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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/>.

CONTENTS

	Page Number
1. DRUGS - GOOD AND BAD	4
2. OBESITY AND EATING	24
3. MENTAL HEALTH TOPICS	36
4. INEQUALITIES AND CHANGES	48
5. FERTILITY, PREGNANCY, BIRTH TOPICS	53
6. ETHICS TOPICS	60
7. TRANSGENDER HEALTH	70
8. SLEEP TOPICS	74

1. DRUGS - GOOD AND BAD

- 1.1. Drug repurposing
 - 1.1.1. Anorexia nervosa
- 1.2. Opioids
 - 1.2.1. Regional prescribing
 - 1.2.2. Latin American perspective
 - 1.2.3. Abstinence
- 1.3. Substance use disorders
 - 1.3.1. Pregnancy as protective
 - 1.3.2. Cannabis and memory
- 1.4. Miscellaneous
 - 1.4.1. Nicotine-free e-cigarettes
 - 1.4.2. Co-production in substance use research
 - 1.4.3. Drug-related celebrity deaths
 - 1.4.4. "Pharmaceutical commons"
 - 1.4.5. Anti-biotic resistance
- 1.5. Appendix 1A - Shen et al (2018)
- 1.6. Appendix 1B - Cipriani et al (2016)
- 1.7. Appendix 1C - Garcia-Orjuela et al (2016)
- 1.8. References

1.1. DRUG REPURPOSING

Drug repurposing is where a medicine designed for one condition/illness is found to be effective with another (unrelated) condition/illness. It saves time and money involved in the creation and testing of new drugs.

One example of drug repurposing is with drugs created for physical conditions applied to mental disorders. Hayes et al (2019) investigated three groups of such drugs:

a) Statins (hydroxymethyl glutaryl coenzyme A reductase inhibitors; HMG-CoA RIs) - to reduce cholesterol.

Previously, Shen et al (2018) performed a meta-analysis of six randomised controlled trials (RCTs) of statins as adjunctive therapy for schizophrenia, and found a reduction in symptoms over twelve weeks (appendix 1A).

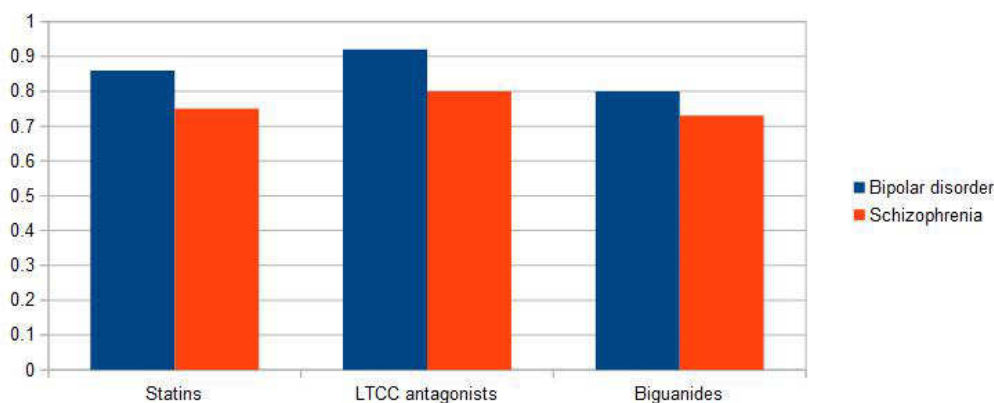
b) L-type calcium channel (LTCC) antagonists (eg: verapamil hydrochloride) - used with cardiac irregularities.

Previously, Cipriani et al (2016) found no effect in reducing bipolar disorder symptoms in a meta-analysis of six RCTs (appendix 1B).

c) Biguanides (eg: metformin hydrochloride) - used with type II diabetes.

Hayes et al (2019) analysed data from the Swedish National Patient Registers for 1973 to 2016. The aim was to see if individuals prescribed any of the above drugs had lower rates of psychiatric hospitalisation for serious mental illness (SMI) during that period compared to when not exposed to the drugs. It was a within-individual design. The focus was upon 142 691 individuals who had a diagnosis of bipolar disorder, schizophrenia, or psychosis. Adjustments during analysis were made for variables like age, number of previous hospitalisations, and use of psychiatric medication.

Psychiatric hospitalisation was reduced during the periods that the sample were taking statins, LTCC antagonists, or biguanides (figure 1.1).



(Data from Hayes et al 2019 table 2)

Figure 1.1 - Adjusted odd ratio for psychiatric hospitalisation for bipolar disorder or schizophrenia when taking one of three drugs (where 1.00 = not taking the drug).

Hayes et al (2019) concluded: "As far as we are aware, this study is the first to suggest that periods of exposure to HMG-CoARIs, LTCC antagonists, and biguanides are associated with lower rates of psychiatric admission and self-harm in patients with SMI. Each of these drugs has a theoretical basis for effectively reducing psychiatric symptoms" (pE6).

- Statins are anti-inflammatory, "with effects on levels of interleukin-1 β , interleukin-6, tumornecrosis factor, and C-reactive protein. Extensive evidence suggests that systemic and neuro-inflammatory processes are involved in the pathophysiology of psychiatric disorders" (Hayes et al 2019 pE7).
- LTCC antagonists are known to have anti-depressants

effects in animal models.

- Biguanides "may potentially improve symptoms in SMI because of underlying disturbed cerebral use of glucose, particularly in brain areas linked to cognitive impairments in schizophrenia" (Hayes et al 2019 pE7).

This study involved a large sample over a long period of time who were compared to themselves (period taking drug versus period not taking drug). But "to be included in the study, individuals had to be prescribed a study drug, suggesting poor physical health, and experience at least 1 outcome, suggesting poor mental health" (Hayes et al 2019 pE7). This limited the generalisability of the findings.

There may have been unmeasured confounding variables, like severity of SMI symptoms.

Because the study used secondary data (ie: collected by someone other than these researchers), it was dependent on the accuracy of the data collection (eg: misclassification of individuals), and limited by the information not collected (eg: treatment adherence).

The study only included SMI that led to psychiatric hospitalisation.

1.1.1.1. Anorexia Nervosa

Anorexia nervosa, in adult in particular, has been treated with drugs developed for other conditions, like anti-depressants (though sufferers of anorexia may also experience depression), and anti-psychotics. One example of a second-generation anti-psychotic ¹ is olanzapine. Its success with anorexia is unclear from previous small-scale studies, leading Attia et al (2019) to undertake a large multi-site placebo-controlled trial.

This was a sixteen-week trial at five sites in North America with individuals diagnosed with DSM-IV-criteria anorexia nervosa, and at least eighteen years old. At the beginning of the study, 75 individuals were randomised to treatment and seventy-seven to placebo. By the end of the study, the treatment group had a significantly greater weight gain than the placebo group (mean increase of 0.26 body mass index (BMI) units per month vs 0.10). This is the equivalent to 1 lb more per month weight gain for a woman of average height. The treatment group reported more side effects.

However, as the researchers noted: "Unfortunately, we found no evidence that olanzapine had a significant

¹ These are newer and chemically different to first-generation anti-psychotics.

impact on the characteristic psychopathological features of anorexia nervosa, such as obsessionality and overconcern with gaining weight" (Attia et al 2019 pp6-7).

Table 1.1 summarises the key strengths and weaknesses of this study.

STRENGTHS	WEAKNESSES
<p>1. Larger sample size than previous studies (eg: 30 adults in study that found no benefits for olanzapine; Brambilla et al 2017).</p> <p>2. Multiple sites.</p> <p>3. "Real-life patients" - ie: with co-morbid psychiatric disorders (eg: mood disorders: one-third currently; anxiety disorders: 40% currently), and taking other medications (eg: 30% anti-depressants). The findings with such patients favours generalisability.</p> <p>4. Good methodological practices (eg: randomisation to treatment or placebo group; blinding of clinical staff to medication).</p> <p>5. Adherence to treatment was based on medicine diaries and monthly pill counts (ie: number of pills left), and end-of-study serum olanzapine levels.</p>	<p>1. Large drop-out - over 40% in both groups (34 individuals in treatment group and 35 in placebo group).</p> <p>2. Short duration.</p> <p>3. Study undertaken with out-patients at five specialist centres (four in the USA).</p> <p>4. All but seven participants were female.</p> <p>5. Exclusion of individuals with psychiatric problems that required immediate attention, like suicidality, and medical or neurological problems. "Participants could not be in intensive out-patient treatments such as partial hospital or day programmes" (Attia et al 2019 p2).</p>

Table 1.1 - Key strengths and weaknesses of Attia et al (2019).

1.2. OPIOIDS

Talking about painkillers and professional sport, King (2014) argued that research would be "especially productive if undertaken in a way that refused the spurious and often harmful distinctions between 'licit' and 'illicit' drugs that permeate social and political life, and instead analysed these substances together. After all, most street drugs begin life as 'wondrous new tools of medicine', in the words of historian David Herzberg (2010), and some drugs, like steroids and prescription painkillers, are used in both licit and illicit ways. Moreover, each category of substance - legal/illegal - depends upon the other for its meaning. This binary relationship is based not on the pharmacological properties of drugs but on political

ideologies about those who are perceived to use them. As such, distinctions between the licit and the illicit help legitimise the terrible toll of the war on drugs on poor and racialised communities... and guarantee that punitive and selective approaches to substance use will inevitably fail" (pp185-186).

King (2014) placed opioid use in the USA in its historical context - "medical consumption was part of what constituted a good middle-class life" (p186). This has been called the "pharmaceuticalisation" of society (Williams et al 2011).

King (2014) described a tension here: "On the one hand, the ability to consume drugs freely to function – as a productive worker, a self-responsible citizen, or, in the case of alcohol, a fun-loving and socially well-adjusted member of the society – is an expectation, if not an obligation of proper citizenship... On the other hand, consumer subjects are required to exercise unceasing self-discipline lest their ingestion practices become excessive or unseemly" (p186).

King's (2014) focus was on prescription painkiller use by professional American football (NFL) players, which embodied this tension ². The "legitimate" use to deal with the pain of injuries versus the stories of opioid dependence of ex-players. King (2014) felt that the "narratives about the 'prescription drug epidemic', and about former NFL players, are helping to unravel the hierarchical distinction between prescription opioids and street opioids that has held sway for so long" (p187).

The "unhelpful" distinction between licit and illicit is based around "the ways that drugs are used or 'misused'" (King 2014). So, "prescription opioid use becomes viewed as a problem only when its procurement or ingestion deviates from methods approved by professional authority; that is, when it is taken in greater quantities than prescribed, when it is stolen from a pharmacy, when it is sold by a person with a prescription to a person without one, when it is procured by a patient who is 'doctor shopping', or when the drug's slow release formula, touted by its manufacturer as a deterrent to addiction, is subverted by the simple act of crushing the pill with a thumbnail and then snorting or injecting the fine white powder that results" (King 2014 p188).

Still on sport, Dunn (2015) referred to two stories of the misuse of prescription tranquillisers (used to induce sleep) by elite swimmers in Australia around 2012.

Prescription substances (PS) are "not generally banned in sport, however some PS may be or may be related

² Over half of retired NFL players surveyed by Cottler et al (2011) admitted to using prescribed opioids during their playing career, and three-quarters of these to misusing them (and 15% still) (Dunn 2015).

to substances which are. For instance, methylphenidate is a prohibited substance in-competition..., yet can be prescribed as treatment for attention-deficit hyperactivity disorder (ADHD) under such trade names as Ritalin and Concerta" (Dunn 2015 p102).

Dunn (2015) argued that sporting bodies should test for prescription drugs, as with performance enhancing substances, but "from an altruistic position of protecting their players' health" (p103).

He continued: "Punitive sanctions may be appropriate for instances where performance-enhancing substances are detected; indeed, athletes themselves support tougher sanctions in these cases... However, this line blurs when the substance detected has little or no performance enhancing properties, and must become even more ambiguous when it comes to PS. [...] Adopting a true harm minimisation policy that does not seek to punish athletes for substance use in the first instance may help to not only understand the underlying causes of substance use amongst this group but also assist the sporting community to act upon them" (Dunn 2015 p104).

1.2.1. Regional Prescribing

In the USA opioid prescriptions and linked deaths have increased significantly in recent years, and Mordecai et al (2018) were concerned about a similar rise in the UK. Deaths attributed to opioids in England and Wales, and Scotland have nearly doubled between 2001 and 2011 (around 500 to around 900) (Giraudon et al 2013).

Mordecai et al (2018) focused on opioid prescribing in primary care in England between 2010 and 2014. Prescriptions of eight opioid drugs increased over the study period, but there was also regional differences found, "with nine out of ten of the highest prescribing areas located in the north of the country, and there was an association between social deprivation and higher opioid prescription" (pe228).

Mordecai et al (2018) explained: "The strong relationship found between Indices of Social Deprivation and opioids prescribed is likely to be at least in part attributable to the higher prevalence of chronic pain in people of lower socio-economic status. In 2011, 40% of males and 44% of females in the lowest income quartile met the criteria for chronic pain (British Pain Society definition), compared with 24% and 30%, respectively, in the highest quartile. Additionally, there is a strong association between unemployment and poor outcomes in chronic pain" (pe230).

There were three key methodological issues related to this study:

i) On the positive side, the data covered the entire country for the eight most commonly prescribed opioids. However, this missed lesser-prescribed ones (eg: pethidine).

ii) The number of prescriptions was converted into equivalent mg of morphine, but "there is no universally agreed method for this calculation" (Mordecai et al 2018 ppe229-230).

iii) There was no information on the reasons for prescription (eg: chronic or acute pain), nor on over-the-counter drugs (eg: codeine).

1.2.2. Latin America Perspective

Pacurucu-Castillo et al (2019) observed: "The opioid epidemic has been declared one of the worst national health crises in the United States, its growth having started in the 1990s. The U.S. Surgeon General has advised against the indiscriminate prescription of opioid analgesics. Drastic control measures were announced by the U.S. Government, after reports that opioid abuse leads to 1,000 visits per day to hospital emergency rooms and kills 78 people per day in the United States" (p1). But these authors pointed out that the situation "looks different in Latin America".

One problem is the limited evidence on the subject for this part of the world. In terms of the few studies, the findings include (Pacurucu-Castillo et al 2019):

- Argentina (2017) - 0.1% of 12-65 year-olds have used heroin, opium and morphine (lifetime prevalence).
- Columbia (2013) - 1.7% ever used opiates.
- Garcia-Orjuela et al (2016) studied the patients at one hospital in Columbia between 2011 and 2014, and 1.8% met the criteria for opioid dependence (appendix 1C).

Pacurucu-Castillo et al (2019) outlined factors in Latin America related to drug use and abuse:

a) Market differences - Some countries have opioids marketed and demanded for pain relief as the key issue (eg: Brazil), while others have illegal substance problems (eg: Mexico).

b) Gender - "In Latin America, addiction among women is seen more negatively than addiction among men. This view results in diminished social acceptability and higher levels of rejection and public criticism for women with drug addiction, perhaps leading to less help-seeking

actions by relatives and acquaintances. The situation is undoubtedly related to socio-cultural factors, family structures, community networks, and even political conditions" (Pacurucu-Castillo et al 2019 p3).

c) Medical professionals - "Most problems begin with the excessive prescription of the drug by the physician, but then the patient takes the initiative to abuse the prescribed drug for its euphoric effects or as an attempt to control eventual withdrawal symptoms" (Pacurucu-Castillo et al 2019 p4).

d) Co-occurring disorders - Opioid users are often likely to have another psychiatric disorder (eg: depression - up to half compared to around one-quarter in the general population).

e) Legal acceptance - Variable amounts of legal opioid possession from country to country (eg: Mexico 2 g of opium; Ecuador 4 g).

f) Public health issues - "Pain is undoubtedly the main referent between legal and illegal use of opioid medications, and cancer is the clinical condition most amenable to their use" (Pacurucu-Castillo et al 2019 p4).

g) Prevention - Countries vary in their programmes.

Pacurucu-Castillo et al (2019) ended with this advice for governments in Latin America concerning opioid abuse: "Any attempt to counteract the current situation must combine strong policies; education campaigns; professional alertness; and the joint work of health authorities, medical professionals, social leaders, and pharmaceutical companies. It is crucial to establish or strengthen appropriate policies for providing information on and producing, importing, and marketing opioids. With pain management as a triggering factor for the increase in opioid use, prescription practices, therapeutic protocols, advertising styles, and regulatory instruments must constitute a harmonious as well as effective armamentarium for pain control efforts" (p5).

1.2.3. Abstinence

Maintenance to abstinence (MTA) programmes aim to wean substance users off the substitute (maintenance) drug (eg: opioid users and opioid agonist medications like methadone).

Gossop et al (2003) compared methadone reduction with three other treatments - in-patient, residential rehabilitation, and methadone maintenance over 4-5 years. All approaches reduced the frequency of heroin use and

non-prescriptive methadone use, and injection and needle sharing. The residential rehabilitation treatment was best for abstinence from heroin. "Moreover, the availability of residential rehabilitation in those with opioid use disorder is of particular importance as this population is more likely to suffer homelessness and social exclusion limiting their access to out-patient services" (Southey et al 2019 p3).

