnaire at <https://doi.org/10.1371/journal.pone.0128337.s002>.



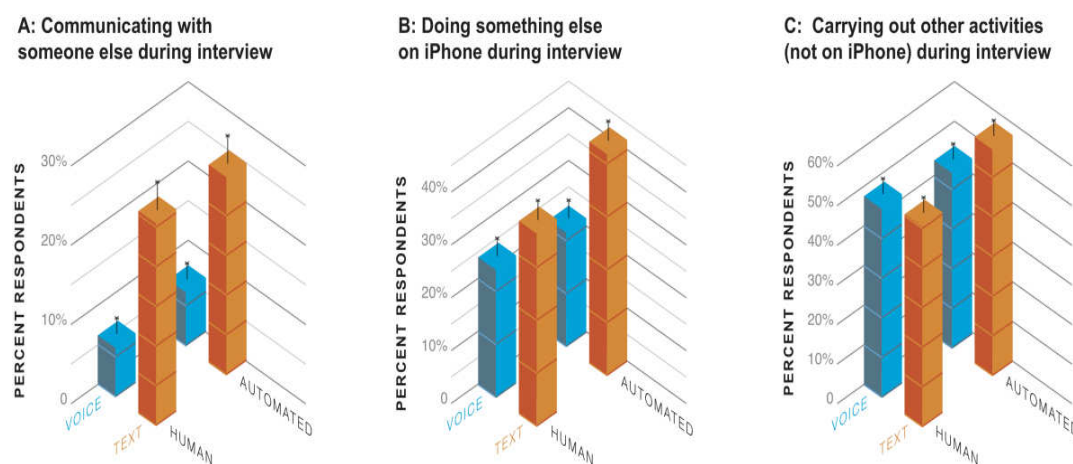
It was found that answers were more precise with text, and more socially undesirable behaviours were reported with automated text (figure 8.3).



(Data from Schober et al 2015 figure 5)

Figure 8.3 - Percentage of participants admitting selective socially undesirable behaviour by condition.

In the debriefing questionnaire, participants were asked about multi-tasking during the interview, which was more common with text (figure 8.4).



(Source: Schober et al 2015 figure 6)

Figure 8.4 - Multi-taking during interview.

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## **9. CHILD SEXUAL ABUSE AND ADULT MENTAL DISORDERS: GETTING AN ACCURATE PICTURE**

- 9.1. Studies and issues
- 9.2. Child maltreatment and depression
  - 9.2.1. Addiction problems
- 9.3. References

### **9.1. STUDIES AND ISSUES**

Behaviours hidden from public view are by their very nature difficult to study, and especially difficult to quantify. One such behaviour is child sexual abuse (CSA).

Studies tend to be retrospective more often than prospective, and the sample can vary between the general population and clinical populations (eg: individuals receiving adult mental health treatment). Retrospective studies involve asking adults to think back to their childhood and report their experiences. Recall-based questionnaires can be anonymous, and thereby maintain privacy and confidentiality. But there are concerns about the accuracy of the recall, let alone the willingness to report experiences.

In a review of child maltreatment, Hardt and Rutter (2004), for example, found that around one-third of adults did not seem to recall abuse that had been substantiated by government agency records. Recall of abuse has also been found to vary across adulthood, between childhood and adulthood, and between siblings experiencing the same maltreatment (Mills et al 2016). In terms of the unwillingness to report to researchers, reasons include embarrassment, defence against negative emotions, and protection of the abuser (Mills et al 2016). Furthermore: "Adults with no or minimal mental health issues tend to under-report agency-documented adverse childhood experiences, while those with psychological problems are more likely to retrospectively report them" (Mills et al 2016 pp87-88).

Prospective studies use contemporaneous information from child protection authorities, for instance. This is an impartial, non-subjective source, but not objective in the sense that only a proportion of cases of child maltreatment are reported to the authorities. For example, in Australia, such sources give a prevalence of 2% for CSA, whereas self-reports vary between 15% for boys to 30% for girls (Mills et al 2016).

