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Health: Mostly Heart

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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/. See also material at https://archive.org/details/orsett-psych.

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1. DIAGNOSIS

1.1. TROPONIN

"Many people attend hospital with chest pain and suspected myocardial infarction, with statistics showing that chest pain accounted for approximately 5% of emergency admissions in 2017–18 [in the UK]. It is important to diagnose people suspected of having an myocardial infarction as early as possible to ensure quick and effective treatment. However, only around 20% of emergency admissions for chest pain will have an myocardial infarction and there are many other causes of chest pain. Tests that can quickly tell which patients do not have myocardial infarction could avoid unnecessary hospital admissions, waiting time and anxiety" (Westwood et al 2021 pxxi).

The use of high-sensitivity cardiac troponin (hs-cTn) assays is common practice in this situation. An elevated cardiac troponin value as seen in a blood sample establishes a diagnosis of myocardial injury [1]. Cardiac tropinins T and I peak after 12-48 hours after acute myocardial infarction (AMI) (Lazar et al 2022) [2]. Put very simply, troponins are found in large amounts in the blood if the heart is "in pain".

The view of hs-cTn assays as the gold standard measure dates from the early 21st century, though the biochemistry was known from the 1960s (Lazar et al 2022). Troponins are specific to the heart, whereas other biomarkers previously used (eg: aspartate transaminase) are not cardio-specific (Lazar et al 2022).

Very low concentrations of cTn have been seen in the blood of healthy individuals due to natural heart cell turnover, while troponin release occurs in other cardiac

[1] The standard threshold of the 99th percentile upper reference limit is used, which varies between men and women (34 ng/L and 16 ng/L respectively) (Lee et al 2019).

[2] "Troponins are structural proteins found in the troponin complex within skeletal and cardiac muscle thin filaments. The troponin complex consists of three subunits (I, T, and C) and along with calcium ions plays an important role in the regulation of muscle contraction. Each molecule has a specific role in the muscle contraction process: troponin T attaches the troponin complex to the actin filament, troponin C acts as the calcium binding site, and troponin I inhibits interaction with myosin heads in the absence of sufficient calcium ions" (Lazar et al 2022 p2).

situations also (Lazar et al 2022).

Various methods have been used to assay troponin, of which hs-cTn assays are the latest. "High-sensitivity troponin assays are used to detect troponins, but at a much lower concentration than classical assays. These assays offer several advantages, first of all being the fact that they are highly sensitive, thus providing faster recognition of AMI (rule-in/rule-out). They are also very precise, with small coefficient of variation even at the 99th percentile, in the reference population" (Lazar et al 2022 p4).

A more sensitive method has shown that there are natural variations in troponin levels - for example, higher in men than women, age-related, and higher in the early morning hours (Lazar et al 2022).

Other consequences of hs-cTn assays include the central role of biomarkers in the diagnosis of AMI, the speed of establishing diagnosis, and in predicting long-term mortality (Lazar et al 2022).

Westwood et al (2021) searched sixteen academic databases for studies published between 2013 and 2019 on hs-cTn assays, and found 37 relevant studies. Clinical effectiveness was the ability of a test to rule-in or rule-out AMI. A test within four hours of hospital admission followed by a second test 1-3 hours later was most effective. "Health economic analyses indicated that high-sensitivity tests may be considered value for money compared with standard troponin tests, which require repeat testing at 10–12 hours" (Westwood et al 2021 pxix).

As with any review of different studies, there were methodological differences between the studies, including patient inclusion and exclusion criteria, location and setting, outcome measures, and hs-cTn assay used (nine different products were reviewed).

Elevated troponin levels were shown to predict mortality in patients with covid-19 and underlying cardiovascular disease in a US study (Majure et al 2021). Data on all patients at hospitals in New York within the Northwell Health system in March and April 2020 were analysed, of which 6247 had an assessment of troponin within 48 hours of hospital admission. Three categories were distinguished - normal troponin level (71% of the sample), mild elevation (15%), and severe elevation (14%).

Compared to the normal level, patients with mild elevation were twice as likely to die during hospital

admission, and those with severe elevation five times more likely.

In the USA, for example, screening for cardiac troponin has become standard irrelevant of clinical presentation (Lee et al 2019). Lee et al (2019) warned that indiscriminate testing could contribute to "diagnostic uncertainty". These researchers showed that many patients admitted to hospital with suspected ACS have high troponin levels. The data came from the Emergency Department at the Royal Infirmary of Edinburgh, Scotland for eleven days in July 2013. All patients during the study period without suspected ACS and receiving a hs-cTn assay were included (n = 918). Four groups were distinguished for analysis purposes (men: <3, 3-6, 7-34, >34 ng/L; women: <1, 2-4, 5-16, >16 ng/L). The prevalence of elevated cardiac troponin was one in eight. This group was more likely to be older, and to have co-morbid conditions, for instance, as well as to have died at thirty days and one year after hospital admission than the lowest troponin group.

1.2. COMPUTERISED TOMOGRAPHY CORONARY ANGIOGRAPHY

Swift diagnosis is also aided by non-invasive computerised tomography coronary angiography (CTCA). But who should receive CTCA?

That is, what level of risk of coronary artery disease after presentation at hospital with acute chest pain. In particular, low- or intermediate-risk chest pain patients. Gray et al (2022) reported a randomised controlled trial that found no benefits for such groups of patients ("Rapid Assessment of Potential Ischaemic Heart Disease with CTCA" (RAPID-CTCA)).

The trial took place in thirty-seven hospitals in the UK with over 1700 patients between 2015 and 2019. The main outcome measure was death or subsequent myocardial infarction at one year follow-up. Approximately half the participants received early CTCA (ie: within 24 hours of hospital admission) and the others received standard care with no CTCA.

