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1. COMPRESSION SOCKS

The benefit of exercise is an inverted u-shape. For example, while light and moderate jogging extends life, strenuous jogging has a mortality rate similar to sedentary individuals. "It has been postulated by Van Houten [et al 2015] that the reduction in vagal activity that accompanies strenuous and prolonged exercise and contributes to increased intestinal damage, may explain this apparent contradiction of the benefits of exercise in individuals who engage in high volumes of intense exercise. While this remains to be substantiated, there is clearly a link between the integrity of the intestinal barrier and health" (Zadow et al 2020 p2461).

Intestinal damage can include gut bacteria escaping into the bloodstream, which impacts the immune system and increases susceptibility to pathogens. One of the mechanisms of intestinal damage through exercise is the blood flow to the skin to reduce body heat and away from the intestines (or splanchnic area - organs in abdominal cavity) (Zadow et al 2020).

"Therefore, identifying strategies that maintain splanchnic blood flow during exercise could prove beneficial for reducing exercise-induced intestinal damage and associated consequences" (Zadow et al 2020 p2462).

Compression garments are one possibility, specifically compression socks. Zadow et al (2020) performed an experiment during the 2016 Gold Coast Marathon in Australia. Forty-six runners volunteered to participate, and half of them wore foot-to-knee compression socks during the race. Blood samples were taken pre-marathon and five minutes after finishing, and analysed for intestinal fatty acid-binding protein (I-FABP) concentration (a marker of intestinal damage).

I-FABP concentration was higher in both groups between the two measures, but it was significantly higher in the no-sock (control) group post-marathon. "This suggests that the known circulatory benefits of lower-limb compression garments extend to their use during exercise, increasing central blood flow and thus reducing intestinal damage" (Zadow et al 2020 p2463).

Running in compression socks had previously been found to help general blood circulation (eg: 10 km race; Castilho Junior et al 2018).

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2. DIAGNOSTIC SELF-TESTS

Watson and McCartney (2025) summed up the situation thus: "Rapid advances in diagnostic technology, coupled with persuasive advertising, have resulted in a surge of direct-to-consumer self-tests, often sold under the banner of 'wellness'. Marketed as tools for empowerment and early detection, these self-tests promise convenience and autonomy and are promoted as tools for individuals to proactively manage their health. Self-testing can also offer an anticipated alternative route for health management, given the challenges in accessing primary care. But behind the glossy marketing lies multiple difficulties with real world use, and considerable potential for harm" (p1).

Two linked studies reported on diagnostic self-tests or direct-to-consumer tests available in the UK in 2023 - Davenport et al (2025), and Hillier et al (2025). Tests available in UK supermarkets, for example, include for male fertility, vitamin D deficiency, the menopause, and cancer (Coombes et al 2025).

There are a number of issues highlighted by Watson and McCartney (2025), including:

i) The impact on healthcare services of poor quality tests - ie: "the downstream consequences of interpreting and acting on dubious test results" (Watson and McCartney 2025 p1).

ii) False positive test results (ie: the test says the individual has the disease when they do not) can lead to anxiety, and unnecessary treatment ¹.

iii) False negative tests results (ie: the test says the individual does not have the disease when they do) can lead to false confidence, and delays in medical help seeking.

iv) Use of the wrong test - eg: using a self-test for "bowel health" to detect the "early stages of colon cancer" (Watson and McCartney 2025 p1).

v) Self-tests "should not be dismissed outright

¹ Kleeman (2024) observed in reference to genetic testing that DNA is not necessarily a reliable predictor of "our medical future": "When it comes to health, our genes are more of a weather forecast than an architect's blueprint: they might reveal a predisposition to certain conditions, but they can't say with certainty whether a person will develop a specific health problem in their lifetime. Except in the case of a few serious illnesses, having the genes for a deadly condition isn't a death sentence" (p21).

though" (Watson and McCartney 2025 p1). There are examples of "good" self-tests, like home pregnancy tests. These successful tests usually have clear binary answers - yes (pregnant) or no (not pregnant).

"Empowering individuals to take an active role in their health is an important goal, but if self-tests are to be sold directly to the public, they must be supported by high quality evidence, robust regulation, trustworthy public information, and clear pathways for interpretation and follow up" (Watson and McCartney 2025 p2).

Davenport et al (2025)

AIM - To review the information provided for diagnostic self-tests sold in the UK.

SAMPLING - Thirty direct-to-consumer self-tests assessing 20 biomarkers for 19 different conditions (eg: blood glucose level; group A streptococcal antigen; influenza A antigen and influenza B antigen; vaginal pH) were purchased from supermarkets, community pharmacies, and health and well-being shops within a ten mile radius of the University of Birmingham (the base of researchers). This was a convenience sampling method.

ANALYSIS - Information from the box or the "instructions for use" (IFU) leaflet (or patient information sheet) were analysed, including "characteristics of the device (biomarker, sample type, cost), statements on intended use (purpose, population, clinical condition), instructions for interpreting the results and recommended actions after a test result, and coherence of intended use and post-test recommended actions with national and international guidelines" (Davenport et al 2025 p2).

FINDINGS: Clinical condition to be detected by the test - 29 tests made "some statement about the clinical condition the test was designed to detect either implied by the name of the test... or in the IFU clinical claim" (Davenport et al 2025 pp4-5).

Who should use the test and when - 8 tests provided sufficient information for appropriate use.

Action after the test result - Seven tests provided information (eg: treatment or health behaviour changes), while 27 recommended follow-up with a healthcare

professional.

Interpretation of test results - Twenty tests stated that "a higher value or the presence of a biomarker was associated with the presence of the health condition being tested" (Davenport et al 2025 p9). In the other tests, interpretation of the results was "more complex"; eg: for "two vaginal pH tests a combination of symptoms and the test result were required to distinguish between three different infections" (Davenport et al 2025 p9).