Official data are collected for purposes different to that of researchers, and may lack precision (eg: "sexual abuse" covers a risk of the behaviour through to violent assault) (Mills et al 2016).

These issues in researching CSA make it hard to establish whether there is a causal link to adult mental health problems. For example, Raphael et al (2001) compared 676 adults with court-documented child maltreatment and 520 matched controls. No difference in adult pain was found between the two groups. But when the groups were divided by self-reported retrospective recall of child maltreatment, those maltreated had significantly more pain symptoms in adulthood than controls. This study was an example of one using a clinical population rather than a representative general population sample (Mills et al 2016).

Mills et al (2016) used a general population sample in the form of the Mater-University of Queensland Study of Pregnancy (MUSP) birth cohort in Australia. This covers 7223 pregnant women at a Queensland hospital between 1981 and 1983. The follow-up data were available for 21 years old (3739 children responded to the questionnaire).

Among the questions at this follow-up was this one: "Did any of the following events happen to you before you were sixteen?". Five abuse scenarios were offered (three non-penetrative and two penetrative CSA):

- "Someone exposed themselves or masturbated in front of you";
- "Someone more than five years older than you kissed or fondled your breasts or genitals";
- "You touched or masturbated the genitals of someone more than five years older than you";
- "Someone more than five years older than you had sexual intercourse with you";
- "Someone more than five years older than you had oral sex with you".

These were the retrospective self-report measures.

The prospective data were taken from state child protection agency records up to September 2000, which recorded a risk of maltreatment, the type, and whether the notification to the authorities was substantiated or unsubstantiated.

The MUSP cohort also completed questions about mental health at 21 years old.

Self-reported CSA was 19.3% for males, and 30.6% for females (figure 9.1), while the agency-reported prevalence was 2.5% overall (which was 1.4% for substantiated only cases).

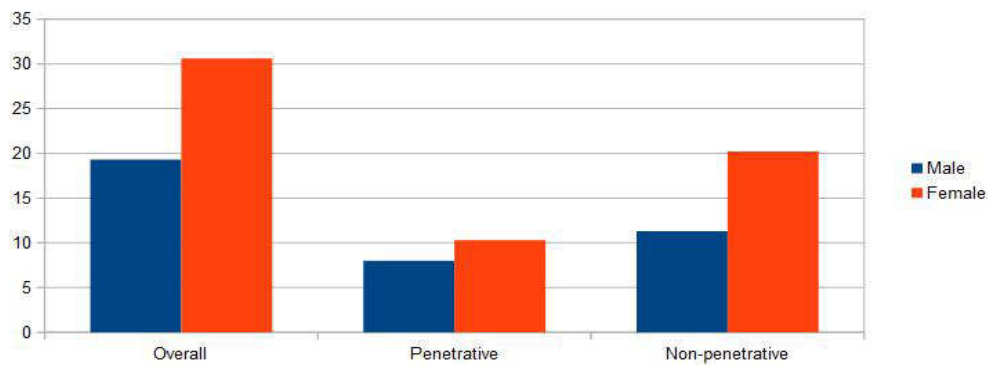
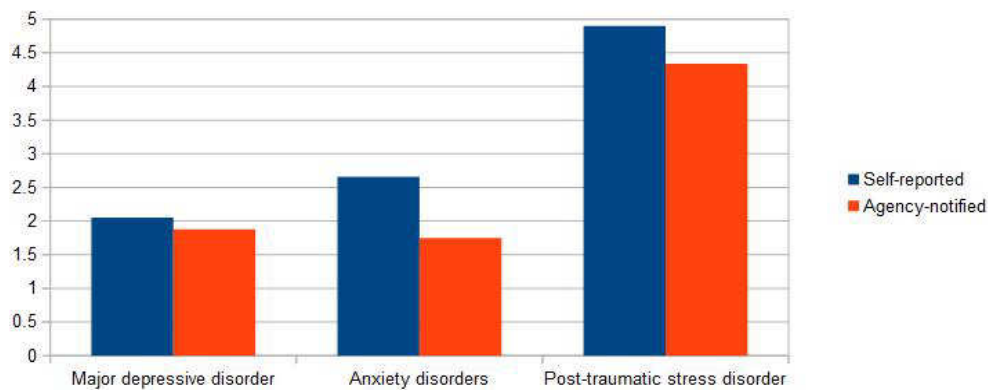


Figure 9.1 - Percentage of respondents self-reporting CSA.

