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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/>.

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1. HEALTH TOPICS

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1.1. OBESITY AND NOT

While preventing obesity is important, treatment in the form of bariatric surgery (BS) for those individuals already obese can be beneficial ¹. For example, a Swedish prospective study of post-BS individuals found sustained and substantial weight loss (eg: over 15% of body weight, over ten years), along with health and quality of life benefits compared to controls (eg: Sjostrom et al 2007).

But up to one-fifth of post-BS individuals do not lose weight (Strimas et al 2014). One factor is pre-existing mental health problems which "may affect patients' ability to adapt and adhere to the post-operative lifestyle changes" (Strimas et al 2014 p73) (eg: post-operative adherence to diet or binge eating). For example, a review of thirty-two studies found that individuals with binge eating disorder before surgery were more likely to show the disorder after the operation (Niego et al 2007).

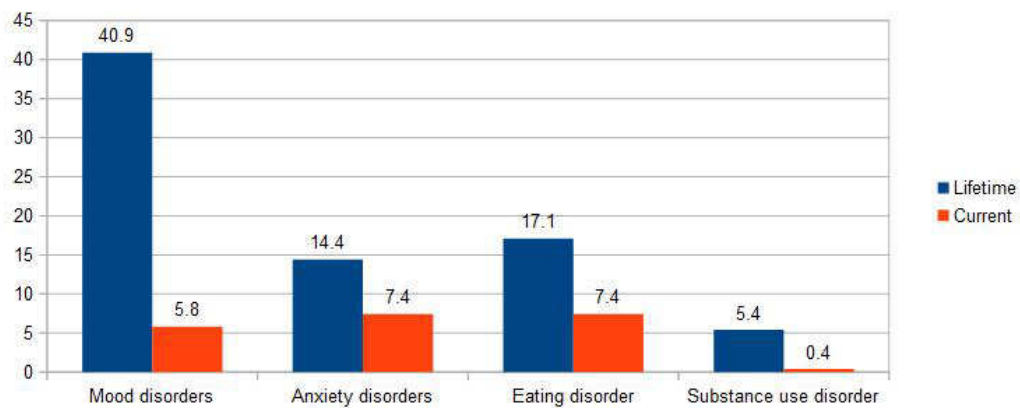
In a Canadian study, over half of a sample BS patients had a pre-existing mental disorder (Strimas et al 2014). The sample was 257 women undergoing a particular type of gastric bypass surgery at a Toronto hospital between 2010 and 2012. The main mental disorders were mood, eating, or affective disorders, or substance use. Specifically, major depressive disorder was most common (lifetime prevalence). Around one-fifth of the sample had a diagnosable mental disorder at the time of surgery (figure 1.1; table 1.1).

Pre-existing psychiatric symptoms are also associated with a greater risk of psychological complications after BS (eg: major depressive disorder and suicide; Omalu et al 2005).

In terms of the women seeking BS, Ghai et al (2014) concentrated on a sample of 148 at a hospital in another city in Canada between 2009 and 2012. Information about body image was collected via psychometric questionnaires.

The women had greater body image disturbance compared to non-obese women in the general population.

¹ BS is considered usually for individuals with a body mass index (BMI) >40 (ie: extremely obese) (Ghai et al 2014).



(Data from Strimas et al 2014 table II p77)

Figure 1.1 - Percentage of sample reporting selected mental disorders prior to surgery.

STRENGTHS	WEAKNESSES
Standardised diagnostic interviews, which established current and lifetime diagnoses. Additional information sought from physicians if necessary.	<p>Risk of patients minimising psychiatric symptoms in order to be accepted for surgery. The researchers admitted that further research "may wish to include a measure of socially desirable responding as a means of statistically controlling for this variable or of completing the psychiatric interview separately from the pre-surgical screening process as part of a research protocol" (Strimas et al 2014 p80).</p> <p>Sample largely middle-aged, more educated, White women, which was not representative of the Canadian population, but similar to other studies of BS populations. "Research has demonstrated that obesity carries greater stigma for females than males..., and perhaps the associated distress motivates females to seek treatment options. It has also been reported that less than half of obese adults are advised to lose weight by their healthcare professional, and middle-aged females with higher levels of education are, in fact, the most likely patients to receive such advice" (Strimas et al 2014 p80).</p>

Table 1.1 - Key strengths and weaknesses of Strimas et al (2014).

Specifically, greater body image dysphoria ², poorer appearance satisfaction ³, and more negative impact of body image on quality of life ⁴, but lower appearance investment ⁵. "The latter finding may suggest that obese women seeking "bariatric treatment are less invested in appearance management compared to non-obese women. Alternatively, it is important to be aware that this finding may also be reflective of a tendency to engage in maladaptive body-avoidance behaviours" (Ghai et al 2014 pp101-102).

BMI was not associated with body image concerns.

The sample was "almost exclusively Caucasian", and relied on self-reported questionnaires.

US Military

The growth in the number of people defined as overweight and obese in the USA in recent years is mirrored in the military. For example, a 5% increase in service personnel defined as obese (BMI ≥ 30 kg/m²) between 1995 and 2008 (Reyes-Guzman et al 2015).

Digging a bit deeper, Meyer and Cole (2019) studied a sample of 189 US soldiers referred to a weight loss programme at the Army Nutrition Clinic in Washington State. The mean BMI was 32 kg/m², and 16% of the sample had the diagnostic criteria of three of five risk factors for metabolic syndrome (eg: high blood pressure, blood glucose, or cholesterol). Low quality diet was common as was low physical activity.

Many of the soldiers had had medical problems in the past year which limited their physical activity. "Weight gain is likely when physical activity is limited but energy consumption is not modified" (Meyer and Cole 2019 p405).

Obesity as a Disease

In 2013 the American Medical Association (AMA) announced that obesity would be viewed as a disease state. Charrow et al (2018) responded: "What is certain,

² Measured by the Situational Inventory of Body Image Dysphoria, Short Form (SIBID-S) (Cash 2002). Twenty items on which individuals rated their negative feelings about their physical appearance in various situations (eg: when trying on clothes; social situations).

³ Measured by the Multi-Dimensional Body-Self Reactions Questionnaire (MBSRQ-AE) (Cash 2000 quoted in Ghai et al 2014). Seven items about satisfaction with one's appearance,

⁴ Measured by the Body Image Quality of Life Inventory (BIQLI) (Cash and Fleming 2002). Nineteen items about the impact of appearance on various domains of quality of life (eg: life satisfaction; social relationships).

⁵ Measured by the Appearance Schemas Inventory-Revised (ASI-R) (Cash et al 2004). Twenty items about the importance of physical appearance to the individual.

is that the decision to categorise obesity as a disease is both a scientific and moral one; it forces us to confront not only the meaning of disease itself but also the implications of medicalising body mass and drawing norms based on its measurement" (p75).

The AMA defined "disease" as a "direct impairment of the normal functioning of some aspect of the body, with characteristic signs and symptoms, and harm or morbidity" (quoted in Charrow et al 2018). Previously, however, a sub-committee within the AMA had argued that there was no clear way to define obesity as a disease (Charrow et al 2018).

The Essentialist argument is that all "diseases" have clearly articulated criteria - often related to suffering, causality, abnormality, and impairment (Charrow et al 2018). "Opponents of the essentialists note that conceptions of disease have changed radically over time - from humours to hysteria to homosexuality. Such distinctions are largely historical and have required that practitioners change disease criteria once conditions are no longer considered a disease" (Charrow et al 2018 p76). At the most cynical, "a disease is whatever a doctor says it is" (Albert et al 1988 quoted in Charrow et al 2018).

Defining a condition as a disease can be as much "a means by which to achieve an end" (Sedwick 1973 quoted in Charrow et al 2018). "That end can increase funding for research, help people feel better about their affliction, or increase awareness about a new illness. Sometimes calling something a disease might also be a means by which to shame individuals, create stigma, or otherwise harm diseased individuals such that they no longer remain diseased" (Charrow et al 2018 p76).

So, "the predominantly medical battle against obesity could then also be explained not because of the potential harmful effects of obesity on health, but by an inclination to medicalise behavior we do not find acceptable" (Vries 2007 quoted in Charrow et al 2018).

But the non-essentialist argument has its own problems, including (Charrow et al 2018):

- Some conditions would never be viewed as a disease even if the label "disease" is given to them.
- Conditions considered as diseases do share some common characteristics.
- Deviation from the norm is not the same as disease (eg: grey hair).

Obesity, like some other conditions, "simultaneously resembles many conditions considered diseases, and many

modes of existence that are not considered diseases at all. For such intermediate conditions, we have the power to decide whether to consider such afflictions diseases based on utilitarian concerns" (Charrow et al 2018 p77). This means that benefit is created by naming a condition as a disease in an ambiguous situation. But Charrow et al (2018) argued that the drawbacks outweigh the benefits, in the form of stigma, and the focus on individual-level interventions. "Once a condition is a disease, many individuals maintain that self-regulatory efforts will be futile and as such embrace their weight as permanent. In studies where obese people read articles that described obesity as a disease, those individuals self-regulated poorly and ate more food" (Charrow et al 2018 pp78-79).

Weight Control Beliefs

Losing weight is linked to weight control beliefs (eg: "I can and should control my weight"). This is the belief that weight is under personal control, and surprisingly, studies showed that "the greater the belief in personal control over weight, the more likely the person was to be binge eating, weight cycling and experiencing low self-esteem" (Laliberte et al 2014 p87).

The alternative belief is that body weight is under biological control, and so individuals should strive for a healthy lifestyle while accepting a "natural" weight. "The belief that 'one should strive for a healthy lifestyle and accept one's natural weight' has been strongly associated with improved body satisfaction, as well as good self-esteem and lower risk of disordered eating" (Laliberte et al 2014 p87).

Laliberte et al (2014) investigated weight control beliefs experimentally with 154 female psychology undergraduates at a university in Canada. Various questionnaires were completed about attitudes towards the body including the seventeen-item Weight Control Beliefs Questionnaire (Laliberte et al 2007). These questionnaires were completed before and after reading information about the biological basis to weight.

Participants showed a significant decrease in the belief that weight is under personal control and a significant increase in the belief in the acceptance of one's weight after reading the educational materials. These changes in attitude were associated with greater body satisfaction and self-esteem, and less disordered eating scores. "Providing people realistic information about weight management appears to allow them to evaluate what is and is not realistically under their control, with resulting improved body satisfaction and self-esteem" (Laliberte et al 2014 p92).

This study did not have a control group, which would

"ensure that the changes observed are not simply the result of variables such as social desirability - for example, readers may have changed their responses to scales in line with what they thought the chapter implied their beliefs should be" (Laliberte et al 2014 p92).

The sample involved individuals not seeking help for weight loss or eating disorders, but was "restricted to young adult, female undergraduate students who were largely of Caucasian, South Asian and Asian descent. While it can certainly be argued that this is a population whereby a 'normative discontent' exists with regards to body satisfaction, the possibility remains that the findings may not generalize to other age groups, cultural backgrounds, or segments of society" (Laliberte et al 2014 p93).

Another limitation was that "the outcomes were measured in terms of self-report only, which were completed immediately after receiving the education material. It is not known whether the changes in beliefs seen would translate into behavioural changes, nor whether the changes would persist over time" (Laliberte et al 2014 p93).

Pro-Anorexia

Connor and Coombes (2014) noted that "[W]omen's embodiment is troublesome. Troublesome embodiment is perhaps best exemplified in the anorexic body. The anorexic body is troubled and is troubling" (p62). The history of extreme thinness in the West includes the "holy anorexics" who "starved for spirituality" in the sixteenth century through to "pro-anorexics" today (Connor and Coombes 2014).

Concentrating on the latter, Connor and Coombes (2014) argued that pro-anorexia is "arguably only found online". It is found in web sites and communities that accept and promote anorexic behaviours. The researchers argued that pro-anorexia is "technological anorexia". They stated: "An alternative theorisation through metaphor enables an understanding of how pro-anorexia functions as the simultaneous reproduction of and political resistance to patriarchal femininity through technology. Here, technology mediates between troubled female bodies and intolerable embodiment. The pro-anorexia movement allows for the illumination of the anorexic struggle for the technological redemption of the female body" (Connor and Coombes 2014 p64).

This fits with Haraway's (1991) cyborg as a metaphor for female embodiment - a way to make sense of the contradictions and "otherness", and changing demands on the female body. Thus, cyborg is "offering a new way to live with discursively constructed bodies that re constantly being updated and rebuilt" (Connor and Coombes

2014 p64).

Based on analysis of pro-anorexia online communities and blogs, Connor and Coombes (2014) developed the cyborg metaphor. For example, the "impossible feast", where the sharing of information about food and weight loss is like eating and never getting full, and never running out of "food".

"These communities are a bring-your-own all-you-can-eat buffet where women can continuously chew through as much information as they want or need in order to shape their bodies and control their emotional experiences. The sites privilege the collection and sharing of this information on a massive scale. Information must be detailed and preferably supported by personal experience. The information is also interconnected through links, stored and retrieved instantly with a click. This is fast and direct access to exponentially expanding data. Pro-anorexics are continually devouring and regurgitating this data, connecting the next woman with the information she needs to modify her troubled body. Thus, this information is constantly being created, consumed and recreated, constructing pro-anorexic knowledge that is multiple, simultaneous, partial and contradictory. This is hybrid knowledge, perpetually in flux" (Connor and Coombes 2014 p65).

I, Bulimia

Frey (2019) reflected on "bulimia as a former bulimic", and used the framework of "embodied reflexivity" (Burns 2003) in her research. This involves the researcher being part of the research (eg: sharing personal experiences with interviewees). The ethnographic material involved interviews with eight bulimic young women in the Netherlands, autobiographical narratives, and reading the literature to "co-produce bulimia in a multi-directional, multi-dimensional narrative" (Frey 2019 p3).

Beginning with the autobiography, Frey (2019) stated: "When I was about thirteen years old, I told a close family member that I wished I had anorexia. She replied that this was a stupid thing to say, but it did not seem necessarily alarming to her. At that time, I was not actively doing bulimia because I wanted to be bulimic, but rather because I wanted to be anorexic. To me it seemed like with anorexia I could be both thin and disciplined, and would also be cared for because of having a serious illness. But no matter how hard I tried, I failed at it, because I reacted to food restriction by bingeing. Purging was then the best way to deal with the fact that I regularly binged on food and fanatically wanted to lose weight – it seemed the most rational thing to do" (p5).

This idea of a "wannabe" anorexic rather than a "real" bulimic was also there in the interviewees. For example, "Alex" said: "Oh my god, I used to be so jealous of people with anorexia. Because it worked, you got so small and so skinny, and all they had to do was avoid food. I was so jealous! And even if now I hear that someone is anorexic, I can't suppress that twinge of 'Oh you're so lucky', which is awful because rationally I know it's like 10 times as bad, they're also damaging themselves. But yeah, when I was bulimic I was like, 'I wish I was anorexic'" (p5).

While "Tanya" described bulimia as "like the failed little sister of anorexia", and she said: "Every time I ate I felt like I failed at anorexia" (p6).

Frey (2019) described a shame of bulimia ("the ugly cousin to anorexia"; "Alex"). She stated: "In the literature on bulimia, I found that in contrast to anorexia, which is popularly associated with control, discipline, and slenderness, bulimia is often associated with out-of-control bingeing, non-normative bodies, and unrestrained sexuality... And whereas food restriction can be symbolically understood as a heroic practice..., self-induced vomiting breaks taboos of bodily fluids and food intake..." (Frey 2019 p7).

The overweight aspect of many bulimics associated with "fat-shaming", while "self-induced vomiting breaks more tabus than just body fluids: it also contradicts norms of food waste" (Frey 2019 p8). "Ellen's" comment caught this last point: "I've heard this a lot: 'You're stupid. People are dying and you're making yourself throw up. This is irrational. You have your life so good, why are you doing it? It's stupid'" (p8).

Some of the interviewees were "proud" of their bulimia. For example, "Laura" said: "I knew I could never be anorexic, I don't have the discipline for it. There was something admirable about people who go that far. [...] Disciplining your body is a trait of anorexic people. Bulimia is more a trait of rebellion. 'Look what I can do, I don't want to be this disciplined'" (p9).

In conclusion, Frey (2019) considered what she had learned: "It is not because I am both researcher and ex-bulimic that I can speak for bulimics. The different ways in which I seek to know bulimia in this article – by writing my own narratives, relating to the literature, interviewing respondents, and so on – can only amount to a partial, imperfect patchwork of how bulimia is done in this context. Even if I have lived experience of bulimia, I don't have any access to a transcendental reality of bulimia outside of these knowledge practices. What results is a 'joining of partial views and halting voices into a collective subject position [Haraway 1988], an extended illness narrative that is embodied, situated, and shared" (p12).

Miscellaneous

The Food Foundation (2019) "The Broken Plate"
(quoted in Clayton 2019):

- Nearly half of food and drink advertising in UK goes on confectionary, sweet and savoury snacks, and soft drinks versus less than 3% on fruit and vegetables.
- Unhealthy foods are around three times cheaper than healthy foods.
- To follow UK Government "Eat Well Guide", it would cost the poorest tenth of households three-quarters of their disposable income (compared to 6% of the richest tenth's income).