CONCLUSION - "The current market and regulatory situation for direct-to-consumer self-tests are likely to make it difficult for the public to make informed decisions about when and how to use them, as well as how to interpret the findings and what subsequent actions should be taken" (Davenport et al 2025 p12).

EVALUATION: Strengths - A range of clinical conditions covered by the tests sampled, and a range of prices (from £1.89 to £39.99).

Weaknesses - Tests sold only by independent pharmacies were excluded, as were tests used for pregnancy and ovulation, and drug testing. The tests were purchased in April 2023. Hillier et al (2025) noted 63 self-tests available in December 2024.

Hillier et al (2025)

AIM - To review the evidence base, clinical performance claims, usability, and safety of diagnostic self-tests sold in the UK.

SAMPLING - As Davenport et al (2025).

ANALYSIS - IFU leaflets analysed for details of supporting evidence, claims about performance of the test, instructions, and safety use. The manufacturers were also contacted about the supporting evidence for their claims (and nine reports were received).

FINDINGS: Performance claims - 24 tests made claims (eg: an "accuracy" value).

Usability and safety - Concerns were raised for 26 tests, "of which 18 were rated as having high risk because the probability of an error was high or the

potential harm was severe" (Hillier et al 2025 p9).

Readability of IFU leaflets - Ten tests were assessed as requiring a reading age equivalent to 13-14 years old, while twenty tests required a reading age higher than that because of "several medical and technical terms" (p12).

CONCLUSION - Improved regulatory oversight of diagnostic direct-to-consumer self-tests was advised, partly because assessment of the tests was limited by manufacturers' unwillingness to provide documentation, and by the limited information on IFU leaflets. Some tests were better than others.

Coombes et al (2025) reviewing both studies focused on four self-tests with the most identified problems - a test for the menopause, one for diagnosis of chronic kidney injury, a vitamin D test, and one to detect an underactive thyroid - produced by two manufacturers.

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3. KRATOM

Medicinal products derived from the fresh leaves of the kratom tree have increased in recent years, particularly outside the tree's native area of South-east Asia. These products have been developed based on the health benefit claims of chewing the fresh leaves (Vicknasingam et al 2024).

What about the evidence to support such claims? Vicknasingam et al (2024) found 53 academic articles published in 2022 and 2023. The articles were grouped based on methodology:

i) Case reports (n = 20) and case series reports (n = 7) - A wide range of cases with little in common from which to draw conclusions.

ii) Surveys (n = 12) - Self-selecting samples answering a variety of questions.

iii) Human trials (n = 6) - Volunteers given kratom-derived substances in controlled conditions, and the effects measured (eg: urinary protein profiles).

iv) Large prevalence surveys - eg: from the US "National Survey on Drug Use and Health" (NSDUH), which included a question on kratom for the first time in 2019, a lifetime prevalence of 0.44% among adolescents (Sharma et al 2022). Higher use among Malaysia youth, for example, at 2.8% (Ismail et al 2022).

Vicknasingam et al (2024) concluded that "there is dearth of reliable data on key epidemiological factors, including the prevalence rates, and on objective and reliable indices of the health/safety profiles of products derived from kratom that are consumed in the United States and other Western countries, as well as of fresh kratom leaves and their water-based preparations that are consumed in South-east Asian countries. Very few studies that are being published are based on rigorous research methodology enrolling large unbiased samples of participants. Additionally, cultivation, harvesting, and processing of kratom plant material in South-east Asian countries and importation, manufacture, and trade of kratom-derived products in the United States are currently not subjected to rigorous regulatory health and safety oversight or standardisation. Consequently, consumers in the United States and in South-east Asian countries are consuming products with not fully known

chemical content, that can be contaminated or adulterated, and may also vary in chemical content and potency from batch to batch" (p289).

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4. AEROBIC EXERCISE AND WEIGHT LOSS

Aerobic exercise at moderate intensity is beneficial for weight loss. Jayedi et al's (2024) meta-analysis established that thirty minutes per week is required, but 150 minutes or more "achieve clinically important reductions" (p2).

A literature search was made for controlled trials lasting at least eight weeks with supervised continuous aerobic exercise (eg: walking; running), and including details of frequency (sessions per week), duration (minutes per session), and intensity. Intensity was divided into light, moderate, and vigorous based on maximum heart rate - 40-54%, 55-69%, and 70-90% respectively - or maximum oxygen consumption (20-39%, 40-59%, and 60-85% respectively), or metabolic equivalents (METs) (1.6-2.9, 3.0-5.9, and 6.0-9.0 respectively).

Weight change was measured in kg primarily, but also in waist circumference (cm), body fat percentage, fat mass (kg), area of visceral adipose tissue (cm²), or area of sub-cutaneous adipose tissue (cm²), as well as health-related quality of life score, and medication reduction (eg: anti-diabetic medications).

One hundred and sixteen randomised controlled trials published before May 2024 were included in the meta-analysis. Overall, each 30 minutes per week of aerobic exercise was associated with a reduction in body weight of 0.52 kg, or 0.56 cm in waist circumference, or 0.37% body fat percentage, for example. These benefits continued in a linear relationship until 300 minutes per week of exercise. Health-related quality of life also improved with more exercise, but there was a small risk of adverse events (eg: musculo-skeletal symptoms).

The studies included in the meta-analysis had a number of methodological differences despite the strict inclusion criteria, including:

i) Country - 71 trials performed in North America, Europe, and Australia, and only two in Africa and four in South America.

ii) Samples - Mostly studies included only one sex (47 women only and 30 men only), and both obese and overweight participants (72 studies). Many trials included individuals with co-morbid health conditions, like type 2 diabetes.

iii) Exercise - Training programmes that increased

with time or not, and duration (from 55 to 300 minutes per week). Adherence to the programme (eg: 80% and over in 48 studies, but no information in sixty studies), and study drop-out (less than 20% in most studies).

iv) Confounding factors - Overall, insufficient data on dietary habits, and smoking status, for instance.