In terms of the main outcome measure, the prevalence was 5.8% of the CTCA group and 6.1% of the comparison group (which was not statistically significant). However, there was an association between CTCA and reduced invasive angiography.

1.3. GLOBAL REGISTRY OF ACUTE CORONARY EVENTS (GRACE)

The "Global Registry of Acute Coronary Events" (GRACE) programme was started in 1999 "to resolve major uncertainties into what constitutes an acute coronary syndrome (ACS), to define how patients with an ACS are treated, and to characterise their outcomes" (Fox et al 2010 p1095). A database exists with which a clinician can compare their practice and "identify opportunities to improve practice. GRACE complements information from randomised trials in selected populations: it defines how practice is applied in a large 'real-world' reflection of the full spectrum of acute coronary disease" (Fox et al 2010 p1095).

The main GRACE data came from 123 hospitals in fourteen countries, while GRACE2 (Expanded GRACE) included 154 hospitals with follow-up between 1999 and 2009 (ie: a total of 247 hospitals in thirty countries). The first 10-20 patients per site per month were added to the database (to give over 102 000 patients in total) (Fox et al 2010).

Suggestions for improving quality of care have been made using the data. For example, Nallamothu et al (2007) found that delays in use of thrombolytic drugs had negative consequences for patients with ST-segment elevation myocardial infarction (STEMI). While Fox et al (2006) developed a prediction tool for outcome at six months after discharge for an ACS (ie: myocardial infarction of death).

Table 1.1 lists the main strengths and weaknesses of GRACE.

STRENGTHS	WEAKNESSES
Large multi-national sample. Full spectrum of hospitals that deal with ACS. Long-term data. First 10-20 patients to avoid "selection bias". Standardised reporting form.	Not all hospitals in particular countries or regions. Data gaps (eg: 15% of patients at six-month follow up; Fox et al 2010). Unmeasured variables. Not as rigorous as randomised controlled trials. Low-income and African countries under-represented.

Table 1.1 - Main strengths and weaknesses of GRACE.

"The spectrum of acute coronary syndromes (ACS) [3] consists of a heterogeneous group of patients with considerable variation in clinical outcome" (Elbarouni et al 2009 p392). Thus, the correct management of an individual is crucial. This has led to "risk stratification" using criteria like the GRACE risk score (RS). This was developed using a cohort of over 11 000 patients by Granger et al (2003) [4].

Elbarouni et al (2009), for example, found that the GRACE RS was "a valid and powerful predictor of adverse outcomes" (p392) among over 12 000 Canadian patients. Patients were divided into three groups for analysis - low, intermediate, and high GRACE RS. The high-risk group was significantly more likely to have in-hospital death than the low-risk group.

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[3] ACS has been defined as "symptoms consistent with cardiac ischaemia and at least one of the following: abnormal cardiac biomarkers, electrocardiogram changes consistent with ACS, and/or a documented history of coronary artery disease" (Elbaroumi et al 2009 p393). Safi et al (2021) described ACS as "a collective term for (1) unstable angina pectoris (chest pain during rest related to ischaemia or hypoxia of the heart muscle); (2) non-ST-elevation myocardial infarction (NSTEMI); or (3) ST-elevation myocardial infarction (STEMI)" (p6).

[4] "The components of the GRACE RS are age, heart rate, systolic blood pressure, Killip class, cardiac arrest, ST-segment deviation, serum creatinine, and initial cardiac biomarker status" (Elbarouni et al 2009 p394).

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2. PSYCHOLOGY AND HEART PROBLEMS

2.1. SCAD AND ANGINA

Spontaneous coronary artery dissection (SCAD) is a form of acute coronary syndrome (ACS), which can result in angina later (Tulloch et al 2024) [5]. It is a "unique clinical condition" with a separation of the coronary artery wall, and "a broad spectrum of clinical manifestations" (Gurgoglione et al 2023 p1). It is "multi-factorial and may involve the complex interaction between predisposing factors (including genetic, hormonal, inflammatory, vascular and psycho-social features) and precipitating stressors, such as emotional and physical triggers" (Gurgoglione et al 2023 p2) (appendix 2A).

The prevalence of angina ranges from less than 1% to 15% depending on the study (Kang 2023) [6]. Angina is a prevalent symptom of coronary artery disease, but also of non-coronary artery related conditions, like respiratory disease, or anaemia. While "alterations in pain sensitivity and stimuli via the vagal nerve fibres that are shared with the heart can result in non-cardiac chest pain resembling angina, which can be induced by gastro-intestinal disorders" (Kang 2023 p2).

Adams et al (2018) compared 22 SCAD patients with 66 ACS matched patients admitted to one hospital in Melbourne, Australia between 2000 and 2015 in terms of characteristics. The SCAD group was significantly more

[5] SCAD was first described in 1931 (Turner et al 2023). Modern imaging has shown that SCAD accounts for around 4% of all acute myocardial infarction cases (Turner et al 2023).

[6] SCAD predominantly affects younger women (below 60 years old) (Murphy et al 2022). One review (Franke et al 2021) calculated a mean age of 51 years old, and 84% of cases were female. SCAD has been reported among younger men after intense exercise (Adlam et al 2018). The lack of traditional cardiovascular risk factors is another characteristic of SCAD (Liang et al 2014). Half of the cases studied by Saw et al (2019) in Canada were described as idiopathic (ie: did not fit a common pattern of causes). SCAD is believed to be one of the leading causes of pregnancy-associated myocardial infarction (Hosseini et al 2024).

likely to be female, younger (mean age: 49 vs 61 years), and have no diabetes. They had a higher prevalence of anxiety, depression or previous neuropsychiatric illness (52% vs 1.5%). This was a case-control study that looked back at patient records for information.