References

Albert, D.A et al (1988) Reasoning in Medicine: An Introduction to Clinical Inference Baltimore: Johns Hopkins University Press

Burns, M (2003) Interviewing: Embodied communication Feminism and Psychology 13, 2, 229-236

Cash, T.F (2002) The situational inventory of body-image dysphoria: Psychometric evidence and development of a short form International Journal of Eating Disorders 32, 3, 362-366

Cash, T.F & Fleming, E.C (2002) The impact of body-image experiences: Development of the body image quality of life inventory International Journal of Eating Disorders 31, 4, 455-460

Cash, T.F et al (2004) The assessment of body image I: An extensive revision of the appearance schemas inventory International Journal of Eating Disorders 35, 3, 305-316

Charrow, A et al (2018) Obesity as disease: Metaphysical and ethical considerations Ethics, Medicine and Public Health 7, 74-81

Clayton, A (2019) Can supermarkets live up to their name? Ethical Consumer 178, 11-12

Connor, G & Coombes, L (2014) Gynetic organisms: Pro-anorexic techno bodies Ethnicity and Inequalities in Health and Social Care 7, 2, 62-71

Frey, I (2019) Anorexia's failed little sisters: Reflections on researching bulimia as a former bulimic Social Theory and Health (<https://link.springer.com/article/10.1057/s41285-019-00100-5#citeas>)

Ghai, A et al (2014) Body image concerns in obese women seeking bariatric surgery Ethnicity and Inequalities in Health and Social Care 7, 2, 96-107

Haraway, D.J (1988) Situated knowledges: The science question in feminism and the privilege of partial perspective Feminist Studies 14, 3, 575-599

Haraway, D.J (1991) Simians, Cyborgs and Women: The Reinvention of Nature New York: Routledge

Laliberte, M.M et al (2007) Controlling your weight versus controlling your lifestyle: How beliefs about weight control affect risk for disordered eating, body dissatisfaction and self esteem Cognitive Therapy and Research

31, 6, 853-869

Laliberte, M.M et al (2014) The impact of education on weight control beliefs Ethnicity and Inequalities in Health and Social Care 7, 2, 86-95

Meyer, S & Cole, R (2019) Army body composition programme study results concerning: Enrolees are more over fat than expected Military Medicine 184, 400-408

Niego, S.H et al (2007) Bing eating in the bariatric surgery population: A review of the literature International Journal of Eating Disorders 40, 4, 349-359

Omalu, B.I et al (2005) Suicides following bariatric surgery for the treatment of obesity Surgery for Obesity and Related Diseases 1, 4, 447-449

Reyes-Guzman, C.M et al (2015) Overweight and obesity trends among active duty military personnel: A thirteen-year perspective American Journal of Preventive Medicine 48, 2, 145-153

Sedwick, P (1973) Illness: Mental and otherwise Hastings Center Studies 1, 19-40

Sjostrom, L et al (2007) Effects of bariatric surgery on mortality in Swedish obese subjects New England Journal of Medicine 357, 8, 741-752

Strimas, R et al (2014) Psychopathology in severely obese women from a Canadian bariatric setting Ethnicity and Inequalities in Health and Social Care 7, 2, 72-85

Vries, J (2007) The obesity epidemic: Medical and ethical considerations Science and Engineering Ethics 13, 1, 55-67

1.2. BIOECONOMY

The Unproven

Datta (2018a) began: "Rapid advances in stem cell (SC) research have evolved into two distinct innovation pathways. One is the approved therapy pathway based on conclusive clinical trial evidence in accordance with existing internationally accepted regulatory frameworks of (bio)pharmaceutical discovery. The other is the direct-to-consumer pathway whereby experimental SC therapies (SCTs) without conclusive evidence of safety and efficacy are administered directly to patients by clinicians in private clinics. Not surprisingly, direct-to-consumer SCTs (DSCTs) raise substantial ethical, legal and social issues..." (p559).

SCT involves SCs from an individual's bone marrow which are "harvested", and "purged" before re-infusion into the donor. "This is unlike the laboratory-based site-of-action of (bio)pharmaceuticals and represents a paradigm shift from in vitro (outside the organism) halt-and-prevent approach of pharmaceuticals (and to a large extent biopharmaceuticals) to in vivo (inside the organism) repair-and-regenerate processes of SCs" (Datta 2018a p561).

Datta (2018a) concentrated on DCST clinics in the USA, China, and India. Such clinics can be small-scale

and will challenge the large pharmaceutical companies. Datta (2018a) noted that the "unproven DSCT market far outstrips the global approved SCT market in quantity of therapies supplied and is dominated by new entrants ranging from micro (<10 employees), small (10 to 50 employees) and medium enterprises (<50 employees)" (p568).

SCT fits with "personalised medicine" as SCTs "require each individual (autologous) cell sample to be processed individually in contrast to existing mass-produced (bio)pharmaceuticals. This also means that the decentralised, point-of-care-based SCT production processes do not use the factors of production and distribution used by existing and mainstream models of (bio)pharmaceuticals, which remain centred around a handful of incumbent pharmaceutical majors represented..." (Datta 2018a p563).

Datta's (2018a) conclusion was that DCSTs offered "the opportunity for micro, small and medium level new entrants... to enter the incumbent-centric resource-intensive global bioeconomy" (p573). "Governance voids" on SCTs (ie: lack of legislation or evidence-based recommendations) may "bolster DCST expansion" (Datta 2018a).

Many DSCTs may be described as experimental (eSCTs) or "unproven" in the "evidence-based medicine" (EBM) literature ⁶. But patients and their families ("users") may pay more attention to social media content from other users (user-to-user engagement) than EBM labels. Surveys have found that around one-third of adults "sought information related to other patients' experiences with their disease" (Datta 2018b p352).

Sharpe et al (2016) pointed out that among "individuals interested in stem cell tourism... internet was the most commonly cited source for information-seeking, ... [with most using] stem cell clinic websites [and] social media" (quoted in Datta 2018b).

Datta (2018b) analysed 868 Facebook posts and twenty testimonials on eSCTs and multiple sclerosis (posted between 2011 and 2016). "Conversations revealed that participants stepped beyond the boundaries of 'unproven' to evaluate the trustworthiness and credibility of

⁶ Datta (2018b) noted that "the effect of a negative label like 'unproven' instead of a label like 'experimental' for experimental SCTs is that 'unproven' not only casts eSCT practitioners as charlatans but also frame users as 'gullible' and lacking the capacity to make good health choices... without provider intervention... Thus, the construct of 'unproven' not only assumes a moral high ground that presupposes scientific evidence as the only legitimate way of knowing therapeutic safety and efficacy but also public trust in its legitimacy. In this sense, 'unproven' frames public trust in eSCTs within the boundaries of scientific evidence and delegitimises those stepping beyond those boundaries when considering 'other' forms of evidence like user experiences" (p354).

evidence. Decisions to do so were tied to distrust in processes, actors and institutions underpinning scientific evidence, especially those perceived to have commercial linkages, but did not extend to distrust in scientific evidence itself. Participants widely believed in the systemic collusion between 'big pharma' (perceived as dishonest) and regulators, in particular, the US Food and Drug Administration (FDA)" (Datta 2018b p356). Put simply, there was a mistrust of the institutions of EBM.

This meant that users had to find their own ways to evaluate "evidence". Scientific evidence (eg: original academic papers) was trusted by some, as was other users' views, evaluations, and experiences with the disease. Negative views were stated as well as positive ones.

Datta (2018b) felt that the view of users as gullible and lacking the capacity to make good choices was simplistic. "Participants not only conducted exhaustive reviews of disease-specific evidence but made rationalisations of risks and benefits in their individual cases" (Datta 2018b p359).

However, Datta (2018b) observed, "what is conspicuous by its absence (in the conversations analysed here) is the reference to provider-created public advisories warning users against undertaking eSCTs as well as academic papers by bioethicists or sociologists. This absence suggests that users rely on evaluating basic research evidence themselves or its interpretations by large credible bodies with public accountability (eg: UK Parliament reports) and experiential data from other participants" (p359). Disease experience was given high value.

Pharmaceutical Knowledge-Making

Pharmaceuticals involve raw materials, production, licensing, and distribution, as well as their actual discovery/creation ("knowledge-making"). Pollock (2014) pointed out that the latter has been concentrated in the West/Global North - "the locus of 'refined knowledge'", and the non-West/Global South as "reservoirs of raw fact" (Comanoff and Comanoff 2011 quoted in Pollock 2014).

Pollock (2014) explored pharmaceutical knowledge-making with ethnographic research at "iThemba Pharmaceuticals" in South Africa, which was founded to discover drugs for tuberculosis, HIV, and malaria. Put simply, the company is involved in the basic science and synthetic chemistry that has traditionally been done by large pharmaceutical companies in the West ("Big Pharma").

"A distinct aspect of doing research on TB, malaria, and HIV in South Africa rather than in a site in the Global North is that the scientists have personal

experience and intimacy with the diseases that they are researching" (Pollock 2014 pp861-862). This is summed up by one of the scientists at the company: "Actually, my interest in drugs started when I was about 15 or 16. I got struck by malaria the first time ever. And I was so sick I thought I was going to die. I had never been so sick in my life. So I thought, after I recovered, I thought I'm going to make a difference to helping people" (p862).

The company and scientists were also embedded in their place. "An African pharmaceutical response is particularly charged in post-apartheid South Africa, a context in which ideologies of neo-liberalism, democracy, HIV denialism, and pharmaceutical-based activism all intertwine and contest each other" (Pollock 2014 p866).

This is seen in the comments of one scientist: "If we are seen to be producing our own drugs for our own diseases, it will increase our standing in international science. I think it will make the South African people feel less helpless towards these diseases. If they know that South Africa is providing something for them, we are looking after ourselves... I think the difference it will make is if the drugs come out of South Africa, there's going to be a difference in the sense people have of South Africa. It's not going to be a concrete difference of it works or doesn't it, because obviously a drug is a drug. But it should help us produce them more cheaply. It should help build international confidence in South Africa, and it should help even the people on the street to feel looked after by their country. Not to feel like a third world country relying on the rich countries of the world" (pp865-866).

Pollock (2014) summed up: "Pharmaceutical knowledge production in South Africa is both post-colonial and global, and scientists involved in drug discovery there speak of it both as offering 'African solutions for African problems' and as a way for African scientists to participate in the global networks of innovative science. The ethical stakes of science in the service of the people are inextricable from the epistemological and financial stakes of creating novel IP [intellectual property]. The promise of drugs affordable to Africans and relevant to their needs jostles with the promise of global prestige for African scientists. In ways both literal and metaphorical, iThemba's and South Africa's place 'on the map' matters. For the bench scientists involved, the project is rooted in personal experience, a sense of democratic citizenship, and the complicated promise of working at 'home'" (p867).

References

- Comanoff, J & Comanoff, J.L (2011) Theory from the South: Or, How Euro-America is Evolving Toward Africa Boulder, CO: Paradigm Publishers
- Datta, S (2018a) An endogenous explanation of growth: Direct-to-consumer stem cell therapies in PR China, India and the USA Regenerative Medicine 13, 5, 559-579
- Datta, S (2018b) Emerging dynamics of evidence and trust in online user-to-user engagement: The case of "unproven" stem cell therapies Critical Public Health 28, 3, 352-362
- Pollock, A (2014) Places of pharmaceutical knowledge-making: Global health, post-colonial science, and hope in South African drug discovery Social Studies of Science 44, 6, 848-873
- Sharpe, K et al (2016) A dichotomy of information-seeking and information-trusting: Stem cell interventions and children with neurodevelopmental disorders Stem Cell Reviews and Repairs 12, 4, 438-447

1.3. POLYSUBSTANCE USE

Using several substances (polydrug use) among individuals seeking treatment for substance-related problems varies in official statistics from European countries. For example, in Switzerland the figure was 16.5% for 2013-15, with opioids and cocaine being the most common primary substances used (Maffli and Astudillo 2018).

Overall, 120 different combinations were identified in the Swiss national monitoring system data, but the most frequent combinations were cannabis/alcohol, tobacco/alcohol, and cocaine/alcohol. Alcohol was common in polydrug use, even though it may not have been the primary substance being treated for, and this has been confirmed in other countries (Maffli and Astudillo 2018).

Individuals with polydrug use "do not have one homogenous profile" (Maffli and Astudillo 2018). For example, younger individuals used alcohol/cocaine, or opioids/cocaine, or alcohol/cocaine, while "marginalised populations" (eg: unemployed) were more likely to use opioids and another substance (Maffli and Astudillo 2018).

Kataja et al (2018) analysed twelve YouTube videos on personal experiences of polydrug use (eg: "Drug combinations - the good and the bad"). Two different primary messages were perceived by the researchers - sobriety, and controlled use.

In the former case, five videos involved six women telling their personal story (including painful events) to encourage "complete sobriety" (ie: no use of any drugs). The stories followed a pattern of polydrug use seen as a solution to another problem, like depression, but, in time, the drug use became the problem. The only solution being sobriety, however hard that may be. A near

death experience was often the trigger for change, as described by one vlogger: "I was fallen over against the couch with my arm out, needle on the floor and I was turning blue [...] I was blue blue like dead blue [...] I flat-lined for two minutes and 32 seconds as my body shut down, all my organs shut down, my brain shut down" (p192).

The benefits of the radical change to sobriety were the encouraging end of the video - eg: "You can always give yourself a second chance that there's always another chance for you to be happy and sober and you can actually have a reason to live and to set goals that you need to set or fulfil the dreams that you want" (p192).

The other videos, all but one by men, encouraged controlled use of drugs, and cautioned about the risks of combining drugs. There were less personal details included. The videos "plead for a more liberal outlook on life, according to which drug use is not condemned but drug users are rather seen as smart individualised and responsible consumers who are aware of the risks of their chosen lifestyle" (Kataja et al 2018 p194).

Table 1.2 summarises the key differences between the two types of videos.

	Sobriety	Controlled Use
View on drugs	"symbolise the worst enemy" (p194)	"even act as helpers toward an ideal intoxication (when properly used" (p194)
Negative bodily experiences (eg: withdrawal)	presented as helpful in motivating abstinence	"expressed as the opponents implying that the use has slipped out of control" (p194)
Positive bodily experiences (eg: highs)	"presented as opponents that hamper quitting drugs, as they tempt the users to return to their old habits" (p194)	provide information about the effects of different substance combinations
Friends	Non-drug users can help, but drug-users hinder	Drug-users help
Overall message	temperance, which included healthy lifestyle and aspirations generally	less clear-cut message
General discourse on drugs	fits with "abstinence discourse"	fits with "harm reduction discourse"
Presenters	female	mostly male

Table 1.2 - Key differences, highlighted by Kataja et al (2018, between sobriety and controlled use videos.

San Mauro Martin et al (2018) outlined a situation of growing importance that there is "evidence that today's older people may be relatively heavier drinkers than previous generations, although historically older people have tended to drink less than any other age group ... Older drinkers consume alcohol far more often than any other age group, despite drinking comparatively little. The body of an older person is less able to clear the same levels of alcohol as in previous years, so alcohol remains in the body longer, producing a cumulative effect" (p199). This is exacerbated with the use of prescription and non-prescription medications.

San Mauro Martin et al (2018) investigated the use of medications and alcohol in a sample of 342 65-96 year-olds in Madrid, Spain. Questionnaires were completed which included total alcohol intake and types, and medication(s) used. Just under half the sample (47%) consumed medications and alcohol, but the figure was significantly higher for men (67%) than women (40%). Medication and alcohol was higher in the 60-69 year-olds, and declined with age (eg: 50% vs 42% of ≥ 80 year-olds).

The sample was opportunity, and the data were self-reports.

References

Kataja, K et al (2018) Sharing risk experiences of polydrug use on YouTube Drugs and Alcohol Today 18, 3, 188-197

Maffli, E & Astudillo, M (2018) Multiple substance use among patients attending treatment for substance-related problems in Switzerland Drugs and Alcohol Today 18, 3, 178-187

San Mauro Martin, I et al (2018) Prevalence of alcohol and medication use among elderly individuals in Spain Drugs and Alcohol Today 18, 3, 198-204

8.4. MISCELLANEOUS

Sedentary Behaviour

Sedentary behaviour "refers to sitting or lying while expending low amounts of energy" (Heron et al 2019 p625), and it is distinct from physical inactivity.

Sedentary behaviour has been linked to negative health consequences (eg: cardiovascular disease). Heron et al (2019) calculated a cost to the NHS in the UK of £0.7 bn per year of prolonged sedentary behaviour (\geq six hours of waking time) by around one-third of the population (using 2016-17 data). The study also calculated that around 70 000 deaths could be avoided by reducing prolonged sedentary behaviour.

"Pyjama paralysis" is a colloquial term used to

describe where older hospital in-patients spend their time in nightwear and in bed when they do not need to remain in bed. Prolonged bed rest is detrimental to recovery with a rapid decline in muscle strength and aerobic capacity, for example (Oliver 2017).

More formally, it is called "hospital associated deconditioning", and defined as "generalised weakness or loss of fitness because of muscle non-use" (Faieta et al 2019 p384) ⁷.

Experimentally, the impact of ten days of bed rest on healthy older adults has been studied by Kortebein et al (2007; 2008). Eleven healthy 60-85 year-olds volunteered for ten days of continuous bed rest. Multiple measures of physical functioning were taken before, during, and after.

Kortebein et al (2007) reported a loss of lean tissue from the legs, which was greater than the loss of younger adults in bed for 28 days. Kortebein et al (2008) outlined the reduction in aerobic capacity of the participants.

Altogether, three main areas of physical decline were noted:

- Lower leg strength and power - eg: stair ascent power significantly declined (ie: time to climb ten steps as fast as possible).
- Maximal aerobic capacity - approximately 10% decline when cycling for three minutes on an exercise bike.
- Physical performance - eg: steps per minute during a five-minute walk declined.