The meta-analysis confirmed the benefits of moderate exercise in weight loss with the more the better to a certain point. This fits with previous meta-analyses on the subject (eg: Armstrong et al 2022).

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5. DRINKING

- 5.1. Water and hydration
- 5.2. Caffeine
- 5.3. References

5.1. WATER AND HYDRATION

Maintaining hydration is crucial. "The body's balance of water intake and output is tightly regulated to keep the concentration of salts and minerals, or electrolytes, in our blood at a precise level. To prevent dehydration, hormonal and neural mechanisms are activated, stimulating thirst to encourage water intake and increased water absorption by the kidneys to decrease water output" (Cox 2023 pp40-41).

The first question is how much to drink in a day for optimal health. Official estimates in the USA in the mid-20th century calculated 2.5 litres based on 1 millilitre of water per kilocalorie of food eaten (with 2500 kilocalories per day as the norm). This is viewed as an overestimate as it did not take into account the fluid ingested in food (Cox 2023).

More recently, research with water labelled with an isotope of hydrogen calculated 1.5 to 1.8 litres per day for men and 1.3-1.4 litres for women (eg: Yamada et al 2022). This figure, of course, is an average and the amount of water required varies with physical activity, and ambient temperature (Cox 2023).

Kavouras (2019) explained how a mistaken belief that the majority of people with free access to water are dehydrated has emerged: "if exercise-induced dehydration leads to increased urine biomarkers, then elevated urinary biomarkers should correspond with water deficit and dehydration. So, when we read data indicating that a majority of children, adults, and athletes have elevated levels of urinary osmolality² or specific gravity we mistakenly conclude that a large portion of the population is dehydrated. Furthermore, when we read data indicating that a majority of people across the world do not meet the dietary guidelines for water intake we also conclude that most people are dehydrated" (p471).

This author took data from the "National Health and Nutrition Examination Survey" (NHANES) in the USA as an

² Urinary osmolality is the concentration of particles like sodium in the urine and it is used as a marker of hydration.

example. Individuals classed as "low-drinkers" (eg: 1694 mL/day) and as "high-drinkers" (eg: 7934 mL/day) have "nearly identical plasma osmolality" (279 and 280 mmol/kg respectively) (Kavouras 2019 p471).

Is it possible to drink too much? Hyponatremia is where the kidneys cannot cope with the amount of water and the sodium content of the blood is diluted dangerously. In everyday life this is rare (Cox 2023).

Not drinking enough is more of an issue. For example, a study with mice on lifelong sub-optimal hydration found inflammation, and accelerated age-related degeneration of key organs in the body, such that life was shortened by six months (the equivalent to fifteen years in humans) (Allen et al 2019).

Dmitrieva and Burg (2011) slowly reduced water intake over fifteen in mice of different ages (3, 18, and 27 months old) (from 56% to 33% of gel food with no additional water available). "With reduced water intake 3 months old mice maintain water balance, as indicated by a near constant weight (that initially even increases slightly). In contrast, 18 and 27 month old mice become dehydrated (lose weight) when there is less than 50% water in their gel food, and dehydration becomes progressively severe as water intake falls further. The dehydration is greater in 27 month old than 18 month old mice. Fast recovery of weight after water intake increased supports the conclusion that the weight loss during water restriction was caused by dehydration" (Dmitrieva and Burg 2011 p2).

Blood sodium levels are elevated with mild dehydration (or "underhydration"; table 5.1), and this is detrimental. Dmitrieva et al (2023) used serum sodium as a proxy for "hydration habits" in their analysis of data from the "Atherosclerosis Risk in Communities" study (over 15 000 US middle-aged adults followed for over 25 years). Serum sodium of 142 mmol/L or more was associated with an increased risk of chronic diseases, and premature mortality compared to the normal range (135 to 146 mmol/L).

Negative water balance is associated with ageing such that older adults are "more prone to dehydration" (Dmitrieva and Burg 2011 p1). This is due in part to the reduced concentration of urine (ie: more water), and "inadequate water intake because of inappropriately decreased thirst" (Dmitrieva and Burg 2011 p1).

"Insensible water loss" describes water loss through the skin, and through exhaling, up to half of total water

loss. This type of water loss was found to increase with age in mice (Dmitrieva and Burg 2011).

- Dehydration - "the condition that results from excessive loss of water from a living organism" (US National Library of Medicine 2018 quoted in Kavouras 2019).
- Alternatively, "dehydration refers to the process of losing water, while hypohydration is the state of water deficit, and rehydration is the process of gaining water from a hypohydrated state towards euhydration [fluid balance]" (Kavouras 2019 p471).
- Adolph and Associates (1969) talked of "voluntary dehydration", where not enough is drunk in relation to rapid sweating.
- Other terms include "insufficient hydration", "sub-optimal hydration" or "pre-dehydration" (Kavouras 2019).
- Underhydration - "encompassing low water intake (consuming less than the reference values), in the absence of total body water deficit, thirst or elevated plasma osmolality ³, while the water homeostatic mechanism has been activated as indicated by elevated vasopressin and urine biomarkers" (Kavouras 2019 p472).
- Loss of water to the equivalent of 2% of body weight is the operationalisation of mild dehydration (Kavouras 2019).

Table 5.1 - Terminology.

Thirst is quenched at the basic level by water, but in the modern world, there are many alternatives available, described as "functional beverages" (eg: energy and sports drinks). Sports drinks, for example, are isotonic, hypotonic or hypertonic ⁴ (containing carbohydrates and salts) with the purpose of replenishing lost electrolytes, say. "Most of these sports drinks were designed for high performance. For most people, exercising half an hour to an hour, they might lose 1 litre of fluid at the most, which can easily be replaced with four cups of water over the couple of hours following exercise" (David Rowlands of Massey University quoted in Cox 2023).