Chronic angina can be linked to mental health problems. Tulloch et al (2024) surveyed 97 adults with SCAD in Canada. A number of questionnaires were completed, including the "Seattle Angina Questionnaire" (SAQ) (Spertus et al 1995), "Patient Health Questionnaire-9" (PHQ-9), "Generalised Anxiety Disorder-7" (GAD-7), and the "Cardiac Anxiety Questionnaire" (CAQ) (Eifert et al 2000; appendix 2B).

About one-fifth of the sample reported symptoms of probable clinical depression and/or generalised anxiety, while 40% had cardiac-related anxiety in the clinical range. These mental health scores were negatively associated with SAQ sub-scale scores (physical limitation; angina stability; angina frequency; angina treatment satisfaction; quality of life; table 2.1). The "data suggest that chronic angina is strongly linked to mental health symptoms among patients who have experienced SCAD" (Tulloch et al 2024 pi57).

- Physical limitation - 9 activities limited by chest pain, chest tightness or angina in past 4 weeks: eg: dressing yourself; climbing a hill or a flight of stairs without stopping; running or jogging.
- Angina stability/frequency - "Over the past 4 weeks, how many times have you had chest pain, chest tightness or angina?".
- Treatment satisfaction - "How satisfied are you that everything possible is being done to treat your chest pain, chest tightness, or angina?".
- Quality of life - "Over the past 4 weeks, how much has your chest pain, chest tightness, or angina interfered with your enjoyment of life?".

(Source: Spertus et al 1995 appendix)

Table 2.1 - Items from SAQ.

Also using the PHQ-9 and GAD-7 with 158 US SCAD survivors, Liang et al (2014) found that 33% had received treatment for depression and 37% for anxiety since the SCAD event. At the time of the survey (September 2011 -

February 2013), 32% of the sample were taking medications for depression and/or anxiety. Younger age at SCAD was associated with higher depression and anxiety scores.

All but four participants were female, and 95% of the overall sample were White. The sample had higher income and educational level than the general population. There was a gap between the SCAD event and the survey (ie: longer than six months).

Three hundred and ten SCAD survivors in Australia completed measures of current anxiety and depression when surveyed by Murphy et al (2024) between two months and eighteen years after the event. The prevalence of anxiety and depressive symptoms were around 20%, and this figure did not vary with time since SCAD. Significant variables associated with anxiety and depression were the absence of a close confidante, financial strain, having a mental health diagnosis pre-SCAD, and obesity. Not being in paid employment was specific to anxiety only, and younger age, and not knowing another SCAD survivor were associated with depression only.

The study involved volunteers, who had already agreed to participate in a larger study, and so may not have been representative of all SCAD survivors. The data were self-reported, and based on recall. Only 5% of the sample was male.

The sample was larger than most other studies, and standardised measures of anxiety and depression were used. The response rate was high (over 70%), and the participants' SCAD had been confirmed by coronary angiogram in most cases.

Angina is linked to psychological distress in that the former can lead to the latter (eg: Tsai et al 2019; table 2.2), but also that psychological distress is associated with poorer cardiovascular disease outcomes. "For instance, people with higher levels of psychological distress may be unlikely to participate in cardiac rehabilitation programmes and change their lifestyles such as quitting smoking and increasing physical activities, which then leads to adverse outcomes" (Kang 2023 p2).

Kang (2023) analysed data from the "UK Household Longitudinal Study" (UKHLS) on psychological distress and angina. The UKHLS has collected yearly data since 1991. Kang (2023) compared 1081 participants with angina, and 8821 age- and sex-matched controls without angina. Psychological distress was measured by the GHQ-12, and

- Data collected in the "Nutrition and Health Survey in Taiwan" (NAHSIT) between 2005 and 2008 were analysed (n = 2080 adults). The "Five-Item Brief Symptom Rating Scale" (BSRS-5) (Lee et al 2003) was used to measure five dimensions of psychological distress (sleep disturbance, anxiety, hostility, depression, and inferiority). A cut-off of 5-6 out of 20 was used. Angina was measured by nine items (eg: "chest pain or discomfort was felt when walking fast or climbing a slope").

- Overall, 3.6% of the sample were categorised as having angina, and 8.8% of participants had a BSRS-5 score of six or above. The BSRS-5 score was significantly associated with angina, and individuals with psychological distress were three times more likely to have angina than individuals with no psychological distress.

Table 2.2 - Details of Tsai et al (2019).