In terms of wider benefits, Southey et al (2019) reported on a voluntary MTA programme for opioids as part of a residential rehabilitation programme in New South Wales, Australia. Data were available for 2013 to 2017 (n = 86). Half of the participants completed the twelve-week programme (completers), and they were compared to non-completers.

Southey et al (2019) summed up the findings: "The MTA program appears to improve the mental health and quality of life of those with opioid addiction through involvement in the program, regardless of whether or not they complete the program. Only depression, anxiety and stress reduced more markedly in program completers. Quality of life and psychological distress improved for both completers and non-completers but this improvement was not significantly higher among completers" (p8).

Length of stay in a residential programme has been found to predict recovery (eg: Turner and Deane 2016).

Southey et al's (2019) study did not have comparison data for non-residential MTA programmes, maintenance treatment, or other types of residential programmes.

1.3. SUBSTANCE USE DISORDERS

The prevalence of substance use disorders is put at around 10% in Western countries like the USA (Brady 2019).

Introducing the latest research, Brady (2019) noted that the "better understanding of substance use disorders can improve prevention and treatment efforts and is critical to public health" (p87). Such studies include:

a) The interaction of particular genes and stressful life events (ie: "differential susceptibility to the impact of stress"; Brady 2019), and substance use disorders among adolescents (Tay et al 2019).

b) Long-term effects on memory of marijuana use by adolescents (Morin et al 2019).

c) Differences in brain structure between substance dependent individuals and non-dependent controls, particularly in the insula and medial orbitofrontal cortex (Mackey et al 2019).

d) Changes in the brain of dependent individuals who achieved abstinence with a twelve-week programme, and maintained it for six months after (Yip et al 2019).

e) The benefits of once-per-month extended-release injectable naltrexone³ over once-daily administration of oral naltrexone for individuals with opioid use disorders (Sullivan et al 2019). "Relapse is often associated with impulsive decision-making, environmental cues, and stressful life events. A long-acting antagonist may give an individual an opportunity to extinguish the learned association between environmental and internal cues and drug use" (Brady 2019 p88).

1.3.1. Pregnancy as Protective

In a 2013 survey of US women of childbearing age, around 10% admitted to drinking alcohol while aware that pregnant, and 2% binge drinking (quoted in Edwards et al 2019). These percentages were less than among non-pregnant women of the same age.

With reference to the last decade, Edwards et al (2019) pointed out that "even as past-30-day alcohol consumption and binge drinking have increased among non-pregnant U.S. women, these behaviours have decreased among pregnant women" (p138).

So could pregnancy be a protective factor for alcohol use disorder? Edwards et al (2019) answered this question in the affirmative with Swedish data.

Over 300 000 mothers aged 18-35 years when pregnant matched were matched to five unrelated control women (born in the same month between 1975 and 1992). Rates of ICD10-criteria diagnosed alcohol use disorder were significantly less among pregnant than control women. "Pregnancy is also associated with reductions in alcohol use disorder among partners, though to a lesser extent than among mothers" (Edwards et al 2019 p143).

1.3.2. Cannabis and Memory

Adolescent cannabis use is around 3% of individuals daily, but nearly 30% ever in their lifetime in the USA (Schuster et al 2018). There are concerns about the long-term effects on the brain of adolescent use.

Concentrating on memory, cannabis use is associated with deficits, while abstinence leads to remittance of memory deficits. Hanson et al (2010) found benefits after

³ Naltrexone is an opioid antagonist - ie: it works on synapses where opioids bind. The upshot is suppression of the desire for opioids.

three weeks of abstinence, while Roten et al (2015) noted improvements in verbal memory over 4-8 weeks (compared to continued users). But these two studies did not randomise participants to abstinence or not (Schuster et al 2018).

But Schuster et al's (2018) study did so with 88 16-25 year-olds in Boston, USA. The individuals, who used cannabis at least weekly, were randomised to thirty days of abstinence or a matched control (continued use) group. Abstinence was based around a contingency management programme that paid the individuals to attend hospital visits (to measure urine) and for abstaining. Cognition was measured by standardised tests at baseline and then once a week during the study. For example, one test of memory was the Delayed Matching to Sample Task, where an example pattern (sample) is shown followed by four choices (match). The delay between sample and match was varied from 0 to 12 seconds.

The abstinence group had significantly better memory scores than the control group at weeks 1, 2, 3, and 4 of the study. "Declarative memory, particularly encoding of novel information, was the aspect of memory most impacted by cannabis abstinence. Those who maintained abstinence learned more words than those who continued to use cannabis" (Schuster et al 2018). Interestingly, other aspects of cognition, like attention did not improve with abstinence.

This study had no control group of non-users, nor measurements of the participants' cognitive abilities before initiation of cannabis use, so Schuster et al (2018) admitted, "it is difficult to interpret the role of cannabis in affecting domains that did not improve more among abstainers compared to non-abstainers, such as tasks of attention, visual span capacity, short-term visual recognition memory, and verbal delayed recall".

They continued: "There are several possible explanations: (1) deficits predate cannabis use, (2) deficits from cannabis exposure are permanent or long-lasting, (3) substantial practice effects in the control group wash out the ability to detect subtle between-group differences, or (4) cannabis does not adversely impact attention or these other domains, thus no improvement over practice effects would be evident with abstinence" (Schuster et al 2018).

The study measured cognitive abilities once a week, so it was unable "to determine a more precise time point when memory improvement occurred during the first week of abstinence" (Schuster et al 2018).

1.4. MISCELLANEOUS

1.4.1. Nicotine-free E-cigarettes

E-cigarette liquids containing nicotine are not

legal in Australia, but there are concerns that these "nicotine-free" products do contain nicotine (Chivers et al 2019).

Ten brands were purchased and analysed by Chivers et al (2019). "Nicotine was detected in six e-liquids; the levels in three (1.3, 1.4, 2.9 mg/mL) were comparable with those of commonly available low dose nicotine e-liquids. The fact that nicotine was present has important implications for addiction and health, and reflects its use in the e-cigarette liquid manufacturing process" (Chivers et al 2019 p1). An acutely toxic chemical (2-chlorophenol) (eg: used in insecticides) was also found in all the e-liquids.

Chivers et al (2019) explained the findings as due the same manufacturing facilities being used for nicotine-free e-liquids, nicotine e-liquids, and other chemical products rather than deliberate adulteration.

1.4.2. Co-Production in Substance Use Research

Quoting Beresford (2003), Cairns and Nicholls (2018) pointed out "that while objectivity and dispassion are one route to truth, when it comes to research involving people 'the greater the distance between direct experience and its interpretation, then the more likely resulting knowledge is to be inaccurate, unreliable and distorted'" (p6).

These authors were advocating co-production in substance use research. Co-production involves service users or "experts by experience" in the research process. More formally, Cairns and Nicholls (2018) defined it as: "Where possible, working in equal partnership with stakeholders with respect to designing, delivering and communicating research. Approaching research as a collaborative effort which draws on the strengths of everyone involved. Recognising that the knowledge held by all parties is valuable and carries equal, though different, potential" (p7).

Co-production has some key principles (Cairns and Nicholls 2018):

- Equality - "mutual respect: valuing everyone's experience, and, as it were, assuming the person you are talking to knows something you do not" (p8).
- Co-operation - working with participants in "meaningful collaboration".
- Participation - active, rather than passive, involvement in the research.

Examples of co-production in substance use research

include:

- Working with 13-18 year-olds to evaluate an alcohol misuse change programme (Clark and Laing 2018).
- Presenting the "recovery journey" of substance misusers (Edwards et al 2018).

1.4.3. Drug-Related Celebrity Deaths

Professional athletes begin "drugs of abuse" for two main reasons (Just et al 2016):

- Performance enhancer model (including to fight pain);
- Abuse and addiction model (eg: to reduce stress).

"Many of these motives apply to celebrities as they are under constant pressure to perform and to appear healthy and productive. Opioids have a soothing effect on many of these issues. Therefore the risk for developing an addiction may be generally elevated for celebrities, especially in those with an increased prevalence of musculo-skeletal pain" (Just et al 2016 p1).

Just et al (2016) collective retrospective data up to June 2016 on drug-related celebrity deaths. From the Internet, publicly available information was found on 220 celebrities (between 1970 and 2015). "Celebrity" was defined as "a person that (i) had a Wikipedia entry and (ii) had a Wikipedia entry devoted to her or him due to their own, substantial achievements" (Just et al 2016 p2). Most drug-related celebrity deaths occurred between 25 to 40 years old.

Just et al (2016) noted "an increase of drug-related celebrity deaths in the 21st century with a statistically significant increase of prescription opioid involvement. Also we were able to show that prescription opioids as well as heroin were significantly associated with a younger age at death compared to all drug-related celebrity suicides, while other prescription drugs were significantly connected with an older age at death" (p3).

The researchers continued: "The increased use of prescription opioids in the U.S. in the 21st century corresponds to our finding that the involvement of prescription opioids was significantly associated with a more recent year of death" (Just et al 2016 p3).

This study involved English websites only, "which may have led to a selection bias towards U.S celebrities" (Just et al 2016 p3).

Furthermore, the researchers admitted, "the perception of who we regard as celebrity might have changed during the study period, even more so after the

rise of social media. Reporting bias might be present as historic reporting of cause of death may have changed over the study period. Pain medications and suicides may have been under-reported in early years due to social acceptability issues, resulting in an apparent increase in those deaths in later years. This effect could have been reinforced by the improvement of toxicological identification methods during the study period. This might have significantly changed the results. Also we cannot control for the total number of celebrities which is most likely on a continuous rise as the entertainment industry itself is continuously growing. This is why we cannot claim that the percentage of celebrities, who suffered a drug-related death, has been rising" (Just et al 2016 p3).

1.4.4. "Pharmaceutical Commons"

In recent years, pharmaceutical research and development (R&D) has seen "open innovation" based on sharing rather than the protection of property rights and patents by private companies. "Whether by sharing chemical libraries, establishing patent pools or placing clinical data in the public domain, improving research productivity seems to demand a greater willingness to abdicate full control over one's own resources" (Lezaun and Montgomery 2015 p4). For Munos and Chin (2009), "sharing could be the key that allows companies to access the vast creative, intellectual, and technological resources required to tackle the formidable challenge of turning the riches of the genome into a treasure trove of new treatments" (quoted in Lezaun and Montgomery 2015).

This sharing of "intellectual capital resources" is most evident in drugs for "neglected tropical diseases" (nineteen diseases prevalent in low-income countries including malaria and tuberculosis), argued Lezaun and Montgomery (2015). They stated: "Greater R&D investment cannot be encouraged by further strengthening intellectual property rights (IPRs), for 'a market monopoly incentive is irrelevant when market prospects are absent' (Trouiller et al 2002). In a situation widely described as 'market failure'..., and where the traditional profit incentive is seen as inoperative or too uncertain to warrant risky expenditures on research, the key is to create new communities of sharing, to trigger processes of reciprocal exchange that will reactivate the circulation of resources. Actors with the relevant expertise and capabilities – academic institutions, governments, philanthropic organisations and, critically, pharmaceutical companies – must join forces and launch new collaborative ventures" (Lezaun and Montgomery 2015 pp4-5).

The manifestation of this idea is product development partnerships (PDPs) that involve for-profit and not-for-profit actors. For example, the Medicines for Malaria Venture, founded in 1999, co-ordinates the research on drugs to combat that disease (including with funding from the Gates Foundation) (Lezaun and Montgomery 2015).

"These ventures are all dedicated to creating new circuits of exchange among corporate, academic, and governmental organisations, and they share at least three key features: their focus on the development of new medical technologies (drugs, vaccines, and microbicides), their self-proclaimed 'virtual' nature, and their emphasis on the pooling of proprietary resources as the key mechanism of enhanced collaboration. 'Virtualism' refers here to the claim of being unencumbered by large investments in fixed capital resources or specific research trajectories, a freedom from costly legacies and socio-technical lock-ins that allows PDPs to spawn diverse alliances and thereby multiply the number of projects under development. The sharing of proprietary assets, on the other hand, is the act that founds these public-private pharmaceutical projects, gives them concrete content, and demarcates their boundaries. Each project is constituted by the pooling of private goods, such as patents, compounds, data, facilities, or expertise" (Lezaun and Montgomery 2015 p6).

1.4.5. Anti-Biotic Resistance

"Anti-biotics kill by selective toxicity", Landecker (2016) pointed out, and "Anti-biotic resistance arises when microbes gain the capacity to evade these drugs" (p20). She coincided anti-biotic resistance as a means "to build a concept of the biology of history: how human historical events and processes have materialised as biological events and processes and ecologies" (Landecker 2016 p21).

In terms of the history of science, the discovery of anti-biotics in the mid-twentieth century was a key event. "Diseases that previously could not be stopped and catastrophic bacterial infections from suppurating wounds were abruptly and seemingly magically cleared up" (Landecker 2016 p25). Soon came "bioprospecting" as scientists searched for new anti-biotics, while industry sold anti-biotics to farmers to improve the growth of their livestock, for example.

"Medical history was therefore also environmental history. Within ten years of isolation, penicillin production was global in scale and scope, spurring prospecting and cultivation of other soil micro-organisms. The metabolisms of microbes were joined to those of animals and humans in new ways, at scale.

Animals were brought inside from outdoor cultivation and fed anti-biotics. They grew to market size on the same amount of food in less time, contributing to post-war increases in meat consumption" (Landecker 2016 p27).

Anti-biotic resistance was "a constant shadow", and penicillin resistance was even detected in a patient one year after its first use in 1941. "Anti-biotic resistance was recognised as a problem and yet seemed not to be an urgent one. Complacency prevailed: another drug could always be found, existing drugs could be further altered, and it was assumed to be an infrequent problem affecting non-compliant patients. It was thought that mutation events would be rare, remaining limited to a mutant's descendants, channelled by vertical genetic inheritance. Thus resistance was experienced as a spur to discovery of drugs working by the same principle, not as a fundamental challenge to the model" (Landecker 2016 p28).

To the question, did humans cause anti-biotic resistance, Landecker (2016) answered "both no and yes". "On the one hand, no: neither anti-biotics nor anti-biotic resistance are of human origin. Humans got anti-biotics from microbes [...] On the other hand, the human role in anti-biotic resistance is evident: just because it already existed doesn't mean that it had the scale, mode and tempo that it does now" (Landecker 2016 p38; 39). Humans have generated "evolutionary pressures" on bacteria which is "the unintended biology of biotechnological control" (Landecker 2016 p41).

In the 1990s, there emerged, what Landecker (2016) called, "a biopolitical rationality of anti-biotic resistance" with individuals and groups publicising anti-biotic resistance in "no less than apocalyptic terms".

Returning to the idea of "a biology of history", anti-biotic resistance has led to "the control of the substances that were the previous technologies of production" (Landecker 2016 p44).

Landecker (2016) ended: "Also implicated are social and cultural analyses of biomedicine and health, as this case pushes us to see that concepts and tools, and economics and politics of life are changing, but so are biologies. Our theories and empirical work should speak to the complex materiality of life adapting to management and manipulation at enormous scale well beyond the frame of human intention. The history of anti-biotics is not behind us, it is in us. Such is the nature of life today" (p44).

1.5. APPENDIX 1A - SHEN ET AL (2018)

Shen et al (2018) found six RCTs that investigated adults with schizophrenia or psychosis given statins or a placebo as well as anti-psychotic medication. The Positive and Negative Syndrome Scale (PANSS) (Kay et al

1987) (in five studies) or the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen 1989) were the primary outcome measures.

In total, 169 participants received statins and 170 placebo, and the data were combined in the meta-analysis. The treatment group showed significant improvements in positive and negative symptoms ⁴ (PANSS score) compared to the placebo group, overall ⁵.

In further analysis, only some classes of statins (eg: simvastatin, but not lovastatin) showed a benefit ⁶, and 12-week use was most effective. "However, these findings should be considered with caution due to the limited number of studies included in these analyses of sub-groups" (Shen et al 2018 p86).

The six studies included in the meta-analysis varied in methodology, including:

- Class statin and dose.
- Anti-psychotic medication (risperidone most common).
- Duration of study (six weeks - 6 months).

1.6. APPENDIX 1B - CIPRIANI ET AL (2016)

Cipriani et al (2016) found six double-blind RCTs that compared LTCC antagonists with placebo or another drug for individuals with a primary diagnosis of bipolar disorder. Data from seventeen observational studies were also found.

The RCTs compared verapamil (LTCC antagonist) with a placebo (2 studies) or lithium (4 studies). The meta-analysis of the data found no difference between verapamil and the placebo or lithium in improving the symptoms of bipolar disorder.

Data from the observational studies suggested that LTCC antagonists had side effects (eg: headaches; changes in blood pressure and heart rate), interacted with other drugs, and were potentially lethal in overdose.

Despite these findings, Cipriani et al (2016) did not want to dismiss the use of LTCC antagonists because "the scientific rationale for targeting calcium channels in bipolar disorder has strengthened significantly in the past few years" (p1328).

⁴ Positive symptoms include hallucinations, while negative symptoms include catatonia, for example.