In terms of body fluid loss during prolonged exercise, Rowlands et al (2022) performed a meta-analysis of studies of hypertonic, isotonic and hypotonic sports

³ Concentration of electrolytes in the blood.

⁴ "Sports drinks containing carbohydrates and electrolytes can be formulated to be more (hypertonic), similar (isotonic), or less (hypotonic) concentrated than body fluids" (Rowlands et al 2022 p350).

drinks and waters. Twenty-eight relevant studies were found.

Hypotonic drinks were calculated to maintain better central hydration (using a measure called delta percent plasma volume; dPV) when consumed during continuous exercise (of up to 180 minutes) than isotonic drinks. It was assumed that hypotonic drinks were also better than hypertonic and non-carbohydrate drinks, and water, but the evidence was limited for direct comparisons.

There were methodological differences between the studies which included the measure of hydration, exercise form, length and intensity, beverage formulation (eg: carbohydrate and electrolyte concentrations; presence of sodium), sample (including gender and size), environmental conditions, the presence of a no-drink control, and the drink ingestion rate.

5.2. CAFFEINE

"Caffeine is the most widely consumed psychoactive drug in the world and one of the most comprehensively studied ingredients in the food supply. It occurs naturally in the leaves and seeds of many plants and has a taste bitter enough to deter pests. Natural sources of dietary caffeine include coffee, tea, and chocolate. Synthetic caffeine is also added to products to enhance their stimulant properties. Historically, this addition was limited to soda-type beverages, but over the past decade, caffeine has been added to a diverse variety of foods and non-food items to promote arousal, alertness, energy, and elevated mood" (Temple et al 2017 p1).

Estimates of caffeine consumption are just that, estimates, because of differences between products. However, for example, in the USA, adult daily caffeine consumption was calculated at 180 mg per day (equivalent to two cups of coffee) in one study, while it was 25 mg/day for 2-11 year-olds and 50 mg/day for teenagers in one cohort (Temple et al 2017).

Temple et al (2017) commented: "Trends in caffeine consumption have been stable among adults for the past two decades. Among children aged 2-19 years old, caffeine consumption increased significantly from the 1970s through the 1990s. This increase was also marked by a decrease in dairy consumption and an increase in soda consumption. More recent data suggest that caffeine consumption has remained stable among this age group since the 1990s, a finding similar to that in adults. This stability is somewhat surprising, given the marked

increase in the number, variety, and availability of caffeinated beverages introduced in the past decade" (p2).

Caffeine is most associated with coffee, but it is also found in energy drinks (and along with their sugar content, this has raised some concerns). It is the quantity consumed, particularly by children and adolescents, that is the issue (Fox-Skelly 2024) (table 5.2).

Generally, 2-3 cups of coffee per day can be "considered as part of a healthy diet" (Peter Kistler of the Baker Heart and Diabetes Institute in Melbourne, Australia quoted in Fox-Skelly 2024). Beneficial effects include concentration and alertness improvements, reduced risk of depression, Parkinson's disease, and cardiovascular diseases (Fox-Skelly 2024).

- Energy drinks vary in caffeine concentrations from 2.5 to 171 mg per 28 mL (compared to 77 to 150 mg for a cup of coffee), while 50 g of sugar in a can or a bottle is not uncommon (Costantino et al 2023). Other substances include taurine and guarana. "The prospect of taurine in tandem with caffeine bolstering concentration, reaction time, and emotional state has sparked investigation, although conclusive evidence on combinatorial cognitive effects remains elusive" (Costantino et al 2023 pp2-3).
- Costantino et al (2023) reviewed the evidence on the potential health risks of excessive energy drink consumption. 96 relevant studies were found published in English between 2009 and early 2023.
- Nine cases of cardiac arrest, three of them fatal, were identified among healthy humans as a direct result of energy drink consumption. Though there may be a "plausible under-reporting" (p25) of deaths.
- Experimental animal studies showed the acute and chronic effects of the components of energy drinks (eg: combination of caffeine and taurine).
- The researchers recommended one can (250 mL) per day, and regulation of the sale of energy drinks to "minors". More research on the long-term effects is required.

Table 5.2 - "Dark side of energy drinks".

Caffeine can improve performance in different sports, like cycling (which has been well studied). For example, Trujilla-Colmena et al (2024) reported a

controlled study with eleven young recreational cyclists in Spain. The participants completed a time-trial on a fourteen kilometre cross-country course in the same weather conditions twice, once after the consumption of 3.00 mg per kg body weight of caffeine one hour before cycling, and once after 0.04 mg/kg of caffeine (the placebo) ⁵. The order of performing the two trials was counterbalanced between participants.

The participants were significantly faster after the caffeine, and the mean heart rate was higher, but there was no difference between the conditions in perceived exertion/fatigue afterwards. The improvement in performance was about 4%.

The study showed that "caffeine enhanced endurance, expressed by a lower time to complete the distance and the capacity to sustain a higher mean heart rate during the trial while maintaining participants' perceived fatigue. The benefits of caffeine were observed mainly during the first half of the course..." (Trujilla-Colmena et al 2024 p9).

This research used a real cycling course, whereas previous studies often used a stationary exercise bike in a laboratory.

Studies of the pharmacological actions of caffeine suggest an anti-depressive effect. "Caffeine has complex effects in the central nervous system, largely mediated by antagonism of adenosine A2a and A1 receptors, including an increased turnover of several monoamine transmitters, such as serotonin, dopamine, and noradrenaline... Therefore, central deficiency of monoamines may be improved by caffeine, which enhances dopaminergic neurotransmission... A deficiency of central monoamines is one of the features of depression..." (Lucas et al 2014 p384).