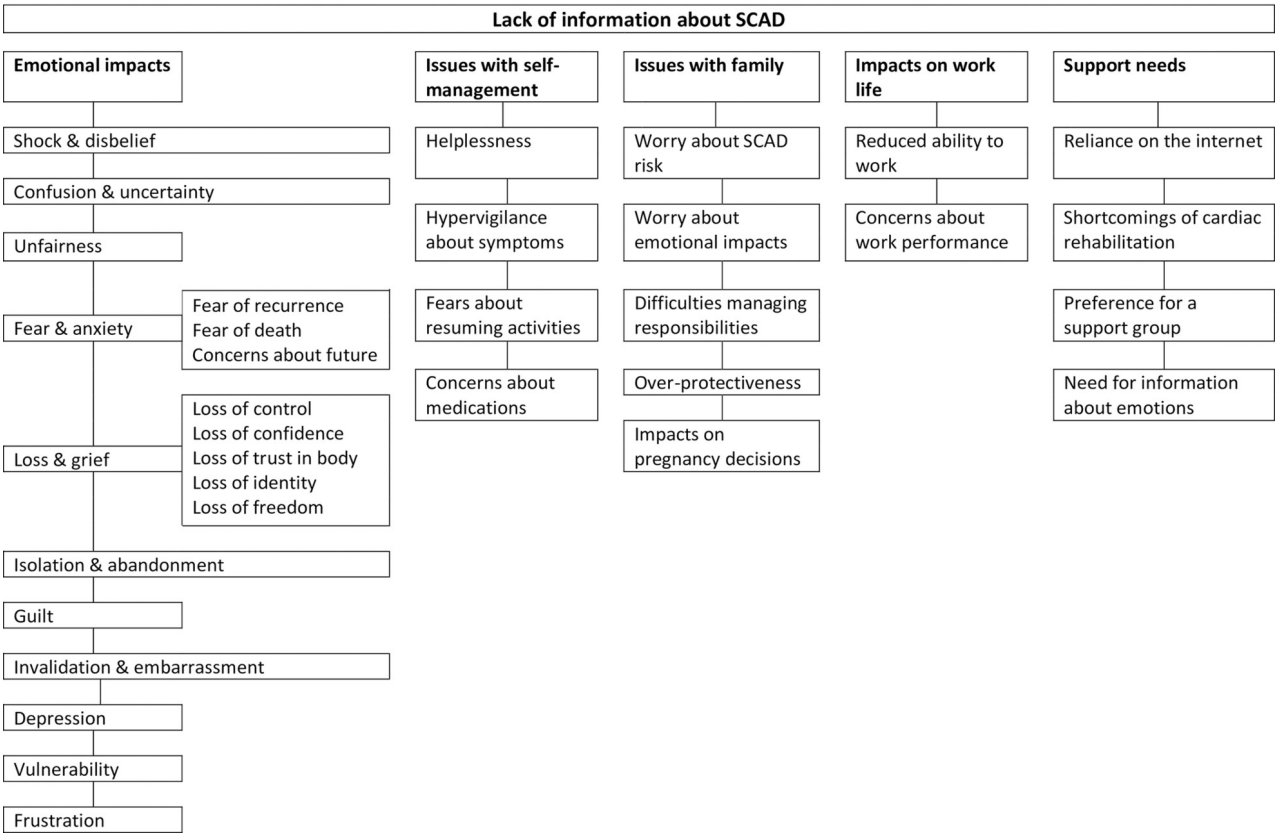
angina by the question, "Has a doctor or other health professional ever told you that you have any of these conditions? Angina" (p3).

Individuals with angina reported higher psychological distress overall, as well as specifically depression and anxiety, loss of confidence, social dysfunction, and anhedonia.

2.2. QUALITATIVE RESEARCH

In terms of qualitative research, Murphy et al (2022) involved 30 SCAD survivors in Australia (27 were female) in one of seven online focus groups about the psycho-social impacts of their condition. The discussions were transcribed and analysed, producing one over-arching theme, five main themes, and 26 sub-themes (figure 2.1).

The over-arching theme was "lack of information", including about the cause of SCAD, its management, and future course (prognosis). "Participants talked extensively about lack of knowledge about SCAD amongst their treating health professionals, from the time of presentation at the hospital emergency department through to later consultations with cardiologists and general practitioners (GPs). Participants stated that many health professionals 'had never heard of SCAD' and often 'knew nothing about it', and commented that health professionals were not aware of differences between SCAD-related heart attack and typical atherosclerotic heart attack..." (Murphy et al 2022 p3).



(Source: Murphy et al 2022 figure 1).

Figure 2.1 - Themes and sub-themes.

The five main themes were:

i) "Emotional impacts" (table 2.3).

ii) "Issues with self-management" (table 2.4).

iii) "Issues with family" - The sub-themes included worry about emotional impacts on family, difficulty managing family responsibilities, and over-protectiveness of family members.

iv) "Impacts on work life" - "SCAD impacted negatively on work in a variety of ways. Some participants had missed new work opportunities, while others had reduced or modified work hours or tasks to reduce their work pressure since the SCAD. Some had retired or stopped paid work, noting either that their work capacity had decreased: 'I can't do what I used to do, which is hard to accept', or that they had brought retirement forward: 'I used it as an excuse really'.

SUB-THEME	COMMENT OR QUOTE
Shock and disbelief	"something just out of the blue" (p5).
Confusion and uncertainty	"there's a lot of uncertainty, in what should happen, what shouldn't happen, what is or isn't the treatment. There seems to be no continuity. Whether that's due to lack of information, lack of knowledge from cardiologists. My GP didn't even know what a SCAD was" (p6).
Unfairness	"I'd been looking after myself, so why me?" (p6).
Fear and anxiety	eg: fear of recurrence.
Loss and grief	eg: loss of control, self-confidence, and trust in body.
Isolation and loneliness	"I felt completely deserted once I left hospital, completely. I was very scared and looking for someone to give me some guidance, and there was nobody. I felt completely deserted. From the hospital and the doctors, no-one knew, no-one was telling me anything" (p8).
Guilt	"I thought what have I done wrong" (p8).
Invalidation and embarrassment	"They say 'well, you're probably a bit overweight, do you have cholesterol, what's your blood pressure like?' Well actually everything is fine, this has nothing to do with your traditional plaque in your arteries. But you have to explain that. It makes me annoyed" (p8).
Depression	"you are all over the shop, emotionally and mentally. You do get a bit teary, because it's such an overwhelming thing to be hit with. It's hard to stay positive" (p9).
Vulnerability	"you have to suddenly think of yourself as a vulnerable person" (p9).
Frustration	"fatigue has been the biggest thing, not being able to do the things I would normally do" (p9).

Table 2.3 - "Emotional impacts" sub-themes.