After adjustment for confounding variables like family income and gender, individuals with self-reported CSA were just over twice as likely to have a history of major depressive disorder (MDD) than non-recall of CSA individuals, and over one and a half times more likely if agency-reported CSA. The same was true for a lifetime history of anxiety disorders, especially post-traumatic stress disorder (PTSD) (figure 9.2).



(Data from Mills et al 2016 tables 2 and 3 p90, and table 4 p91)

Figure 9.2 - Adjusted odds ratios for lifetime prevalence (where no self-reported or agency-notified CSA = 1).

Around 40% of individuals with agency-substantiated-CSA did not report it to the researchers. Is this failure to recall or failure to disclose? Mills et al (2016) offered another possibility that "some of the cases of notified, or even substantiated, child sexual abuse may have been reported to the agency primarily on the basis of unacceptable exposure to risk of CSA - for example, children living in the same household as a known child

sex offender" (p91).

This study confirmed that most cases of CSA go unreported to authorities.

Mills et al highlighted the important point for them: "A striking finding of this study was the strong and consistent independent association between both self-reported and agency-notified CSA and post-traumatic stress disorder (PTSD). Across all measures of exposure e penetrative and non-penetrative CSA, agency-notified CSA, and agency-substantiated CSA - the odds ratios for PTSD after adjustment were significant, ranging from 2.7 to 5.5. These results suggest that while PTSD is a less common condition than MDD or broadly categorised anxiety disorders, it has a particular relevance as a relatively specific outcome following CSA" (p91).

The researchers accepted the following key limitations to their study:

i) The attrition rate of the MUSP cohort - Only 52.4% of the original cohort completed the follow-up questionnaire at twenty-one years old, and only 2508 of them gave enough information about adult mental health problems to be included in the analysis. Drop-out from the MUSP cohort, as is common in such longitudinal studies, was greater among those experiencing social disadvantage, and those exposed to agency-reported child maltreatment.

ii) Both the self-reported and official data lacked detail about the CSA (eg: severity, duration, relationship of victim to perpetrator).

iii) No details of other traumatic life events collected, so it was not possible to establish causality between CSA and PTSD.

iv) Anxiety disorders is a broad category, and may have masked the relationship between CSA and a specific anxiety disorder (eg: phobia, obsessive-compulsive disorder).

Other limitations include:

- Follow-up at 21 years old - CSA may have been relatively recent and thus individuals were loathed to report it, while mental health problems may not develop until later life.
- Having five scenarios of CSA was quite limited - It ignores other types of CSA (eg: watching sexually explicit material), and uses the difference of "more than five years older".

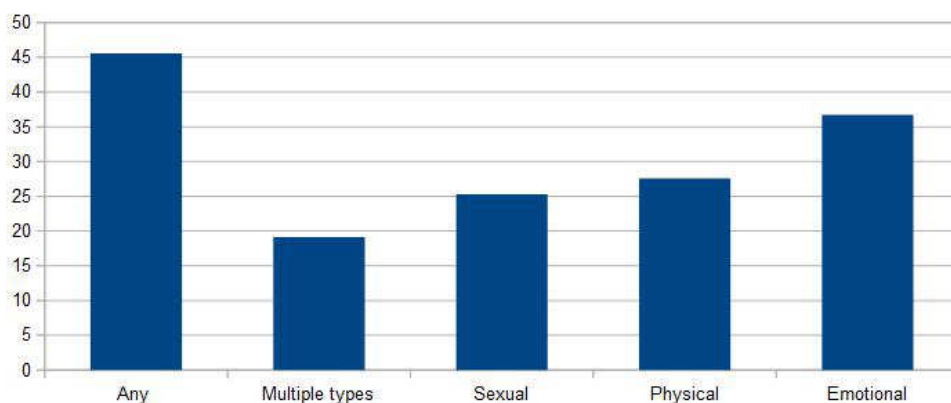
- Agency-reported data - The risk of misrecording; the degree to which the authorities investigated will influence the substantiated/unsubstantiated outcome (eg: threshold for formal investigation); families moving out of Queensland were categorised as "unable to complete".