Can this be observed in humans as a reduced risk of suicide among large coffee consumers? Lucas et al (2014) analysed US data from three cohorts - the "Health Professionals' Follow-up Study" (over 51 000 male health professionals 40-75 years old when began in 1986), "Nurses' Health Study" (121 700 female nurses aged 30-55 years in 1976), and "Nurses' Health Study II" (over 116 000 female nurses aged 25-42 years in 1989). Full data were available on approximately 210 000 individuals for Lucas et al (2014).

Food frequency questionnaires had been completed by the participants of the cohorts at various times, and the

⁵ Technically the participants performed the trial four times, twice for each condition.

key items were "coffee with caffeine", "decaffeinated coffee", "non-herbal tea", carbonated soft drinks (with or without caffeine), and chocolate. Measures and amounts of the items were standardised (eg: 137 mg of caffeine per cup of coffee (8 oz/237 ml). The outcome measure was death by suicide and self-inflicted injuries.

Overall, 277 deaths from these means were documented. After adjusting for variables, like smoking, alcohol consumption, and marital status, higher coffee consumption was associated with lower suicide risk. For example, those consuming four or more cups of coffee per day had half the risk of those who drank less than one cup per week. There was no relationship for decaffeinated coffee or tea consumption. The researchers commented: "The lack of association between decaffeinated coffee and suicide risk suggests that caffeine, rather than other coffee components, contributes to this association. However, consumption of decaffeinated coffee was low and we cannot exclude the possibility that an inverse association with suicide risk could exist for higher consumption" (Lucas et al 2014 p382).

The data were observational, and so causation cannot be established.

Though caffeine is the main constituent of coffee, there are over 100 other biologic agents in the beverage, and this observation led Chieng et al (2022) to investigate coffee sub-types and cardiovascular disease using UK Biobank data. Coffee consumption was self-reported for instant, ground/filter, and decaffeinated, and the outcome measures were incidence of cardiovascular disease, and mortality (from it).

The final data set contained nearly 500 000 participants with an average age of 58 years, and follow-up of twelve years. Of these, 22.4% self-classified as non-coffee drinkers, and they were the comparison group. Cardiovascular disease was reported in about one-tenth of the sample during follow-up (and 60% of those died). Coffee consumption (of any type) was associated with lower risk of cardiovascular disease, and mortality compared to non-drinkers. Four to five cups per day was the maximum before negative effects emerged. An inverted U-shape for coffee consumption and outcomes was found, overall.

The study assumed that coffee consumption at baseline (2006-2010) remained unchanged throughout follow-up.

Negative effects of caffeine reported by Temple et

al (2017) in their review included an impact on the cardiovascular system, negative behavioural outcomes in children, and sleep disturbances, while there was no clear relationship for dehydration and diuresis. "Death from caffeine ingestion appears to be rare" (Temple et al 2017 p6).

As well as negative effects, "sensitivity to caffeine varies wildly. Some people can guzzle three cans of energy drink in quick succession with little effect, while others aren't so lucky" (Fox-Skelly 2024 p39). Temple et al (2017) concluded a review of the evidence on caffeine that its consumption is relatively safe for healthy adults, but "that for some vulnerable populations, caffeine consumption could be harmful, including impairments in cardiovascular function, sleep, and substance use" (p1). Vulnerable populations include pregnant and lactating individuals, children, adolescents and young adults, and individuals with certain health conditions (eg: heart-related; mental illness) (Temple et al 2017).

The gut microbiome is involved in the metabolism of coffee, and such that certain bacteria are specialists (eg: more Bacteroides in the gut of coffee drinkers; Gonzalez et al 2020). Manghi et al (2024) showed a specific gut microbiome member, Lawsonibacter asaccharolyticus, in coffee drinkers (and to a lesser extent with decaffeinated coffee) using data from "ZOE Personalised Response to Dieting Composition Trial" (ZOE PREDICT), the "Mind-Body Study" (MBS) ⁶, and the "Men's Lifestyle Validation Study" (MLVS) ⁷. Nearly 23 000 participants in these studies in the USA and the UK had provided stool samples which allowed genetic analysis of the gut bacteria. Data from a further 54 000 participants were available from public data sets. This research revealed "a metabolic link between a specific gut micro-organism and a specific food item" (Manghi et al 2024 p3120).

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6. THE POLITICS OF EXHAUSTION AND MENTAL HEALTH

Haggar and Kienzler (2025) asserted: "Seeking asylum in the UK can be a long, complex and difficult process shaped by tough immigration policies" (p1), and the process is "characterised by uncertainty and a poor quality of life" (p2). These authors continued that the situations and processes "can be considered forms of structural violence – systemic social, political, and economic inequalities that harm people seeking asylum both directly and indirectly... They stem from entrenched systems and power structures that limit access to resources and opportunities, contributing to poor health and mental health outcomes among those seeking asylum" (Haggar and Kienzler 2025 p2). The upshot is what has been called a "politics of exhaustion" (eg: Welander 2020), which impacts the mental health of those seeking asylum.

The "politics of exhaustion" describes "the convergence of punitive migration practices designed to wear down the resilience of those seeking asylum by making their lives as difficult as possible. As such, it is a 'tool of governance and control' to deter settlement... Similarly, Ansems de Vries and Guild (2018), consider the notion of politics of exhaustion as 'the felt effects of the stretching over time of a combination of fractured mobility, daily violence and fundamental uncertainty' (p2157). The authors further highlight the concept's subjective dimension considering that it affects the quality of life, wellbeing and health of people seeking asylum... Such 'politics of exhaustion' subject people seeking asylum to 'slow', 'structural' forms of violence... in that social structures and arrangements perpetuate inequities and prevent people from meeting their basic needs and potentials" (Haggar and Kienzler 2025 p3).