References

Dock, W (1944) The evil sequelae of complete bed rest Journal of the American Medical Association 125, 1083-1085

Faieta, J et al (2019) Reducing the effects of hospital-associated deconditioning: Post-acute care treatment options for patients and their caregivers Archives of Physical Medicine and Rehabilitation 100, 384-386

Heron, L et al (2019) Direct healthcare costs of sedentary behaviour in the UK Journal of Epidemiology and Community Health 73, 7, 625-629

Kortebein, P et al (2007) Effect of ten days bed rest on skeletal muscle in healthy older adults Journal of the American Medical Association 297, 1772-1774

Kortebein, P et al (2008) Functional impact of ten days of bed rest in healthy older adults Journal of Gerontology: Medical Sciences 63A, 10, 1076-1081

⁷ The detrimental effects were first reported in the 1940s (eg: Dock 1944).

Ready-to-Use Therapeutic Foods

"Ready-to-use therapeutic food" (RUTF) refers to "packaged, durable and easily dispensable food products that initially emerged as a humanitarian technology in zones of crisis - such as famine, war or natural disaster - where immediate intervention is necessary to preserve life" (Pentecost and Cousins 2018 p9). These are "nutraceuticals" (Street 2014) - ie: "foods that have been 'transformed' and 'enhanced' through technological or design processes, such as the fortification of foods with vitamins and minerals, the biofortification of food through plant breeding for nutrient-rich crops and the manufacture of dietary supplements" (Pentecost and Cousins 2018 p9).

However, RUTFs are used more widely than in humanitarian crisis zones, as in South Africa, where the "foods" are given to underweight pregnant women and HIV-positive individuals (Pentecost and Cousins 2018). RUTFs have become a normal part of care. "The everyday provision of RUTF here is not enacted as part of a humanitarian vision for saving lives, but as part of a much broader future-making project, predicated on an ambivalent politics of welfare provision and consumer citizenship" (Pentecost and Cousins 2018 p12).

While in India, Street (2014) has shown "the ways in which the nutraceutical industry has shifted from offering health supplements to the middle classes at risk of so-called 'lifestyle diseases' to including the marketing of fortified foods to poor and rural communities 'in a language of humanitarianism'" (Pentecost and Cousins 2018 p12).

These changes in the use of RUTFs is part of what Pentecost and Cousins (2018) called "the temporary as the future". "RUTF provision to the undernourished pregnant woman as part of state policy thus rests on an anticipatory logic that does not seek to save lives in the immediate sense, but to secure life as capital in the long term. RUTF thus appears alongside antenatal care as a reproductive technology to secure the future, recalling Donna Haraway's [1997] suggestion that agribusiness technologies and computers in financial capitals are as much reproductive technologies as sonograms and in vitro fertilisation" (Pentecost and Cousins 2018 p13).

References

Haraway, D.J (1997) Modest_witness@second_millennium. Femaleman_meets_oncomouse New York: Routledge

Pentecost, M & Cousins, T (2018) The temporary as future Anthropology Today 34, 4, 9-13

Street, A (2014) Food as pharma: Marketing nutraceuticals to India's rural poor Critical Public Health 25, 3, 361-372

Sociology of Complementary Medicine

Gale (2014) noted that "complementary and alternative medicine (CAM) and traditional medicine (TM) are important social phenomena. National and regional studies in the 'developed' world have shown high usage of CAM, especially for those with chronic diseases, such as cancer... In the 'developing' world, traditional medicines can be the 'mainstay' of health care delivery, particularly in remote or rural areas" (p805).

But the terminology for these practices can vary. Gale (2014) made two points here: "First, that naming is an exercise in power that in this field tends to be reflective of 'Western' biomedical dominance internationally and, second, that the dualism evident in most terms and definitions used is a product of historical social construction" (p806).

Broom (2002) observed: "Weak assertions ['we are scientific', 'we are holistic'] become hard facts as they find their way into textbooks, lectures and publications. In this way, they become symbolic of particular groups and organisations, and ultimately such representations come to be viewed as reflective of the natural order" (quoted in Gale 2014).

The binary of biomedicine and "alternative" practices is not always clear-cut as definitions and categories change over time, and both of them include great diversity themselves. Furthermore, similarities between practitioners are ignored as well as growing "integrative" approaches (Gale 2014).

"Medical pluralism" (Cant and Sharma 1999) (or "hybridity"; Frank and Stollberg 2004) has been used to describe, for example, users or consumers who "tend to make choices based on pragmatism and perceived therapeutic effectiveness rather than philosophy or scientific evidence" (Gale 2014 p810). Some writers have argued that integrative medicine can be empowering for the patient (eg: cancer patients; Smithson et al 2010).

It is possible to also see the use of CAM as health activism or resistance to the power of biomedicine and its control of the body (Gale 2014).

"Probably the most ubiquitous question in wider society about CAM is 'Does it work?'" (Gale 2014 p814). A sociological response might critique the criteria by which this question is answered. The apparently objective criteria of science are, in fact, products of social processes. An alternative approach, developed through

medical anthropology, is the concept of "body-stories" (Gale 2011) to describe the individual's experience of illness, medicine, and healing (ie: the experiences of embodiment and intersubjectivity) (Gale 2014).

References

- Broom, A (2002) Contested territories: The construction of boundaries between alternative and conventional cancer treatments New Zealand Sociology 17, 2, 215-234
- Cant, S & Sharma, V (1999) A New Medical Pluralism? London: UCL Press
- Frank, R & Stollberg, G (2004) Conceptualising hybridisation on the diffusion of Asian medical knowledge to Germany International Sociology 19, 1, 71-88
- Gale, N.K (2011) From body-talk to body-stories: Body work in complementary and alternative medicine Sociology of Health and Illness 33, 2, 237-251
- Gale, N.K (2014) The sociology of traditional, complementary and alternative medicine Sociology Compass 8/6, 805-822
- Smithson, J et al (2010) Cancer patients' experiences of using complementary therapies: Polarisation and integration Journal of Health Services Research and Policy 15, sup 2, 54-61

Evolutionary Medicine

Evidence has emerged in recent years that early-life effects influence adult development (and even future generations) in conditions like obesity and type 2 diabetes. How and why has natural selection come favour this developmental plasticity?

Kuijper et al (2019) considered this question: "Natural selection is a process for maximising (inclusive) fitness, but this is very much a constrained optimisation problem – bounded by physical and energetic constraints imposed by the ecological and social environment, by constraints on information, and by the apparatus of genetic and cellular machinery" (p2).

"Evolutionary medicine" has developed as a field to answer such questions. Two key insights on disease have come from this discipline (Kuijper et al 2019):

- Natural selection "works" on certain traits to enhance survival, not health.
- The response of traits to natural selection is limited by certain constraints.

Evolutionary medicine makes use of the concept of mismatches as in a novel environment not experienced in evolutionary history (evolutionary mismatch) or during a life-time (developmental mismatch). The latter depends on predictive adaptive responses (PARs). "For example,

certain responses to early-life malnutrition ... are likely to be the result of a prediction in utero of later-life nutritional environments, but will result in malprediction when individuals are faced with nutrition-rich diets later in life (often resulting in metabolic disorders" (Kuijper et al 2019 p2).

Reference

Kuijper, B et al (2019) Developing differences: Early-life effects and evolutionary medicine Philosophical Transactions of the Royal Society B 374, 20190039

Cancer Facts?

The lifetime chance of a cancer diagnosis in the UK is 1 in 2 (Goodman 2019), but there are risks than an individual can reduce. However, health messages can often seem confusing (Goodman 2019).

There are a number of factors that are involved in this confusion, including:

i) Research issues

- New and emerging evidence can mean that previously non-risk factors become risk factors (eg: injuries and skin cancer - possible link; Goodman 2019).
- Controlled experimental studies on carcinogens are usually with laboratory animals, but the applicability to humans can be debatable.
- Problems in controlling confounding factors in human studies.
- Simple links between cause and effect are rarely obvious (eg: lifetime heavy smoker who does not develop lung cancer).
- Problems with identifying all the interconnecting factors, and how they interconnect.
- The role of genes, and our knowledge about them.

ii) Information issues

- Articles on the Internet by "enthusiasts" that can best be described as "misinformation" (eg: anti-perspirant and breast cancer ("very unlikely") Goodman 2019).
- Vested interests funding research to show what they

want or hide what they do not want known (eg: tobacco industry historically).

- Media "scare stories" (eg: mobile phone use and brain cancer in "Observer" July 2018 ("unlikely with moderate use") Goodman 2019).

Table 1.3 outlines some risk factors as known at this point.

FACTOR	RISK
Overweight/obesity	General cancer - definitely
Tobacco	Lung - definitely
Sun/UV radiation	Skin - definitely
Hepatitis B and C	Lymph and liver - definitely
Human papillomavirus	Cervical - definitely for some strains
Alcohol	General - yes, but unlikely in moderation
Talcum Powder	Ovarian - possibly
Coffee	General - unlikely in moderation
Power lines	General - unlikely
Stress	General - unlikely
Aspartame (artificial sweetener)	Brain - no conclusive evidence
Water fluoridation	Bone - unlikely

(Source: Goodman 2019 p37)

Table 1.3 - Some risk factors for cancer.

Malvezzi et al's (2019) analysis of European Union (EU) data predicted a general decline in cancer mortality for 2014 to 2019. The marked decline in cigarette smoking in recent years is seen as important, along with screening and early diagnosis and treatment, while the ageing population, and obesity are negative factors, particularly for breast cancer.

References

Goodman, J.R (2019) Confused about cancer? New Scientist 9th February, 34-37

Malvezzi, M et al (2019) European cancer mortality predictions for the year 2019 with focus on breast cancer Annals of Oncology 30, 5, 781-787

Body Temperature

Normal body temperature was determined as 37 °C in 1868 (Hausmann et al 2018). But there is evidence that the temperature fluctuates over the 24-hour period. Smartphone technology has allowed researchers to gather data on the subject.

Hausmann et al (2018) collected data from 329 US participants via a crowdsourcing app for the iPhone. Participants took their temperature with a thermometer at various times of the day, and recorded the information on the app along with physical symptoms.

The mean normal temperature was 36.5 °C, with variations from 36.1 °C (between 3-5 am) to 36.7 °C (between 4-6 pm). Mean male body temperature was lower than women's (36.5 vs 36.6 °C).

Participants collected "real-life" data, but there was no way to verify the thermometer readings.

Reference

Hausmann, J.S et al (2018) Using smartphone crowdsourcing to redefine normal and febrile temperatures in adults: Results from the Feverprints Study Journal of General Internal Medicine 33, 12, 2046-2047

Four Loko Effect

In the USA in 2010, there were cases in the news of severe alcohol intoxication from a fruit-flavoured, caffeinated, alcohol drink called "Four Loko". The Food and Drug Administration (FDA) asked the manufacturers to remove the caffeine (which the company claimed was comparable to a cup of coffee) (Siegel 2011).

The concern was that the caffeine exacerbated the effects of the alcohol. For example, some authors "suggested that the stimulant effect of caffeine may antagonise the soporific effect of alcohol and that 'lengthened time awake theoretically allows greater alcohol intake before loss of consciousness' (Weldy 2010)" (Siegel 2011 p358).

Siegel (2011) found no studies on time-to-unconsciousness comparing caffeinated and non-caffeinated alcoholic drinks, while the research on the caffeine-alcohol interaction was mixed. This led Siegel (2011) to state that "the evidence that caffeine is the agent responsible for the alleged displays of excessive intoxication seen following consumption of the original formulation of Four Loko and similar beverages is not overwhelming" (p358).

An alternative explanation is that drinks like Four Loko "provide alcohol in an unusual context. It has been

known for many years that drugs in general, and alcohol in particular, have a greater effect if they are administered in the presence of unusual cues rather than in the presence of cues typically associated with the drug. Thus, if you present alcohol in a manner divorced from the usual alcohol-associated stimuli, the effects of the alcohol are enhanced. That is, the drug-experienced individual does not display the expected tolerant response to the drug when it is administered in the presence of cues not previously associated with the drug" (Siegel 2011 p358).

Siegel (1976) has called this "the situational specificity of tolerance". For example, the same amount of caffeine injected into the bloodstream has a greater effect on blood pressure than drinking a cup of coffee (Siegel 2011).

In terms of experiments with alcohol, McCusker and Brown (1990) gave beer to students in a simulated beer (usual form and context) or alcohol mixed with sweetened carbonated water in an office setting (unusual form and context). "Based on several objective measures of intoxication, the unusual context group became more inebriated than the usual context group" (Siegel 2011 p359).

Applying these ideas to Four Loko, Siegel (2011) explained that "many people have become very drunk after consuming Four Loko because the drink provides a novel context for alcohol administration; alcohol tolerance, having been acquired in the context of different cues, may not be exhibited in the context of Four Loko cues. Perhaps the rather unwieldy phrase 'situational-specificity of tolerance' should be renamed the 'Four Loko effect'" (p359).

References

McCusker, C.G & Brown, K (1990) Alcohol-predictive cues enhance tolerance to and precipitate "craving" for alcohol in social drinkers Journal of Studies on Alcohol 51, 494-499

Siegel, S (1976) Morphine analgesic tolerance: It situation specificity supports a Pavlovian conditioning model Science 193, 323-325

Siegel, S (2011) The four-loko effect Perspectives on Psychological Science 64, 4, 357-362

Weldy, D.L (2010) Risks of alcoholic energy drinks for youth Journal of the American Board of Family Medicine 23, 555-558

Ingestion

Children under three years old ingest objects as they learn to explore the environment - most commonly coins, followed by "toy parts" (Tagg et al 2019). Spitz (1971) reported that coins pass through the infant's body

in 3-6 days with no adverse effects.

Tagg et al (2019) recruited six volunteer health-care professionals to swallow a "Lego mini-figure head" (roughly 10 x 10 mm in size). Participants kept a stool diary for three days prior to swallowing, and during the period of ingestion. The average time taken was 1.71 days (ranging from 1.14 to 3.04 days), and stool consistency did not change during ingestion.

References

Spitz, L (1971) Management of ingested foreign bodies in childhood
British Medical Journal 4, 469-472

Tagg, A et al (2019) Everything is awesome: Don't forget the Lego
Journal of Paediatrics and Health 55, 8, 921-923

Sunshine

Concern over too much sun and the negative risks has grown in recent years, while the possibility of vitamin D deficiency, for instance, from too little sun has been pushed into the background. Vitamin D is used by bone and muscle cells, but also the immune system (Geddes 2019).

Recent studies have suggested that vitamin D can prevent upper respiratory tract infections, for instance, while mice exposed to UV (ultra-violet) light (as in sunlight) were less likely to develop an autoimmune condition (Geddes 2019).

A large-scale Swedish longitudinal study (Melanoma in Southern Sweden; MISS) (table 1.4) found that women who spent more time in the sun lived longer, despite the increased risk of skin cancer. Over eleven years of follow-up, there were 2545 deaths, and sun avoiders were double the highest sun exposure group (Lindqvist 2018).

- In 1990 MISS began with 29 518 women with no history of cancer, who responded to a request from researchers.
- Sun exposure habits were measured by 4 questions:
 - i) "How often do you sunbathe during the summertime?" (never; 1-14 times; 15-30 times; >30 times).
 - ii) "Do you sunbathe during the winter, such as on holidays to the mountains?" (no; 1-3 days; 4-10 days; >10 days).
 - iii) Do you use tanning beds?" (never; 1-3 times/year; 4-10 times/year; >10 times/year).
 - iv) "Do you go abroad on holiday to swim and sunbathe?" (never; once/1-2 years; once/year; two or more times/year).
- All the answers were grouped in five overall categories, from 0 (avoiding sun) to 4 (highest sun exposure).

Table 1.4 - Melanoma in Southern Sweden (MISS).

One possibility is that sunlight reduces blood pressure via UV-activated nitric oxide, and this improves life expectancy (Geddes 2019).

Dermatologist Richard Weller admitted: "I am conflicted... Sunlight is good and bad" (quoted in Geddes 2019). The answer is short periods in the sun, appropriate to the skin type, and an awareness of the UV index (ie: strength of the sun) (table 1.5) (Geddes 2019).

	Light skin:		Dark skin:	
	Winter	Summer	Winter	Summer
Tropical latitudes (ie: close to equator)	5-10	1-5	30-45	15-20
Higher latitudes (eg: UK)	Difficult to make any vitamin D	5-10	Difficult to make any vitamin D	25-40

(Source: Geddes 2019 p31)

Table 1.5 - Approximate number of minutes needed in midday sun to get daily dose of vitamin D.

References

- Geddes, L (2019) Let the sun shine New Scientist 16th March, 28-32
- Lindqvist, P.G (2018) The winding path towards an inverse relationship between sun exposure and all-cause mortality Anti-Cancer Research 38, 1173-1178

Fasting-Mimicking Diet

Fasting-mimicking diets (FMDs) involve reducing food intake to one-tenth of normal amount, say, for a period of days. Rangan et al (2019) reported benefits of such a diet in mice with inflammatory bowel disease (IBD)- like symptoms.

A four-day FMD was used, which involved 50% of normal calorie intake on Day 1, and 10% of normal intake subsequently. The control group diet was two-day water-only fasting, and half the mice in the study had dextran sodium sulfate-induced colitis, which mimics human IBD.

Reference

- Rangan, P et al (2019) Fasting-mimicking diet modulates microbiota and promotes intestinal regeneration to reduce inflammatory bowel disease pathology Cell Reports 26, 2704-2719

Non-Communicable Diseases

"Non-communicable diseases" (NCDs) is a commonly used term, but it "lacks a consolidated definition" (Blundell and Hine 2019 p5). The World Health Organisation (WHO) emphasised that it means "chronic diseases... not passed from person to person" (ie: non-infectious) (quoted in Blundell and Hine 2019). NCDs usually include cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes (Blundell and Hine 2019).