⁵ The one study using SANS found no significant difference.

⁶ Shen et al (2018) stated: "Based on the series of findings, we speculated that simvastatin improved psychiatric symptoms, especially negative symptoms may be via the increase of central dopamine receptors, the up-regulation of muscarinic receptor and NMDA [N-methyl D-aspartate] receptor binding, and the influence of serotonin transporter (SERT) functions" (p91).

1.7. APPENDIX 1C - GARCIA-ORJUELA ET AL (2016)

The clinical records of all patients treated for dependency to legally prescribed opioids at the University Hospital in Medellin, Columbia, between 1st January 2011 and 31st December 2014 were reviewed. In total, 3332 patient records in the study period, of which sixty fulfilled the DSM-IV criteria for opioid dependence.

This "includes three or more of the following, occurring at any time in the same 12-month period: (a) tolerance, (b) withdrawal, (c) the substance is often taken in larger amounts or over a longer period than was intended, (d) there is a persistent desire or unsuccessful efforts to cut down or control substance use, (e) a great deal of time is spent in activities necessary to obtain the substance or recover from its effects, (f) important social, occupational, or recreational activities are given up or reduced because of substance use, (g) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance" (Garcia-Orjuela et al 2016 p2).

There were equal numbers of men and women, and the median age was 43 years old. The treatment of pain was the main initiator of opioid use.

Thirty-seven individuals consumed more than one opioid type at a time, and 19 combined opioid with other substance misuse (eg: alcohol).

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2. OBESITY AND EATING

- 2.1. Obesity
 - 2.1.1. Images of obesity
- 2.2. Eating for health
 - 2.2.1. Vegan stigma
- 2.3. Miscellaneous
 - 2.3.1. Sedentary behaviour
 - 2.3.2. Transcranial direct current stimulation and expectation
 - 2.3.3. Paying for food safety
- 2.4. Appendix 2A - "Fat capital"
- 2.5. Appendix 2B - Transgenerational transmission
- 2.6. References

2.1. OBESITY

Adding fat to the waist (belly) is seen as a risk factor for health ⁷. For example, every inch added to the average waistline of a nation (above the healthy level), increased annual health care costs by around 4% (in a Danish study) (Wallis 2018).

As individuals reach middle-age, the resting metabolism slows by 1-2%, and excess fat is deposited around the abdominal organs (visceral fat) (as opposed to under the skin - sub-cutaneous fat). The former releases fatty acids directly into the liver, for instance, rather than into the general circulation (Wallis 2018).

But is visceral fat (or "belly fat") a cause or a marker of later health problems? There is some disagreement about the answer (Wallis 2018).

An idea that has appeared in recent years relates to dietary inflammatory index (DII) (Cavicchia et al 2009). This was developed to score diets for inflammatory properties (ie: reactions of the immune system, like increased C-reactive protein). The Mediterranean diet with fruits, vegetables, fish, and fibres has a low DII score, whereas the "unhealthy" Western diet has a high one (Varkaneh et al 2018).

So, a high DII score is linked to health problems like high blood pressure, and cardiovascular disorders, via obesity. But the studies are not all in agreement about the relationship between DII and obesity (Varkaneh et al 2018).

This led Varkaneh et al (2018) to perform a meta-analysis on this relationship. Twenty-two relevant studies were found that compared body mass index (BMI) in high and low DII groups. Overall, there was a significant

⁷ "Fat" may have a good side in biotechnology (appendix 2A).

positive association between DII score and BMI/obesity.

2.1.1. Images of Obesity

Gard and Wright (2005) commented that the images of obesity in the media "is as much to do with a social and cultural response to particular kinds of bodies as it has to do with health" (quoted in Couch et al 2015).

Couch et al (2015) interviewed 142 obese adults in Australia about their perceptions of news reporting about obesity. Six main themes were elicited from the analysis:

i) "Simplistic and inaccurate reporting that blames and shames" - news coverage that was "superficial, unrealistic, inaccurate, unfair, or unhelpful" (Couch et al 2015 p5).

The consequences was a "culture of stigma" as one woman commented about her experience: "The idiots who yell out comments to me when I'm trying to do something positive, like ride my bike home... It [the news] almost feeds those people and allows them to be more abusive because they look in the paper, and the paper is on a slightly subtler level, doing the same thing" (p6).

ii) "Weight loss success stories" - eg: one woman noted: "[The media] will talk to you when you've lost the weight, when you're a champion, but they don't want to talk to you beforehand" (p6). Another female participant noted that "a lot of stories... I think are probably unrealistic and that people can feel as if they're second class citizens because they can't do what someone else has done" (p6).

iii) "Freaks and enemies" - stories of severely obese individuals like "freak shows": "Forklifts needed to lift obese dead people in funeral homes; obese people needing specialised facilities and equipment to weigh them on which would normally be used for machinery or animals; walls knocked down to get an obese person out of their house; cranes used to lift obese people; hospital beds not big enough; and women who were so fat they were not able to go to hospital to have their babies" (Couch et al 2015 p6).

iv) "Absence of obese voices" - "The news hasn't taken the time to sit down and speak to someone obese. Not one person has come up to me in the media and said, 'Tell us your story? How did this happen and why did this happen and what is it that made it happen?' Questions like that are important questions" (female participant; p7).

v) "Absence of identity" - "Participants

specifically referred to their perceptions of how images of 'headless fatties' stereotyped and dehumanised obese individuals..., such as one participant commenting, 'Where the heads are blurred out and you've just got this huge one and a half meter wide bum in a tracksuit wobbling down the street'" (Couch et al 2015 p7).

vi) "Limited news consumption" - many participants admitted to not paying attention to obesity news reporting - eg: "I tune off, tune out. It depresses you so you don't want to know" (female participant; p7).

These themes captured the "lived impact" (Boere 2013) of obesity news reporting. Couch et al (2015) commented: "Our study suggests that the news media focus on spectacle, deviance, personal responsibility, and exclusion acts effectively as forms of social sanction and control, and contributes to the wider social regime of control and management of obese bodies" (p8).

The authors argued that this type of reporting can be seen in relation to panopticon and synopticon. Panopticon is Foucault's (1979) idea of surveillance of the many by the few as a means of social control. The surveillance is through medical institutions assessing, classifying, and diagnosing, and thereby creating "norms". This, then, becomes internalised as self-surveillance (Couch et al 2015). "Persons themselves and their bodies are turned into 'objects', 'self-surveillance emerges as a practice of control' (Eckermann 1997)" (Couch et al 2015 p3).

Synopticon (Mathiesen 1997) describes how the mass media is involved in this process, particular the many viewing the few (eg: celebrities' successes and failures). The viewing of the spectacle and deviance act as tools of social control. "The synopticon 'directs and controls or disciplines our consciousness' (Mathiesen 1997) through a whole system of messages, produced by many different media stories, rather than isolated single ones. News stories which highlight the importance of personal responsibility are an integral part in this system of messages, alongside stories which highlight deviance. This synoptical system of messages encultures the audience by creating a general understanding of the world; it produces and reproduces norms" (Couch et al 2015 p9).

Holland et al (2011) analysed the newspaper reporting of a health report presented to the Australian Government called "Australia's Future 'Fat Bomb'" in 2008. The report focused on obesity and overweight among middle-aged Australians and the projected consequences in the next twenty years.

The researchers described the framing of the report by the newspapers under the following headings:

a) The "fattest nation" frame - The idea that obesity rates were growing to the point of overtaking the USA were picked up by all the eight newspapers studied - eg: "Australia pips US as world's fattest nation"; "A nation of fatties - Australia outweighs United States on obesity scales" (p36). The report did not actually make any international comparisons (Holland et al 2011).

b) "The news value of 'fresh figures'" - The stories tended to use the "fresh figures" of the report to challenge any doubters - eg: "However, even leading nutritionist Jenny O'Dea from the University of Sydney - who recently claimed Australia's childhood obesity epidemic had been exaggerated - has backed the new figures, which suggest that the crisis for adults has been drastically underestimated" (from "The Age"; p37).

c) "Report provides a platform for denigrating obese people" - Phrases like "fat arses", "flabby flesh", and "unsightly slob" appeared in columns moralising on the "national disgrace" of obesity.

d) Dissent - Little mention of methodological issues with the report's figures (eg: representativeness of the sample), and under-reporting of contrary evidence.

Holland et al (2011) summed up: "In terms of tone and content there were no significant differences in initial news stories on the Fat Bomb report between tabloid and broadsheet newspapers. Each framed the report as further evidence of the reality and the extent of the obesity 'epidemic' or 'crisis' and the need for urgent action to address it. The lead author of the report was the only source quoted in the majority of stories and his comments were uncritically reproduced" (p42).

2.2. EATING FOR HEALTH

"Nutritional epigenetics" is the idea that nutrients/food affects the regulation of gene expression, particularly in relation to cancer, obesity, and diabetes (Landecker 2011).

Concentrating on the "experimental formalisation of food in nutritional epigenetics", Landecker (2011) noted "a larger historical context in which food is increasingly simultaneously alimentary and therapeutic - increasingly a tool for intervention in the health and character of present bodies and those of future generations" (p168).

The experimental work is usually with inbred mouse populations, and the changes in particular genes. For example, a gene coding for agouti signalling protein can be altered produce "obese yellow syndrome" - a yellow

coat and hyperphagia (overeating) ⁸ - and "even if food is restricted, these mice will become fatter on the same amount of food" (Landecker 2011 p175). Different diets can be tested with these particular populations to see which "colour" mice develop. "The ability to manipulate gene expression and thus phenotype with diet is the most notable feature of this mouse model system" (Landecker 2011 p176).

To sum up, "the basic logic of nutritional epigenetics is that the outside environment, in this case the kind and quantity of food eaten by a parent or an infant mouse, changes the inside constitution of the mouse at the molecular level. This is not a mutation - a change in genetic sequence - but a change in the potential of genes to be expressed in the body as protein products. The molecules in food affect the kind and number of molecules attached to DNA, and these molecules end up affecting the kind of body an organism has" (Landecker 2011 p176).

The idea that food affects physiology is not new, but it is "about food that affects the very systems that metabolise food; for example, the presence or absence of nutrients may cause the body to be built with different numbers of cells in its digestive organs, or to have more or less receptors for metabolic hormones" (Landecker 2011 p176). More than that, the nutritional environment of the pregnant mother can "act to 'set' the range of possibility for gene expression for the life of the organism and perhaps that of its descendants" (Landecker 2011 pp176-177) (appendix 2B).

Nutritional epigenetics is part of the "molecularisation" of biology (Rose 2006), which "involves the progressive perception, manipulation, conceptualisation and capitalisation of molecular spaces and processes in the body in life science" (Landecker 2011 p179). In the case of the experiments with mice, the diet fed has been transformed into molecules to manipulate to see the visible effects on gene expression.

Applying these points to humans, there is the rise of "functional foods" with "the emphasis on particular biologically active substances rather than on genes (or lack thereof), but the molecular optic here is also intensely cultivated. Food scientists, companies and consumers increasingly push toward foods that are supposed to carry a health benefit above and beyond the nutritive value provided by the caloric content, vitamins or minerals in that food... The anti-oxidant is a good example of the functional food; regardless of the nutritive value of the foodstuff, the anti-oxidant is supposed to reduce damage to cells and DNA from oxygen

⁸ The opposite is a brown coat and thinner.

free radicals in the body, and thereby protect the consumer from cancer or other diseases" (Landecker 2011 p186).

Landecker (2011) continued: "We are living in a time of the reconfiguration of food as medicine, as curative or preventive therapy; foods are central to the work consumers undertake to affect their present and future health or to work toward the 'perfect, imperishable' body (Chrysanthou 2002). Aimed at what Stefan Beck [eg: Beck and Niewohner 2006] has called the 'preventive self', even health foods and 'whole' foods are promoted for their abundance of beneficial molecules or their freedom from harmful ones; spinach becomes a 'good source of phytonutrients' in nutritionist framing (Pollan 2007). Conversely, food can also figure as the carrier of molecular substances that act as toxins or misplaced signals that perturb the body's regulation. That in this time food appears in nutritional epigenetics as a kind of mass molecular milieu for the epigenetic topography of populations is then one particular manifestation and intensification of this shift" (p187).

The irony is that "functional foods" are often portrayed and perceived as "natural" when in reality they are "synthetic". Scrinis (2008) suggested renaming them "functionally marketed foods", "for it is their mode of emphasising component nutrients and claimed health benefits over other aspects of a foodstuff that distinguishes them from other kinds of food" (Landecker 2011 p186).

2.2.1. Vegan Stigma

The choice of particular foods, like meat, can be as much a social decision as a practical one. Markowski and Roxburgh (2019) considered this in relation to "vegan stigma" (ie: the negative perception of individuals who eat no animal flesh or products).

These researchers set up five focus groups at a mid-west US university to discuss food choices. The participants included vegetarians (n = 14), vegans (n = 4), and omnivores (n = 16).

A key question in the focus groups was, "what comes to mind when thinking about vegans as people?". The responses included some positive comments, but the majority were negative (particularly by non-vegans). For example, among the vegetarians, vegans were viewed as attention-seeking, or regarding themselves as morally superior - eg: "Someone will say, 'I can't eat that - I'm vegan'. And it's like, 'Oh, you're vegan'. Like, you have to say it - you can't just say you can't eat it" (vegetarian 1); "Like it's kind of a moral war... I feel like some people that I have encountered, people who are vegan, have kind of, just like, this air about them"

(vegetarian 2) (p5).

The omnivore groups added the perception of vegans as aggressive - eg: "They're really vocal with their veganism and try to kind of like, force it down people's throats sometimes" (omnivore 4) (p5).

The researchers noted three ways the non-vegans responded to these perceptions:

i) Social distancing - eg: not having vegans as friends.

ii) Anticipating vegan stigma - the non-vegans were aware of the negative perceptions. For example, omnivore 6 stated: "Kind of like with your friends, if you become a vegan, they're like, 'Hey you wanna get a beer and a burger?' You're like, 'No, I'll get a water and some leaves or something'" (p6).

iii) Behavioural distancing - eating certain foods to show that the individual was not a vegan (eg: vegetarians and eggs).

Markowski and Roxburgh (2019) noted this last response in relation to reducing meat consumption in the USA for health reasons: "Unless made easier socially as well as personally, our results suggest that meat consumption reduction and plant-based diet adoption may still be met with significant resistance due in part to the shared negative sentiments associated with those who are meat-free and plant-based" (p8).

2.3. MISCELLANEOUS

2.3.1. Sedentary Behaviour

Sedentary behaviour (eg: sitting for hours at a time) has been linked to negative health outcomes (eg: cardiovascular diseases; mortality). Diaz et al (2019) investigated whether replacing sedentary time with light intensity physical activity (LIPA) or moderate-to-vigorous intensity physical activity (MVPA) reduced the health risks.

The data came from the REGARDS (Reasons for Geographic and Racial Differences in Strokes) study in the USA, which recruited over 30 000 over 45s between 2003 and 2007. Accelerometer data for one week were available for 7999 participants. Physical activity was counted in one-minute epochs, and during a day, a total of 0-49 was defined as sedentary, 50-1064 as LIPA, and >1065 as MVPA. The outcome measure was all-cause mortality.

It was calculated that replacing 30 minutes of

sedentary behaviour with 30 minutes of LIPA reduced the mortality risk by 17%, and 30 minutes of MVPA reduced the risk 35%. So, "movement in itself (doing 'something'), irrespective of intensity, is beneficial" (Diaz et al 2019). Less active individuals gained more from physical activity than more active participants.

The accelerometer could not distinguish between sitting and standing, so standing would be defined as sedentary, suggesting an overestimation of sedentary time. Furthermore, only seven days of data were collected.

2.3.2. Transcranial Direct Current Stimulation and Expectation

Transcranial direct current stimulation (tDCS) is a possible treatment for eating-related conditions, like frequent food cravings and over-eating. But studies on single-session tDCS to the dorsolateral prefrontal cortex find contrary results - reductions in food consumption and craving, reductions in craving but not eating, and no reductions in either (Ray et al 2019).

Ray et al (2019) argued that the difference in findings depended upon expectation of treatment outcomes (ie: the patient's beliefs about the treatment). Even in studies with sham tDCS as a control, patients can tell and thus have different expectations. "Active stimulation induces transient physical sensations such as itching and tingling throughout the session... while the standard sham condition delivers current only for the first and last minute of the session. Hence participants are more likely to guess that the active condition is the real one..., logically increasing the likelihood of treatment expectations" (Ray et al 2019 p2). Furthermore, sham tDCS produces a placebo effect.

Ray et al (2019) reported a manipulation of expectation study with seventy-four US students divided into four conditions:

1. Received sham tDCS and told beforehand sham (ie: no expectation of improvement).
2. Told sham, but received real tDCS (ie: no expectation of improvement, but if treatment works, there will be improvement).
3. Told real, but got sham (ie: placebo effect).
4. Told real, got real (ie: expectation and treatment).

The expectation was created by the phrase by the

experimenter, "people tend to crave less and eat less junk food after real tDCS" (p2). After twenty minutes of the tDCS condition, food craving was measured by rating images of food, and actual eating by 20 minutes alone in a room with sweets and cookies.