## 9.2. CHILD MALTREATMENT AND DEPRESSION

In their meta-analysis, Nelson et al (2017) found that "childhood maltreatment, especially emotional abuse and neglect, represents a risk factor for severe, early-onset, treatment-resistant depression with a chronic course" (p96).

These researchers found 184 relevant studies published before late November 2013 that covered child maltreatment and adult depression. The main findings were:

i) About half of individuals with depression reported childhood maltreatment, and one in five depressed individuals had experienced more than one type of maltreatment (figure 9.3).



(Data from Nelson et al 2017 table 1 p99)

Figure 9.3 - Percentage of individuals with depression reporting childhood maltreatment.

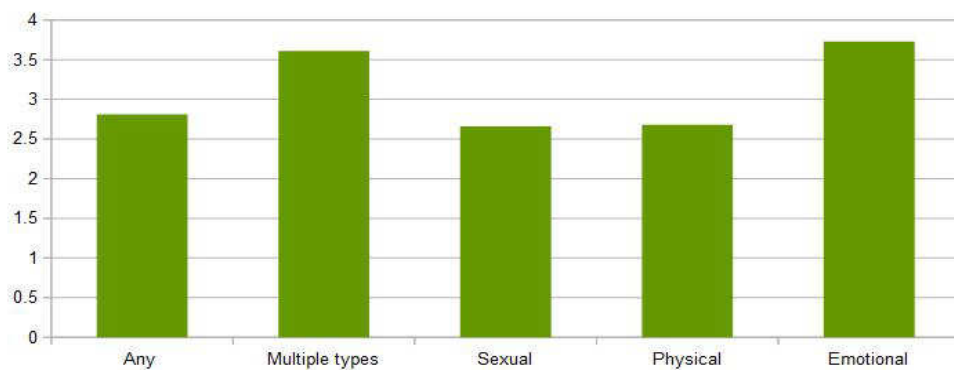
ii) The risk of depression was increased two to four-fold by childhood maltreatment as compared to no maltreatment (figure 9.4) <sup>64</sup>.

iii) Depression severity was significantly

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<sup>64</sup> A meta-analysis of 124 studies by Norman et al (2012) found that emotional abuse increased the risk three-fold and physical abuse 1.5 times.





(Data from Nelson et al 2017 table 1 p99)

Figure 9.4 - Increased risk of depression based on maltreatment (where 1 = no maltreatment).

positively correlated with childhood maltreatment severity.

iv) Onset of depression was earlier in adulthood for individuals with childhood maltreatment than not (23 vs 27 years for first depression onset).

v) The risk of chronic course of depression (ie: more severe and/or longer) was twice as likely with maltreatment as not.

vi) The risk of treatment non-responding depression was about twice as likely with maltreatment as not <sup>65</sup>.

Among the sub-types of maltreatment, emotional neglect was "the most commonly reported form of childhood maltreatment in individuals with depression, and emotional abuse was shown to be the most closely related to depression severity" (Nelson et al 2017 p102).

Nelson et al (2017) stated that "it appears inadequate to regard childhood maltreatment as a unitary phenomenon when considering its effects on depressive disorders" (p96).

Meta-analyses are based on other studies, and, as in this case, there is often heterogeneity in findings which a mean effect can hide. There are also variables, like time and length of maltreatment, and perpetrator, which studies will vary in their ability to control for.

Most studies were retrospective, and asked adults to recall their childhood.

<sup>65</sup> Nanni et al's (2012) found 1.5 times more likely.