Others felt they had returned to work too early and were not ready, or would have preferred to work less but were not in a position to do so" (Murphy et al 2022 p11).

v) "Need for psycho-social support" - eg: SCAD-tailored cardiac rehabilitation programmes; cognitive-behavioural therapy (CBT) to deal with uncertainty.

SUB-THEME	QUOTES AND COMMENTS
Hyper-vigilance about physical symptoms	"Participants indicated that since their SCAD they had become highly focussed on their body and physical symptoms, including racing pulse, irregular heartbeat, and chest pain. Many had experienced 'shocking and persistent chest pain' since the SCAD, noting that this was 'very disconcerting'. Many had become 'hyper-alert and hyper-sensitive to anything that happened in my body'. They commented that this hyper-vigilance was 'tiring' and 'made me feel like I was probably seen as a hypochondriac'. Side-effects of medications sometimes mimicked signs or symptoms of heart attack, exacerbating fear and concern: 'all that sensation around your chest, and heartburn, it just freaks you out'. Some participants had decided to stop taking certain medications due to the intensity of side effects" (Murphy et al 2020 p9).
Helplessness and incompetence	"Due to its non-atherosclerotic nature and in the absence of traditional CVD [cardiovascular disease] risk factors, SCAD left people feeling helpless in managing their condition: They noted that SCAD-related heart attack is 'harder to manage because you can't blame it on things you can change' and 'there's no way you can fix it by the normal heart attack strategies'. This lack of control created fear: 'normally with a heart attack, you get back to exercise, eat right, and you can fix this. But with SCAD I thought ''how am I going to fix this? How am I going to help myself?'' I didn't know, so that's why I was frightened'" (Murphy et al 2022 p9).
Fears and confusion about normal activities and exercise	"It's that constant analysis about whether something you want to do is something that you can or should do. Whereas before you'd just go and do it, without a second thought. It is a big adjustment" (p10).
Concerns about medications	"why am I on cholesterol medication when I don;t have a cholesterol problem?" (p10).

Table 2.4 - Quotes and comments related to the theme of "issues with self- management.

Uncertainty was key to many of the themes and sub-themes. "The importance of uncertainty in illness has received considerable attention over the past three decades and has been investigated in both cardiac and non-cardiac chronic conditions. Mischel's [1990] 'Model of Uncertainty in Illness' proposes that uncertainty results when the patient is unable to determine the meaning of the illness or diagnosis, or is unable to accurately predict the likely trajectory and outcomes. Uncertainty is particularly high in illnesses with

unclear diagnoses, treatments and management guidelines, and in those with high risk of recurrence. It is not surprising, therefore, that uncertainty is high following SCAD given its relative rarity, unclear cause and trajectory, lack of consistent guidelines for management, and high recurrence rate. Uncertainty is associated with lack of information provision, and leads to reduced capacity for self-management, poor quality of life, and increased risk of depression" (Murphy et al 2022 p13).

Another relevant theory is "Self-Determination Theory" (SDT) (eg: Ryan and Deci 2017), which links well-being to three psychological needs - autonomy, competence, and relatedness. Scad challenges all three of them. "First, there is a threat to autonomy: participants felt a loss of control over their body and their health, and a loss of freedom to be the person they had previously been and to live as they had previously lived. That SCAD cannot be managed through lifestyle change exacerbates feelings of helplessness in being unable to 'fix' the condition or actively minimise the risk of recurrence" (Murphy et al 2022 p13).

The researchers continued: "Second, a sense of incompetence arises: participants felt confused, anxious, fearful, vulnerable, frustrated, depressed and, as already noted, extremely uncertain. Consequently, there is an eroding of previously intact self-confidence and self-esteem, resulting in a lack of mastery and efficacy to manage the condition and other aspects of life" (Murphy et al 2022 pp13-14). Relatedness was challenged as participants felt unsupported, misunderstood and isolated, both from health professionals and the general population, mostly because of the lack of understanding about SCAD.

In another qualitative study, Godoy et al (2024) identified five themes in their semi-structured interviews with 24 female and one male SCAD survivors in England (table 2.5).

Turner et al (2023) performed a literature review on the patient experience of SCAD. Five relevant studies were found published before June 2023 and included in four academic databases.

The researchers distinguished a major theme - "perceived lack of information about SCAD for patients" - and two minor themes - "living with emotional responses after SCAD", and "recovery needs after SCAD".

THEME	QUOTATION
Mental well-being (eg: shock about diagnosis; anxiety)	"Emotionally it's deeply impacted me because I didn't know about SCAD. I had no idea that as a healthy physically fit... I really take care of myself and then this happened that has thrown me and the fact that there's a recurrence possibility it's just... yeah. I really have a sense of my own frailty".
Physical activity (pre-SCAD physically active, now not)	"My life is being physically active. I love running, cycling, playing squash, and like 6 weeks before, I'd run a half marathon, like running is everything I do. So, not being able to do that and no clear instruction on how quickly I'll get back to that was just kind of everything".
Cardiovascular rehabilitation (eg: concern about exercising again)	"Cardiac rehab is the best of all, you know, options. I would rather do it under the support of somebody that's a professional, than be attempting to do it myself. That doesn't mean to say I am not nervous about it".
Healthcare professionals (eg: lack of awareness about SCAD)	"I'm still perplexed as how the cardiac rehab team have got posters up about it and gave me leaflets and the card to put in my wallet should I be admitted to A&E [Accident & Emergency]. Cardiac rehab team know about it, and in the same hospital albeit it's a different building, the cardiology team are still unaware of this".
Information (eg: lack of information for patient)	"It's so frustrating because so little relatively is known about SCAD and what causes it, and you know. I've asked so many questions, but yeah, people say, well that's just not known yet, that's just an unknown, so that's frustrating" (pA7).