Participants told that there were receiving real tDCS (conditions 3 and 4) had lower craving scores than participants told sham (conditions 1 and 2). The craving score did not vary with actual receiving of tDCS or not. The same was true for actual eating - mean consumption of around 400 kcals in conditions 3 and 4 versus 550 kcals in conditions 1 and 2 (ie: 37% less), while the mean consumption of 450 kcals was recorded in conditions receiving real or sham tDCS (ie: no difference).

2.3.3. Paying for Food Safety

Reducing the risk of food-borne illness (eg: food poisoning) is a public good, but how do individuals view such a risk?

Smith et al (2014) used the willingness to pay extra as a measure of risk, and offered around 1600 US consumers three options in their experiment:

- Home test kits for food-borne contaminants that individuals could purchase (individual responsibility for prevention).
- More food safety inspectors (government responsibility for prevention).
- Availability of medicine to combat food-borne illness severity (individual response to sickness).

The degree of choice of these options was varied by the researchers, and the cost of the options.

Smith et al (2014) found that in "the specific case of the risk of food borne illness, it seems clear that consumers are willing to pay to improve food safety and in this survey they preferred the plan that offers them private control over the risk reduction" (p192). It was calculated that individuals would be willing to pay around \$250 per year to combat the risk of food-borne illness, particularly for individual prevention (home test kits).

2.4. APPENDIX 2A - "FAT CAPITAL"

Ehlers (2015) pointed out that "fatness is understood as a bodily deficiency, and 'fat bodies are constructed (and discriminated against) as being unhealthy, ugly, and 'out of place'" (Colls 2007)" (p260). On the other hand, fat (adipose tissue) is viewed

differently in the "domain" of breast reconstruction following breast cancer surgery⁹. In fact, "in this domain it becomes evident that certain forms of fat are considered desirable and good: indeed, fat represents a form of corporeal capital" ["fat capital"] (Ehlers 2015 p260), or what Waldby and Mitchell (2006) called a "tissue economy". Waldby (2002) referred to the "biovalue" of fat in this context, which is "the value extracted from the vital properties of living processes" (Rose 2006).

"Fat is distinct from other forms of excess body material, such as ova, sperm, and embryos, precisely because where it is deemed excessive, it is pathologised. It is also distinct, however, from other forms of pathologised bodily waste (such as faeces, urine, and pus) because of its potential utility in a therapeutic context. Fat becomes biovalue in breast reconstruction because its very vitality - its live-ness, malleability, and capacity - can be harnessed and redeployed, and this takes place 'in order to promise a return to corporeal wholeness' after breast cancer surgery" (Ehlers 2015 p261).

Fat has become a commodity to be traded and profited from as in the neoliberal way. Developments in biotechnology will allow for "fat banks", for instance, where individuals can store surplus fat for future use. Even the gaining of surplus fat for later use - "for instance, if a woman does not have adequate fat reserves to make two full C-cup breasts, so puts on weight over a relatively short period of time in order to achieve the required amount" (Ehlers 2015 p264)¹⁰.

More than that, the discovery of adipose-derived stem cells in fat that could be used in tissue engineering and regenerative medicine.

2.5. APPENDIX 2B - TRANSGENERATIONAL TRANSMISSION

An example of recent work with mice on transgenerational transmission of obesity is Sarker et al (2018).

It has been shown previously that pregnant mice fed a high-fat diet (HFD) have offspring who in later life have hyperphagia (eg: Sun et al 2012). It is suggested that the diet of the mother alters gene expression in the

⁹ In a common form of (autologous) breast reconstruction, fat, muscle, and skin from the lower abdomen is used to make a breast. "While reconstruction using silicone implants has the same end-goal, using fat is generally considered more successful, in that an autologous breast will visually appear and feel more 'natural' than those created through the use of implants: they become fully integrated into the body and respond to changes in body weight, and they enable the crafting of breast ptosis (fall or drooping) that is not achievable with implants" (Ehlers 2015 pp262-263).

¹⁰ A US company is offering "fat bank packages" (Ehlers 2015).

offspring in the womb leading to physiological changes (eg: to hypothalamic appetite regulatory system) (Sarker et al 2018).

There is some evidence that the diet of the pregnant mother may also influence future generations (eg: Dunn and Bale 2011).

Sarker et al (2018) fed female mice (generation 0; G0) a HFD or a normal diet before mating, and during pregnancy and lactation (ie: nine weeks). G1 males were later mated with naive females, and their male offspring (G2) did the same to give the next generation (G3).

Despite a normal diet for G1 to G3 mice, there was evidence of obesity, particularly for G3 males from the HFD G0 mothers (ie: great grandmothers), while G3 females from the same ancestors showed addictive-like behaviours (suggesting that reward centres in the brain had been altered by the G0 HFD).

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3. MENTAL HEALTH TOPICS

- A. Post-deployment screening
- B. ADHD experienced
- C. Left-behind children
- D. Chronic fatigue syndrome
- E. Game transfer phenomena
- F. Screen time
- G. NFL suicide
- H. Personality disorders
- I. Gut microbiome and mental health
- J. Mental health of perpetrators of IPV
- K. References

A. POST-DEPLOYMENT SCREENING

It has been estimated that around 5% of UK military personnel in Iraq and Afghanistan between 2001 and 2014 had post-traumatic stress disorder (PTSD), 20% psychological distress, and 16% alcohol problems (Rona et al 2017). One suggestion to deal with this issue is post-deployment mental health screening.

Rona et al (2017) reported the Post Operational Screening Trial (POST), which evaluated post-deployment screening in the Royal Marines and Army. Four hundred and thirty-four platoons were randomised to receive the intervention or not 6-12 weeks after deployment with reassessments between 10-24 months later. The screening group were offered tailored advice relating to their mental health status, while the control group received general advice, after completion of mental health questionnaires.

Overall, "the provision of tailored help-seeking advice between 6 and 12 weeks after return from deployment was ineffective at decreasing the prevalence of PTSD, depression or GAD [generalised anxiety disorder], and alcohol misuse over a period of 10-24 months... [There was] no evidence to support the idea that informing someone that they were experiencing mental health disorder symptoms encouraged them to seek help from mental health-care providers" (Rona et al 2017 p1418).

So, the study did not support the introduction of this type of post-deployment screening. The researchers offered some explanations for the findings including "the heterogeneity of evolution of mental disorders over time, possible absence of interest in engaging with services in some cases, and potential unwillingness to continue treatment among those who engage with services. Previous research suggests that between a third and half of treated personnel do not show meaningful symptom improvement and that those who improve remain above

thresholds usually used to define caseness after trauma therapy" (Rona et al 2017 p1421).

Interestingly, one-third of the screening group did not view their tailored advice. This "might be because of low interest, mistrust in health services, fear of receiving bad news, or a belief that mental health issues are not personally relevant" (Rona et al 2017 p1419). But those individuals with PTSD, anxiety or depression at baseline were more likely to view the tailored advice.

B. ADHD EXPERIENCED

Attention deficit hyperactivity disorder (ADHD) can be summarised as the characteristics of "a failure to pay attention to details, difficulty organising tasks and activities, excessive talking, fidgeting, and an inability to remain seated in appropriate situations" (Nielsen 2017 p260). The focus of the disorder was originally children, but adults are increasingly being diagnosed (Nielsen 2017).

Concentrating on adults, Nielsen (2017) presented ADHD as "impairment in sense of time and difference in rhythm" (ie: "a certain being in the world"). From interviews with thirteen adult sufferers in Denmark, Nielsen (2017) distinguished three elements of "an embodied experience of being 'out of sync'":

- i) "An inner restlessness and bodily arrhythmia";
- ii) "An intersubjective desynchronisation between the individual and his or her surroundings";
- iii) Difficulties in social skills producing a feeling of "lagging behind socially".

Three quotes from the interviewees give an idea of the experience of ADHD:

- "Kelly" - "I've been very flighty in my thoughts and in my construction of sentences, and earlier, it brought a lot of misunderstandings. I believe I've said a whole word or a full sentence, but I haven't. A word such as 'not' is quite crucial in a sentence! If I have a sentence in my head, and I'm about to say it, but I skip the essence while I keep on talking, it's not hard to see why people don't get it. So in that perspective, there's been many misunderstandings and much frustration and I've been thinking: why can't people understand what I just said. But I haven't necessarily" (p263).
- "Judith" - "It just not there. The sense of time. It's now, now, now. It's about being in the present. That's

how we are. I only just learned about time. Well, not watching the clock and seeing what time it is, but I mean sense of time and having an idea about how long things take. How long it takes to do grocery shopping and knowing when I'll be back home again. Like getting a sense of it" (p265).

- "Lilly" - "I have always been kind of... back then... I distanced myself... and I've just been thinking: my brain is speeding so fast, and it actually... it has always been like that with me. Because it was always racing. 20,000 thoughts. No one had any idea that it was racing like crazy in here. And I remember that, because it was also like that, when I was a kid. I could stay in my own world and those thoughts were just going around and round. I kept to myself. I wasn't open. But I was very observing, I remember that. And was thinking a lot of thoughts. I remember how I felt. And when I was looking at myself in the mirror I remember that inner... I felt like... I was restless inside and I felt like... I don't know..." (p267).

C. LEFT-BEHIND CHILDREN

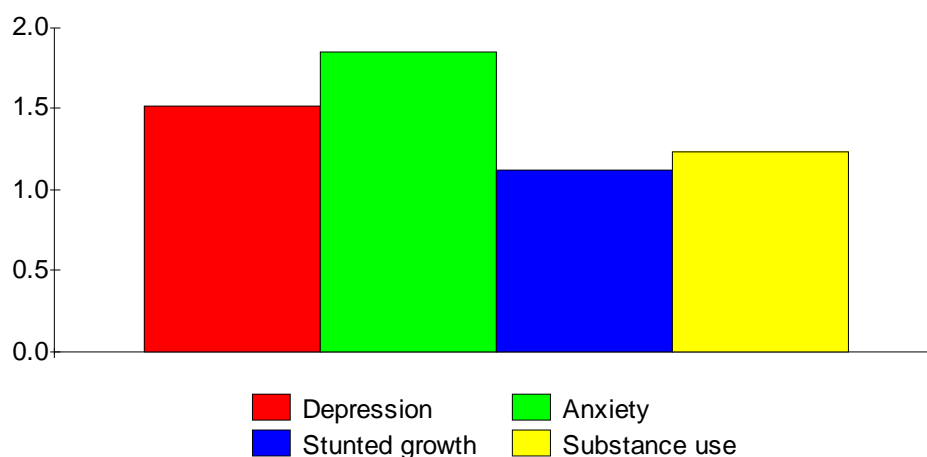
One in seven individuals in the world is a migrant, mostly from rural to urban settings, or from poorer to richer countries. International migrants send over \$US 600 billion per year home to their families, which can include left-behind children (Fellmeth et al 2018). The experience of such children varies.

What about the health status of left-behind children? Fellmeth et al (2018) found 111 studies in their attempt to answer this question. These came from sixteen countries between 1994 and 2017, and totalled over 106 000 left-behind children and adolescents (and over 158 000 of non-migrating parents as comparison).

Meta-analysis showed that compared to children of non-migrating parents, left-behind children had a significantly higher risk of, for example:

- Depression, anxiety, and suicidal thoughts.
- Wasting and stunted growth.
- Substance use (figure 3.1).

In summary, "as a group, left-behind children and adolescents have worse outcomes than children of non-migrating parents, especially with regard to mental health and nutrition" (Fellmeth et al 2018 p2574). There was no overall evidence of health benefits for the left-behind children from parental migration (though there may be economic benefits).



(Data from Fellmeth et al 2018 figure 4)

Figure 3.1 - Relative risk for left-behind children (where 1.00 = risk for children of non-migrating parents).

This general review confirmed country reviews for rural China (Qin and Albin 2013) and the Philippines (Reyes 2008).

Interestingly, Graham et al (2015) reported negative health consequences for other left-behind family members (eg: mothers; other carers).

The review by Fellmeth et al (2018) was unable to establish the factors that explained the poorer health of left-behind children (eg: living conditions; level of other caregiver supervision). "Children of parents migrating because of extreme poverty, disasters, or oppression are likely to have worse health outcomes than children from wealthier migrant families that are financially stable with access to adequate health care. Residing with siblings and relationships between children and their caregivers could also be important" (Fellmeth et al 2018 p2577).

Over four-fifths of the studies in the review came from China, and involved internal, rural-to-urban labour migration.

The studies in the review varied in length of parental migration (minimum of six months), reason for migration (eg: labour; forced by armed conflict), and outcome measures, for instance (Fellmeth et al 2018).

D. CHRONIC FATIGUE SYNDROME

Chronic Fatigue Syndrome (CFS) may originate from immune system dysfunction, though studies are inconsistent about the exact mechanism (eg: C-reactive

protein) (Russell et al 2019). The problem is that individuals with CFS are usually studied after the condition has begun, and so there are unlikely to be pre-illness measures.

An experimental approach would induce the illness, and so take measures before and after the onset. Getting around the ethics of deliberative infection, there is persistent fatigue after treatment of the hepatitis C virus (HCV) with interferon-alpha (IFN-a). Many patients experience CFS-like symptoms after IFN-a treatment has ceased. Thus, it is "a suitable model to mimic the immune trajectory of people who develop CFS, at baseline (ie: before the immune trigger), during the immune trigger, and after the immune trigger has ceased" (Russell et al 2019 p277).

Russell et al (2019) studied fifty-five liver patients in London with HCV treated with IFN-a. Eighteen patients reported persistent fatigue in the six months after treatment, and they were compared to the rest of the sample. The fatigued individuals had differences in immune functioning at baseline (eg: interleukin levels). Russell et al (2019) summed up: "findings from this study support the hypothesis that abnormal immune mechanisms are important in CFS, but only early in the course of the illness, around the time of the trigger, rather than when the syndrome is established. Moreover, our study confirms the importance of the acute fatigue response to the trigger, rather than of the recovery period preceding the illness" (p283).

E. GAME TRANSFER PHENOMENA

Game transfer phenomena (GTP) was first used by Ortiz de Gortari in her dissertation in 2010 to describe "altered sensorial perceptions, mental process, and behaviour transfer from the video game world to real-life context" (Ortiz de Gortari and Griffiths 2016 p470).

Ortiz de Gortari and Griffiths (2015) distinguished three dimensions of GTP:

- i) Inner or outer phenomena - eg: seeing images from the video game superimposed on physical objects in the real world.

- ii) Self-generated or non-self-generated - eg: hearing one's own thoughts.

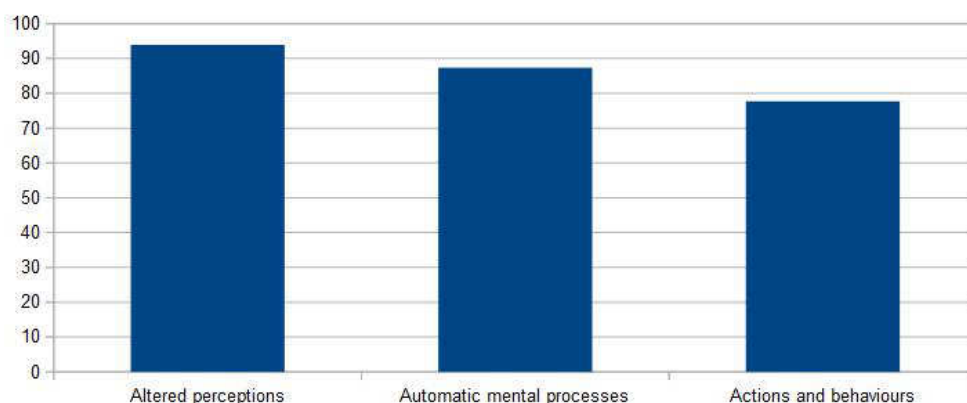
- iii) Voluntary or involuntary - eg: involuntary outbursts using game content.

Ortiz de Gortari et al (2011) interviewed 42 Swedish frequent video gamers aged 15-21 years old, and found four themes related to GTP:

- Dreams - dreaming about aspects of video game.
- Automatic thoughts and urges - thinking about the video game in everyday life.
- Altered perceptions - eg: misperceiving real-life object as something from video game.
- Behaviours - eg: using narrative slang from video game in everyday life.

Poels et al (2014) found three similar themes in their analysis of an online survey completed by 511 "World of Warcraft" gamers - memory recalls from the game in real-life, cognitive biases (eg: attention bias towards video game-related cues), and game content in dreams, daydreams, and everyday vocabulary.

Ortiz de Gortari and Griffiths (2016) reported a larger online survey with 2362 gamers recruited via relevant community forums and Facebook. GTP was reported by almost all respondents, but was not necessarily related to length of playing. Over 90% reported altered perceptions, around three-quarters automatic thoughts, and behaviours (figure 3.2).



(Data from Ortiz de Gortari and Griffiths 2016 table 3 p475)

Figure 3.2 - Frequency of GTP (%).

F. SCREEN TIME

One in four children begin school with deficits and delays in developmental outcomes (eg: language, motor skills) (Madigan et al 2019). Is early digital media use ("screen time") a factor here?