### 9.2.1. Addiction Problems

Experiencing childhood maltreatment is a "potent risk factor" for adolescent alcohol and drug problems (Wardell et al 2016). The question is what causes this link? One answer is impulsivity, which is associated with risk-taking behaviour generally.

Whiteside and Lynam (2001) distinguished four aspects of impulsivity:

- i) Lack of perseverance (ie: difficulty with staying focused);
- ii) Lack of pre-meditation (ie: acting without thinking/planning);
- iii) Sensation seeking;
- iv) Negative urgency (ie: "acting rashly in response to negative emotions"; Wardell et al 2016).

Cyders et al (2007) added positive urgency (ie: acting rashly in response to positive emotions).

In a study of 232 adolescents in Toronto, Canada, Wardell et al (2016) found that negative urgency alone of the aspects of impulsivity mediated the relationship between childhood maltreatment and alcohol and cannabis problems.

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## **10. ISSUES RELATED TO THERAPY**

- 10.1. Choosing and evaluating therapy
- 10.2. Positive psychology interventions
- 10.3. Treatment adherence generally
- 10.4. Appendix 10A - Language and behaviour
- 10.5. Appendix 10B - Technology
- 10.6. References

### **10.1. CHOOSING AND EVALUATING THERAPY**

"Planning and assigning a patient to a treatment that optimises gains and fits the patient's needs is a shared objective among clinicians. However, selecting the most appropriate treatment for each patient can be a nebulous and unreliable task, varying by the clinician's biases and theoretical training and with uncertain or unmeasured results" (Beutler et al 2016 p100).

Three approaches have been used to select the most appropriate treatment or therapy (Beutler et al 2016):

i) Clinicians decide on the treatment based on their experience.

ii) Evidence-based treatment for a specific diagnosis.

iii) The use of evidence-based principles to find a "fit" between treatment, diagnosis, and context.

An example of this latter approach is Systematic Treatment Selection (STS) (Beutler et al 2000). It provides "the clinician with a set of empirically informed guidelines about using different psychotherapeutic strategies depending on a patient's proclivities, needs, and overall profile characteristics" (Beutler et al 2016 p100). Three domains of variables are involved - participant factors, interventions, and relationship qualities (Beutler et al 2016).

Beutler et al (2016) noted that most therapeutic approaches "obtain equivalent effects to one another; diagnostic groupings account for little of the change, and therapist and patient differences, independently of treatment, still account for most of the changes observed" (p101). So an eclectic approach as in STS is better.

Taking the preferences of the client/patient/service user/customer into account with treatment is now given prominence. In relation to therapy, Swift et al (2011) defined it as "the behaviours or attributes of the therapist and therapy that clients value or desire"

(quoted in Cooper and Norcross 2016). "People enter therapy with certain preferences, and it is clear that effectiveness of therapy is closely linked to these. If the therapist's style differs markedly from the patient's ideas about the relationship to which he or she would respond, positive results are less likely to ensue. Addressing and accommodating client preferences have been shown to improve treatment outcomes and reduce client dropout by at least a third" (Cooper and Norcross 2016 p95).

These preferences include (Cooper and Norcross 2016):

- Therapist preferences - personal characteristics of therapist (eg: female);
- Treatment preferences - a particular kind of therapy (eg: CBT;
- Role preferences - "particular behaviours, activities and styles of intervention within the therapeutic work" (Cooper and Norcross 2016) (eg: asking questions; reflecting on childhood).

Meta-analyses have shown that clients who have a preferred versus non-preferred therapy have significantly better clinical outcomes, and satisfaction, and a significantly lower drop-out (Cooper and Norcross 2016).

How to establish clients' preferences? There are a number of ways (Cooper and Norcross 2016):

i) Treatment preference vignettes/decision aids - Clients are presented with written or video-recorded vignettes of different treatments and asked to choose. Such "decision aids" have been linked to greater self-efficacy (Cooper and Norcross 2016). But this method tends to elicit a dichotomous response (ie: treatment A rather than treatment B), and not the magnitude of preference (Cooper and Norcross 2016).

ii) Psychometric questionnaires and inventories - These are structured questionnaire measures that ask clients to rate or score particular therapist activities. For example, the Counselling Preference Form (CPF) (Goates-Jones and Hill 2008) covers ten therapist activities, including "insight skills", like gaining a new perspective on problems, and "action skills" (eg: learning problem-solving strategies for particular situations), while the Preferences for College Counselling Inventory (PCCI) (Hatchett 2015) has ninety items (later reduced to sixty-seven items).