Haggar and Kienzler (2025) explored these ideas in semi-structured interviews with eighteen third-sector services providers for people seeking asylum in England and Wales in mid 2021. The findings can be grouped under three headings (table 6.1):

i) "The exhausting nature of the asylum process" - The interviewees used terms like "wearing down", "grinding down", and "tiring" to reflect the asylum process, while one participant describe the process as

being "stressed, tired, and just exasperated... like when you try and try and it's still not enough" (p4).

The "practice of disbelief" of officials was one aspect, which a lawyer interviewee described thus: "If you're constantly saying, 'I don't believe you' 'I don't believe you', no matter what they do to produce evidence... eventually it tires them out, they think 'well what can I do to get you to believe me?'" (p4). A psychiatrist participant said: "If [immigration officials] can find one or two facts which are questionable, they can say 'this person is not a believable person, and therefore we can disregard the rest of the story'" (p4).

Excessive delays in the processing of claims was another aspect of the system. One participant stated: "The waiting without any answer or information, that is exhausting... having this question in your mind, 'what is going to happen to my life?'... Service providers said the Home Office does not provide status updates on individual asylum claims, leaving people 'stuck in limbo endlessly'" (Hagggar and Kienzler 2025 p4).

Living in deprivation was a further aspect. "While waiting for their claim to be processed, people seeking asylum tend to live in conditions of deprivation driven by discriminatory policies, which were perceived as exhausting. For example, the combination of limited financial support and not being allowed to work was seen to make everyday activities, such as eating, socialising, and taking public transport, into a challenge or a trade-off. A lawyer explained: 'Where do you socialise? You can't pay for that when you have to ration your money'... Deciding how to ration money was perceived as a constant struggle weighing on people's minds: 'The lack of money is always quite exhausting, always having to think about it'... Enduring an inadequate and inappropriate standard of asylum accommodation was further perceived as exhausting. Service providers reported that accommodation was frequently overcrowded, uncomfortable and dehumanising..." (Hagggar and Kienzler 2025 p4).

ii) "The impact of exhaustion on daily life" - "Most service providers heard verbal expressions like: 'I'm tired... I don't know if I'll have the energy for that'..., whilst others shared more concerning expressions, such as 'I'm a zombie'... This was further reflected in physical appearance and body language. Eight service providers highlighted that people seeking asylum could appear tired and lacklustre. A social support volunteer stated: 'over five years of the asylum process

people age like 20 years'... A third of providers noted that exhaustion could impact the ability of people seeking asylum to concentrate and function well day to day, including whilst studying or supporting casework for their asylum claim" (Hagggar and Kienzler 2025 p5).

iii) "The impact of exhaustion on mental health and well-being" - Participants reported that a number of asylum seekers they knew had "reached a point where they 'can't deal with it'..., 'can't cope anymore'..., and 'just don't have any fight left'... This state of exhaustion was perceived as psychologically unsafe, as people could turn to unhealthy coping mechanisms including self-harm, drugs and alcohol: 'We do get a lot of suicidal ideation and disclosure of self-harm because they can't cope anymore'... A mental health worker added that 'a lot of them do turn to drugs and alcohol'..., although religion could act as a protective factor against this. Exhaustion was also perceived to play out by damaging self-esteem and self-worth..." (Hagggar and Kienzler 2025 p5).

- "They come with so much hope and ambition... many will tell me that the way they've been treated here has been the most damaging... they put so much on it and then when they get here, people don't believe them, they're not treated with respect, they're excluded... all those hopes and dreams slowly begin to go... I think the system eventually wears them down" (social worker; p5).
- "One of the physiological reasons for the exhaustion is not only the Home Office delaying a resolution of this, but the brain is also trying to make sense of everything that's happened to them before that in their country, on the journey, the trauma they've had since they've come here, the way people are treating them... they're mentally exhausted because all these messages are going backwards and forwards" (psychiatrist; p6).
- "I think all mental health problems would be exacerbated by exhaustion... you make yourself more vulnerable if you're not able to use coping strategies that are helpful... I would already be vulnerable to schizophrenia and depression, but if I had a bit of social support or I could find activities to do to boost my self-esteem, I would be less likely to show symptoms of it. But if I'm exhausted and apathetic, I won't seek out things to do and I won't seek out help if I need it" (psychiatrist; p6).

Table - Three key quotes from interviews in Hagggar and Kienzler (2025).

Haggar and Kienzler (2025) ended: "In successive attempts to 'control migration', claiming asylum in the UK is becoming tougher than ever. Asylum policy and practice create conditions which restrict the rights of those seeking asylum so severely that they are frequently forced into deprivation and destitution, are routinely treated with suspicion stemming from a deeply rooted culture of refusal in the Home Office, and can be left precariously in limbo for many years due to long processing times. Such practices persist, intersect, and compound to exhaust people seeking asylum, with the aim that they become fed up and leave of their own accord. A 'politics of exhaustion' is enacted here because exhaustion arises as an invisible mechanism of harm through convergent and persistent structurally violent policies. Practices of exhaustion are powerfully engrained, seemingly justified as part of the bureaucratic machinery of the asylum process. There is little political will to improve it" (p7).

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7. ENVIRONMENTAL SENSITIVITY AND MENTAL HEALTH PROBLEMS

The personality trait of sensitivity (or environmental sensitivity or sensory-processing sensitivity) is defined as "a heightened degree of sensitivity to physical, emotional, and social stimuli, such as bright lights, subtle changes in the environment, and other people's moods, combined with deeper cognitive processing of such sensory stimulation" (Falkenstein et al 2025 p1). It is associated with other traits like introversion and neuroticism, and with common mental health problems.