Table 2.5 - Five themes (and quotes) identified by Godoy et al (2024).

a) Perceived lack of information - One study found that about 25% of the sample had received no information about SCAD after diagnosis, while over four-fifths of the remainder found the information "insufficient or inadequate" (Wagers et al 2018).

There was a perceived lack of information about the individual's own SCAD, and about SCAD generally (eg: "triggers"). Consequently, patients conducted their own internet searches often. "Patients with SCAD reported that they felt the provision of more information would alleviate anxiety related to the uncertainty that they experienced following the SCAD event. Furthermore, patients with SCAD felt a lack of control over their condition and feelings of being isolated and alone arising from insufficient information" (Turner et al 2023

p1429).

b) Living with emotional responses - There was a range of emotions reported, summed up by words like "scary", "life-changing", and "caught off guard". "Participants with SCAD had believed themselves to be fit and healthy before their event, and described a 'roller-coaster of emotions' including shock, disbelief, confusion, fear, and anxiety in the aftermath of a SCAD event. Emotional responses after SCAD had had a negative impact on participants' mental health and could persist for months or years after SCAD. Emotional responses such as anxiety accompanied a fear of recurrence and a sense of uncertainty, particularly in the context of a paucity of research and understanding about SCAD itself, its aetiology and management, and a perceived lack of control" (Turner et al 2023 p1429).

c) Recovery needs - Support for both physical and emotional recovery was perceived as important.

The review showed the limited number of studies on the topic. Most participants had accessed specialist services. "Perspectives of individuals not affiliated or volunteering for research are absent" (Turner et al 2023 p1431). The studies were undertaken in North America, Western Europe, and Australia with predominantly female and !largely White cohorts" (Turner et al 2023 p1431).

2.3. FEAR OF RECURRENCE AND PROGRESSION

Clarke et al (2024a) surveyed 293 SCAD patients in Australia about fear of recurrence, of the future, and of death in the six months after their SCAD. The response options were "not at all" (0), "a small amount" (1), "a moderate amount" (2), and "a large amount" (3).

Over 95% of the respondents had some level of worry (ie: scored 1-3) about recurrence, and about triggering another SCAD, while similar numbers had fear of the future, with around 80% having some fear of dying. Around half of the respondents or less scored 3 on the different items. Fear of recurrence was significantly associated with general mental health problems (eg: depression; anxiety).

More generally, "fear of recurrence and progression" (FoRP) of chronic illnesses is "a trans-diagnostic construct used to describe the fear that a disease will

recur or progress, with all related consequences... The construct was introduced as a framework to describe disease-specific distress in chronic illness patients that could not be appropriately described as anxiety in that the fears represent an appropriate response to the real threats of one's disease experience rather than being excessive or out of proportion" (Clarke et al 2025 p1). The concept was originally applied to cancer.

Cardiac-FoRP has been studied in a limited way so far. Clarke et al (2024b) performed a scoping review of qualitative studies on the topic. "Several broad domains of cardiac-FoRP were identified, including concerns around one's health, dying, relationships, treatment, accessing help, roles and responsibilities, and physical activity. Common behavioural responses when patients were confronted with cardiac-FoRP included avoidance, hyperawareness, symptom misattribution, seeking help, and making lifestyle changes" (Clarke et al 2025 p2).

Clarke et al (2025) developed the work on cardiac-FoRP with 241 volunteers (mostly from Australia, New Zealand and the UK) whp had experienced an acute coronary event, cardiac surgery, or a chronic cardiac condition. Participants were presented with 44 cardiac-specific FoRP items (table 2.6). Based on the responses to these items, three groups were distinguished - high- (26% of the sample), moderate- (41%) and low-FoRP (33%) [7]. The high-FoRP group was more likely to be younger, have co-morbid health conditions, high illness uncertainty and cardiac-related distress.

In terms of specific fears, the most common were declining health and recurrence, while hyperawareness was the most common response (reported by over 80% of the sample). "In terms of hyperawareness, many participants reported feeling overly aware of sensations in their body and worried that when they had physical sensations such as chest discomfort, increased heart rate, or shortness of breath, their cardiac disease was progressing or that they were having another event" (Clarke et al 2025 p11).

[7] The percentages in each group were similar to those found among cancer patients (eg: Calderon et al 2024).

- "Your general health and functioning declining"
- "Having another heart event"
- "Becoming unable to engage in activities you enjoy"
- "Feel overly aware of sensations in your body"
- "Feel worried that you are having another event when you have chest discomfort, or when your heartbeat is fast or irregular"
- "Feel worried that your condition is getting worse when you notice changes in your body, such as feeling more fatigued, short of breath, or retaining more fluid"
- "Becoming less of a person"
- "Ageing"

Table 2.6 - Example of items in Clarke et al (2025).

2.4. FATIGUE

Fatigue post-SCAD was studied by Saeed et al (2025) with a Norwegian sample of sixty women. Around 70% reported fatigue, and this was associated with memory and concentration difficulties, sleep disturbance, low energy level, lack of motivation, and frustration, for example. Age was not associated with fatigue (age range of the sample 33-73 years).

Three-quarters of women reported an emotional reaction after SCAD, and one-quarter overall recurrent symptoms (including fear of a new SCAD event). Depression was experienced by a small number of respondents (10%), and 5% of these believed that their depression and fatigue were related.

Most patients used beta-blockers, and this was associated with self-reported fatigue, but discontinuation of that medication was not associated with less fatigue for most people.

2.5. APPENDIX 2A - TRIGGERS FOR SCAD

Rabkin (2022) listed 25 reported underlying predisposing factors or acute triggers of SCAD, mostly physiological. He admitted: "Such a large and diverse list of factors suggests that all these factors cannot

reasonably be 'true' causative factors. Many of these conditions are based on single case reports, small patient groups, or patient groups without controls or comparative groups" (Rabkin 2022 p220).