Cooper and Norcross (2016) developed the eighteen-item Cooper-Norcross Inventory of Preferences (C-NIP)

(figure 10.1), which distinguished therapist versus client directiveness, emotional intensity versus emotional reserve, past orientation versus present orientation, and warm support versus focused challenge.

- I would like the therapist to:

FOCUS ON SPECIFIC GOALS			NO OR EQUAL PREFERENCE	NOT FOCUS ON SPECIFIC GOALS		
3	2	1		-1	-2	-3
			0			

- I would like the therapist to:

HELP ME REFLECT MY CHILDHOOD			NO OR EQUAL PREFERENCE	HELP ME REFLECT ON MY ADULTHOOD		
3	2	1		-1	-2	-3
			0			

(Source: Cooper and Norcross 2016 appendix 1)

Figure 10.1 - Example of items from C-NIP.

The success of therapy or treatment varies with mental disorder. For example, in the case of anorexia nervosa (AN), only half of sufferers are classed as normal-weight upon discharge from in-patient facilities (Gumz et al 2015).

The success of a treatment can be improved by understanding the factors involved in the change process. Gumz et al (2015) did this for AN. Two hundred and thirty-three AN sufferers in Germany completed a number of questionnaires on entry to hospital, and the answers were linked to treatment success on discharge.

Using factor analysis, four factors emerged as important in treatment success or failure:

1. Basic need satisfaction - eg: self-esteem, self-efficacy, and supportive relationships.

2. AN-specific cognitions and behaviours - "disorder-maintaining beliefs".

3. Emotional involvement and commitment to treatment.

4. Alliance and treatment confidence - eg: feeling of being understood by therapist.

Put simply, a successful treatment outcome will be associated with high scores on factors 1, 3 and 4, and low scores on factor 2.

Therapeutic alliance (TA) (ie: the relationship between the client and therapist) is linked to treatment

outcome. Put simply, a warm relationship between client and therapist usually leads to better outcomes.

The TA can also include close family members in some forms of therapy (eg: family therapy) or in some conditions (eg: child and adolescent disorders). There are also occasions when individuals may be "unwillingly brought into therapy by their parent or guardian" (Rienecke et al 2016).

These issues are seen in Family Based Treatment (FBT) for adolescent anorexia nervosa. Rienecke et al (2016) explored the TA with fifty-six patients at a US hospital and their parents (mostly mothers).

Patient TA was associated with improvements in cognitive and behavioural symptoms of anorexia, but not weight gain over the two-week hospital programme. Maternal hostility towards her daughter limited maternal TA in FBT. Mothers' TA was predictive of treatment completion.

Brief mental health interventions in the context of care for physical illness are part of primary care behavioural health (PCBH) (ie: embedded into primary care), and growing in popularity (Funderburk and Shepardson 2015). For example, Nieuwsma et al (2011 quoted in Funderburk and Shepardson 2015) reported moderate success for brief 6-8 session CBT and problem-solving treatment for depression.

Bhugra et al (2016) commented on the use of a variety of terms instead of "mental illness" and "mental disorders". These include "the patient is suffering from mental health", "mental health concerns", "mental health issues", "mental health problems" or "mental ill health". Bhugra et al (2016) were critical: "Although the grammatical coherence of these statements might be challenged, we contend that such linguistic misnomers disguise stigma and add to confusion in the minds of scientists and the public. These terms do a disservice, and contribute to misunderstanding about what constitutes mental illness, mental health, and wellbeing" (p1100).