"Combining diseases under a single classification may secure advocacy and action, as in the case of the neglected tropical diseases (NTDs) with the establishment of the London Declaration in 2012. Defined after the NTDs, the NCD movement has mobilised the global health community and engaged political leaders in a previously neglected public health concern. But is the term fit for purpose into the future?" (Blundell and Hine 2019 p5).

One problem is that the category NCD has grown in its inclusion (eg: mental health problems, disabilities, trauma), while "creating a false dichotomy between diseases with infectious and non-infectious risk factors" (Blundell and Hine 2019 p5). For instance, around one-tenth of human cancers have a viral infection-basis, as do some diseases grouped as cardiovascular diseases (eg: rheumatic fever) (Blundell and Hine 2019).

Blundell and Hine (2019) continued: "The term non-communicable may also cause us to overlook biosocial contagions. Communication of microbes and communication of social risk factors might not be so different: consider how streptococcal infection and nicotine addiction might be 'communicated' across one proffered cigarette. The communication of both these entities is likely mediated by poverty, the tackling of which requires the global health community to engage both political and public awareness" (p6).

Blundell and Hine (2019) made their position clear: "we should scrap the NCD label now. We must stop defining them by what they are not and define them as what they are: 'human-made illnesses'. Cigarettes, recreational drugs and alcohol are sold to the vulnerable, environments are polluted by human activities, mass media and crime on the streets breed conditions for physical inactivity and food poverty is a challenge that exists even in high-income countries" (p6).

Reference

Blundell, H.J & Hine, P (2019) Non-communicable diseases: Ditch the label and recapture public awareness International Health 11, 5-6

Distorted Body Perception

Distortions of body image are part of eating disorders, for example, but Sadibolova et al (2019) found that individuals generally underestimate the volume and overestimate the length of body parts. Forty participants were asked to estimate the volume and length of body parts while wearing a black smock which stopped them from looking.

The estimation of length was based on their hand length or a short stick, and the volume involved the width of their hand or a small cube. Both the largest volume underestimation and length overestimation were for the torso.

Sadibolova et al (2019) asserted that knowledge of perceptual distortions of body image in healthy individuals will help to distinguish the distortions in individuals with clinical disorders.

Reference

Sadibolova, R et al (2019) Distortions of perceived volume and length of body parts Cortex 111, 74-86

Schooling

There is a positive correlation between length of education/educational qualifications, and health and longevity. But establishing the causal nature of the relationship is difficult for various reasons, including (Courtin et al 2019):

a) The presence of common factors for education and health (eg: early life circumstances).

b) The possibility of reverse causation - ie: childhood health influences educational attainment.

c) Whether length of schooling is the same as educational qualifications in relation to health and longevity.

d) What is the biological mechanism underlying the correlation?

e) How to test the correlation in real-life?

In relation to the latter point, the 1959 Berthoin reform raised the minimum school leaving age from 14 to 16 years old in France (ie: for all children born after 1st January 1953), and Courtin et al (2019) used this event in a quasi-experimental study. Data were analysed

from a cohort of French adults, with particular reference to those born 48 months before the reform and those born 48 months after (n = 18 915). Health data were available since 2012 (eg: blood pressure; cholesterol levels; body mass index).

Courtin et al (2019) summed up the findings: "Although there is a clear association between higher educational attainment and lower biological risk profiles in our sample, our results also indicate that a policy that increased schooling duration did not translate into improved health as measured by biomarkers. We find no evidence of health benefits for participants from intermediate and high parental social class, and we find some evidence that the reform may have had negative effects on blood pressure and white blood cells counts for respondents from poorer families" (p383).

The authors offered a possible explanation for their findings in that the Berthoin reform increased schooling leaving age only (ie: it did not require the pupils to gain new qualifications or skills). "This would be consistent with the 'sheepskin effect' [Liu et al 2014], the idea that it is educational credentials which may potentially benefit health, and not the number of years of schooling" (Courtin et al 2019 p384).

Furthermore, no increase in qualifications would have a limited effect on job prospects, and "education is hypothesised to influence health partly by enhancing access to health-promoting resources such as knowledge, social networks and better jobs and earnings" (Courtin et al 2019 p384).

Courtin et al (2019) ended: "Our findings do not necessarily question the notion that education leads to better health, but they suggest that law-mandated increases in schooling duration alone may not be sufficient to improve the health of disadvantaged groups" (p385).

References

Courtin, E et al (2019) Longer schooling but not better off? A quasi-experimental study of the effect of compulsory schooling on biomarkers in France Social Science and Medicine 220, 379-385

Liu, S.Y et al (2014) Sheepskin effects of education in the ten-year Framlingham risk of coronary heart disease Social Science and Medicine 80, 1, 31-36

Health Inequality

US life expectancy is low considering the amount of per capita health expenditure (Stiglitz 2018), and this is worsened by the "deaths of despair" (Case and Deaton 2017) (eg: alcoholism, drug overdoses, suicides).

Health inequality is also caused by access to health care, and level of risk (eg: consumption of poor diet).

Wilkinson and Pickett (2010) argued that income equality (ie: "poverty among plenty") worsens health inequality. The mechanism that translates the social structure into health is stress. Low socio-economic status individuals are in a permanent state of stress which has negative consequences (Sapolsky 2018).

References

Case, A & Deaton, A (2017) Mortality and morbidity in the 21st century Brookings Papers on Economic Activity 1, 397-476

Sapolsky, R.M (2018) The health-wealth gap Scientific American November, 56-61

Stiglitz, J (2018) A rigged economy Scientific American November, 50-55

Wilkinson, R & Pickett, K (2010) The Spirit Level: Why Greater Equality Makes Societies Stronger London: Bloomsbury Press

2. BIOETHICS TOPICS

- 2.1. Rational suicide and physician-assisted death
- 2.2. Bioethical issues
- 2.3. Miscellaneous

2.1. RATIONAL SUICIDE AND PHYSICIAN-ASSISTED DEATH

"Rational suicide" is "a desire for suicide in the absence of diagnosed psychiatric illness" (Dzeng and Pantilat 2018 p853).

Dzeng and Pantilat (2018) argued that three factors together accounted for the increase in this behaviour among older adults:

i) Neoliberalism - Neoliberal policies since the 1970s have "created a culture that redefines citizens as consumers, whereby competition and market-based metrics become dominant ideological forces that permeate all aspects of human life. Neoliberalism changed human relationships within society from a civil sphere that enshrined a commitment to social solidarity and collaboration among fellow citizens to that of a universal market where human beings are pawns in calculations of profits and losses. Rather than emancipation and freedom, the markets created atomisation and loneliness" (Dzeng and Pantilat 2018 p853). Put simply, older adults feel of little value to society.

ii) Technology - "The technology industry has accelerated the broader temporal trends toward ageism and fear of decay... More than ever before, ageing is perceived as something to be vanquished, rather than a natural human experience. The declaration of ageing as a disease, pathologises ageing as an entity to be shunned and avoided, in oneself and others" (Dzeng and Pantilat 2018 pp853-854).

iii) Changing attitudes towards the legalisation of physician-assisted death (PAD) - On the other hand, technology has created the ability to sustain life in serious illness. "Concerns about overly aggressive care at the end of life and of unrelenting suffering have in part fuelled advocacy for PAD, with many people seeing aggressive medical interventions and unrelieved suffering at the end of life as avoidable only through premature self-inflicted death" (Dzeng and Pantilat 2018 p854).

Sulmasy et al (2018) argued that "autonomy alone does not justify PAD, as it must be weighed by the other ethical principles such as justice, beneficence (best interest), and non-maleficence (first do no harm). They

also argue that PAD is not a healing act and can also cause further harm by jeopardising the trust inherent in the physician-patient relationship" (Dzeng 2018 p1209).

Furthermore, they argued that "allowing PAD can send social messages, including one that devalues lives by suggesting that there are certain states that are not worth living. Legalising PAD could slowly change social norms that might encourage suicide contagion, normalise PAD leading to an incremental extension of PAD, and further perpetuate the image of pain and suffering as an inevitable part of death" (Dzeng 2018 p1209).

Dzeng (2018) emphasised the context of the debate with the development of life-sustaining technologies which can "delay death at all costs", and produce longevity over quality of life. "A default of aggressive care in the hospital, financial incentives to overtreat, social pressures to be a 'fighter', and the inherent emotional trauma and fears of death, further encourage a culture of care that prioritises high-intensity care at the expense of humanistic care" (Dzeng 2018 p1209). A desire to combat this approach is part of the growing acceptance of PAD among the public as they "empower themselves against prolonged suffering", Dzeng (2018) suspected.

Levitan (2012) described the idea of "boomericide" - rational suicide for a "Baby Boomer". "Baby Boomers" are a cohort born between the end of World War II and 1960 roughly, and they "value youth, personal fulfilment, and the ability to remain active after retirement and generally have negative attitudes toward ageing" (Balasubramaniam 2018 p999). They also face institutional end-of-life care more than previous cohorts, and these factors may account for the interest in rational suicide (Balasubramaniam 2018).

Psychiatric Patients

PAD for terminally ill individuals is different to psychiatric patients. "Unlike a stage four terminal cancer patient, those suffering from mental illness are supposedly not facing an impending death from their disorder that is reasonably foreseeable... A pivotal question is whether separate and additional safeguards should be required for psychiatric patients than for those with terminal or general medical conditions" (Waring 2019 p2). Individuals with long-term (treatment-resistant) major depression are a prime example here, and a wish to die can be high.

But a wish to die is not always the same as wanting PAD. "A wish to die can have various meanings, eg: it can be a wish to allow a terminal illness to take its course and to 'let death put an end to severe suffering', a wish

to spare others from dealing with the burden of oneself, a wish to preserve self-determination, a wish to end a life that is now without value, or a wish 'to move on to another reality'. A wish to die can also have various functions, eg: as an appeal for attention, a vehicle to talk about dying, or 'a means for re-establishing agency'. Wishes to die can fluctuate widely between these meanings and functions" (Waring 2017 p3).

In terms of incurability, which is often a criteria for PAD, Downie and Dembo (2016) distinguished between individuals where no treatment is available, and where treatment is available but individuals find it unacceptable (ie: treatment refusal). The former includes where available treatment has been tried and did not work (or are not likely to work) (Waring 2019).

Capacity to decide is an issue, particularly in "all-consuming depressions in which persons lose any sense of what life without depression was or could be like" (Waring 2019 p8).

Subjective Experience of Wishes to Die

Ohnsorge et al (2019) observed that wishes to die (WTD) among patients undergoing end-of-life care have "multi-dimensional reasons, hold subjective meanings, and consist of diverse and dynamic intentions, which in addition are weighed against each other over time. A WTD does not always contain a wish to hasten death. It is not uncommon for patients' wishes with regard to living or dying to change from WTD (and even wishes to hasten death) into wishes to live and also the other way around, even in the final weeks of life" (p2).

Among cancer patients, a small number express WTD (eg: 12% of 377 Canadians; Wilson et al 2016), but the figures vary depending on the definition of WTD used in the study (Ohnsorge et al 2019). Among individuals with neurological diseases, slightly more report WTD, but less for organ failure patients (Ohnsorge et al 2019).

In terms of the motivations for WTD, pain and fatigue are commonly mentioned, along with existential-spiritual and non-physical reasons like "depression, demoralisation, hopelessness, a sense of abandonment, fear of the future, fear of losing control or the sense of self, the perception of being a burden to others, poor family cohesion or social support, high levels of anxiety, and existential suffering" (Ohnsorge et al 2019 p3).

Ohnsorge et al (2019) interviewed thirty cancer and 32 non-cancer patients, and their families and healthcare

professionals to give a total of 248 persons. The semi-structured interviews in palliative care facilities in Switzerland covered the "anatomy of the WTD" - the intention (what the wish aims for), the motivation (why the wish is there), and the social interactions related to WTD.

The findings were grouped into "trajectories" based on type of patients:

1. Patients with neurological diseases.

Intentions - A WTD for when life became unbearable.

Motivations - Worries about burdensome and the "image of a total loss of sovereignty".

Social interactions - "Observing the suffering of other people with the same illness often brought people with ALS [amyotrophic lateral sclerosis] or MS [multiple sclerosis] to wonder what kind of development, symptoms or state of health they themselves would find unbearable. Sometimes these observations gave rise to the expression of a hypothetical WTD. One man with MS, remembering a friend with MS who spent months in a state of dementia in which she did not recognise anyone, said: 'No. I mean, if I realised that something isn't good any more like this [ie: the dementia in his friend with MS], then I wouldn't want to live any longer'" (Ohnsorge et al 2019 p10).

2. Patients with organ failure.

Intentions - "After the experience of an acute life-threatening health crisis, however, alongside their wishes to live many of these patients also developed a hypothetical WTD for the future, wanting to avoid having to go through another crisis" (Ohnsorge et al 2019 p11).

Motivations - "Patients reported that coping with a life-threatening crisis required enormous amounts of physical and psychological energy. Some explained that they had already accepted that they were 'dying', and found it difficult to readjust and continue living. The burdensome experience of previous crises (eg: acute respiratory crisis) and the fear of having to go through another made some patients consider the possibility of hastening dying, and some then decided to let death happen at the next crisis" (Ohnsorge et al 2019 p11).

Social interactions - Physicians usually rejected the WTD at moments of acute crisis. "These physicians held that such a decision required thorough communication and longer reflection than was possible in a state of crisis.

One person who came to the emergency department... said that the physician 'at that moment broke his will'..., because he refused to follow his patient's request to stop treatment. Retrospectively, however, the patient agreed with the physician's decision" (Ohnsorge et al 2019 p12).

3. Frail elderly patients.

Intentions - "As in the other patient groups, frail persons... also expressed a variety of intentions in WTD, ranging from sporadically expressed WTD without any wish to hasten death..., to hypothetical wishes to die at some point in the future..., to concrete requests to hasten death" (Ohnsorge et al 2019 p13).

Motivations - The WTD was often connected to aspects of ageing (eg: loss of function; loss of interest in life). One woman's words are an example here: "When you have [...] to relinquish things piece by piece in old age, it's difficult up here. In your head. That's what [bothers me] most, it's really a matter of life. [...] If that's life... you're born. You have all these years. And when you go back, all that goes backwards again. And you have to experience so much where you think, no, that can't be possible. [...] It's really not easy! [...] I just hope that it doesn't last much longer. It no longer really has meaning for me, you know. I'm not clinging to anything. [...] I have no more desires. It's here, but do what you want for all I care. It doesn't mean anything to me anymore" (p14).

Social interactions - The feeling of not being needed by anyone was reported, as in one participant's words: "...what am I here for actually, and the children are grown up, they have their own life, you don't have anything to say any more. So I could just go, I think I could just go. [...] I'm not needed any longer" (p14).

4. Patients with cancer.

Intentions - A stronger concrete WTD than other patients, and many of the interviewees here were members of a Swiss right-to-die organisation.

Motivations - "Many interviewees wished to die because of the high physical and psychological burden of symptoms such as pain, dyspnea, chronic nausea, fatigue, anxiety or depression. They wished to die so that death could put an end to severe suffering, to a situation that was seen as an unreasonable physical or psychological demand, or to end a life they felt was now without value" (Ohnsorge

et al 2019 p15).

For example, this woman said: "You know, I have battled with this stupid cancer for a year and a half. I really tried all the operations, tried all the chemo, and as long as there was even a tiny bit of hope, just the tiniest bit, I still travelled to Lausanne to have an operation, I did everything, but the moment they said, we can't do any more for you, I said, okay, now it's finished, now I can't fight any more, now I don't even want to fight any more, I would like to die now, I'd like to go now. That was quite clear for me" (p16).

Social interactions - Less concern about being a burden to others as the patients' dependence were for a shorter time and less heavily than other groups. Relationships with family members both improved and deteriorated.

Altogether, the patient groups were similar in having "hypothetical WTD" (ie: if the worse happened), though this was triggered differently. "For neurological patients, it was when they had to consider starting tube feeding or respirator support. The onset of advanced breathlessness, spasmodic contractions or immobilisation that significantly compromised quality of life and indicated the proximity of death, and moments when deciding to initiate palliative sedation, were other important time-points for neurological patients. Patients with organ failure experienced time-restricted WTHD [wishes to hasten death] during an acute crisis and for future crises. Patients with cancer often reflected on a WTD soon after the initial diagnosis, the first relapse, significant aggravations, and during the shift from curative into palliative care (if understood as a clear 'cut' in patient-physician communication: 'there is nothing we can do'; 'then I stopped fighting')" (Ohnsorge et al 2019 pp19-20) (table 2.1).

In terms of the motivations, Ohnsorge et al (2019) felt that they were "able to show very clearly that the strain of engaging with life again after a life-threatening health crisis, the feeling of being stuck in an in-between state, the unpredictability and great complexity of illness, could all be a motivation for a WTD. The continual repetition of thinking they were going to die, and then having to start again and find their way back into life, was described by these patients as demanding enormous amounts of energy. Some wanted to die because they felt the effort to be too much. Others said they wished to die because they did not want to feel stuck in an 'intermediate state' in which they were not dying, but not living well either. Finally, one patient expressed a wish to die because of the fact that their pathologies finally became so complex that treatments were mutually exclusive" (p18). Table 2.2 summarises key differences between the four groups.