"Although some benefits of high-quality and interactive screen time have been identified, excessive screen time has been associated with a number of deleterious physical, behavioural, and cognitive outcomes. While it is possible that screen time

interferes with opportunities for learning and growth, it is also possible that children with delays receive more screen time to help modulate challenging behaviours. For example, toddlers who struggle with self-regulation have been shown to receive more screen time than those without difficulties" (Madigan et al 2019 ppE1-E2).

In terms of establishing the direction of association, Madigan et al (2019) analysed data from the "All Our Families study" in Alberta, Canada. This involves over 3000 pregnant women between 2008 and 2010. Data were collected at 24, 36, and 60 months old, including measures of developmental progress, and mother-reported use of particular electronic mediums on a typical day (eg: watch TV; use a computer or gaming system).

On average, total screen time was 17 hours per week at two years old, 35 hours at three years old, and ten hours at five years old. Altogether, "higher levels of screen exposure relative to a child's average level of screen time were associated with significantly poorer performance on developmental screening tests at the next study wave relative to a child's average level of developmental milestones but not vice versa" (Madigan et al 2019 pE4). Thus, greater screen time at 24 months old was associated with poorer developmental scores at 36 months, and 36 months and 60 months respectively, giving a clear direction of association.

The researchers offered an explanation: "When young children are observing screens, they may be missing important opportunities to practice and master interpersonal, motor, and communication skills. For example, when children are observing screens without an interactive or physical component, they are more sedentary and, therefore, not practicing gross motor skills, such as walking and running, which in turn may delay development in this area. Screens can also disrupt interactions with caregivers by limiting opportunities for verbal and non-verbal social exchanges, which are essential for fostering optimal growth and development" (Madigan et al 2019 pE5).

The key methodological issues with this study included (Madigan et al 2019):

i) Changes in technology and technology use over the study period. Smartphones, for example, were of limited use in 2011 (the first data collection point), and classed as "other screen-based device".

ii) Measurements relevant here were not taken before 24 months old.

iii) "Screen time" was treated as a unidimensional

variable - ie: no distinction in media content quality (eg: educational).

iv) Use of maternal reports only (ie: no paternal measures).

v) The controlling of variables during analysis (eg: gender; maternal education level), but some relevant ones may have been missed (eg: time mother spent with child and screen).

In terms of the key strengths of this study, it was a large-scale, longitudinal study, which was able to show the direction of association.

G. NFL SUICIDE

There has been recent concern about chronic traumatic encephalopathy (CTE) among retired American football (NFL) players from concussion and head injuries during the game. A feature of CTE is suicide, though this is disputed (Webner and Iverson 2016).

Webner and Iverson (2016) pointed out that there is limited information about suicide by retired NFL players. These authors rectified the problem using publicly-available information. Between 1920 and 2015, there have been over 26 000 professional NFL players, of which twenty-six individuals had completed suicide (but nearly half since 2009).

Webner and Iverson (2016) concluded that "it is possible that specific types of neuropathology associated with CTE, such as depositions of hyperphosphorylated tau in perivascular regions of the brain and depths of sulci, contribute to the development of depression and suicidality in some people, but this has not been established empirically" (p1720). However, other studies have found at-risk factors like mental health problems, and chronic pain and opioid use among retired players (Webner and Iverson 2016).

H. PERSONALITY DISORDERS

How many people in the adult general population suffer from a personality disorder (PD)? Studies vary in their answer for Western countries, so Volkert et al (2018) performed a meta-analysis (which establishes an average from a number of studies).

Firstly, the researchers had to find relevant studies, for which they focused on 1994 to mid-2017. The search terms "PD", "axis-II disorders" and "prevalence" were used in three relevant academic databases, while the references in one study were used to find further

studies.

Three inclusion criteria were set:

- Prevalence rates of adults (16 years old and over) In Europe, North America, Australia or New Zealand.
- Standardised PD diagnosis by DSM IV or 5, or ICD-10.
- Published in English or German.

Ten studies met these criteria (reported in 27 articles) ¹¹, and they were rated for methodological quality using a version of the Newcastle-Ottawa Scale (Wells et al 2004). This gives a score of potential bias, which in this study was 0-5 (where a higher score is less risk of bias). Elements scored in a study included sample representativeness and size, details of non-respondents, and diagnosis of PD. Most of the studies had a low risk of bias (ie: good quality methodological), but the difference between respondents and non-respondents was rarely investigated.

Overall, the mean prevalence rate for any PD was 12% (range 6-20%). "Hence, personality disorders have a similar prevalence to physical health conditions, like low back pain and chronic respiratory diseases (approximately 12 and 7% each in high-income adult populations), and are much more prevalent than diabetes mellitus and cardiovascular diseases (each approximately 3% in high-income adult populations) or depressive and anxiety disorders (each approximately 6%)" (Volkert et al 2018 p714).

For individual PDs, the rates included 1.9% for borderline, 3% anti-social, and 1.2% narcissistic.

In total, over 113 000 individuals were included in the studies, which varied in methodological elements, including:

- Country of study - seven countries, and most studies from the USA (n = 4).
- Diagnostic interview - eg: Structural Clinical Interview for DSM Disorders Axis II; International Personality Diagnostic Examination.
- Prevalence time period - eg: lifetime (ie: ever); last five years.
- Sampling - random or representative; some stratification by ethnicity.

¹¹ Initially, 1427 records found, which was narrowed to 75, and 48 of these excluded (eg: no standardised diagnosis; use of DSM-III criteria).

- Age - ranged from 16 to 94 years with mean 33-51 years.
- Gender - ranged from 50 to 63% females.
- Type of PD - most common was borderline (in nine studies).
- Sample size - from 557 to 43 093.
- Details of statistical analysis varied.
- Expert-rated measures/clinical interviews vs self-reports - prevalence estimates lower with former method. "Self-report measures, which are more economic to use, have been criticised for overestimating prevalence, whereas diagnostic interviews require clinical expertise, intensive training and are more time consuming" (Volkert et al 2018 p714).

I. GUT MICROBIOME AND MENTAL HEALTH

The human microbiota includes all micro-organisms (bacteria, eukaryotes, archaea, and viruses) within the human body, and the microbiome is these microbes and their genes (Malan-Muller et al 2018). Malan-Muller et al (2018) considered the role of the gut microbiome in anxiety disorders.

Studies of the microbiota-gut-brain (MGB) axis (ie: the bidirectional communication between the brain and gut microbiota) have mostly involved animals, usually with germ-free (GF) individuals (ie: no microbiota). For example, the microbiota of the high-anxiety GF mouse strain are transplanted via faecal sample into the low-anxiety GF mouse strain. Behaviour changes have been observed (Malan-Muller et al 2018).

Experimental manipulation like this is easier with non-human animals, whereas the human studies tend to be observational. For example, a comparison of the faecal microbiota of individuals with and without major depression. Studies vary in their findings on bacterial diversity (eg: some show increased in depressed individuals and some show less diverse) (Malan-Muller et al 2018).

The nearest to manipulation of the microbiota in humans is the use of probiotics (live, beneficial micro-organisms). A few controlled trials have been tried, which show "some potential" for probiotics to change behaviour positively (in relation to anxiety disorders). However, methodology is an issue. "Probiotic trials require careful design as several factors may influence the outcome of such interventions, including confounding factors and matching of patients and controls. Comparing

the results of these studies is complicated by the between-study differences, such as differences in probiotic strains, treatment duration, outcome measures, as well as gender and age distribution. In addition, samples sizes are relatively small and larger cohorts would be required to verify these findings" (Malan-Muller et al 2018 p95). Consequently, Malan-Muller et al (2018) would only accept that probiotic intervention studies "could be" used with individuals with anxiety disorders.

J. MENTAL HEALTH OF PERPETRATORS OF IPV

The mental health of victims of intimate partner violence (IPV) is well researched, but less so the mental health of the perpetrators.

Sesar et al (2018) reported a review of the literature published between 1987 and 2017. In total, 137 recent articles were found.

The following aspects of mental health were reported:

i) Anger and hostility - Some evidence of differences between violent and non-violent men here. But definitions of the concepts vary and need to be clearer.

ii) Anxiety disorders - Post-traumatic stress disorder (PTSD) and IPV, in particular, but also high frequency of generalised anxiety disorder (GAD), panic disorder, and social phobia.

iii) Depression - Both male and female perpetrators, but males are more likely to manifest their symptoms of depression in anger.

iv) Suicidal ideation and behaviour - Attempted suicide is high among male perpetrators, but the research is less clear about suicidal thoughts.

v) Personality disorders - eg: narcissistic personality disorder and anti-social personality disorder in both sexes. "Different forms of personality disorders are associated with different types of violent behaviour towards intimate partners... The differences are not just manifested in the type of violent behaviour but also, in the incidence of violent behaviour and stress reaction to a violent situation" (Sesar et al 2018 p229).

vi) Other behaviours - eg: alcoholism (very common); problem gambling.

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4. INEQUALITIES AND CHANGES

- 4.1. Life expectancy
 - 4.1.1. Geography
 - 4.1.2. Gender
- 4.2. Changing diseases
- 4.3. Appendix 4A - Measuring ageing
- 4.4. References

4.1. LIFE EXPECTANCY

Deeg et al (2018) reported data from the Longitudinal Ageing Study Amsterdam which showed increases in total life expectancy and cognitive healthy life expectancy over the last quarter of a century in the Netherlands, but, at the same time, life expectancy in good physical health was declining ¹².

Crimmins (2018) asked: "Does it make sense that as mortality declines and life expectancy increases, healthy physical life expectancy does not increase?" (p1582). She considered some answers:

- Not study flaws as the Amsterdam study was well designed.
- The findings confirm other studies around the world (though comparisons can be limited by the different definitions used).
- The success of extending life with medical improvements means that more people with illnesses and disabilities do not die.
- Improvements in early life experiences that affect later cognitive health (eg: increased educational levels and reduced cognitive decline).

4.1.1. Geography

One inequality in life expectancy is geographical. Dwyer-Lindgren et al (2017) reported an example of this with data for the USA between 1980 and 2014 based at county level.

In 2014, the nation-level life expectancy was 79.1 years overall, and 76.7 for men and 81.5 for women. However, the gap between the lowest (eg: in eastern Kentucky, South and North Dakota) and highest (eg: in central Colorado) at county level was 20.1 years.

¹² Measuring ageing has its difficulties (appendix 4A).

Overall, life expectancy at birth increased by around five years during the study period. "This masks massive variation at the county level; however, counties in central Colorado, Alaska, and along both coasts experienced much larger increases, while some southern counties in states stretching from Oklahoma to West Virginia saw little, if any, improvement over this same period" (Dwyer-Lindgren et al 2017 p1005).

In terms of the reasons for the inequalities in life expectancy, the following factors were important:

- Socio-economic (eg: median household income for county; percentage of population below the poverty line).
- Race/ethnicity (eg: differences in unemployment rate).
- Behavioural and metabolic factors (eg: prevalence of obesity; cigarette smoking).
- Health care factors (eg: physicians per 1000 population).

To paint a simple picture, low life-expectancy counties had a large number of households below the poverty line, and ethnic minorities, unhealthy behaviours including obesity, and fewer health care facilities, for example.

4.1.2. Gender

Crimmins et al (2019) considered gender differences in health and mortality. "Common generalisations are that men live shorter but healthier lives and that women live longer lives but in worse health. Such generalisations are an oversimplification, and sex differences in health cannot be described so succinctly" (Crimmins et al 2019 p135). Crimmins et al's (2019) view was that "in some aspects of health, men do worse; in others, women do worse" (p135).

These researchers analysed nationally representative data from a variety of countries under four main headings:

i) Life expectancy - Generally, male life expectancy is lower than that of females around the world. Though this difference has been reduced by changes in societies (eg: similar numbers of men and women smoking in the USA in recent years), or increased as it is "highly contingent on the circumstances in which people live and mortality-related epidemiological conditions such as disease dominance, public health infrastructure, and healthcare resources" (Crimmins et al 2019 pp137-138). For example, the life expectancy gap is ten years in Kazakhstan, but much less than a year in Nepal (Crimmins et al 2019).

ii) Disability - Men report less disability in self-reported surveys. In terms of studies with objective measures of functioning in later life (eg: Wheaton and Crimmins 2016), "women have lower grip strength... and slower gait speed... Results for chair stands and tandem stand... indicated men were more mobile and had better balance. Although the differences between countries in the performance of men and women are variable, we can conclude that men are stronger and faster" (Crimmins et al 2019 pp138-139).

iii) Diseases - The differences are inconsistent with men more likely to have heart attacks (ie: lethal conditions), and women more likely to have arthritis (ie: debilitating conditions), for example.

iv) Physiological status - eg: hypertension; cholesterol. For instance, based on World Health Organisation data from nearly 190 countries, the "level of hypertension for men exceeds that for women in most countries, but there are several countries where the prevalence of hypertension is higher for women. For high concentrations of total cholesterol, the patterns are reversed, with women having a higher prevalence of risk-level total cholesterol in most countries, yet in some countries men are higher" (Crimmins et al 2019 p142).

Crimmins et al (2019) ended with a summary: "We conclude that men live shorter lives than women at present. Women have more functioning problems now at least partly because they are not as strong, mobile, or steady as men. Currently, men have more lethal conditions, whereas women have more disabling chronic conditions. Men and women have somewhat different health problems; one sex cannot be characterised as having better health. Our strongest conclusion is that male/female differences in health are highly dependent on historical time and geographic location" (p145).

4.2. CHANGING DISEASES

Changes in the modern world like urbanisation, and economic inequality, as well as to the climate, are "creating conditions in which diseases emerge faster and spread further" (Moyer 2018).

Concentrating mainly on the USA, Moyer (2018) noted the following patterns:

a) Increases in rates of hepatitis A, Legionnaires' disease, and other infections carried by viruses, bacteria, and parasites in the cities.

For example, a two-thirds increase in Legionnaires' disease in New York city between 2016 and 2017. The city

environment aids this increase with, for instance, large water towers on buildings where the bacteria that cause this disease can breed as well recent changes to save energy (eg: reducing the water temperature and flow).

b) The return of infectious diseases, once thought in decline, based in economic inequality.

Individuals in poverty are more likely to live in unclean conditions, have poor nutrition, experience stress and work when sick, have limited health care facilities, and abuse substances - "all known infection risk factors" (Moyes 2018).

Individuals in low-paid jobs, who have to work when ill because of lack of sick pay, who work in restaurants may lead to the spread of diseases throughout the population.

More generally, Riley (2018) noted biological differences in bacteria between rich and poor areas of the same city with the case of streptococcal strains in Salvador, Brazil. The strain in the slum areas was more resistant to vaccines than the strains in the wealthy neighbourhoods.

Climate change is increasing how diseases spread as in the "migration" of diseases with rising temperatures. For example, the mosquito-borne virus, Rift Valley fever, which infects livestock mostly (but also humans) first recorded in Kenya in the 1930s, but has appeared in the Arabian peninsula in the 21st century (Parshley 2018).

4.3. APPENDIX 4A - MEASURING AGEING

"While everyone ages, the rate at which aging occurs is heterogeneous, and between-person variations in the pace of aging manifest as differences in susceptibility to death and disease" (Liu et al 2018 p3). So, how to measure ageing?

One method is to compare observable characteristics of the individual to the general population at a certain chronological age, and so it is possible to say that a person is younger or older than expected on a biological or physiological level.

Liu et al (2018) proposed an alternative called "Phenotypic Age" (PA), which describes "mortality risk among persons of the same chronological age, using data from a variety of multi-system clinical chemistry biomarkers. In general, a person's Phenotypic Age signifies the age within the general population that corresponds with that person's mortality risk. For example, 2 individuals may be 50 years old chronologically, but one may have a Phenotypic Age of 55 years, indicating that he/she has the average mortality risk of someone who is 55 years old chronologically,

whereas the other may have a Phenotypic Age of 45 years, indicating that he/she has the average mortality risk of someone who is 45 years old chronologically" (p4).

The researchers applied the concept of PA to data from the Fourth National Health and Nutrition Examination Survey (NHANES IV) in the USA. Over 11 400 adults aged twenty years old and older were the sample. Nine biomarkers, including mean cell volume, C-reactive protein, and glucose, were used to calculate PA.

It was found that individuals with "the highest Phenotypic Ages relative to their chronological ages had much steeper declines in survival over the approximately 12.5 years of follow-up" (Liu et al 2018 p11).

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5. FERTILITY, PREGNANCY, BIRTH TOPICS

- 5.1. PTSD and childbirth
- 5.2. Pregnancy and breast cancer
 - 5.2.1. A sociological view
- 5.3. Fertility add-ons
- 5.4. Abortion denied
- 5.5. References

5.1. PTSD AND CHILDBIRTH

Post-Traumatic Stress Disorder (PTSD) as diagnosed by accepted criteria (eg: DSM-IV) (table 5.1) has been estimated in up to 7% of women in the general population after childbirth (though 1-2% is an agreed rate)¹³, but maybe three times higher among at risk groups (eg: stillbirth women) (Ayers et al 2008).