Gurgoglione et al (2023) investigated the predisposing factors for SCAD with an Italian sample. Sixty-four individuals with suspected SCAD who attended the University Hospital of Parma between January 2013 and October 2022 were involved. Traditional and non-traditional cardiovascular risk factors were classified. Stress in the 24 hours prior to hospital admission were also recorded.

Overall, 64% of participants had precipitating stress (n = 41 individuals), divided into emotional distress (n = 31) (defined as "being strongly upset about something, feeling tense or nervous, worried, and/or extreme or unusual emotional distress"; p2), and physical exertion (n = 10) (defined as "extreme or unusual physical exertion"; p2). So, one-third of the sample had no precipitating stressors in the 24 hours prior to admission.

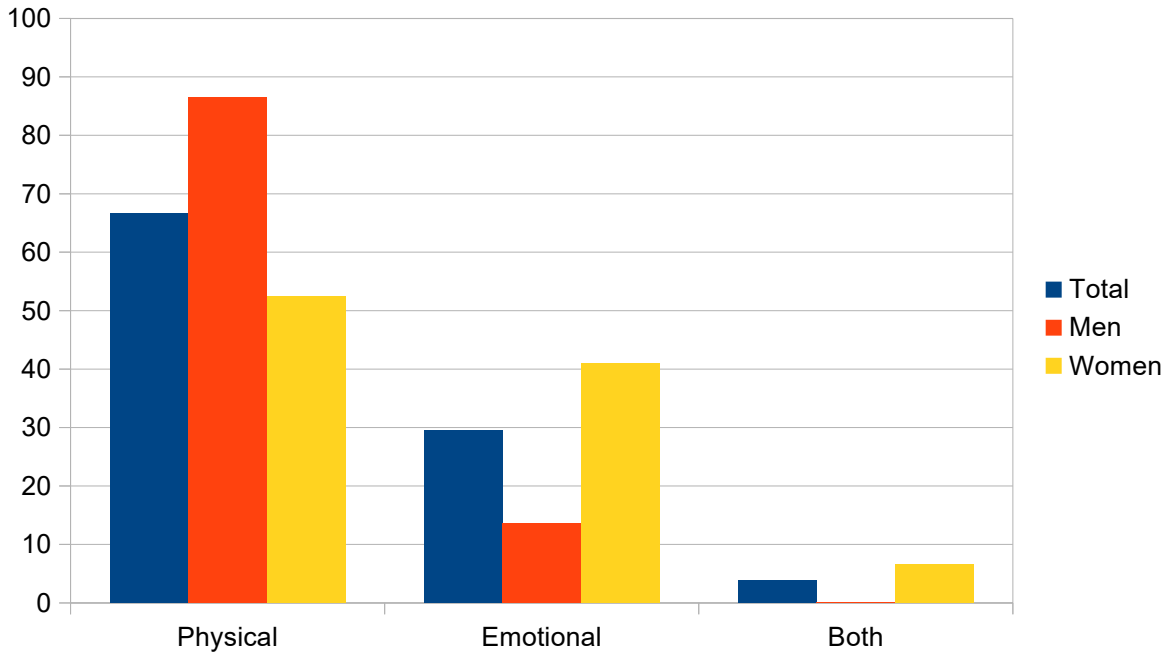
Emotional stressors were associated with being female (though overall 56 members of the sample were female). There is the theory that "emotional stressors elicit more frequently SCAD in women, while physical efforts are prevalent in male population" (Gurgoglione et al 2023 p4). Two previous studies supported the importance of emotional stressors in SCAD - Saw (2014): emotional stressors around twice as common as physical ones, and Daoulah et al (2021): 40% of an Arab Gulf sample reported emotional triggers.

Gurgoglione et al (2023) concluded that "emotional stressors leading to SCAD may identify a SCAD sub-type with specific features and more frequently reported chest pain" (p6).

Hosseini et al (2024) performed a review of case reports and case series on stress prior to SCAD. Ninety-three such studies covering 105 patients were included (published prior to January 2023). Evidence of physical stress was found for two-thirds of patients, and emotional stress in 30% of cases. Physical stress (eg: lifting heavy objects; intense exercise) was more common in male patients (86% overall) than females (59%), but the opposite for emotional stress (eg: family-related issues) (14% of men vs 48% of women) (figure 2.2).

It was hypothesised that the stressor leads to "a

sudden catecholamine surge" [8] which causes the damage to the heart seen in SCAD, though "this mechanism has not been fully investigated" (Hosseini et al 2024 p7).



(Data from table 2 Hosseini et al 2024).

Figure 2.2 - Stress prior to SCAD (%).

Rabkin (2022) examined the relationship between emotional stressors and SCAD in a systematic literature review. A search of two academic databases were made up to July 2022. Eight relevant case reports among eighteen articles (published in English) were found (table 2.7).

Heart problems after hearing about the death of a close friend or family member was common in the case reports. Studies without a comparison group (n = 5) were mostly retrospective with self-reported measures of stress (and SCAD in some cases), and a sizeable minority of participants recalled stress before their SCAD event.

Five studies had comparison groups, though the retrospective method and self-report measures were also used. Generally, there was no excess perceived stress in the SCAD group compared to the non-SCAD group in a meta-analysis of three of the studies.

The consequences of SCAD were emotional and psychological, even similar to post-traumatic stress

[8] Catecholamines are hormones, like adrenaline, released in the "fight or flight response".

disorder (PTSD) in some cases.

"In conclusion, chronic psychological stress, anxiety, or depression is not associated with the development of SCAD, however acute emotional stress may be a factor precipitating SCAD in some patients" (Rabkin 2022 p219).