They argued: "Abandoning mental illness as a concept means that the seriousness with which the patient understands their problem is not followed up by the professionals. Additionally, using terms such as 'mental health issues' or 'mental health concerns' can seem to imply such experiences are less severe, or less chronic, or less worthy, and maybe even positively valued states of suffering with no connection with illness, disease, or pathology" (p1100).

Slightly mischievously they asked: "Hypertension, diabetes, ischaemic heart disease, and dermatitis are all chronic conditions, and are not called 'physical health issues' or 'concerns', so why should depression, anxiety, and severe mental illnesses like schizophrenia be called

mental health problems?" (Bhugra et al 2016 p1100) <sup>66</sup>.

## 10.2. POSITIVE PSYCHOLOGY INTERVENTIONS

Positive psychology interventions (PPIs) aim to improve subjective well-being (SWB) and reduce depressive symptoms. They were originally proposed by Seligman et al (2005), and include exercises like "Three Good Things" (where individuals keep a diary of three good things per day they have experienced), or the "Gratitude Visit" (to thank an individual who has been kind to them).

The evidence for the benefits of PPIs is mixed - "from substantial to negligible" (Woodworth et al 2016). Studies have tended to compare an intervention group with a control group, whereas Woodworth et al (2016) argued that N-of-1 designs (single case research) <sup>67</sup> (Barbot and Perchec 2015) allow "the examination of individual change in SWB".

If two groups are compared at one point in time, then it misses individual changes in the variable measured over time (ie: within-individual or intra-individual variability). Single case research is able to cover the latter. But in order to have the rigour of an experimental design, the individual is studied in different conditions (ie: they are their own comparison).

Barbot and Perchec (2015) summed up the key issue for traditional group comparisons (nomothetic approaches) and single case research: "While nomothetic approaches offer a general model reflecting the development of an 'ideal-sample-average individual', they still may not apply to each individual in the sample (ie: true on average but not in general). Reciprocally, idiographic approaches are challenged to make inferences from the individual level to the population level" (p64).

Woodworth et al (2016) investigated three PPIs over 9-10 weeks with fifteen volunteers in Tasmania, Australia. A counterbalanced N-of-1 design was used where participants completed a sequence of exercises in one phase, and the reverse order in the second phase. No overall change in SWB was found. Woodworth et al (2016) concluded: "Although such interventions may produce between-group changes in well-being, this does not necessarily mean they produce clinically relevant intra-individual changes" (p28).

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<sup>66</sup> Hayes et al (2003) outlined "acceptance and commitment therapy" (ACT), which assumes "destructive normality" (ie: "ordinary human psychological processes can themselves lead to extremely destructive and dysfunctional results and can amplify or exacerbate unusual pathological processes" (p6)). Language and rule-governing behaviour play a part in this process (appendix 10A).

<sup>67</sup> Also called "idiographic" (Barbot and Perchec 2015) or "idiothetic" (Lamiell 1998) designs.

### 10.3. TREATMENT ADHERENCE GENERALLY

Treatment and therapy can require many daily care activities (eg: two hours per day for proper management of type 1 diabetes; Heckman et al 2015), and the risk of non-adherence is high, particularly when the behavioural interventions are burdensome and/or frequent (Heckman et al 2015). "More is not always better, and increases in patient burden are a primary determinant of reduced adherence and effectiveness. Thus, the optimal dose for any behavioural intervention is that which results in maximum adherence" (Heckman et al 2015 p31).

Adaptive treatment strategies (or dynamic treatment regimens) tailor treatment to the patient/client, and change the programme to avoid unnecessary treatment, and thereby reduce overburden and fatigue (Heckman et al 2015) <sup>68</sup>.

Treatment burden (ie: "how much effort is required for a given health behaviour"; Heckman et al 2015) can be measured by the Treatment Burden Questionnaire (TBQ) (Tran et al 2014), which covers factors like taking medication, doctor visits and tests, social impact of treatment, and financial burden. Total scores negatively correlate with adherence and quality of life (ie: low burden - high adherence, and vice versa) (Heckman et al 2015).