Similarities of wishes to die in all four trajectories (neuro, organ failure, frailty, cancer)

- WTD are complex and dynamic;
- WTD appear frequently in the experience of dying;
- subjective meaning of WTD includes a) intentions, b) motivations, c) social interactions;
- a variety of intentions of WTD are present in all patient groups;
- WTD can be fluctuant and change over time, even close to dying;
- WTD can contain various wishes next to each other: wishes to live, various wishes to die with or without wishes to hasten death;
- hypothetical WTD expressed in all groups;
- hypothetical WTD of persons who think themselves close to dying are more realistic and concrete than those who think themselves far from dying;
- in all groups there are particular moments or incidences that trigger a WTD;
- feelings of 'being a burden to others' appear as reason for WTD in all trajectories.

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(Source: Ohnsorge et al 2019 table 3)

Table 2.1 - Similarities of WTD between the four groups of patients.

Ohnsorge et al (2019) concluded: "Illness-related considerations alone do not give a comprehensive insight into the entirety of the WTD, but provide important information on (a) the challenges that particular patient groups commonly face and that might lead to the formulation of a WTD; and (b) what to investigate when wanting to understand the WTD of a particular patient. Looking at the WTD through a 'trajectory lens' shows that people dealing with similar trajectories are often confronted with similar questions and concerns due to facing common challenges. These challenges set the conditions under which WTD are articulated" (p21).

Differences and typical patterns of wishes to die among the four trajectories	
Neuro	<p>Hypothetical WTD: should conditions in future become unbearable.</p> <p>Fears behind hypothetical WTD: physical suffocation, dependence on others and on breathing support, being rendered immobile, fear of being completely dependent and losing sovereignty.</p> <p>For some, hypothetical WTD served the function of being in control when confronted with increasing loss of autonomy.</p> <p>Points in the illness trajectory that triggered a WTD: considering starting tube feeding or respirator support, the onset of advanced breathlessness, spasmodic contractions or immobilization, significantly compromised quality of life and deciding to initiate palliative sedation.</p> <p>Advanced care planning can counteract a WTD.</p>
Organ failure	<p>Wish to hasten death can appear during a life-threatening crisis.</p> <p>Hypothetical WTD: should there be another life-threatening crisis, to avoid unwanted experiences and pain.</p> <p>Motivations for a WTD: significant deterioration of health, fear of the next life-threatening crisis, feeling of being stuck in a state between life and death, too much effort of starting life after crisis, the unpredictability and great complexity of illness.</p> <p>Points in the illness trajectory that triggered a WTD: during an acute crisis.</p>
Frailty	<p>Approaching death is not an abstract future event, but something to relate to and ponder about.</p> <p>Repetitively expressed WTD are often specific to this patient group.</p> <p>Motivations for WTD: Feelings of being worthless, of alienation from society and other generations, physical deterioration, loss of activity, increasing dependence, institutionalization, the loss of friends and relatives, feeling of estrangement, perceptions of a change in thought processes, general loss of interest in life, social isolation and loneliness besides more objective factors described by other studies.</p> <p>Together with cancer patients, fear of being a burden to others strongest in this patient group.</p> <p>Points in the illness trajectory that triggered a WTD: giving up one's home, moving into care facilities, loss of important relationships or physical abilities.</p>
Cancer	<p>WTD often expressed in situations of high physical burden and emotional suffering.</p> <p>Frequent hypothetical WTD for the future.</p> <p>Motivations for WTD: to let death put an end to severe suffering, to end a situation perceived as unreasonably demanding, or to end a life they felt was now without value, wanting to control of future events, lack of a longer-term perspective and hopelessness due to the clear awareness of approaching death.</p> <p>Together with frail elders, fear of being a burden to others strongest in this patient group.</p> <p>Points in the illness trajectory that triggered a WTD: diagnosis, relapse or diagnosis of metastasis, significant aggravations or during the shift from curative into palliative care.</p>

<https://doi.org/10.1371/journal.pone.0210784.t004>

(Source: Ohnsorge et al 2019 table 4)

Table 2.2 - Differences of WTD between four groups.

References

- Balasubramaniam, S (2018) Rational suicide in elderly adults: A clinician's perspective Journal of the American Geriatrics Society 66, 998-1001
- Downie, J & Dembo, J (2016) Medical assistance in dying and mental illness under the new Canadian law Journal of Ethics in Mental Health 9, 11
- Dzeng, E (2018) Can growing popular support for physician-assisted death motivate organised medicine to improve end-of-life care? Journal of General Internal Medicine 33, 8, 1209-1211
- Dzeng, E & Pantilat, S.Z (2018) Social causes of rational suicide in older adults Journal of the American Geriatrics Society 66, 853-855
- Levitan, P (2012) Boomericide: From Woodstock to Suicide Portland, OR: Portlandia Press
- Ohnsorge, K et al (2019) Wishes to die at the end of life and subjective experience of four different typical dying trajectories. A qualitative interview study PLoS ONE 14, 1, e210784 (Freely available at <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0210784>)

Sulmasy, D.P et al (2018) Physician-assisted suicide: Why neutrality by organised medicine is neither neutral nor appropriate Journal of General Internal Medicine 33, 8, 1394-1399

Waring, D.R (2019) Wishing you won't be here: Medical assistance in dying for psychiatric patients Ethics, Medicine and Public Health 8, 1-10

Wilson, K.G et al (2016) Mental disorders and the desire for death in patients receiving palliative care for cancer BMJ Supportive and Palliative Care 6, 2, 170-177

2.2. BIOETHICAL ISSUES

Mill (1972) imagined a "marketplace of ideas" (as in the capitalist model of buyers and sellers) that "rational or reasonable citizens engaged in rational, mutual, intellectual competition in such a venue will eventually produce a morally acceptable decision on any issue, no matter what the issue and decision are" (Cooley 2018 p54). Originality of ideas will be like a new product in the marketplace.

"In today's world, each marketplace of ideas' reality is very different from its idealised version that expects people to be rational and act rationally. In a world in which fake news, authoritarianism, and deception have so much sway, it might be argued that Mill's position is naïve at best, and dangerous at worse. Although free exchange of ideas can be a valuable form of decision-making, in general, it is only as good as those researchers and other stakeholders who comprise the marketplace" (Cooley 2018 p55).

Cooley (2018), however, did not want to abandon the marketplace, even if individuals are not rational, but argued for a filling of the marketplace with reasonable thinking. "The practical way to deal with bad free speech and false ideas is to fill the markets with researchers and other stake-holders, who are reasonable in the sense they are inclined to adopt reasonable outcomes and ways to achieve them, are adequate critical thinkers, and want to make decisions that make the world a better place for themselves and others" (Cooley 2018 p55).

Organ donation

Chaim and Duguet (2018) pointed out that "recent studies on organ donations in Arab or Islamic countries show that Muslims in general are more willing to donate while alive, but are reluctant to donate organs from the (brain) dead" (p89). Why is this the case?

Chaim and Duguet (2018) summarised the various reasons reported in surveys, including:

- Lack of understanding of the transplantation process.

- Lack of understanding of the concept of brain death.
- Misunderstanding of who owns their body (themselves or God).
- Mistrust of hospital authorities.
- Fear of disfiguration of the body, and how that affects the individual on Judgment Day.
- Fear of stigma from the local community.

Muslim scholars have debated the issue, including suggestions to increase organ donation, like harvesting organs from executed criminals without their prior consent, or financial compensation to families of post-mortem donors. Both of these ideas have also been discussed generally (Chaim and Duguet 2018).

Another issue which is relevant to organ transplantation generally is the difference between presumed (or assumed) consent and explicit consent. The latter is seen in organ donation schemes where individuals must opt-in (ie: consent before death) as opposed to opt-out with the former (ie: the individual must explicitly say before death that they do not want to donate) (Chaim and Duguet 2018).

In 2017 in South Africa, the first living donor liver transplantation from an HIV-positive mother to her HIV-negative infant was performed. Traditionally, HIV-positive living donors are rejected because of the risk of transmission, but there is a serious shortage of donors, and "it was highly likely that the child would die before a deceased donor liver could be procured" (Etheredge et al 2019 p287).

Etheredge et al (2019) were writing 21 months after the transplant, and both mother and child were well. The development of HIV is a risk not a certainty for the child.

What are the ethical issues for such transplants generally? The relevant points include (Etheredge et al 2019):

- Immediate benefits (ie: life-saving) outweighed "risk of an uncertain future".
- Good survival and treatment for HIV today.
- Refusal of mother's option to donate is an infringement of her autonomy.
- Refusal is against the child's best interests.

- The child has no say in future (eg: living with HIV).
- How and when to disclose to the child.
- Whether to give the child HIV-treatment before symptoms appear (ie: anti-retroviral therapy (ART) prophylaxis), particularly if the ART interacts with immunosuppression therapy to prevent rejection of the new liver.

Etheredge et al (2019) summarised the key questions for medical staff: "Is it ethical to save a child's life through transplant while at that same time knowingly exposing them to HIV? Is it ethical to place the burden of this decision on a parent who may stop at nothing to save the life of their child? Is it ethical to deny HIV-positive people the option of living donation even when they are otherwise eligible to donate? To definitely determine whether the child does or does not have HIV infection, is a provocative treatment interruption of ART ethically justifiable, given the potential consequences?" (p290).

Torres et al (2019) reported a case study of an "organ swap" (bi-organ paired exchange). It involved a healthy daughter and her mother who was on kidney dialysis, but the daughter could not donate a kidney because of the potential of kidney disease in later life. Of the two sisters, one had liver disease, but the healthy sibling's liver was unsuitable for transplant. So, a swap was created where the healthy sister gave a kidney to the mother, and the daughter donated half her liver to the ill sister (Wilson 2019).

One ethical issue related to the idea of a "fair swap". "In theory, a liver is worth more than a kidney, because people with kidney failure can survive for many years on dialysis, but there is no equivalent for liver failure" (Wilson 2019 p9). Helping their relatives indirectly was sufficient for the donors (Wilson 2019).

The process is complex (involving four operations on the same day), but it could increase the availability of live donors, and overcome problems where relatives cannot directly donate for some reason (Wilson 2019).

Xenotransplantation

Xenotransplantation is "the transplanting of organs, cells or tissues from one species to another" (Hodge 2018 p59). The promise of this in relation to organ donation from genetically modified pigs, say, is great, particularly with a shortage of human donors and increasing demand.

"To be sure, given the extraordinarily high odds

against the success of xenotransplantation - rejection of the xenograft, the potential transmission of unknown diseases from a family of porcine endogenous retroviruses, the life expectancy of a pig being about 15 years verses the life expectancy of a human - the science has had several positive gains world-wide" (Hodge 2018 p61). But there are ethical issues, most importantly related to animal rights.

To briefly summarise two different views here. Firstly, Immanuel Kant, who "believed that non-human animal's lack of rational capacity and moral worth meant that rational human animals can use them for their purposes, just as long as the latter weren't cruel to the former" (Hodge 2018 p63). On the other hand, Peter Singer (1993) called such a view "speciesism": "The idea of using animals as a source for organ donation is an example of speciesism, premised as it is on the idea that animals are things for us to use as best suits our own interests, without much concern for the interests of the animals themselves. Perhaps the easiest way to see this is to ask yourself the following question; why should we be prepared to accept the use of organs from animals, but not be prepared to take them from human infants who are, and always will be, less intellectually developed than the nonhuman animals?" (quoted in Hodge 2018).

Fishman and Patience (2004) highlighted the potential infection risk with xenotransplantation - either by diseases that are common to the donor and recipient species, or those that are dormant in the donor but become active in the recipient (including through genetic mutation), or donor-recipient incompatibility that causes problems. Hodge (2018) observed that "we can certainly envision an almost science-fiction like crisis where a pathogen is passed from person to person due to a virus mutation from the disharmony of pig-to-human transplantation. If this occurs, we may most likely not have an immediate cure for a disease of this kind, making the consequence(s) quite dire" (p62).

Determining Death

Related to the question of human organ transplantation is the definition of death (table 2.3). This can include brain death, or ceased circulatory or respiratory functions for 2-5 minutes (Donation after Circulatory Death (DCD) protocols (Lizza 2018).

Shah and Miller (2010) argued that brain death is a "legal fiction", but no harm is done to such individuals by taking their organs and the recipients benefit. Lizza (2018) saw brain death as "a true criterion for determining death" (p83).

- Establishing when a person is dead has always troubled human societies, and different ways have been used. For example, in Ancient Greece, a finger was cut off before cremation to check (Teresi 2018).
- For a long time, with the development of medicine, the answer was when the heart stopped and breathing ceased (cardiopulmonary death). But the coma situation challenged this criteria (Teresi 2018).
- A committee at Harvard Medical School in 1968 proposed that the individual in a coma should be "unreceptive" with "no movements" and "no reflexes" to determine death⁸. But EEG measures of brain waves are better (Teresi 2018).

Table 2.3 - Determining death.

Shewmon (eg: 2010) proposed a continuum of biological states from sickness to decomposition, and one point along the continuum is designed as "death".

"Irreversibility" of function is important to others, like Bernat et al (2010) - "the function will not be restored because it will neither return spontaneously, nor will return as a result of medical intervention because resuscitation efforts will not be attempted" (quoted in Lizza 2018).

Lizza (2018) preferred "to include not just permanent cessation of function but psychological, social, and cultural factors that go beyond strictly biological ones" (p83). This fitted with Shewmon's (2010) idea of two "death-related moments or events":

i) "Passing away" or "civil death" - "the end of the organism's relation to the rest of the world".

ii) "Deanimation" - an organism's "metaphorical end".

The former is relevant to organ transplantation (Lizza 2018).

Returning to the debate about brain death, Lizza (2018) referred to the "decapitation gambit". For example, a decapitated rooster is able to run around for a short period. It makes commonsense that a "warm and moving body" is not dead, but this is also contrary to another commonsense understanding of death. "Most people would not identify themselves with their decapitated

⁸ Brain dead patients make spontaneous and reflexive involuntary movements. For example, finger movements most commonly, in fifteen of 38 patients in an Argentine study (Saposnik et al 2000). While two of 400 patients in Spain showed upper-limb movements (Marti-Fabregas et al 2000). It is important that families are told about this, as movement can be taken as a sign of recovery or potential recovery (Ahmad 2000).

bodies. They think that decapitation would mean their death. Their lives would be over, and they would regard the decapitated body with no brain function as their sad remains" (Lizza 2018 p85).

Fear of Death

Kagan (2018) asked: "is fear of death a rationally appropriate response?". She offered three criteria in response:

i) The thing feared is bad - On the one hand, a good thing (life) is removed, but, on the other, "there is nothing that being dead is like. It involves no kind of experience at all, so it is not intrinsically bad" (Kagan 2018 p127).

ii) The likelihood of the feared event happening - "Fear of death is inappropriate because death is certain. But what is not at all certain is when you are going to die. Perhaps, then, what we should be afraid of is not loss of life per se, but rather the possibility that we will die sooner rather than later" (Kagan 2018 p127).

iii) An assessment of the certainty of the event and how bad it will be - Fear is appropriate when there is uncertainty about the event happening and/or how bad it will be, like a burglar striking, which may or may not happen, and who may or may not attack you in the process (Kagan 2018).

Kagan (2018) ended: "Obviously, fear that death may come soon can make sense among the very sick or the very aged. But for the rest of us, I think, it is typically misplaced. If you are reasonably healthy and yet you say to me, 'I am terrified of death', then all I can say in response is that I believe you, but terror is inappropriate. It doesn't make sense, given the facts" (p127).

Queering Bioethics

Wahlert and Fiester (2012) introduced the idea of queer bioethics, including the aims "to place sexuality and gender identity in the core of ethical discussions brought about by advances and renegotiations of normality in biology and medicine", and "to place the so-called less powerful central stage" (eg: LGBTQI - lesbian, gay, bisexual, trans, queer or intersex) (Sudenkaarne 2018 p119).

Key concepts are heteronormativity and cisnormativity. The former "refers to the systematic

assumption of heterosexuality, from which seemingly follows the unproblematic legitimacy of organising bioethical practices accordingly. Cisnormativity refers to the assumption that there are two distinct (if not indeed categorical/essential), gender binaries of male and female, from which seemingly follows the unproblematic legitimacy of organising bioethical practices accordingly" (Sudenkaarne 2018 p118).

Sudenkaarne (2018) continued: "Hetero- and cisnormativity are also often accompanied by the assumption that gender can be divided into social (gender) and biological (sex), whereas a queer approach to sex... is that it is physiology that is also gendered socially, not through so-called objective discovery" (pp118-119).

Sudenkaarne (2018) used the case study of surrogacy in Finland to show queer bioethics in action. In 2011, surrogacy was recommended by the national ethics board as an infertility treatment for married couples where it was physically impossible to have a child due to malfunctions or absence of a uterus. A queer bioethics would "analyse whether the case in question honours the diversity of families and relationships across and within the LGBT(QI) population or does it prioritise heterosexual marriage" (Sudenkaarne 2018 p122). Wahlert and Fiester (2014) proposed a queer bioethics inventory (or checklist) which can be summed up in the question: are queer and non-queer individuals treated equally (Sudenkaarne 2018).

Population Health Programmes

Population health is defined as "the health outcomes of a group of individuals, including the distribution of such outcomes within the group" by the US Institute of Medicine (quoted in DeCamp et al 2018). It can be based on local geography, or where healthcare is received, for instance. But there is a tension, DeCamp et al (2018) pointed out: "Population health has the potential to improve patient care and health outcomes for individual patients. However, specific population health activities may not be in every patient's best interest in every circumstance, which can create ethical tensions for individual physicians and other health care professionals" (p370).