Summarising discussions of experts, Ayers et al (2008) noted: "We know very little about whether PTSD following childbirth is a direct result of birth or purely a continuation of PTSD in pregnancy. Although the majority of prevalence studies have measured PTSD symptoms in relation to childbirth, few have examined trauma history, PTSD symptoms in relation to other traumas, and PTSD in pregnancy" (p242).

Furthermore, the course of PTSD after birth is unclear with different studies finding increases, decreases or no change over time. "It is possible that the course of PTSD following childbirth may differ to following other events because women have daily contact with their baby, which could either exacerbate symptoms or reduce avoidance through acting as a form of exposure" (Ayers et al 2008 p242).

- A - Trauma involves "actual or threatened death/serious injury".
- B - Re-experiencing (eg: recurrent distressing dreams).
- C - Avoidance and numbing (eg: avoid places and reminders).
- D - Arousal (eg: difficulty sleeping).

Table 5.1 - Key criteria for diagnosing PTSD in DSM-IV.

There are a few studies of fathers, and there are estimates of up to 5% of them experiencing PTSD after their partner's childbirth. But the studies tend to be

¹³ In Beijing, perinatal post-traumatic stress disorder (PPTSD) symptoms ranged from 1 to 12% of Chinese mothers (Zhang et al 2018).

self-reported rather than fully diagnosed (Ayers et al 2008).

In terms of the questionnaires used to measure PTSD, general ones may not be specific enough (eg: do not include fear of childbirth). There are specific questionnaires like the Perinatal Post-Traumatic Stress Disorder Questionnaire (PPQ) (Demier et al 1996), but they are "not widely validated" (Ayers et al 2008).

Ayers et al's (2016) meta-analysis found fifty studies (up to May 2015) on PTSD measured at least one month after childbirth. From these, the researchers distinguished three groups of risk factors for PPTSD:

a) During pregnancy - eg: depression; fear of childbirth; poor health; pregnancy complications; a history of PTSD.

b) At birth - eg: negative subjective experience; low perceived control or agency; lack of support from staff.

c) Post-natal - eg: depression; poor coping and stress.

There is a wider question of "whether the phenomenology of PTSD following childbirth is the same as PTSD after other events" (Ayers et al 2008 p245).

Ayers et al (2008) continued: "There are many potential ways in which birth differs from other traumatic events including that it is predictable, usually entered into voluntarily, involves huge physiological and neuro-hormonal changes, is largely viewed by society as a positive event, and yet can involve breeches of bodily integrity that not all other traumatic events involve. It was noted from clinical experience that distress after birth often appears to be associated with the loss of the expected or desired birth, which may make it different to other traumatic events. Similarly, there may be different consequences for a woman when she is expected by other members of her society to have had a positive experience. The experience of childbirth as a traumatic event may also differ from others in that it almost inevitably involves several individuals: the woman, her partner, the baby and care staff, adding a level of complexity to the event" (p245).

5.2. PREGNANCY AND BREAST CANCER

Breast cancer risk is reduced for women who have had children. Husby et al (2018) found that the key was a pregnancy lasting 34 weeks or longer.

Data on 2.3 million women who had been pregnant in Denmark between 1974 and 2014 were analysed, and then replicated with data on 1.6 million women in Norway. Those who developed breast cancer after childbirth were compared to those who did not have cancer.

Generally, first childbirth before 30 years old reduced the risk of later breast cancer, but no benefits for first child over thirty. Additional childbirths further reduced the risk. Pregnancy lasting 34 weeks or longer was associated with a reduced risk of breast cancer of over 10%, but no benefits for pregnancies lasting 33 weeks or less.

So, this is a "novel finding that pregnancy-induced breast cancer is obtained within a narrow time window, late in pregnancy" (Husby et al 2018 p3).

This study has a number of key methodological strengths:

- Very large, population, sample (with little risk of selection bias).
- Prospective study (and no concerns with recall bias).
- Classification of pregnancy and diagnosis of cancer by medical professionals (though a small possibility of misclassification).
- Long-term follow-up.
- Statistical analysis controlled for confounding factors like socio-economic status.

5.2.1. A Sociological View

Modern culture has been described as a "risk society" (ie: the focus on "debating, preventing and managing risks"; Beck 2006). The notion of risk, for Giddens (1999), comes from being "increasingly preoccupied with the future (and also with safety)". "Risks represent those possible futures or outcomes that are seen to be undesirable and to be avoided. They are the possible futures that threaten the status quo; they are events or situations positioned as the 'other' of safety" (Ehlers 2016 p82).

The upshot is health management, which is "a variety of strategies that identify, treat, manage, or administer those individuals, groups or localities where risk is seen to be high" (Rose 2007 quoted in Ehlers 2016).

Ehlers (2016) focused on breast cancer here, and how the biopolitics of health management "orients the

biological – living beings – towards life in a regulatory fashion. This imperative to (make) live – or, the affirmation of life – is productive, in the sense that it produces ways of living/life. However, such a regulatory affirmation of life should not necessarily be seen as neutral or liberatory. In terms of illness and health (in both biomedical and broader social understandings), regularisation operates in such a way that only certain trajectories for life are encouraged or viewed as acceptable, generally ones that incorporate biomedical rationalities into the governing of self" (p82).

From this comes the "survivor narrative" (or "survivor culture" or "survivor politics" ¹⁴) which emphasises "oft-repeated incantations of 'surviving cancer'" (Ehlers 2016). Though some women find this narrative empowering, Steingraber (1991) noted it "at the same time denies the uncertainty of our prognosis" (quoted in Ehlers 2016). In medical terms, prognosis is the predicted course of an illness. But in sociological terms, Jain (2007) talked of "prognosis time" ¹⁵, where the individual experiences the world differently. However, "within the experience of living in prognosis, safety cannot be absolutely quantified, though it remains an ideal that the individual understandably seeks to achieve" (Ehlers 2016 p85).

Ehlers (2016) continued:

Ambiguity, uncertainty, and the fear or realities of death, however, comprise the experience of living in prognosis. The pink-ribbon campaign and breast cancer culture more generally elide these complexities, focusing instead on cheeriness, consumerism, and what Barbara Ehrenreich has called the reckless optimism of 'bright-siding', or the relentless pursuit of positive thinking (2009). Survivor politics insists on the disavowal of death by foregrounding what can be seen as the refusal to be overcome by cancer: while those women who have lost their lives to breast cancer are remembered in major breast cancer rallies, it is usually in the form of privatised loss (by friends or family who carry the name of the lost-loved-one) rather than comprising and integral part of the formalised ceremony—which is centred on survival. And the endless drive for 'the cure', so present in public breast cancer campaigns, functions to not only foreground an elusive

¹⁴ As seen in pink ribbon campaigns and rallies of support, and sponsored events to raise money. What has been called "pink militancy" (Krupar 2012).

¹⁵ "Time shifts, in prognosis, in the sense that one must re-orient themselves to time: one cannot know how long the cancer was there (this requires a questioning of the past); death becomes central and operates as an active loss, rather than something that happens at the end of a life-span; lifespan itself must come under review; the future is constantly anticipated while it simultaneously dissolves into the past (what are my chances in light of survival rates — my end is foreshadowed at the beginning [in the prognosis]); life becomes counterfactual in the sense that one might look back and yearn for a different story or see points of time where the story might have turned out differently; and, finally, life in prognosis is explicitly measured in time, in terms of the stages of treatment and disease" (Ehlers 2016 p91).

biomedical 'promise' but also to deny or suspend the sheer terror, pain, suffering, and death that accompanies breast cancer diagnosis, treatment, and the experience of life in prognosis (pp89-90).

5.3. FERTILITY ADD-ONS

Women undergoing in vitro fertilisation (IVF) in private clinics can be offered additional services (eg: pre-implantation genetic screening; thyroid anti-bodies; sperm DNA tests), alternatives, or treatments for preservation of fertility. These can be expensive, but what is the evidence for these "extras"?

Heneghan et al (2016) reviewed 38 interventions/add-ons offered in UK fertility centres. Systematic reviews were found for 27 interventions. Only five of the interventions were found to improve live birth outcomes, while the remainder had insufficient evidence or poorer birth outcomes. Of the eleven interventions without systematic reviews, no evidence at all was found for three.

In terms of advice from the National Institute for Health and Clinical Excellence (NICE), eleven interventions were recommended for specific women (eg: with thyroid disease), six for research purposes only, two not recommended, and the remainder had no guidance.

Heneghan et al (2016) lamented the lack of clear evidence and advice for patients and clinicians. They stated: "Patients are unlikely to have specialist skills in seeking and critically appraising clinical evidence. For complex issues such as genetic screening we consider the HFEA's [Human Fertilisation and Embryology Authority] advice, that 'you should talk to your GP to go through the options available', unreasonable, as there is likely to be insufficient knowledge available to correctly reflect the potential benefits and harms of such interventions" (p3).

5.4. ABORTION DENIED

Abortion is a hotly debated topic, and much of the debate is focused upon the mental health of the woman, both after an abortion or after denial of a wanted abortion. "Scientific evidence shows that most women's emotional and mental health are not negatively affected by having an abortion, while some research shows short-term harm to mental health from being denied a wanted abortion" (Greene Foster et al 2018 p1054).

What about the consequences of denial of abortion upon the child born? Generally, comparing unintended and intended pregnancies, children of the former have increased risk of poorer health outcomes, including low

birth weight, due to maternal behaviour during pregnancy, and bonding issues later (Greene Foster et al 2018). But pregnancy intention is usually reported to researchers after birth. "Such a retrospective measurement may be flawed; women may change their designation of a pregnancy as intended or unintended based on the circumstances of raising the child. Certain women might be less likely to report an unintended pregnancy than others. In addition, not all pregnancies that are unintended at conception are unwanted; some may be happy surprises" (Greene Foster et al 2018 p1054).

Attempting to overcome these problems, Greene Foster et al (2018) reported data from the Turnaway Study (2008-2016), where women who wanted an abortion were denied it in the USA. The women were denied because they were beyond the gestational age limit. This group comprised 146 women and their children, and they were compared to women who received an abortion but subsequently had another child (n = 182). The main outcomes measures were child health-related by five years old.

There was no differences in most of the outcomes between the two groups. However, there was poorer maternal bonding in the denied group, and these children were more likely to live in maternal-reported poverty.

Greene Foster et al (2018) concluded that "access to abortion enables women to choose to have children at a time when they have more financial and emotional resources to devote to their children" (p1059).

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6. ETHICS TOPICS

- 6.1. Conflict of interests
- 6.2. Privacy versus access
- 6.3. Ethical decisions in psychiatry
- 6.4. Reproductive ethics
 - 6.4.1. "Three-parent IVF"
 - 6.4.2. Human embryo research
- 6.5. Oxford Utilitarianism Scale
- 6.6. Appendix 6A - Bioethics
- 6.7. References

6.1. CONFLICT OF INTERESTS

Gilmore et al (2018) lamented the health promotion partnership in the UK between Public Health England (PHE) and Drinkware (a charity funded by the alcohol industry): "Commercial companies survive by profiting from the things they produce, and for those producing tobacco, alcohol, or unhealthy foods, that profit motive inevitably runs counter to health. These industries have adopted common and successful strategies to prevent, undermine, dilute, or constrain measures designed to curtail their activities. Their actions include a focus on personal responsibility for health harms; championing the rights of the individual to adopt unhealthy behaviours as a matter of personal freedom; attacking critics; dismissing research findings as 'junk science'; funding alternative research that provides pro-industry results; investing in corporate social responsibility activities to enhance reputation; mounting legal challenges; and, crucially, opposing and avoiding effective health regulation by promoting voluntary codes and partnerships with government" (p1).

The PHE/Drinkware strategy encourages "alcohol-free days a week", placing the emphasis of problem drinking on a small number of individuals who drink every day rather than the amount of alcohol drunk (eg: limits of fourteen units per week). Gilmore et al (2018) argued that the alcohol industry supports this campaign because "it thinks the campaign will be ineffective or will divert attention from other more effective policies to reduce alcohol consumption that the industry fears more, such as minimum unit pricing" (p1).

Furthermore, "through Drinkaware, the alcohol industry gains valuable engagement with PHE, establishes working relations with PHE staff, and may even secure a seat at the table when other alcohol harm initiatives are planned and executed" (Gilmore et al 2018 p2).

6.2. PRIVACY VERSUS ACCESS

Social media has allowed individuals to share their health and illness stories (what Ostherr (2018) called the "patient-driven illness narratives"). In the past, these stories would have been shared with family and close friends, but now the Internet makes them available to all.

"Patients' illness narratives have emerged as vivid counter-narratives to official accounts, challenging traditional models of biomedical expertise as they circulate through robust networks of engaged citizens concerned with health care, often termed 'e-patients' (Ferguson and Frydman 2004). Members of these groups have developed extensive online activist communities, demand access to their own health data, conduct crowd-sourced experiments, and 'hack' health problems that traditional medical experts have failed to solve. In this way, e-patients can be seen as practicing a form of 'citizen science' (Hand 2010) in medical contexts as a means of creating alternative models of patient-physician partnership" (Ostherr 2018 p4).

E-patients demand access to their medical data. For example, Hugo Campos wore a small implanted electronic device designed to record his heart activity. The data created by this device were sent to his doctor, and could be accessed via a consultation. Campos (in the USA) has campaigned for direct access to that data (Ostherr 2018). The argument is presented "in terms of privacy and ownership, asking: Who owns the data? Who controls access to the data? In whose interest is 'privacy' invoked – the patient's or the manufacturer's?" (Ostherr 2018 p7).

The manufacturers of the device have been one of the barriers to Campos, claiming that the data are highly technical, and need experts (doctors) to interpret it to avoid "a lot of angst" (company spokesman quoted Ostherr 2018).

The alternative to patient-driven illness narratives is "clinic-driven illness narratives" based around electronic health record (EHR) systems (Ostherr 2018). These biomedical data are kept in the closed system of medical record-keeping (ie: privacy-based). The two types of knowledge of the different narratives are "disconnected forms of knowledge and meaning that exist in separate realms" (Ostherr 2018 p13).

Ostherr (2018) took this view in her conclusion: "The risks of third-party exploitation of data shared in online patient communities are real. However, the necessary response is not to firewall open patient resources online, thereby undermining their benefits alongside their harms, but rather to open up clinical EHR networks to more diverse forms of input, with greater

privacy protections" (p14).

She continued: "The great strength of patient stories in platforms outside traditional clinical settings is their rich detail, their unrestrained narration, the varied and unfiltered affective states they register, the wild heterogeneity of sources and types of information they include, and the multiplicity of voices they present. Most of these variables continue to be excluded from EHRs..." (Ostherr 2018 p15).

6.3. ETHICAL DECISIONS IN PSYCHIATRY

Case 1

A woman ("Jane Doe") without identification and under-dressed for winter is found wandering in a city. "She is internally preoccupied, mumbling to herself and laughing, and religiously preoccupied, which she expresses through her belief that the physician is an angel" (Thurin et al 2019 p36). A psychiatrist is unable to make a clear diagnosis because of lack of information. It is suggested that more invasive tests are required - eg: lumbar puncture for cerebrospinal fluid to look for infections. But the patient does not have capacity to consent to such tests, it is felt.

Should the medical team proceed anyway? Thurin et al (2019) answered "yes" based on the principles of beneficence (acting in the patient's best interest), and justice (making a diagnosis without full information would be discriminatory). Autonomy is secondary. "When patients are too ill to communicate, understand, or reason through a given decision, physicians work under the premise that the patient needs and wants help" (Thurin et al 2019 p38).

Subsequently, family members of Jane Doe are found, and give details of her history of psychosis. However, the patient is refusing the appropriate medication, and has been doing so, which explained her wandering in the city.

Should the medical team apply for permission to force treatment? Beneficence again is the key ethical principle, so Thurin et al (2019) argued for "yes".

Case 2

"Bill" has a history of major depression, and chronic kidney disease. Anti-depressants may benefit the former, but be a risk for the latter. Bill can consent to such medication.

Should the psychiatrist prescribe these drugs? "Yes" is Thurin et al's (2019) answer based on the following ethical principles:

- Autonomy - Bill wants the treatment.
- Beneficence - The drugs will reduce the depression and suicide risk.
- Non-maleficence (treatment should not cause harm) - Close monitoring of the kidney function with regular tests.

However, the anti-depressants do not help, and the depression becomes worse. Electro-convulsive therapy (ECT) is a possibility, but Bill "worries about 'electroshock' therapy and whether it will be painful or make him 'like a zombie'" (Thurin et al 2019 p37).

Can Bill give appropriate consent or not in his condition? A psychiatrist must consider autonomy and beneficence in the decision based around capacity. "Capacity is a fluid ability that changes based on the question, the circumstances, and the ability of the patient to understand and manipulate necessary information. Disruption in cognition and mood can affect these abilities. The question of informed consent in patients with mental illness has been empirically evaluated in numerous studies. Overall, these studies have shown that, although patients with mental illness tend to have more difficulty with decision making for treatment, the majority maintain the capacity to make treatment decisions. Alternatively, some have questioned the ideal of truly informed consent, on the basis of numerous situational, psychological, and neuropsychiatric factors that can influence rational decision making" (Thurin et al 2019 p38).