The "Highly Sensitive Person Scale" (HSPS) (Aron and Aron 1997) has been developed to measure it. Smolewska et al (2006) described three underlying factors in the HSPS - "(a) Ease of Excitation (EOE), which refers to being easily overwhelmed by internal or external stimuli (eg: 'Are you more than others affected by moods of other people?'); (b) Low Sensory Threshold (LST), which refers to unpleasant sensory arousal from external stimuli (eg: 'Do you become unpleasantly aroused when a lot is going on around you?'); and (c) Aesthetic Sensitivity (AES), which refers to being susceptible to beauty and the arts (eg: 'Are you deeply moved by the arts or music?')" (Falkenstein et al 2025 p2).

Falkenstein et al (2025) performed a literature review on sensitivity and mental health problems, finding 37 relevant studies. Meta-analysis showed a positive correlation between sensitivity and depression, and anxiety, overall. Sensitivity was also associated with psychosomatic symptoms, obsessive compulsive disorder, post-traumatic stress disorder, agoraphobia, and social phobia.

The studies in the review mostly involved convenience samples (particularly of female students), were correlational (ie: could not establish causality), and were based self-reports.

The explanations for the association between high sensitivity and mental health problems included that such individuals "feeling often and quickly overwhelmed in everyday life because of perceiving more stressors could promote a recurring sense of learned helplessness in the individual - a mental state that contributes to depression and anxiety" (Falkenstein et al 2025 p3) (eg: Benham 2006). Or over-rumination by sensitive individuals (eg: Lionetti et al 2022). While Brindle et al (2015)

"hypothesised that individuals high in sensitivity are more aware of their negative emotional states while also showing lower self-efficacy regarding how they might change their negative emotional states. In other words, an increased awareness of negative emotional states in someone who lacks the emotional-regulation skills to overcome these could cause recurring feelings of helplessness and negative affect in the individual" (Falkenstein et al 2025 p3).

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8. HEALTH CARE AND THE ENVIRONMENT

- 8.1. Health data
- 8.2. Environmental footprint
- 8.3. Co-benefits policy
- 8.4. References

8.1. HEALTH DATA

The global improvements in population health in the last century could well be reversed with future climate change, particularly in lower- and middle-income countries. Orton et al (2025) stated: "The degree to which climate events directly affect physical and/or mental health, or impact one or more pre-existing health conditions, requires a new approach to epidemiological analysis. Essential to understanding and addressing the interaction of climate on patient health is the documenting and interpreting of patient-centric, timely, and comprehensive health data which can be linked to key climate and environmental variables" (p1).

Digital health data can help identify sub-populations and individuals most at risk from the negative health impacts of climate change.

Orton et al (2025) offered a preliminary list of environmental and climate variables relevant to future health:

- i) Excess heat.
- ii) Drought in areas where drought uncommon/less severe.
- iii) Wildfires.
- iv) Flooding from rainfall on already saturated land.
- v) Rises in sea levels.
- vi) Changes in ocean climate.

8.2. ENVIRONMENTAL FOOTPRINT

Samuel et al (2025a) stated: "Globally, national healthcare sectors contribute approximately 5.5 % to their country's greenhouse gas (GHG) emissions..."

Healthcare also contributes to other environmental harms, including the production of toxic and non-toxic waste, water use, and effects on biodiversity... Calls have been made for the healthcare sector to address its adverse environmental impacts... and many healthcare systems internationally have committed to develop low-carbon health services" (p1). How to do this while maintaining quality of care?

Samuel et al (2025a) investigated the attitudes to this topic in twelve focus groups in the UK with members of the general public. Each focus group involved imagining a 35 year-old patient with a persistent cough and what care they would expect from the National Health System (NHS), along with the environmental impact of that care, and what could be improved in the future.

All participants (n = 82) recognised that the NHS should be reducing its environmental harm, but this concern was secondary to the health needs of themselves and loved ones. For example, one participant said: "when you're in pain, the idea of considering some potentially remote and possibly distant, you know, distant in terms of time effect is not one that's going to actually be very, be very valid" ("G10E"; p5). Another participant stated: "I know quite a few doctors [and] they would not think about the environmental impact, because they would think 'this is what the patient needs'... I think, what we said before about the guilt... I feel like they would rather take the guilt of the environmental impact than the guilt of potentially losing a patient" ("G01E"; p5).

The participants felt that receiving healthcare required "hard work" (eg: travel to hospital or clinic; time waiting for an appointment), and so care about the environment was very much in the background. As one person said: "if you could walk into your GP, have an appointment get seen on the same day... you might say, 'Oh, how can I do this in a greener way' but, because it's such a struggle to get even, you know, even seen..." ["G06I"]. Consequently, because of the amount of investment in caring that was required, their caring responsibilities towards themselves and their loved ones overshadowed other caring responsibilities (to, for example, the environment)" (Samuel et al 2025a p6).

One experience reported by a participant showed the difficulties individuals perceived: "I was once offered... for... vertigo, between the week of pills, or one injection. And I have a phobia of needles. And if I was told that the injection would be much better for the environment... I'd then have to decide whether my phobia was like... I'd likely go home and cry..., and be..., be

really upset if they were to give me that choice... Putting the [choice on me], it's like essentially saying, are you a good person?" ("G06C"; p7).

8.3. CO-BENEFITS POLICY

"Co-benefits" is "a policy framing underpinned by the idea that the positive effects of a particular policy will also produce benefits (co-benefits) in other policy areas" (Samuel et al 2025b p1). An environment-health co-benefits framing has become common - ie: environmental harm mitigation policies will also bring population health benefits. "Framing the benefits of environmental policies in terms of direct health co-benefits is particularly appealing because of the immediate visible and tangible improvements to individuals and their communities... This includes, for example, low carbon, active transport, which improves physical health and reduces exposure to harmful pollutants; eating fewer meat products, which reduces farming emissions and is associated with lower cardiovascular and cancer risk; efficient housing, which saves energy and reduces cold and damp related illnesses; sustainable prescribing, which reduces pharmaceutical production and avoids harmful effects of over-medicating; and protecting or enhancing biodiversity, which is related to improved mental and physical health outcomes" (Samuel et al 2025b pp1-2).