For example, a screening programme with an upper age cut-off point can lead to underscreening of healthy individuals over the age limit and overscreening of unhealthy individuals within the age range as efforts are made to meet the targets of the programme (DeCamp et al 2018). Such a screening programme produces average benefits for the group, but discourages "appropriate individualised clinical decision-making" (DeCamp et al

2018).

DeCamp et al (2018) considered population health programmes (PHPs) in the light of ethical principles:

i) Beneficence (act in the patient's best interests) and non-maleficence (do no harm) - A doctor may be distracted from the medical issues of the individual by the demands of PHP targets, while, at the organisational level, there may be a preoccupation with the cost of the programme.

ii) Respect for the person and their autonomy - Patients are encouraged to undertake screening, for example, without a full discussion of the risks and benefits because it is the PHP being implemented at the moment. Standardisation, generally, can fail to accommodate social and cultural differences.

iii) Justice - The benefits and burdens of PHPs are not always shared equally across all patients, or the design of programmes with patient input, but not from patients who will use the programme.

"Difficult to reach" patients are often missed by PHPs (eg: individuals not using the Internet; speaking a "minority" language) (DeCamp et al 2018).

Assisted Reproductive Technology

Despite the widening availability of Assisted Reproductive Technology (ART), people living with Human Immunodeficiency Virus (PLHIV) can lack access to it (eg: one-third of US fertility clinics offer the service; Gross et al 2018). Part of the problem in the USA, at least, is the federal recommendation for separate laboratory and storage facilities for reproductive tissue from PLHIV (known as "universal precautions", and the "double set-up") (Gross et al 2018) ⁹.

The developments in anti-retroviral therapy has meant that PLHIV have the possibility to "live a long, healthy life and to procreate with minimal risk of horizontal or vertical transmission (between partners or mother-to-child, respectively. In this setting, the reproductive interests and rights of PLHIV have been widely recognised, and their reproductive intentions resemble those of the general population" (Gross et al 2018 p31).

Gross et al (2018) reflected on the rights of equal

⁹ This system is not used in other places, like Canada and Europe (Gross et al 2018).

access to ART for infertility among HIV-positive and HIV-negative individuals. They found over fifty papers in medical journals in the last 25 years on the ethics. Two main issues have been discussed - (a) the risk of transmission of HIV to partners, offspring, or healthcare workers, and (b) the short lifespan of PLHIV. Current medical evidence refutes these arguments as reasons for not providing ART to PLHIV (Gross et al 2018).

For example, Zafer et al's (2016) meta-analysis of forty studies found no HIV transmission from a HIV-positive woman to her HIV-negative partner (ie: HIV-discordant couple) via ART, while there were "no reports of HIV transmission to mother or infant when using standardised sperm processing techniques" (Barnhart et al 2009 quoted in Gross et al 2018).

The American Society for Reproductive Medicine (ASRM) Ethics Committee had "no reports of HIV infection of laboratory personnel resulting from processing the gametes/embryos for serodiscordant couples using current laboratory protocols. Cross-contamination of the gametes or embryos of other couples in the same laboratory has also not been reported" (quoted in Gross et al 2018). So, "no scientific evidence to support the use of the 'double set-up'" (Gross et al 2018 p41).

On the positive side, the "creation of a family is a basic human right", according to the ASRM (Gross et al 2018).

Mitochondrial Replacement Therapy

Mitochondrial replacement therapy (MRT) is where third-party mitochondria is used to replace the "faulty" mitochondria, and thus overcome mitochondrial diseases like Leigh's disease. Media headlines have labelled the process "three-parent families" (Harris 2016).

One argument against MRT is the confusion for the child in having three genetic parents (though the third-party DNA in the donated mitochondria is less than 1% of genetic material and it does not transmit any traits; Harris 2016). Harris (2016) dismissed this point:

"Although children might be confused if they are told that they have three genetic parents, only a very confused person would think - let alone say - any such thing. If I were a child for whom the alternative to having some third-party DNA in my genome - DNA that influences nothing about my nature, save only my susceptibility to disease and suffering - was mitochondrial disease, I doubt I would be complaining about an identity crisis. If, on the other hand, I were condemned unnecessarily to a life of pain and illness, I would really have something to complain of..." (p12).

Another objection to MRT is the future child who has been the product of MRT cannot consent to its use. Again

Harris (2016) dismissed this point: "I am afraid that I fail to see any ethical issues that arise in connection with future generations as involving issues of consent. They do not, for the simple and sufficient reason that there are no such people in existence capable of either giving or withholding consent. All would be/might be parents make numerous decisions about issues that might affect their future children. They do this all the time without thinking about the consent of the children..." (p12).

He continued: "Thus utter disregard of the relevance of such consents is this potential child's only chance of existence, and therefore so long as the best guess is that the child's eventual life would not be intolerably ghastly, it would be in that child's interests to be created" (Harris 2016 p13).

IVF Add-Ons

Spencer et al (2016), for example, reported that UK fertility clinics were making claims about in vitro fertilisation (IVF) "add-ons" (extra services/procedures) that were not supported by evidence of efficacy. Zemyarska (2019) asked: "Is it ethical to provide IVF add-ons when there is no evidence of a benefit if the patient requests it"?

The answer can be given based on three principles:

i) Autonomy - As the evidence for add-ons is often unclear or untested rather than clearly negative, "patients should not be denied the autonomy to, within reason, endeavour to maximise their chances of success" (Zemyarska 2019 p348).

On the other hand, medical responsibility means that it is "a clinician's right and responsibility to prioritise their professional judgment over the patient's autonomy and reject requests which exceed what is potentially beneficial or can be deemed sensibly permissible. Particularly vulnerable patients must be additionally protected against making irrational or unfavourable decisions, as their autonomy might be compromised. Patient pressure and competition between IVF clinics contribute to the coercion to offer such therapeutic or diagnostic add-ons due to concerns of diminished clientele and financial losses. Clinicians and units alike should remember, however, that their primary aim is to treat, not to profit, so providing adjunct IVF treatments against medical and moral rationale must be refused, even at the risk of losing a patient" (Zemyarska 2019 p348).

ii) Beneficence - To do the best for the patient, doctors should prioritise the treatment that is "most

impactful and beneficial".

On the other hand, emotional and psychological benefits may accrue the patient, particularly in unsuccessful fertility cases (eg: feeling of closure; sense of involvement).

iii) Non-maleficence - In order to do no harm, "ethics dictates that it is acceptable to provide a treatment only if the potential benefit is equal to or greater than the potential harm. Hence, unless and until there is evidence that would warrant their use, IVF add-ons with above minimal risk of adverse side effects, acute or long-term health damage, as well as those with untested safety, should not be provided" (Zemyarska 2019 p349).

There is also a duty to the potential child. "In this context, clinicians must be vigilant of unreasonable or unsafe patient pressure, always striving to balance the potential gain for the parents against any risk of harm to the resulting children. After all, the professionals who are involved in creating the embryos have a duty to them to protect them" (Zemyarska 2019 p350).

To sum up, "providing additional tools for IVF that lack evidence of a benefit might be morally acceptable if there is true informed consent, a potential of cost-effective physiological or psychological benefit and a minimal risk of harm. Ethical principles must always be considered in conjunction, with non-maleficence prioritised over beneficence and autonomy, particularly with regard to the future of the embryos that have been created and any potential children which might be born as a result. Additionally, it is imperative that desperate and vulnerable patients be protected against financial and emotional exploitation, as well as harm and disinformation, during the course of their infertility treatment" (Zemyarska 2019 p350).

Biobank Consent

Biobanks are repositories of biological material donated by individuals usually for research purposes. But should informed consent be sought and obtained for each separate research project ("specific consent") or is donation in the first place one-off consent ("broad consent")?

Against the former is that "seeking specific consent every time a sample – or personal data derived from a sample – is used for a new purpose, or by a new party, poses a considerable financial and administrative burden on researchers and a 'drag' on research. Given that samples and personal data can be reused at points in time

remote from the original acquisition, actually contacting the donor may be hard and become more difficult over time" (Manson 2019 p291).

The problem with "broad consent" is it "cannot be informed consent: how can it be when the future, specific, research uses (or users) are not yet known" (Manson 2019 p2910).

Ploug and Holm (2016) proposed an alternative, not just for biobanks but all health data, of "meta-consent". This is "the idea that people should be asked how and when they would like to be presented with a request for consent. That is, people should be asked to design how they in the future would like to provide consent to the use of their personal health data and biological material. By expressing a preference for how and when to provide consent, people can be said to provide consent on a meta level" (Ploug and Holm 2016 quoted in Manson 2019).

Manson (2019) was critical of this approach: "To simply allow people to choose whichever framework they wish might seem to be an irresponsible way of 'solving' the biobank consent debate. By analogy, people have different preferences about taxation systems. However, it does not solve debates about the proper level of taxation for all to allow individuals to choose the tax regimen that they prefer" (p292). Furthermore, all participants may choose "specific consent" which produces all the burdens of that approach.

Manson (2019) argued that biobanks could offer "broad consent" because donors do not have to donate. "Biobanks, in general, do not need to recruit any particular individual. What is needed is a sufficiently large number of participants of various types. It does not wrong any particular potential participant to ask her if she is willing to consent in a certain way (provided it meets the appropriate standards – and that is what the ongoing biobank consent debate is about). If this participant does not like the 'terms', she does not have to consent to giving a sample. If she does not consent, then others will" (Manson 2019 p293).

Ploug and Holm (2019) defended their approach – "meta-consent" is "not a matter of consenting or refusing consent. It is a matter of designing future consent requests from researchers" (p295). "Meta-consent" forms can be designed that are specific to the biobank, and/or cover many variations, including private/public use, commercial/non-commercial, national/international, and type of research. So, an individual could ask for specific consent to be sought for commercial tissue analysis, for instance, but give blanket consent to public use of health databases. Modern communication technology should make contacting donors straightforward

(Ploug and Holm 2019).

Ploug and Holm (2019) commented that "biobank research is highly dynamic. The research questions change radically over time as do the methods used to answer them. Doing healthcare research into heritable diseases has changed completely with the introduction of whole genome/exome sequencing with a host of implications for research participants, many of which could not be clear to anyone when participants initially gave their consent to the proposal that researchers could use their samples and data to do 'research into heritable diseases'" (pp296-297).

For Ploug and Holm (2019), "meta-consent" is a better way to request donor's consent in the long run than "broad consent".

Direct-to-Consumer Genetic Tests

Single nucleotide polymorphism genotyping arrays ("SNP-chips") are able to test for genetic variations in an individual's genome at many DNA locations. SNP-chips are cheap, and are the basis of direct-to-consumer (DTC) genetic testing, but they are not as good as the "gold standard" of DNA sequencing (Weedon et al 2019).

SNP-chips are accurate for common genetic variants in the genome, but highly inaccurate for rare variants (like the breast cancer genes, BRCA 1 and 2). Weedon et al (2019) compared DTC SNP-chips with gold standard methods for detecting the BRCA genes in UK Biobank data (n = 49 908).

For rare pathogenic BRCA variants, the SNP-chips had a false detection rate of around 85% (ie: false positives). Women with such variants would be recommended for further screening and treatment, which is unwarranted.

Weedon et al (2019) ended: "Clinicians and researchers should be aware of the poor performance of SNP-chips for genotyping rare genetic variants to avoid counselling patients inappropriately or investing limited resources into investigating false associations with badly genotyped variants" (p5).

References

Ahmad, K (2000) Brain-dead can make involuntary movements Lancet 355, p206

Barnhart, N et al (2009) Assisted reproduction for couples affected by human immunodeficiency virus in California Fertility and Sterility 91, 4, supp, 1540-1543

Bernat, J et al (2010) The circulatory response determination of death in organ donation Critical Care Medicine 38, 963-970

Chaim, V.R & Duguet, A-M (2018) Debates in Islamic bioethics on how to

increase organ donations: Between presumed consent and explicit consent
Ethics, Medicine and Public Health 7, 88-94

Cooley, D.R (2019) Editorial: Controversies in bioethics II:
Marketplaces of ideas Ethics, Medicine and Public Health 7, 54-58

DeCamp, M et al (2018) Ethical issues in the design and implementation
of population health programmes Journal of General Internal Medicine 33, 3,
370-375

Etheredge, H.R et al (2019) Needs must: Living donor liver
transplantation from an HIV-positive mother to her HIV-negative child in
Johannesburg, South Africa Journal of Medical Ethics 45, 287-290

Fishman, J.A & Patience, C (2004) Xenotransplantation: Infectious risk
revisited American Journal of Transplantation 4, 9, 1383-1390

Gross, M.S et al (2018) Assisted reproduction and HIV: Separate but
not equal Ethics, Medicine and Public Health 7, 29-44

Harris, J (2016) Germline modification and the burden of human
existence Cambridge Quarterly of Healthcare Ethics 25, 6-18

Hodge, D.A (2018) Xenotransplantation, trust, and trustworthiness:
Ethical issues for African Americans Ethics, Medicine and Public Health 7,
59-67

Kagan, S (2018) Don't fear the reaper. Lawton, G & Webb, J (eds) Big
Questions Amazing Answers (revised ed) London: New Scientist

Lizza, J.P (2018) Is brain death a legal fiction? Ethics, Medicine and
Public Health 7, 82-87

Manson, N.C (2019) The biobank consent debate: Why "meta-consent" is
not the solution? Journal of Medical Ethics 45, 291-294

Marti-Fabregas, J et al (2000) Decerebrate-like posturing with
mechanical ventilation in brain death Neurology 54, 224-227

Mill, J.S (1972) On liberty. In Acton, H.B (ed) Utilitarianism, On
Liberty and Contributions on Representative Government London: J.M Dent &
Sons

Ploug, T & Holm, S (2016) Meta consent - a flexible solution to the
problem of secondary use of health data Bioethics 30, 721-732

Ploug, T & Holm, S (2019) The biobank consent debate: Why "meta-
consent" is still the solution! Journal of Medical Ethics 45, 295-297

Saposnik, G et al (2000) Spontaneous and reflex movements in brain
death Neurology 54, 221-223

Shah, S.K & Miller, F (2010) Can we handle the truth? Legal fictions
in the determining of death American Journal of Law and Medicine 36, 540-
585

Shewmon, D.A (2010) Constructing the death elephant: A synthetic
paradigm for the definition, criteria, and tests for death Journal of
Medical Philosophy 35, 256-298

Singer, P (1993) Practical Ethics New York: Cambridge University
Press

Spencer, E.A et al (2016) Claims for fertility interventions: A
systematic assessment of statements on UK fertility centre websites BMJ Open
6, e013940

Sudenkaarne, T (2018) Queering bioethics: A queer bioethical inventory
of surrogacy Ethics, Medicine and Public Health 6, 117-125

Teresi, D (2018) Plight of the living dead. In Lawton, G & Webb, J
(eds) Big Questions Amazing Answers (revised ed) London: New Scientist

Torres, A-M et al (2019) Bi-organ paired exchange - sentinel case of a liver-kidney swap American Journal of Transplantation 19, 9, 2646-2649

Wahlert, L & Fiester, A (2012) Queer bioethics: Why its time has come Bioethics 26 (supp 1), ii-v

Wahlert, L & Fiester, A (2014) Repaving the road to good intentions: LGBT healthcare and the queer bioethical lens Hastings Center Report 44 (supp 4), S56-S65

Weedon, M.N et al (2019) Very rare pathogenic genetic variants detected by SNP-chips are usually false positives: Implications for direct-to-consumer genetic testing BioRxiv (<https://www.biorxiv.org/content/10.1101/696799v1>)

Wilson, C (2019) Kidney-for-liver swap New Scientist 6th April, p9

Zafer, M et al (2016) Effectiveness of semen washing to prevent human immunodeficiency (HIV) transmission and assist pregnancy in HIV-discordant couples: A systematic review and meta-analysis Fertility and Sterility 105, 3, 645-655

Zemyarska, M.S (2019) Is it ethical to provide IVF add-ons when there is no evidence of a benefit if the patient requests it? Journal of Medical Ethics 45, 346-350

2.3. MISCELLANEOUS

Human Germline Editing

Lander et al (2019) called for a global moratorium on human germline editing (HGE) - ie: "changing heritable DNA (in sperm, eggs or embryos) to make genetically modified children" (p165)¹⁰. This moratorium does not apply to research.

HGE could be used for "genetic correction" (editing a gene mutation that causes a disease) or "genetic enhancement" (improving individuals) (eg: "incorporating new instructions into a person's genome to enhance, say, their memory or muscles, or even to confer entirely new biological functions, such as the ability to see infra-red light or break down certain toxins"; Lander et al 2019 p166).

There are a variety of different issues related to HGE, including (Lander et al 2019):

a) Technical - "Although techniques have improved in the past several years, germline editing is not yet safe or effective enough to justify any use in the clinic" (Lander et al 2019 p166).

b) Scientific - A need to understand the long-term biological consequences of HGE. For example, altering a

¹⁰ Meanwhile, the full cloning of non-human animals has been achieved in over twenty mammalian species, including sheep, mice, rats, dogs, and macaque monkeys (Liu et al 2018). Other forms of gene manipulation are common with animals (appendix 2A).

version of the gene SLC39A8 decreases the risk of developing hypertension, and Parkinson's disease, but increases the risk of developing schizophrenia, Crohn's disease, and obesity (Lander et al 2019).

c) Medical - "Some argue, especially in the popular press, that germline editing is urgently needed to stop children from being born with severe genetic diseases. But couples who know they are at risk of transmitting a severe disease-causing mutation already have safe ways to avoid doing so. They can use in vitro fertilisation (IVF) in conjunction with pre-implantation genetic testing (PGT), prenatal testing, sperm donors, egg donors, embryo donors or adoption. In particular, use of IVF followed by genetic screening of the embryos to ensure that only unaffected ones are transferred to the person's uterus, guarantees that a couple will not have children with the genetic disease" (Lander et al 2019 p166).

d) Ethical - "The societal impacts of clinical germline editing could be considerable. Individuals with genetic differences or disabilities can experience stigmatisation and discrimination. Parents could be put under powerful peer and marketing pressure to enhance their children. Children with edited DNA could be affected psychologically in detrimental ways. Many religious groups and others are likely to find the idea of redesigning the fundamental biology of humans morally troubling. Unequal access to the technology could increase inequality. Genetic enhancement could even divide humans into sub-species" (Lander et al 2019 p167).