It is important for a psychiatrist to present the costs and benefits of ECT to the patient. This should include the risks of forgoing the treatment, outcome statistics of the treatment, and possible side effects of it.

After discussions with Bill, he says "it's up to you". The psychiatrist worried that this "reflects Bill's hopelessness and that he is not fully participating in the decision-making process, again calling into question his capacity to make this treatment decision and, therefore, his ability to provide informed consent. An important component of informed consent is the concept of voluntariness, or an individual's ability to act in accordance with an authentic sense of self and freedom from undue influence" (Thurin et al 2019 p39).

Thurin et al (2019) continued: "In physician-patient communication, there can be hidden, sometimes unintended, messages from providers to patients that influence what information they share; what questions they ask; and, ultimately, what decisions they make. Bill may interpret the way the psychiatrist discusses the efficacy of ECT and the act of promoting it as a primary treatment choice

as the psychiatrist's personal preference. In doing so, Bill may feel that he has to agree or risk disappointing the psychiatrist" (p39). Involving other parties in the decision may help (eg: other medical professionals, family members).

The psychiatrist decides, against his judgment, to try another drug instead of ECT. Thurin et al (2019) pointed out: "In this case, it may actually be a violation of the principle of beneficence that the psychiatrist opted to proceed with another medication trial when medications have been ineffective to date and there is a more effective treatment option available" (p39).

6.4. REPRODUCTIVE ETHICS

6.4.1. "Three-parent IVF"

"Mitochondrial replacement therapy" (MRT) (or "three-parent IVF") involves a couple undergoing in vitro fertilisation (IVF) having the mitochondrial DNA of a third-party donor added (Schaefer and Labude 2017)¹⁶.

Baylis's (2013) arguments against this type of IVF related to potential harms - to egg donors; to the offspring; to specific interest groups; to society. Rulli (2017) questioned the "life-saving" potential of the procedure. "Three-parent IVF is a way of bringing healthy individuals into existence. While this may be a good thing, the procedure should not be attributed to the value of a life-saving treatment" (Schaefer and Labude 2017 p1577).

Schaefer and Labude (2017), on the other hand, argued that banning or restricting the use of MRT could be violating the "procreative rights" of individuals, and the right to genetic affinity (ie: to have a child that is genetically related to the parents). For some people, "the importance of genetic continuity is intricately linked to the general sources of meaning in life" (Schaefer and Labude 2017 p1578). To prohibit MRT would deny women with particular mitochondrial disorders "the opportunity to have healthy genetically related children" (Schaefer and Labude 2017 p1578).

Schaefer and Labude (2017) illustrated it thus: "a woman with disordered mitochondria may face a dilemma: have a child naturally, risking significant mitochondrial disease in her offspring, or adopt or secure a gamete donor, giving up on her central project of having genetic affinity with her children. MRT would resolve this

¹⁶ Note that "the term 'three-parent IVF' is a misnomer, since the contribution of the mitochondrial donor is too trivial to merit calling that donor a parent" (Schaeffer and Labude 2017 p1579).

dilemma by allowing such women to have healthy, genetically related children. By banning MRT, governments essentially shut off a reasonable opportunity to secure genetic affinity with her children" (p1578).

However, Schaefer and Labude (2017) were not arguing for unregulated MRT.

6.4.2. Human Embryo Research

In vitro human embryos are the true "test-tube babies", where embryos are experimentally sustained for a short period of time (eg: 7 days). Researchers are able to study the causes of early miscarriages, and certain degenerative diseases, for instance (Cavaliere 2017).

In the UK, there is a 14-day limit on such embryos laid down in the 1990 Human Fertilisation and Embryology Act. This point was chosen because the 14th day of development "signals the emergence of the primitive streak in the human embryo, a precursor of the brain and the spinal cord" (Cavaliere 2017 p3). It was also a compromise between those who saw human life as beginning at conception (and thus were against any research on in vitro embryos), and researchers seeing the benefits of study.

There has also been the practical issue that sustaining in vitro embryos beyond seven days has not been possible. However, researchers are increasing this time (eg: 12 days in 2016). This has opened up the question of whether to extend the 14-day limit.

The benefits of the research is the main argument for extension (ie: beneficence), along with technical feasibility (ie: in vitro embryos will be sustainable for longer in the near future).

Cavaliere (2017) considered these arguments (appendix 6A). The potential benefits of future research can be caught up in the "often-hyped claims concerning the benefits of new technological possibilities" (p7). This is the assumption that scientific progress is linear, and so benefits gained in the past will continue from future research.

Advocates also argue that the benefits for society outweigh any costs. But such research has "a societal cost of offending certain moral feelings on the value of early human life, and not respecting certain strongly held convictions on how we ought to treat human embryos. Thus, individuals who hold such views may find themselves feeling alienated from or devalued by society" (Cavaliere 2017 p7).

One argument against extending the 14-day limit is "the slippery slope argument". "The slippery slope argument against embryo research is approximately like this: embryo research should not be allowed/the limit

should not be extended because allowing research on embryos in a very early stage of their development/extending the limit beyond day 14 will lead to the permissibility of research on fetuses and newborns. The argument voices the concern that once we become accustomed to research on pre-embryos, we will extend the permission for research on embryos on a later stage of development; once we become accustomed to this too, then we will allow research on fetuses and babies" (Cavaliere 2017 p8).

Cavaliere (2017) herself favoured compromise and "respecting value pluralism" ¹⁷ based on two arguments:

i) Trust - A 14-day limit maintains public trust based on the following logic:

"a) Scientific research is important because it improves people's lives and it should be allowed to carry on;
b) Public trust is necessary to carry on scientific research;
c) Therefore, public trust in scientific research ought to be preserved" (Cavaliere 2017 p9).

ii) Respect - A 14-day limit respects the competing views on the subject, particularly the moral status of the embryo. This is important within a democracy.

Cavaliere (2017) ended: "I have argued that the 14-day limit for embryo research is not valuable in spite of being a solution of compromise, but rather because of it. The idea of a democratic society is that even those who do not accord intrinsic value to the human embryo should respect value pluralism and accord moral worth to opposing views. For this reason, any proposal to change the 14-day rule needs careful evaluation of the scientific feasibility and effective benefits of embryo research; it needs an extensive inquiry into public attitudes concerning embryos; and it needs a deliberative process that takes these elements into account. It does not need positions that consider only the beneficence of research and its technical feasibility" (p10).

6.5. OXFORD UTILITARIANISM SCALE

Utilitarianism is "the impartial maximisation of the

¹⁷ Referring to Brownsword (2008), Wilson (2011) observed that "we should not consider moral pluralism a problem for bioethics, but should see it as the source of its socio-political utility: providing 'outsiders' with the chance to broker compromises and facilitate 'the process of practical decision-making'" (p136).

greater good" (Kahane et al 2018 p134). It is seen in common moral dilemmas that involve sacrificing one person to save five others, for example.

Kahane et al (2018) distinguished between a negative and a positive version of utilitarianism in their development of the Oxford Utilitarianism Scale (OUS). This constructed from over 1000 participants online responding to seventy-seven items, which after factor analysis produced two key factors:

- "Impartial beneficence" (IB) (positive utilitarianism)
 - eg: "It is morally wrong to keep money that one doesn't really need if one can donate it to causes that provide effective help to those who will benefit a great deal".
- "Instrumental harm" (IH) (negative utilitarianism) -
 - eg: "It is morally right to harm an innocent person if harming them is a necessary means to helping several other innocent people".

Five items relating to IB and four for IH made up the final version of the OUS (table 6.1).

- Impartial Beneficence (IB) items:

1. If the only way to save another person's life during an emergency is to sacrifice one's own leg, then one is morally required to make this sacrifice.
2. From a moral point of view, we should feel obliged to give one of our kidneys to a person with kidney failure since we do not need two kidneys to survive, but really only one to be healthy.
3. From a moral perspective, people should care about the well-being of all human beings on the planet equally; they should not favour the well-being of people who are especially close to them either physically or emotionally.
4. It is just as wrong to fail to help someone as it is to actively harm them yourself.
5. It is morally wrong to keep money that one doesn't really need if one can donate it to causes that provide effective help to those who will benefit a great deal.

- Instrumental Harm (IH) items:

1. It is morally right to harm an innocent person if harming them is a necessary means to helping several other innocent people.
2. If the only way to ensure the overall well-being and happiness of the people is through the use of political oppression for a short, limited period, then political oppression should be used.
3. It is permissible to torture an innocent person if this would be necessary to provide information to prevent a bomb going off that would kill hundreds of people.

4. Sometimes it is morally necessary for innocent people to die as collateral damage—if more people are saved overall.

(Each item scored: strongly disagree (1) to strongly agree (7))

(Source: Kahane et al 2018 p146)

Table 6.1 - Oxford Utilitarianism Scale.

6.6. APPENDIX 6A - BIOETHICS

The term "bioethics" first appeared in the 1970s, and has since become "the label for growing external scrutiny of science and medicine, with philosophers, lawyers and theologians serving on federal commissions and working in dedicated centres for bioethics" (Wilson 2011 p122) ¹⁸. Rose (2006) described "a bioethical encirclement of biomedical science and clinical practice" (quoted in Wilson 2011), while others highlighted "a fundamental shift in the location and exercise of biopower: with new actors determining the development of policies and biomedical technologies that, in turn, play a crucial role in governing the health of individuals and populations" (Wilson 2011 p122).

Wilson (2011) noted two main criticisms of bioethics:

i) Too formal in terms of philosophical principles, and so "divorced from the expectations of the patients it claims to represent" (Wilson 2011 p122).

ii) Justifying new scientific medical technologies, and "instead of providing a challenge to biomedicine and acting on behalf of patients, it serves to insulate science and medicine from threatening questions about new technologies and, through an increasingly bureaucratic process, provides 'ethical warrants' that allow research to proceed" (Wilson 2011 p122).

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¹⁸ The phrase "ethics industry" was used in one newspaper in the 1990s (Wilson 2011).

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7. TRANSGENDER HEALTH

- 7.1. Mental health
- 7.2. Uterine transplantation
- 7.3. References

7.1. MENTAL HEALTH

Garofalo (2016) asserted: "Healthcare is a fundamental right of every human being; however, transgender ¹⁹ people have often been overlooked in their pursuit of the highest quality healthcare, in part, because they face significant barriers when it comes to basic needs, including social support, education, housing, employment, and access to medical and mental health services. Among the many disparities facing transgender people are extreme levels of violence and harassment, and experiences of discrimination in the healthcare environment. Transgender people, particularly transgender women from communities of colour, are the highest risk demographic group in the United States for the acquisition of HIV. Transgender people are also at increased risk for mental health and substance use issues, including higher risk for depression, post-traumatic stress, and attempted suicide" (p1).

Concentrating on mental health, gay, lesbian and bisexual individuals experience higher rates of depression than heterosexuals, and transgender individuals even higher rates than that (eg: Landers et al 2009), and also for suicides (eg: Grant et al 2011) ²⁰. "In a heteronormative society, non-traditional gender identity and sexuality influence self-esteem. Internalised transphobia, a discomfort with one's own transgenderism as a result of internalising society's normative gender expectations, can negatively affect health outcomes among transgender people. For many transgender individuals, feelings of shame, isolation, anger, sadness, loss, and even self-rejection or questioning of one's identity can lead to depression symptoms..." (Su et al 2016 p13).

Su et al (2016) reported the details of an 67-item online survey with 770 lesbian, gay, bisexual, and transgender (LGBT) Nebraskans in 2010. Ninety-one

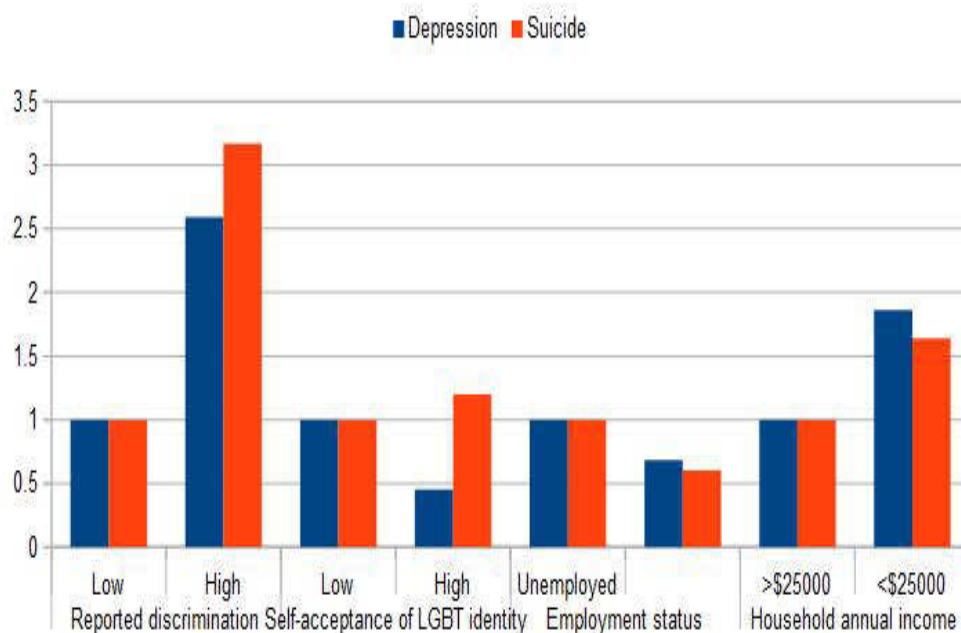
¹⁹ Transgender is "an umbrella term for persons whose gender identity, gender expression, or behaviour does not conform to that typically associated with the sex to which they are assigned at birth" (Su et al 2016 p12). "Trans*" is sometimes used (Morgan 2015).

²⁰ Eg: 48% of trans* people under 26 years old have attempted suicide ever (and 30% in the last year), and 59% considered it (vs 6% of the general population) (Trans Mental Health Survey 2012 quoted in Morgan 2015).

respondents self-identified as transgender.

Transgender individuals were significantly more likely to report depression in the past week (54%) than the rest of the sample (33%), and significantly more likely to have attempted suicide ever (38 vs 16%).

For the transgender individuals, two variables were significantly associated with depression - reported discrimination increased the risk, while LGBT identity acceptance reduced it. Attempted suicide was linked to discrimination, and low income, but employment reduced the risk (figure 7.1).



(Data from Su et al 2016 table 3 p17)

Figure 7.1 - Odds ratio of depression symptoms and ever attempted suicide based on certain variables.

The study used a volunteer sample (table 7.1) recruited via LGBT-friendly publications and public venues as well as via friends in the Omaha metropolitan area. Thus, it was not possible to say if the sample was representative. Individuals who did not self-identify as LGBT may not have volunteered. Furthermore, being an online survey excluded individuals without access to computers or the Internet.

All measures were self-reported, so there is a risk of recall bias.

Advantages	Disadvantages
<p>1. The only way to access relevant participants as no central register exists of LGBT individuals (ie: "hidden population").</p> <p>2. Less ethical concerns over coercion with individuals who choose to participate.</p>	<p>1. No way of knowing if the sample is representative of the whole population of LGBT individuals in the area.</p> <p>2. Certain individuals are more likely to volunteer than others (eg: more sociable).</p>

Table 7.1 - Key advantages and disadvantages of volunteer sampling for this study.

7.2. UTERINE TRANSPLANTATION

"Traditionally, infertility has been an unfortunate consequence of the realignment of a transgender person's body with their gender identity" (Jones et al 2019 p152). One possibility to overcome this problem is uterine transplantation (UTx), which has been tried generally. Jones et al (2019) reported 42 UTx procedure performed worldwide, and at least twelve live births.

Could UTx work for male to female (M2F) transgender women? Jones et al (2019) discussed the medical issues. UTx involves "the transplantation of the uterus, including the cervix, a cuff of vagina, the surrounding ligamentous and connective tissues, as well as the major blood vessels to the level of the internal iliac vessels. The uterus is then placed orthotopically in the pelvis of the recipient, where it is structurally supported using the uterosacral, round and broad ligaments laterally, the bladder peritoneum anteriorly, and the vagina and paravaginal tissues inferiorly" (Jones et al 2019 p152). With transgender women, this would only be possible after completion (or as part) of gender reassignment surgery, though surgery would long and challenging.

Fertility would be via in vitro fertilisation, for instance, with the individual's own sperm frozen prior to gender reassignment, and a donor egg. Birth be by caesarean section "owing to concerns regarding the mechanical strain of labour" (Jones et al 2019 p155).

Jones et al (2019) felt that there was "no overwhelming clinical argument against performing UTx" with transgender women, despite the challenges for medical practitioners. They concluded: "The reproductive aspirations of M2F transgender women deserve equal consideration to those assigned female at birth and, subject to feasibility being shown in the suggested areas of research, it may be legally and ethically impermissible not to consider performing UTx in this population" (Jones et al 2019 p155). The relevant ethical issues are justice and equality (Jones et al 2019).