With the growth of the co-benefits approach, there are two challenges, according to Samuel et al (2025b): "first, how to measure and assess co-benefit relationships and policy measures - including issues with how best to model data, which variables to use in analysis and how to account for unintended consequences - and second, issues around implementing co-benefits approaches in practice... In terms of the latter, concerns have been voiced about systematic and organisational barriers associated with a lack of resources and capacity..., siloed thinking, a lack of integration between departments working on different policy objectives and the use of different technical language and political realities across these departments" (pp2-3).

Oliveira and Thorseth (2016) also noted that "co-benefits consistently states facts and numbers that have created a shared belief, especially present in policy documents, that co-benefits are good and desirable... the idea of co-benefits itself holds a latent notion of some kind of rightness" (quoted in Samuel et al 2025b).

Samuel et al (2025b) explored co-benefits of policies around environmental harms associated with healthcare, and health benefits in twelve focus groups with eighty-two members of the UK public. "Co-benefits framings resonated with participants, who perceived this approach as useful for prioritising healthcare needs while valuing the environment. However, when participants tried to frame co-benefits as a solution, they struggled to reconcile complexities" (Samuel et al 2025b p1).

The complexities can be seen in the following quotes which show distrust on policy decisions. For example, a male participant voiced scepticism succinctly: "Four hospitals closing just sounds like cost-cutting and green issues are just an excuse" (p9). A female participant expressed similar views: "Just the first thing for me is I'm just suspicious, is it about the better access to care – for whom? Why is it better? How is it better? Maybe it might be better environmentally, if it's closer to you, you might have more options to get there in an environmentally friendly fashion. Yeah. But, you know, what's not in here is for cost reductions. And I can imagine that would be behind this kind of initiative" (p9).

The researchers pointed out a subjective aspect to the views about co-benefits. Put simply, a positive attitude about policies to reduce environmental harm as long as it did not impact the individual's access and experience of healthcare. For example, there had a previous debate in the media about a caesarean birth having a greater carbon footprint than a vaginal birth, and the impact upon the mother's decision to choose the mode of birth (Samuel et al 2025b).

Samuel et al (2025b) commented: "The subjective nature of co-benefits approaches, alongside issues of (dis)trust, raises a key policy-related question: who should determine which health and care needs – needs that our findings and others have shown to reflect differing preferences among patients... – should align with co-benefits policies associated with mitigating the environmental harms of healthcare? Our participants richly grappled with the complexities of this question" (pp9-10).

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9. MENTAL HEALTH OF GESTATIONAL SURROGATES

Gestational carriers (ie: surrogate pregnancies) have an increased risk of new-onset mental health problems. Potential risk factors (beyond those of pregnancy) include "the emotional effect of separation from the newborn, maintaining relationships with the intended parents and child, and societal scrutiny about their decision to pursue gestational carriage" (Velez et al 2025 p2) ⁸.

Velez et al (2025) analysed data from Ontario, Canada, from the "Better Outcomes Registry and Network Ontario" database of all births between early 2012 and early 2021. Three groups were distinguished - gestational carriage (n = 758), and non-gestational carriage (subdivided into unassisted conception and IVF (in vitro fertilisation)). The main outcome measure was new-onset mental illness based on hospital admission or outpatient visit.

The rate of new-onset mental illness was calculated per 100 person-years, which was 6.9 for gestational carriers compared to 5.2 for unassisted conception and 5.0 for IVF non-gestational carriers.

Standards of practice in Ontario involved a mental health screening of potential surrogates, which meant that these individuals should have been mental illness-free before the pregnancy. "However, mental health professionals report challenges in conducting comprehensive assessments, particularly when using instruments that frequently elicit defensive response patterns that make them difficult to interpret. In the current study, 19.0% of gestational carriers had a documented diagnosis of mental illness before pregnancy" (Velez et al 2025 p6).

Gestational carriers usually undergo IVF, which increases the chances of multi-foetal pregnancies and of pregnancy complications that "could lead to, or exacerbate mental illness" (Velez et al 2025 p6).

The gestational carriers were different to other groups on a number of measures - for example, more likely to reside in lower-income areas, be obese, and have chronic hypertension.

The researchers accepted two more limitations - namely, the dependence upon the accuracy of the database, and the wide range of mental disorders included in the

⁸ The brain changes during pregnancy (appendix 9A).

outcome measure.

APPENDIX 9A - PREGNANT BRAIN

Pritschet et al (2024) mapped changes in the maternal brain from pre-conception (three weeks before IVF), through pregnancy, to two years post-partum using regular neuroimages. In summary: "Pronounced decreases in grey matter volume and cortical thickness were evident across the brain, standing in contrast to increases in white matter micro-structural integrity, ventricle volume and cerebrospinal fluid, with few regions untouched by the transition to motherhood" (Pritschet et al 2024 p2253).

This was a case study of a healthy 38 year-old woman who underwent 26 magnetic resonance imaging (MRI) scans.

It should not be surprising that there are neuroanatomical changes during and around pregnancy because "the maternal body undergoes profound physiological adaptations to support the development of the foetus, including increases in plasma volume, metabolic rate, oxygen consumption and immune regulation. These rapid adaptations are initiated by 100-fold to 1,000-fold increases in hormone production, including oestrogen and progesterone. These neuromodulatory hormones also drive significant reorganisation of the central nervous system" (Pritschet et al 2024 p2253).

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