A particular mutation in the CCR-5 gene has been found to protect individuals against HIV (Samson et al 1996). In 2018, a scientist in China announced editing of this gene in two babies (ie: to protect against future HIV risk) (Normile 2018). This case raised a number of ethical and methodological issues (Cyranoski 2018).

For example, despite the protection that this mutation "provides against HIV, and possibly other pathogens such as smallpox and flavivirus, and although it facilitates recovery after stroke, it also appears to reduce protection against certain other infectious diseases such as influenza" (Wei and Nielsen 2019 p909). Furthermore, in an analysis of UK Biobank data on over 400 000 individuals, Wei and Nielsen (2019) found that having two copies of the mutation (known as delta32) increased all-cause mortality by 20%.

Appendix 2A - Knockout Macaques

A number of genes have been found that are involved

in the circadian clock that controls body rhythms like temperature, feeding, and sleep and waking. One gene is the Brain and Muscle ARNT-Like 1 (BMAL1), which, when deleted in mice, produced disruption of the rhythms, glucose intolerance, and premature ageing (Qiu et al 2019).

The applicability of mouse models to humans means that non-human primates are being used. Qiu et al (2019) deleted the BMAL1 gene in ten cynomolgus monkeys (*Macaca fascicularis*). These BMAL1 knockout monkeys showed disrupted rhythms in hormones, and altered phases of sleep, as well as "behaviours resembling anxiety, depression, and schizophrenia in humans" (Qiu et al 2019 p88).

References

Cyranoski, D (2018) First CRISPR babies: Six questions that remain Nature (30th November) (<https://www.nature.com/articles/d41586-018-07607-3>)

Lander, E et al (2019) Adopt a moratorium on heritable genome editing Nature 567, 165-168

Liu, Z et al (2018) Cloning of macaque monkeys by somatic cell nuclear transfer Cell 172, 881-887

Normile, D (2018) Shock greets claim of CRISPR-edited babies Science 362, 978-979

Qiu, P et al (2019) BMAL1 knockout macaque monkeys display reduced sleep and psychiatric disorders National Science Review 6, 87-100

Samson, M et al (1996) Resistance to HIV-1 infection in Caucasian individuals bearing mutant alleles of the CCR-5 chemokine receptor gene Nature 382, 722-725

Wei, X & Nielsen, R (2019) CCR5-delta32 is deleterious in the homozygous state in humans Nature Medicine 25, 909-910

Missing Diversity

Genome-wide association studies (GWAS) compare millions of genetic variants in individuals with and without a disease in large datasets, and they allow the identification of variants linked to the risk of a disease and its treatment. But these datasets are not representative of ethnic groups (Williams 2019).

Sirugo et al (2019) reported that four-fifths of the individuals in the GWAS datasets held by the US National Human Genome Research Institute and the European Bioinformatics Institute were White European. So, "the lack of ethnic diversity in human genomic studies means that our ability to translate genetic research into clinical practice or public health policy may be dangerously incomplete, or worse, mistaken. For example, attempts to use estimates of genetic risk from European-based studies in non-Europeans may result in inaccurate

assessment of risk and lack of interventions in understudied populations" (Sirugo et al 2019 p26).

The implications of the limited diversity in the datasets includes (Sirugo et al 2019):

a) Different genes linked to a disease in different populations, and a medication aimed at one gene will be of limited use with the other gene/population.

b) Genetic mutations specific to non-White populations are missed.

c) Knowledge about complex conditions is not generalisable - "For example, there are more than 300 genes involved in retinal disease; over 3000 mutations in 65 genes cause retinitis pigmentosa (RP) with different modes of inheritance... As many of these mutations have only been characterised in Europeans, we know little about the genetic causes of retinal disease across ethnically diverse populations" (Sirugo et al 2019 p27).

d) Differences in genetic architecture (eg: frequency of certain genetic variations in a population) ignored as in small bottlenecked populations and those practicing consanguineous mating (eg: cousin marriage)

e) Risk calculations not applicable - eg: polygenic risk scores (PRS). These are "obtained by computing the effect size of thousands of genetic variants from a discovery sample, then combining and applying them to the genetic profiles from other individuals to predict risk of complex disease" (Sirugo et al 2019 p29). For example, in one study, a PRS for schizophrenia was ten times higher in Africans and African-Americans than Europeans, "but this does not reflect true disease risk" (Sirugo et al 2019 p29).

Sirugo et al (2019) ended: "Despite the plea to include more diverse sampling in genomic studies and the critical knowledge these studies can bring, we recognise that obstacles remain. Recruiting diverse populations can be difficult in many settings, in some cases due to a mistrust in biomedical research stemming from past experiences of exploitation" (p30).

References

Sirugo, G et al (2019) The missing diversity in human genetic studies Cell 177, 1, 26-31

Williams, S (2019) Genetic diversity matters New Scientist 30th March, 22-23

3. MENTAL HEALTH TOPICS

- 3.1. Suicidality
- 3.2. Miscellaneous

3.1. SUICIDALITY

Psychoanalysis and Suicide

Briggs et al (2019) performed a systematic review and meta-analysis of twelve randomised controlled trials evaluating psychoanalysis for suicidal behaviour, and self-harm. There was evidence of a small reduction in attempted suicide in the following year, and in the repetition of self-harm in the following six months (but not twelve months). There were some benefits in well-being, but no overall effect on depression and anxiety symptoms.

The researchers' conclusions were limited by the heterogeneity of the studies, and the quality of the evidence. The methodological differences between studies included:

- i) Sample size - ranging from 30 to 134.
- ii) Sample recruited from accident and emergency outpatients, or from in-patients, for example.
- iii) Participants - adolescents or adults; mostly females; all studies in Western countries.
- iv) Control/comparison group - eg: waiting list or treatment as usual; comparison with other therapy.
- v) Duration, intensity and content of therapy - "This is further complicated by inconsistency of taxonomies of psychoanalytic psychotherapies, reflecting an apparent predisposition in the field for the constant invention of new labels for similar interventions..." (Briggs et al 2019 p326).
- vi) Number of previous episodes of self-harm or suicide attempts.
- vii) Outcome measures and follow-up period.
- viii) Different definitions of self-harm.

Economic Uncertainty and Suicide

Mental health tends to decline in a nation during an

economic downturn, and specifically, suicide increases (Vandoros et al 2019).

This has been confirmed by studies since the financial crisis of 2007-2008 in England, Spain, Greece, Italy, and Ireland, for example, and the correlation between economic recession and suicide is robust over many months and even years (Vandoros et al 2019).

But the World Health Organisation has noted that "many suicides happen impulsively in moments of crisis" (quoted in Vandoros et al 2019). So, could daily fluctuations in economic uncertainty trigger suicide?

Vandoros et al (2019) answered this question with data from England and Wales for 2001-2015 on daily number of suicides according to the Office for National Statistics, and the daily Economic Policy Uncertainty Index (based on financial news in UK newspapers).

During the study period, this index varied from 0 to 1645 (where a higher number is greater uncertainty), and the average number of suicides was 13.22 per day (9.99 for males and 3.23 for females).

The researchers found a short-lived association (ie: same or next day) between uncertainty and suicide. It was calculated that a 1% increase in the uncertainty index was associated with 0.00049 more suicides per day. Put another way: "An increase in economic uncertainty by one standard deviation from the mean is expected to lead to an additional 11 suicides in England and Wales per year, while a fivefold increase would mean an additional 1.7 suicides per week, or 89 more suicides per year" (Vandoros et al 2019 p407).

The magnitude of the effect of uncertainty was higher for males.

The data were aggregated, and so could not explain individual behaviour. The researchers admitted that "as economic uncertainty is unlikely to be the only cause of suicide, this might act as a trigger in moments of crisis" (Vandoros et al 2019 pp408-409).

There was no information on suicide attempts, which can also be impulsive (Vandoros et al 2019).

Self-Harm and Older Adults

Troya et al (2019) reviewed the studies on self-harm by older adults. Self-harm is defined by the National Institute for Health and Care Excellence (NICE) in the UK as "any act of self-poisoning or self-injury carried out by a person, irrespective of motivation" (quoted in Troya et al 2019). This does not include indirect self-harm, like refusal to eat and drink (Troya et al 2019).

The researchers found forty relevant studies (published up to March 2018). The cut-off age used was sixty years old.

The estimated self-harm rate varied between 19 and

65 per 100 000 population ¹¹, with self-poisoning as the majority method (86% of cases). Around one-third of cases had a history of self-harm, and over two-thirds a diagnosis of depression.

The main risk factors were grouped into three types:

- Socio-demographic - eg: being female; living alone.
- Clinical - eg: previous history of self-harm; psychiatric history, particularly depression.
- Other - eg: alcohol and drug use.

Three studies collected qualitative data, and three themes emerged from their interviews - loss of control (eg: due to physical and mental health problems), increased feelings of loneliness and isolation, and "ageing perceived as burdensome and affecting daily living".

"Despite sharing some characteristics of self-harm with younger populations (eg: higher percentage in women, those with psychiatric history and those with a previous episode(s) of self-harm), there is an increased risk of repetition and suicide in older adults" (Troya et al 2019 p195). Older adults who self-harm were over sixty times more likely to commit suicide than younger self-harmers (Troya et al 2019).

Troya et al (2019) reflected on the key methodological differences between the included studies:

i) Terminology and definition of self-harm - "Most of the included studies (n = 29) classified self-harm as attempted suicide, ie: as holding an exclusively suicidal intent, which is not always the case" (Troya et al 2019 p197).

ii) Study design - Over half the studies were observational. "This means that factors such as potential confounders and direction of causality between exposure and outcome could not always be determined for the whole older adult population" (Troya et al 2019 p197).

iii) Sample - Thirty-four studies were hospital-based (ie: individuals who presented for treatment). "Not all self-harm episodes result in hospital presentations, therefore other self-harm episodes (eg: in the community) may not have been comprehensively captured in this review. Therefore, appropriate consideration must be taken when interpreting results from this review to avoid

¹¹ This was based on seven studies only. Though it is lower than younger populations (eg: over 500 per 100 000 among adolescents; Geulayov et al 2018), Troya et al (2019) advised caution about the findings as the studies varied in sample size, study design, healthcare system, and reporting of self-harm/non-suicidal injury, for example.

generalising to the wider population of older adults who self-harm" (Troya et al 2019 p197).

Easier access to hospital patient records explains why few studies were community-based.

The iceberg model (Geulayov et al 2018) proposed three layers of self-harm presentations. The top two layers are visible in the form of hospital presentations with injury, and fatal self-harm (suicide), while the majority is hidden (under the surface) in the community.

iv) Quality of studies - Most of the studies were rated as moderate (n = 28) or high (n = 10) methodological quality using US National Institutes of Health criteria. This scores the presence of appropriate information in the article. Loss of participants during follow-up was a key weakness.

References

Briggs, S et al (2019) The effectiveness of psychoanalytic/psychodynamic psychotherapy for reducing suicide attempts and self-harm: Systematic review and meta-analysis British Journal of Psychiatry 214, 320-328

Geulayov, G et al (2018) Incidence of suicide, hospital-presenting non-fatal self-harm, and community-occurring non-fatal self-harm in adolescents in England (the iceberg model of self-harm): A retrospective study Lancet Psychiatry 5, 167-174

Troya, M.I et al (2019) Self-harm in older adults: Systematic review British Journal of Psychiatry 214, 186-200

Vandoros, S et al (2019) The association between economic uncertainty and suicide in the short-run Social Science and Medicine 220, 403-410

3.2. MISCELLANEOUS

Leonardo da Vinci

Catani and Mazzarello (2019) described the story of Leonardo da Vinci as "one of a paradox – a great mind that has compassed the wonders of anatomy, natural philosophy and art, but also failed to complete so many projects... The excessive time dedicated to idea planning and the lack of perseverance seems to have been particularly detrimental to finalise tasks that at first had attracted his enthusiasm" (p1842).

At the time, his biographer, Giorgio Vasari, stated: "in learning and in the rudiments of letters he would have made great proficiency, if he had not been so variable and unstable, for he set himself to learn many things, and then, after having begun them, abandoned them" (quoted in Catani and Mazzarello 2019). While Pope Leone X, who employed da Vinci in the Vatican, declared: "Alas! this man will never do anything, for he begins by thinking of the end of the work, before the beginning"

(quoted in Catani and Mazzarello 2019).

Based on these and other contemporary observations of the man, Catani and Mazzarello (2019) considered whether he had Attention Deficit Hyperactivity Disorder (ADHD). The key characteristics of this condition are procrastination, the inability to complete tasks, and restlessness of body and mind (Catani and Mazzarello 2019).

Catani and Mazzarello (2019) stated: "We suggest that historical documentation supports Leonardo's difficulties with procrastination and time management as characteristic of ADHD, a condition that might explain aspects of his temperament and the strange form of his dissipative genius. Leonardo's difficulties were pervasive since childhood, which is a fundamental characteristic of the condition. There is also unquestionable evidence that Leonardo was constantly on the go, keeping himself occupied with doing something but often jumping from task to task. Like many of those suffering with ADHD, he slept very little and worked continuously night and day by alternating rapid cycles of short naps and waking" (p1845).

This is an interesting example of diagnosing past figures from historical records using modern categories of behaviours and disorders. It can only be speculative, as ideally diagnosis needs the individual to be present to answer questions.

Using modern categories in the past shows that behaviours and disorders are not just products of their time. This can be viewed as highlighting the universality of the categories over time, or as "psychiatric imperialism".

Reference

Catani, M & Mazzarello, P (2019) Leonardo da Vinci: A genius driven to distraction Brain 142, 1842-1846

Anxiety Disorders

Bandelow et al (2018) presented a meta-analysis that found that psychotherapy and pharmacotherapy were equally effective in reducing anxiety disorder symptoms¹². The researchers focused on the "enduring effects" (ie: whether there is a relapse after a treatment is topped).

Ninety-three controlled follow-up studies (published between 1980 and 2016) for three anxiety disorders -

¹² This was a development of a meta-analysis by Bandelow et al (2015), which covered treatments for anxiety disorders generally.

panic disorder with or without agoraphobia, generalised anxiety disorder, and social anxiety disorder - were found. The data, however, were pooled in the meta-analysis.

The enduring effects of psychotherapy and pharmacotherapy were similar. This finding "casts doubt on the widespread assumption that only psychological treatments have enduring effects and gains achieved with medications are lost soon after they are stopped. However, the good news for patients with anxiety disorders is that the chance of deterioration within 2 years after treatment termination is low, and independent from previous treatment" (Bandelow et al 2018 p336).

The majority of studies involved cognitive-behavioural therapy (CBT), and follow-up for 24 months was common in all cases.

Follow-up studies have methodological problems including confounding factors. "For example, it is common for clinical trial protocols to require participants to refrain from involvement in any other treatments during the active treatment period. However, in follow-up studies, it is almost impossible to control what alternative treatments patients utilise after stopping their original treatment" (Bandelow et al 2018 p337).

Leichsenring and Hoyer (2019) criticised this meta-analysis, including:

a) The inclusion criteria for studies did not require head to head comparisons between the two treatments.

Bandelow et al (2019) replied that there are few head to head studies available.

b) The comparison of the effect of psychotherapy and of pharmacotherapy via separate studies is difficult because of different patient populations, for example.

But every meta-analysis includes studies with different populations (Bandelow et al 2019).

c) The authors had associations with pharmaceutical companies which may have influenced their conclusions ¹³.

Bandelow et al (2019) replied: "We frankly disclosed our conflicts of interest, but this should also be expected from authors publishing in the field of psychotherapy, in particular when they are strongly promoting certain forms of psychotherapy, such as Dr

¹³ The conclusion by Bandelow et al (2018) that caused a response from critics was the assertion that "uncontrolled studies that report stable improvements after a treatment-free follow-up period may overestimate the 'durability' of psychotherapies, as these may be caused by unspecific effects. The often-cited advantage of psychotherapy over pharmacotherapy for anxiety disorders – a longer-lasting improvement – could not be confirmed in our study" (p337).

Leichsenring, who is a fervent advocate for psychoanalysis and has been criticised for possibly biased meta-analyses in the literature" (p54).

References

Bandelow, B et al (2015) Efficacy of treatments for anxiety disorders: A meta-analysis International Clinical Psychopharmacology 30, 4, 183-192

Bandelow, B et al (2018) Enduring effects of psychological treatments for anxiety disorders: Meta-analysis of follow-up studies British Journal of Psychiatry 212, 333-338

Bandelow, B et al (2019) Authors' reply British Journal of Psychiatry 214, 53-54

Leichsenring, F & Hoyer, J (2019) Does pharmacotherapy really have as enduring effects as psychotherapy in anxiety disorders? Some doubts British Journal of Psychiatry 214, p53

Functional Conditions

Listening to individuals talk about their symptoms is important, particularly when no apparent physical cause can be found. This situation has been called "functional disorders", "psychosomatic illness" or "mentally unexplained symptoms", with the emphasis that the person is not faking (Wilson 2019).