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8. SLEEP TOPICS

- 8.1 Falling asleep
- 8.2. Human sleep
- 8.3. Nightmares and suicides
- 8.4. Insufficient sleep
- 8.5. Caregiving
- 8.6. Memory
- 8.7. Dreaming
- 8.8. References

8.1. FALLING ASLEEP

Difficulty falling asleep can be due to bedtime rumination about past events, and/or future ones. Scullin et al (2018) showed the benefits of a to-do list to reduce bedtime rumination about future events.

Writing a to-do list before sleep seems a counter-intuitive solution to rumination, but Pennebaker (1997) has shown many benefits generally from writing about what is on one's mind. So, Scullin et al (2018) tested the following ideas: "One hypothesis is that writing about the future will lead to increased worry over unfinished tasks, thereby increasing sleep onset latency, relative to journaling about completed activities (which, having been completed, should not trigger worry). The alternative hypothesis is that writing a to-do list will 'off-load' those thoughts from consciousness (ie: Pennebaker-like effects), and thereby decrease sleep onset latency, relative to journaling about completed activities (which need not be 'off-loaded' because they have already been completed)" (p140).

Fifty-seven volunteers at a US university either completed a five-minute to-do list or a completed tasks list before sleeping at a sleep laboratory for four consecutive nights. Sleep onset was significantly faster in the to-do list condition (mean: 15 minutes) than the completed tasks list (mean: 25 minutes). Furthermore, the "more to-do list items that one wrote, the faster they fell asleep" (Scullin et al 2018 p142).

In such studies, there is a debate about the control/comparison group. Scullin et al (2018) had an "active control" group as opposed to a no-writing condition (no-treatment control group) or thinking about to-do list (comparison group). The "active control" is "vulnerable to placebo effects because 'control' participants are engaged in a trivial activity that the experimenters themselves do not expect to affect behavioural outcomes" (Scullin et al 2018 p143).

8.2. HUMAN SLEEP

All mammals appear to sleep, but the length of sleep varies greatly between species (eg: 2 hours per 24 hours in elephants to 20 hours per day among bats), depending on predation risk at the sleep site and metabolic rate/foraging needs, for example (Nunn and Samson 2018).

Among primates, humans sleep the least in a 24-hour period, and this is one characteristic of many that led humans to be described as "a spectacular evolutionary anomaly" (quoted in Nunn and Samson 2018).

Samson and Nunn (2015) performed a comparative analysis of primates, and found that both total sleep is less, but REM (rapid eye movement) sleep is more in humans than predicted. They concluded that "human sleep has been shaped by risks and opportunity costs, with risks involving increased predator and conspecific threats from sleeping on the ground, and opportunity costs of sleep involving time lost for building and maintaining social bonds, and fewer opportunities for individual or social learning" (Nunn and Samson 2018 p602).

Nunn and Samson (2018) developed this analysis with a comparison of thirty primate species, and "sleep architecture" (eg: total sleep time, and duration of REM and NREM (non-REM) sleep). Modelling (based on brain size and diet, for example) predicted that humans should sleep for 9.55 hours per night (as opposed to 7-8 hours in reality). REM sleep was predicted to be 14% of total sleep time, but it is actually closer to one-quarter. NREM sleep was expected to be 8.5 hours, but is 5.5 hours on average.

The comparative data on sleep in non-human primates came from studies of captive animals, who are "notoriously bored" (Hamzelou 2018).

8.3. NIGHTMARES AND SUICIDE

Nightmares are "frightening or disturbing dreams that disrupt an individual's sleep to the point of startling them awake" (Titus et al 2018 p59). They are associated with suicidal behaviour, independent of other risk factors, like post-traumatic stress disorder (Titus et al 2018). For example, Sjostrom et al (2007) found that two-thirds of a sample of 165 adults admitted to hospital after a suicide attempt had experienced them.

While Sjostrom et al (2009) found that nightmares were associated with a four-fold increase in repeated suicidal behaviour. The regularity of the nightmares was also important (eg: frequent nightmares and twice the likelihood of death by suicide compared to no nightmares; Tanskanen et al 2011).

8.4. INSUFFICIENT SLEEP

Chronic insufficient or sub-optimal sleep has an impact on many aspects of an individual's life, including daytime performance and fatigue, increased accident risk, a weaker immune response, and anxiety and depression (Sullivan and Ordiah 2018).

Concentrating on the latter, Sullivan and Ordiah (2018) analysed data from the 2012 Behavioural Risk Factor Surveillance System (BRFSS), which is a US nationwide telephone survey conducted by the Centers for Disease Control. Inadequate sleep was categorised for the past thirty days as average number of hours per day, with 7-9 as "optimal", 6 hours as "mildly insufficient", and less than 6 hours "insufficient".

Of the 20 851 responses analysed, 13% were "insufficient" sleep and 24% "mildly insufficient", with the remainder as "optimal". These three groups were compared for measures of anxiety and depression in the last month. Converting the data into odds ratios (where 1 is optimal sleep), individuals reporting insufficient sleep were four times more likely to be "depressed" or "restless", and three times more likely to feel "hopeless" or "nervous". For individuals with mildly insufficient sleep, they were about one and a half times more likely to report the four symptoms. It was calculated that one hour less sleep below six hours per day was associated with a 60-80% increase in the likelihood of the symptoms compared to optimal sleep. The relationship was stronger for women than men.

Sullivan and Ordiah (2018) observed: "Many previous studies have focused on the extremes, often intentionally induced, sleep deficiency, but chronic mild sleep restriction is more common in the general population and these data likely offer a more accurate depiction of real life conditions for many people. Although the odds of depression or anxiety were not as great among this group compared to individuals with more extreme sleep deprivation, there was an increased association of such symptoms compared to individuals who slept for 7-9 hrs" (p3).

The key limitations of this study are:

a) Cross-sectional design which is a "snapshot" at one point in time, and causality cannot be established. It is possible that depression leads to poorer sleep or vice versa.

b) Self reports of sleep and mental health with no independent verification.

c) No distinction between sleep duration and sleep quality.

Chronic sleep loss is associated with increased risk of obesity, and minor weekly shifts in sleep timing (eg: five consecutive nights of short sleep) is associated with weight gain risk, according to human studies (Cedernaes et al 2018).

Concentrating on the physiological changes induced by sleep loss, Cedernaes et al (2018) found that one night of sleep loss can lead to the body storing extra fat (increased adipogenesis) (ie: "altered 'metabolic memory'").

Fifteen young healthy males took part in "a randomised two session within-subject crossover design study" involving one night without sleep and one with sleep or vice versa. Food intake was controlled over the 42 hours of each session. Blood and fatty tissue samples were taken regularly.

The relationship between sleep duration and mortality seems to be U-shaped for adults under 65 years old - ie: short and long sleep duration associated with greater mortality (Akerstedt et al 2018).

"Most studies of sleep duration and its consequences ask for the 'usual' or 'habitual' duration. It is not clear, however, whether individuals refer only to weekdays or take into account weekends. Because there are 5 weekdays and 2 weekend days, it is likely that self-reports of typical sleep duration more strongly reflect weekday sleep" (Akerstedt et al 2018 p2).

Thus, Akerstedt et al (2018) took into account extended weekend sleep in their study of over 38 000 Swedish adults. This is the Swedish National March Cohort (SNMC), which involved individuals who completed a detailed questionnaire in September 1997 throughout the country. The relevant questions here were, "How many hours, approximately, do you usually sleep during a workday/weekday night?", and "How many hours, approximately, do you usually sleep per night on days off?". The response options were <5, 5, 6, 7, 8, or ≥9 hours.

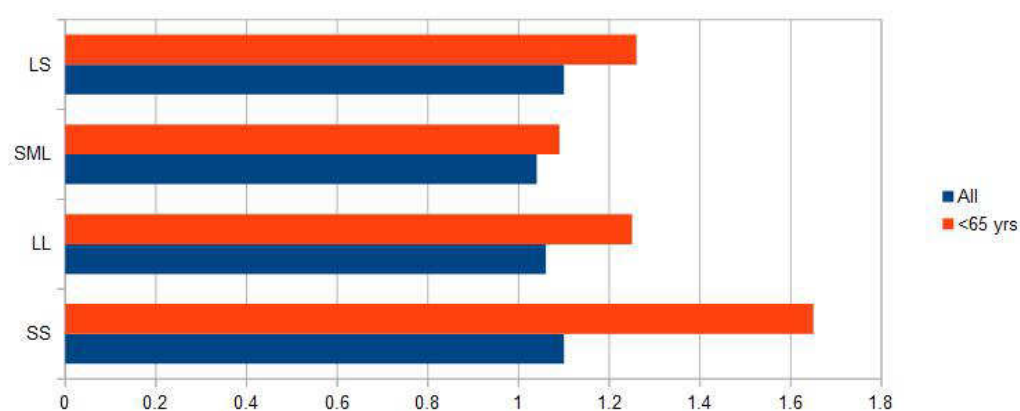
Short sleep was defined as ≤5 hours, and long sleep as ≥9 hours. Potential confounders that were measured included gender, education, body mass index, alcohol intake, physical exercise, coffee intake, and use of sleeping pills. Follow-up for mortality was made until the end of 2010.

For analysis purposes, six groups were distinguished (table 8.1).

The SS group and LL group were associated with higher mortality than the MM group. The SML group did not have a greater risk of mortality suggesting that "short weekday sleep may be compensated for during the weekend" (Akerstedt et al 2018 p8) (figure 8.1).

Name	Weekday	Weekend
SS	short	short
MM	medium (ie: 7 hrs)	medium
LL	long	long
SML	short	medium or long
ML	medium	long
LS 1	long	short or medium
LS 2	medium	short

Table 8.1 - Six groups used by Akerstedt et al (2018).



(Based on Akerstedt et al 2018 figure 4)

Figure 8.1 - Adjusted hazard ratio for mortality (where MM = 1.00).

8.5. CAREGIVING

Informal care is defined as "assistance provided by people from the intimate environment of the dependent person, who do not receive any training or economic compensation" (Sacco et al 2018 p2). It is estimated that around 17% of adults in the USA and 11% in Sweden, for instance, provide such care (Sacco et al 2018). Informal care to an elderly, ill or disabled person can lead to sleep disturbance for the carer.

Sacco et al (2018) reported a study in Sweden using data from the Swedish Longitudinal Occupational Survey of Health (SLOSH). Begun in 2003, SLOSH is a biennial postal survey of over 21 000 working adults aged 16-64 years old. Sacco et al (2018) used data from 2010, 2012, 2014 and 2016 (over 12 000 respondents).

Self-reported sleep disturbance was measured by four questions for the last three months (eg: difficulties falling asleep - "never" (0) to "always/five times a

week" (5)). Informal care for an adult relative was self-reported per working week, and categorised as less or more than five hours per week.

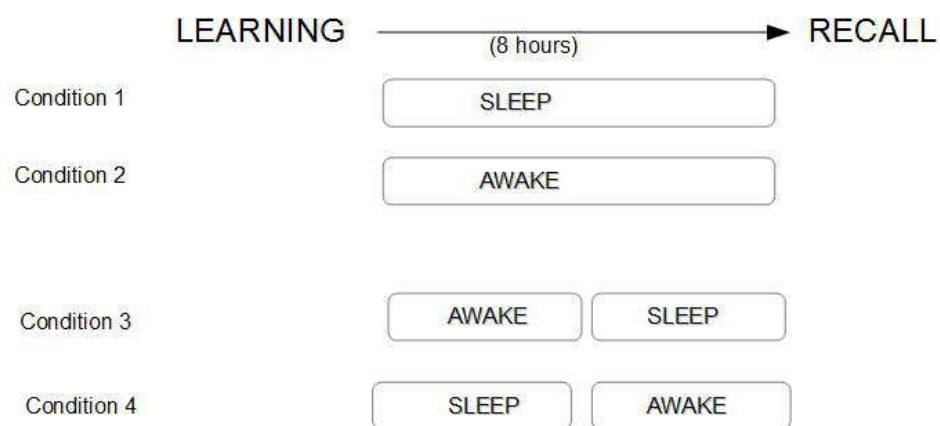
Around 12% of respondents provided informal care for less than five hours and 1.8% for more than five hours per week. "Caregivers were more likely to be female, be older, have a lower education level, report that their life was affected by physical pain or discomfort or by chronic illness, report poorer self-rated health, depressive symptoms, and sleep disturbance, and be in paid work under 20 hours per week" (Sacco et al 2018 p4).

Controlling for other variables like self-rated health, caregiving was associated with reported sleep disturbance, and cessation of caregiving with better sleep. "Even low-intensity care provision was related to sleep disturbance among this sample of carers in paid work" (Sacco et al 2018 p1). But longer hours of caregiving went with greater sleep disturbance.

All data were self-reported, at two-yearly intervals, and no information was available on the nature of the caregiving tasks, and on the care recipients (Sacco et al 2018).

8.6. MEMORY

Ekstrand (1972) showed clearly in experimental work that individuals who sleep between learning and recall do better in retention than individuals who are awake during the intervening period (figure 8.2).



(After Brown and Lewandowsky 2010)

Figure 8.2 - Design of sleep and memory experiments.

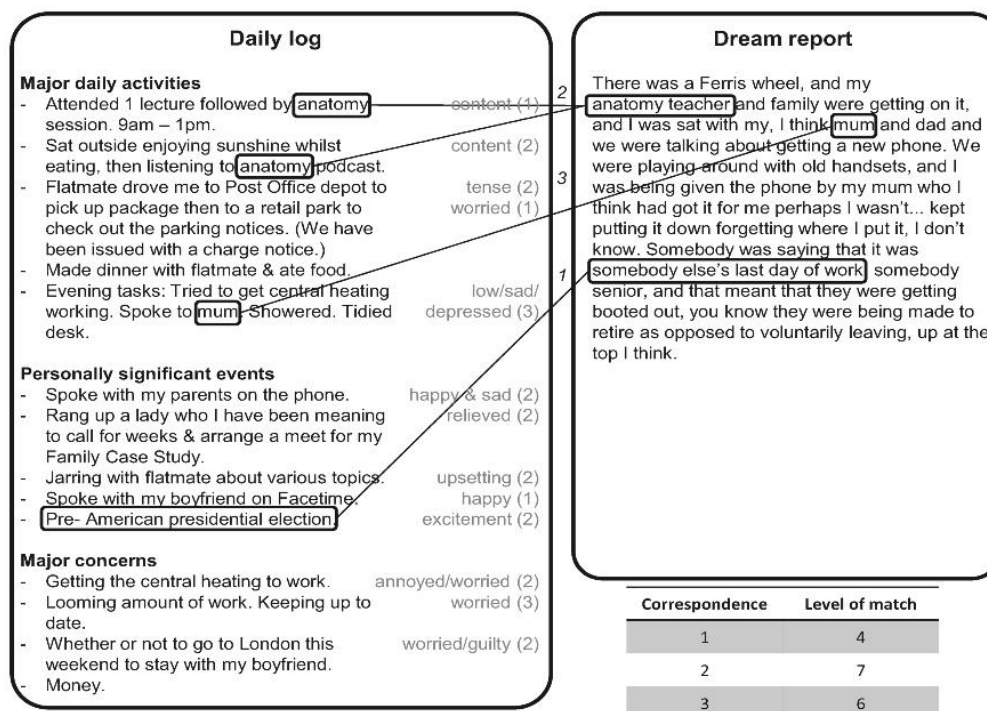
8.7. DREAMING

During REM sleep theta waves at the front of the

brain are seen in electroencephalography (EEG). This plays a role in the processing of recent memories and, particularly, emotional ones (Eichenlaub et al 2018).

Eichenlaub et al (2018) regularly woke twenty healthy volunteers during a night's sleep at a sleep laboratory in Wales. At each awakening individuals reported if they had been dreaming, and if so, the content of the dream. In total, there were 93 awakenings (48 in REM sleep). The majority of the REM awakenings were followed by a dream report, but only half of the non-REM awakenings.

The content of the dreams was compared to diaries of activities kept by the participants for the previous ten days (figure 8.3). The number of waking-life events in the last two days incorporated in dream reports correlated with theta waves in REM sleep, but not with non-REM sleep. The more intense the waking-life events, the more likely it appeared in dream content ²¹. "These results accord with theories ²² that dreaming reflects emotional memory processing taking place in REM sleep" (Eichenlaub et al 2018 p645).



(Source: Eichenlaub et al 2018 figure 2 p640)

Figure 8.3 - Example of scoring of dream content and diary entry.

²¹ Theta activity has been found to be higher in individuals who frequently experience nightmares (Hooper 2018).

²² Eg: Cartwright et al (1998).

This study involved only one night in the sleep laboratory. The researchers admitted that "the use of a multiple-night design is recommended for future studies so as to limit the sleep disturbance due to multiple awakenings within a single night as used in this study, affording an across-night balance of both sleep-stages and sleep cycles, and greater representativeness of REM dreams for the different cycles" (Eichenlaub et al 2018 p645).

Electrical activity in the brain was only measured at the front of the head. Again the researchers admitted that "future studies should use a larger number of electrodes to refine the involvement of frontal and neighbouring central and temporal regions in the correlation between the number of recent waking-life experiences incorporated into REM dreams and REM theta power" (Eichenlaub et al 2018 p645).

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