Sav et al (2013) found a number of themes of treatment burden in a review of studies with medical conditions like asthma, diabetes, and cancer, and mental health. These included physical side effects of medication, cost of care and travel to medical facilities, and time demands of management of the condition. "There is clear evidence that treatment burden is experienced by patients with at least one chronic health condition, and this affects many aspects of their lives" (Heckman et al 2015 p32).

Treatment fatigue <sup>69</sup> is "the psychological fatigue associated with treatment engagement" (Heckman et al 2015). For type 1 diabetes, this is also known as "diabetes overwhelmus", "diabetes emotional distress", and "diabetes burnout" (Fritschi and Quinn 2010). This is measured by, for instance, the Diabetes Distress Scale (Polonsky et al 2005), which includes items like "feelings that diabetes is taking too much of my mental and physical energy", and "feeling overwhelmed by the demands of living with diabetes" (Heckman et al 2015).

Individuals need to see tangible benefits (usually

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<sup>68</sup> Technology can help here (appendix 10B).

<sup>69</sup> Also called pill-fatigue, medication-fatigue, dosing-fatigue, and injection-fatigue in chronic disease management (Heckman et al 2015).



symptom reduction) to continue adherence to treatment (Heckman et al 2015).

Heckman et al (2015) proposed the workload-capacity model, which suggests that treatment fatigue, and non-adherence to treatment can arise in four ways - increased workload through more general demands (ie: daily life) or specifically more demands of treatment (eg: time, effort), or reduced capacity via declining general resources (eg: social support, motivation, finances) or via increased illness burden (eg: intensity, complications).

#### **10.4. APPENDIX 10A - LANGUAGE AND BEHAVIOUR**

Chen (2013) proposed the idea that speaking a language that has a future tense leads to a different perception of the future than in languages using a present tense <sup>70</sup>. For example, an English speaker describing tomorrow's weather would say, "it is going to rain" using the future tense ("is going to"), while a German speaker says literally (in translation), "it rains tomorrow" (ie: using present tense) (Chen 2013).

Primarily, Chen (2013) argued that "grammatically separating the future and the present leads to dissociate the future from the present" (strong future-time reference; FTR), and this makes "the future feel more distant". An upshot of this is less willingness to save for the future. But languages that "equate present and future" (weak FTR) will be "more willing to save for a future which appears closer". This difference is also seen in future-oriented health behaviours.

For example, comparing individuals with identical income, education, family structure, and countries of birth, but speaking different languages (eg: Belgium, Switzerland), Chen (2013) found speakers of weak-FTR languages were one-third more likely to have saved in the past year than strong-FTR language speakers, and a quarter less likely to smoke, for instance.

Chen (2013) believed that the relationship was causal (ie: the FTR nature of the language determined behaviour) rather than the language reflecting deeper differences between the speakers that caused the variations in behaviour.

#### **10.5. APPENDIX 10B - TECHNOLOGY**

Real-time and real-world measures of health

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<sup>70</sup> This fits with the Sapir-Whorf hypothesis (Whorf 1956) that proposed that language influences thought.

behaviour involve information about the moment (eg: prompted self-report) or soon afterwards (eg: daily diary). Mobile and wireless technologies have made the real-time repeated sampling of behaviours and experiences so much easier. This is Ecological Momentary Assessment (EMA) (Riley et al 2015).

Mobile and wireless health (mHealth) technologies include the "smart-watch", which can measure activity/movement, heart and blood pressure, for instance, through to nanosensors on the body (Riley et al 2015).

Real-time information allows for intensively adaptive interventions (IAIs) - ie: adjusting an intervention based on the current situation. For example, Adams et al (2013) developed and evaluated an IAI based on personalised, flexible, daily physical activity goals (ie: number of steps) using feedback and goal achievement. This technique significantly increased steps per day over six months as compared to a static daily goal among overweight individuals.

"IAIs hold considerable promise to improve behavioural interventions" argued Riley et al (2015), but there are key questions to be answered like "how frequently do inputs need to be obtained for the IAI to effectively adapt?". Most IAIs are reactive to real-time data, but could they be used to pre-empt, for example, falls (Riley et al 2015)?

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