O'Sullivan (2016) detailed many case studies, and often medical professionals view the sufferers as pretending. On the other hand, administering potent drugs in the case of "functional epilepsy", say, can be dangerous (Wilson 2019).

Distracting attention has been found to be effective with functional symptoms. For example, an individual with a functional tremor in their right hand is distracted with a task using the left hand, and the tremor stops (Wilson 2019).

Stone and Edwards (2012) advocated showing sufferers that there was no physical basis to their condition (eg: with physiological data). Sethi (2013) preferred to tell his patients "there is no organic basis to the symptomatology and advise that underlying psychogenic factors need to be aggressively addressed rather than say that the events are real, not imagined, or 'all in the mind'" (p869). Stone and Edwards (2013) countered that "neurologists tend to explain the symptoms in purely psychological terms. This can be interpreted by patients as an accusation that they are feigning their symptoms even if this is not what the doctor believes" (p869).

References

O'Sullivan, S (2016) It's All In Your Head: Stories From the Frontline of Psychosomatic Illness New York: Random House

Sethi, N.K (2013) Trick or treat?: Showing patients with functional (psychogenic) motor symptoms their physical signs Neurology 80, p869

Stone, J & Edwards, M (2012) Trick or treat?: Showing patients with functional (psychogenic) motor symptoms their physical signs Neurology 79, 3, 282-284

Stone, J & Edwards, M (2013) Author response Neurology 80, p869

Wilson, C (2019) Mind tricks New Scientist 6th April, 28-32

Diet and Mental Illness

Individuals with severe mental illness (SMI) have a life expectancy on average fifteen years less than the general population. Adverse physical health, primarily cardiovascular disease, explains much of the difference, and diet can play a role in this. Medication is also important - eg: anti-psychotics increase appetite generally, and for sweet foods specifically (Teasdale et al 2019).

Teasdale et al (2019) reported a review of studies of the dietary intake of individuals with SMI. They had statistically significant higher food intake (linked to weight gain), and sodium intake than controls. This conclusion was based on seven studies that collected quantitative data on the topic. Over fifty other studies provided qualitative data.

Any review of studies includes a variations like:

- Country of study - mainly USA.
- Design of study - mostly cross-sectional.
- Participants - eg: community-dwelling vs in-patients; schizophrenia vs all SMI; types of medication used.
- Measurement of dietary intake - eg: validated food frequency questionnaire; food diary.

The key was that these data were self-reports. "Misreporting is a common issue in the general population, with an average energy under-reporting of approximately 20%, and higher in people who are obese (~30%). Given that people with SMI commonly experience additional barriers, including cognitive impairment, lack of motivation and poor memory, misreporting could be expected to be more common, and to have a larger impact, in this population suggesting the findings on energy intake may be an underestimation" (Teasdale et al 2019 p256).

Reference

Teasdale, S.B et al (2019) Dietary intake of people with severe mental illness: Systematic review and meta-analysis British Journal of Psychiatry 214, 251-259

4. SLEEP TOPICS

Sleep and Pregnancy

Poor sleep quality and insufficient sleep are common during pregnancy and after childbirth (Richter et al 2019).

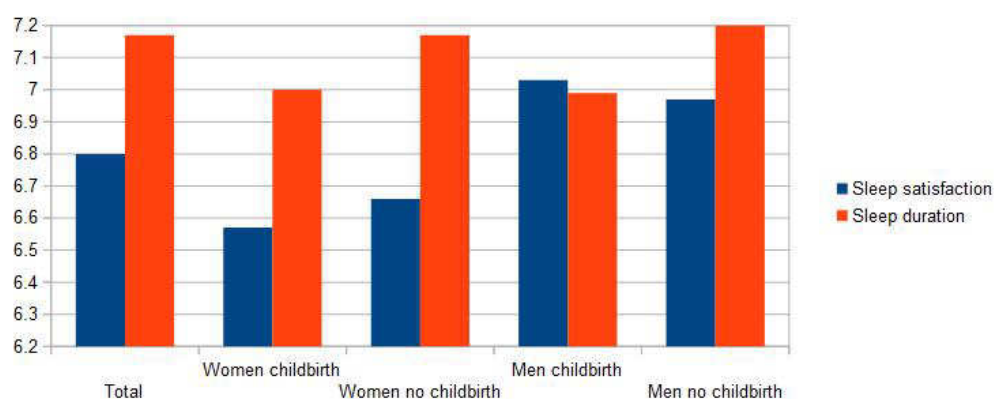
Much of the research has used convenience samples of pregnant women at one (or a small number of) hospital(s). Richter et al (2019) used a representative sample of women and men in Germany (part of the German Socio-Economic Panel). Sleep satisfaction was self-rated on a ten-point scale at annual interviews between 2008 and 2015, along with average weekday and weekend sleep hours. Demographic variables were also taken.

Mothers - Lower ratings of sleep satisfaction in pregnancy and post-partum compared to before pregnancy (average 1.5 points lower). The nadir was the first three months after birth. Sleep duration increased during pregnancy (average of ten minutes per night), but declined after childbirth (average of forty minutes). "Four to six years after the birth of their first child, maternal sleep satisfaction and duration were still lower than pre-pregnancy, after controlling for age... The birth of the second and third children affected mothers' sleep satisfaction significantly less than did the birth of the first child..., whereas the effects on sleep duration were similar after the first, second, and third childbirth" (Richter et al 2019 p5).

Fathers - A small decline in sleep satisfaction after childbirth compared to before pregnancy, and an average decline of ten minutes in sleep duration per night. "Four to six years after the birth of their first child, fathers' sleep satisfaction and duration were still lower than their pre-pregnancy values... after controlling for age. The birth of their second child affected fathers' sleep satisfaction less than did the birth of their first child..., whereas the effect on sleep duration was very similar after the first, second, and third childbirth" (Richter et al 2019 p5).

Men and women experiencing births during the study period reported lower sleep satisfaction and duration than men and women without births (figure 4.1).

Table 4.1 summarises the main strengths and weaknesses of the study.



(Data from Richter et al 2019 table 1)

Figure 4.1 - Mean sleep satisfaction (out of 10) and sleep duration (hours per night).

STRENGTHS	WEAKNESSES
<ol style="list-style-type: none"> 1. Large sample (n = 38 861). 2. Representative sample of German population of childbearing age. 3. Longitudinal panel study over eight years (ie: returning to the same participants annually). 4. Data on both parents. 	<ol style="list-style-type: none"> 1. Single item used for sleep satisfaction. 2. Self-reported measures, where objective ones would be better. 3. Measures taken annually. 4. Secondary data - researchers had no control over the design of the questionnaire, including variables measured.

Table 4.1 - Main strengths and weaknesses of Richter et al (2019).

Sleep Stages

Based on electroencephalography (EEG), which measures the electrical activity of the brain, sleep is divided into stages/types - rapid eye movement (REM), and three stages of non-REM (Stevner et al 2019).

The advance of technology has allowed more detailed study of sleep and the brain. Stevner et al (2019) reported the use of functional magnetic resonance imaging (fMRI) with fifty-seven healthy volunteers, and the discovery of nineteen "recurring whole-brain network states". However, none of these states corresponded to Stage 1 NREM sleep (just after falling asleep) (Stevner et al 2019).

One explanation for sleep growing in popularity

recently is the "synaptic homeostasis hypothesis" (SHY) (Tononi and Cirelli 2003). It suggests that sleep wave sleep (SWS) (or Non-Rem sleep) lowers synaptic strength to save energy ("synaptic downscaling"). Synapses are junctions between neurons, and memories are formed by strengthening certain synapses. SWS does not change the relationship of synapses (ie: memories), but lowers strength of them all, according to this theory (Drew 2018).

So, "total synaptic strength increases during wakefulness and reaches a maximum just before going to sleep. Then, as soon as sleep ensues, total synaptic strength begins to decrease, and reaches a baseline level by the time sleep ends" (Tononi and Cirelli 2006 p50).

Tononi and Cirelli (2006) gave an example with numbers to show the strength of synapses. During SWS "a synapse that after wakefulness had strength of 100 is downscaled to 80, another synapse, which had been potentiated to 150, is downscaled to 120... The synapse with a strength of 5, having being downscaled below a minimum strength, has been 'downselected' or removed altogether" (Tononi and Cirelli 2006 p51).

The SHY makes a number of predictions (Tononi and Cirelli 2006):

a) During wakefulness the strength of synapses increases as new memories are formed.

Evidence - Stimulating a rat's whisker for 24 hours produces an increase in synaptic strength in the area of the brain that responds to input from the whiskers (Knott et al 2002).

b) After days with higher levels of learning, brain activity during SWS will be greater.

Evidence - Extending the hours awake in animals or humans produces greater activity in the following SWS (Cirelli and Tononi 2000).

c) Synaptic downscaling during SWS.

Evidence - Neuroimaging during sleep shows decreases in brain metabolism (Braun et al 1997).

The advantages of synaptic downscaling include saving energy, space saving, and to allow for learning and memory the next day (Tononi and Cirelli 2006). Tononi and Cirelli (2014) stated that "sleep is the price the brain pays for plasticity".

Decreases in synaptic strength have been shown in rats, but "such changes have been described primarily in rodents in their home cage in the absence of novel

experience or learning" (Durkin and Aton 2016 p155).

Durkin and Aton (2016) presented evidence that challenged the SHY. Their experiments involved measuring single neurons in the visual cortex of mice with implanted electrodes. The head-fixed mice were shown a blank screen or a pattern for one-hour sessions. The SHY would predict increased firing of the cell (as the synapses are strengthened) with the visual pattern. This was not found - the firing rates of the neurons were identical for both stimuli.

Neuron activity was also recorded during post-stimulation sleep. SHY would predict a reduction in cell firing as synaptic downscaling occurs, but the researchers found increased activity after both stimuli. Increases in activity were greater in REM sleep. Durkin and Aton (2016) admitted: "One caveat is that in these studies, we directly measured neuronal activity, but not synaptic strength" (p158).

"Knockout mice" have become popular in recent years. These are animals genetically engineered to lack certain genes, which helps to highlight the function of the missing genes.

Related to sleep, Niwa et al (2018) showed that two genes linked to the neurotransmitter acetylcholine are important for REM sleep, and sleep generally. When both the genes ("Chrm1" and "Chrm3") were knocked out, the mice had virtually no REM sleep. There was also a reduction in NREM sleep to a lesser extent.

Previous work had found abundant acetylcholine in the brain stem (eg: cat; Kodama et al 1990), and cortex during REM sleep (Niwa et al 2018).

Sleep Learning

The idea that an individual can learn new material while asleep (sleep learning) has appeared in science fiction (eg: Huxley's "Brave New World" in 1932), and popular culture (eg: "PsychoPhone" marketed in the USA in the 1920s) in the mid-20th century (Paller and Oudiette 2018).

Science of the time was slightly less ambitious. For example, LeShan (1942) reported playing a tape saying "my fingernails taste terribly bitter" six times per night to boys who bit their nails two hours after they fell asleep. After 54 nights of this, eight of twenty boys had stopped biting their nails (compared to none of the control group).

A recent version of this study (Arzi et al 2014) presented the odours of tobacco and rotten fish together during sleep to smokers who wanted to quit. These individuals lit up significantly less in the following

week than controls (table 4.2).

Controlled studies of sleep learning new material tend to find that information played during the night was recalled only if individuals had been awake (Paller and Oudiette 2018).

- This research shows the "implicit acquisition of entirely new associations during sleep" (Arzi et al 2014 p15382).
- Arzi et al (2014) used olfactory aversive conditioning which paired the smell of cigarettes with an aversive odour (based on the principles of classical conditioning). Sixty-six healthy smoking volunteers were involved in the study in Israel. Participants were divided into three groups:
 - i) Olfactory aversive conditioning - During a night's sleep, the two odours were released together into the room for short periods (during REM and stage 2 NREM sleep).
 - ii) Wake control - Participants sat in a room awake and the two odours were released individually into the room for short periods.
 - iii) Unpleasant odour alone control - Only the unpleasant odour was released during a night's sleep.
- The outcome measure was the number of cigarettes smoked in the seven days after the smells compared to the seven days beforehand (as self-reported).
- There was a significant reduction in cigarettes smoked in the olfactory aversive conditioning group only. A reduction from around 13 cigarettes per day on average to around ten. The other two conditions showed little change.

Table 4.2 - Arzi et al (2014)

An alternative approach has focused on sleep improving learning that took place beforehand. For example, Rasch et al (2007) required participants to learn the location of objects while smelling a rose before sleep. The odour of a rose was presented during different stages of sleep. The following day recall of the location of the objects was improved with the cue of the smell during SWS (Paller and Oudiette 2018).

Oudiette and Paller (2013) reported the use of sounds as the cues in a technique called "targeted memory reactivation" (TMR). Prior to sleep participants learned the location of fifty objects while sounds were played for some (eg: picture of a cat and meow sound). During SWS the sound was played quietly to the sleepers. Recall of these objects was better on awakening.

TMR's success has been linked to the sleep spindle (originating in the thalamus) in EEG recordings of sleep (Paller and Oudiette 2018).

Overall, sleep learning seems able to preserve

memories from the preceding day and improve learning before sleep rather than learn new material from scratch during sleep.

Though work with mice (DeLavilleon et al 2015) has suggested an intriguing/disturbing possibility. Mice explored a new environment, and this caused "place cells" in the brain to fire. It has been shown that these cells fire during sleep, suggested that memory is replayed. The researchers stimulated the brains of the sleeping mice when particular place cells fired, but not others. Subsequently, the animals spent more time at the locations associated with these memories. What is exactly happening in terms of the memories of the mice is unclear as it may be conditioning that led to the choice of location (Paller and Oudiette 2018).

Insomnia and Heart Problems

There is a positive correlation between insomnia and cardiovascular disease (CVD), but establishing causality is not easy. For example, self-reports of insomnia are influenced by confounding factors, like chronic illness, socio-economic status, and lifestyle factors (Larsson and Markus 2019).

Larsson and Markus (2019) sought to overcome these problems by examining genetic variations among over 1.5 million individuals in publicly available data (including the UK Biobank). Specific genes known to be associated with insomnia were examined.

Genetic liability to insomnia was found to be associated with significantly higher risk with most forms of major CVDs. The increased risk was modest, however (eg: 1.1 times greater risk of stroke with the "insomnia genes" than not).

The causal relationship seems to be that the genes related to insomnia are also associated with increased body weight and risk of type 2 diabetes, as well as other physiological changes that increase the risk of CVD.

However, the researchers could not rule out "other causal pathways leading to insomnia that cause CVD" (Larsson and Markus 2019 p797).

The different types and forms of insomnia were not distinguished, and the participants were primarily of European descent (Larsson and Markus 2019).

References

Arzi, A et al (2014) Olfactory aversive conditioning during sleep reduces cigarette-smoking behaviour Journal of Neuroscience 34, 46, 15382-15393

Braun, A.R et al (1997) Regional cerebral blood flow throughout the sleep-wake cycle. A H2(15)O PET study Brain 120, 1173-1197

Cirelli, C & Tononi, G (2000) Gene expression in the brain across the sleep-waking cycle Brain Research 885, 2, 303-321

Delavilleon, G et al (2015) Explicit memory creation during sleep demonstrates a causal role of place cells in navigation Nature Neuroscience 18, 4, 493-495

Drew, L (2018) Wonder of slumber. In Lawton, G & Webb, J (eds) Big Questions Amazing Answers (revised edition) London: New Scientist

Durkin, J & Aton, S.J (2016) Sleep-dependent potentiation in the visual system is at odds with the synaptic homeostasis hypothesis Sleep 39, 1, 155-159

Knott, G.W et al (2002) Formation of dendritic spines with GABAergic synapses induced by whisker stem in adult mice Neuron 34, 2, 265-273

Kodama, T et al (1990) Enhancement of acetylcholine release during paradoxical sleep in the dorsal tegmental field of the cat brain stem Neuroscience Letters 114, 277-282

Larsson, S.C & Markus, H.S (2019) Genetic liability to insomnia and cardiovascular disease Circulation 140, 9, 796-798

LeShan, L (1942) The breaking of a habit by suggestion during sleep Journal of Abnormal and Social Psychology 37, 3, 406-408

Niwa, Y et al (2018) Muscarinic acetylcholine receptors Chrm 1 and Chrm 3 are essential for REM sleep Cell Reports 24, 2231-2247

Oudiette, D & Paller, K.A (2013) Upgrading the sleeping brain with targeted memory reactivation Trends in Cognitive Science 13, 3, 142-149

Paller, K.A & Oudiette, D (2018) Sleep learning gets real Scientific American November, 20-25

Rasch, B et al (2007) Odour cues during slow-wave sleep prompt declarative memory consolidation Science 315, 1426-1429

Richter, D et al (2019) Long-term effects of pregnancy and childbirth on sleep satisfaction and duration of first-time and experienced mothers and fathers Sleep 42, 4, zsz015

Stevner, A.B.A et al (2019) Discovery of key whole-brain transitions and dynamics during human wakefulness and non-REM sleep Nature Communications 10: 1035

Tononi, G & Cirelli, C (2003) Sleep and synaptic homeostasis: A hypothesis Brain Research Bulletin 62, 2, 143-150

Tononi, G & Cirelli, C (2006) Sleep function and synaptic homeostasis Sleep Medicine Reviews 10, 49-62

Tononi, G & Cirelli, C (2014) Sleep and the price of plasticity: From synaptic and cellular homeostasis to memory consolidation and integration Neuron 81, 12-34