STUDY	DETAIL
Anisman & Joelson (2006) - case report	"Upon hearing of the death of her brother, a previously healthy 35 year-old native American woman experienced the sudden onset of crushing retrosternal pain" (quoted in Rabkin 2022)
Smaardijk et al (2020) - no comparison group	172 women with SCAD in the Netherlands completed questionnaires (eg: "Perceived Stress Scale" (PSS-10)) in retrospect. Half of the respondents reported high perceived stress in the month before SCAD
Krittanawong et al (2019) - comparison group	66 360 patients in the USA with SCAD compared to a control group of ACS without SCAD. Significantly higher prevalence of depression, anxiety, and emotional stress in the SCAD group compared to the non-SCAD group

Table 2.7 - Example of the three types of study found in Rabkin's (2022) literature search.

2.6. APPENDIX 2B - CARDIAC ANXIETY QUESTIONNAIRE

The CAQ was developed to measure "heart-focused anxiety" (HFA), which is "the fear of cardiac-related stimuli and sensations because of their perceived negative consequences" (Eifert et al 2000 p1039). In its construction, 63 items were collected from the literature and from interviews with cardiology clinic outpatients. "Items were aimed at addressing the core features of HFA, including fears and worries about heart disease, fear of chest pain and other heart-related sensations, heart-focused attention, help and reassurance seeking, and avoidance of activities believed to elicit cardiac symptoms" (Eifert et al 2000 p1041).

Each item was scored from 0 (never) to 4 (always). The 63 items were presented to 188 US patients at a cardiology unit. Item analysis of the responses (eg: removal of similarly worded items; low discrimination) reduced the number of items to the final eighteen (table 2.8). The final questionnaire was given to 42 outpatients of the same clinic to establish reliability and validity. Total scores can vary from 0 to 72, with a higher score

signifying greater anxiety.

Factor analysis produced three underlying factors: I - "fear" (worry about chest and heart sensations; 8 items); II - "avoidance" (avoiding activities that could trigger symptoms; 5 items); and III - "attention" (heart-focused attention and monitoring; 5 items).

- "I avoid physical exertion" (factor II).
- "If tests come out normal, I still worry about my heart" (factor I).
- "I check my pulse" (factor III).
- "I get frightened" (factor I).
- "I have difficulty concentrating on anything else" (factor I).

(Source: Eifert et al 2000 appendix A)

Table 2.8 - Items from the CAQ.

Wedegartner et al (2020) investigated HFA in a sample of 107 German adults with stable heart failure. A questionnaire was completed which included the CAQ, and measures of general anxiety and depression, quality of life, cognitive problems, self-care (ie: following medical recommendations), and personality. The CAQ score was the outcome measure.

High HFA was significantly predicted by high general anxiety, high on the personality characteristic conscientiousness, low quality of life, and lack of physical activity. Poor renal function (ie: low estimated glomerular filtration rate) was a medical predictor of HFA.

Nearly 90% of the sample was males (Caucasian), and the patients came from one medical centre. Individuals with depression were excluded, which the researchers admitted could produce selection bias as "depression is a common condition in patients with heart failure and the co-morbidity of anxiety and depression is high" (Wedegartner et al 2020 p385).

2.6.1. Cardiac Distress

The term "cardiac distress" has been coined to describe the emotions after a cardiac event. It is

defined as "a persistent negative emotional state rather than a transient state; involving multiple psychosocial domains; that challenges a patient's capacity to cope with living with their heart condition, the treatment of the condition, and the resultant changes to daily living; and challenges the person's sense of self and future orientation" (Jackson et al 2018 quoted in Le Grande et al 2023).

The "Cardiac Distress Inventory" (CDI) was developed to measure it. The original (long form) has 55 items (Jackson et al 2022) covering eight sub-scales (fear and uncertainty; disconnection and hopelessness; changes to roles and relationships; overwhelm and depletion; cognitive challenges; physical challenges; health system challenges; death concerns), while the short form (CDI-SF) has twelve items (le Grande et al 2023) (table 2.9).

In past four weeks ("no distress" (0) to "severe distress" (3)):

- "Thinking I will never be the same again" (fear and uncertainty sub-scale)
- "Not knowing what the future holds for me" (fear and uncertainty)
- "Feeling lonely" (disconnection and hopelessness)
- "Withdrawing from people" (disconnection and hopelessness)
- "Being unable to deal with stress" (overwhelm and depletion)

Range of total scores: 0-36; >13 = cardiac distress

(Source: Le Grande et al 2023)

Table 2.9 - Items from the CDI-SF.

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3. MEDICATIONS

3.1. STATINS

One way to approach cardiovascular disease (CVD) in a population is with preventive measures. The use of statin therapy [9] is a good example. "Across randomised trials, statin therapy has been reliably shown to reduce rates of CVD irrespective of age, sex, CVD risk and co-morbidities, with more potent statin regimens achieving larger reductions in low-density lipoprotein cholesterol (LDL-C), demonstrating larger CVD risk reductions" (Mihaylova et al 2024 pxxi).

What about the widening of statin use in the population? Mihaylova et al (2024) reported a modelling study comparing statin and placebo using "Cholesterol Treatment Trialists' Collaboration", the "UK Biobank" cohort, and "Whitehall II" data. in total, over 600 000 UK participants.

The researchers calculated that low cost statin therapy would be "highly cost effective" for all adults aged 40 years and above in the UK.

Collins et al (2016) summed up the conclusion from large-scale randomised controlled trial evidence (table 3.1) as reducing the risk of major vascular events (eg: coronary death) by "about one-quarter for each mmol/L reduction in LDL cholesterol during each year (after the first) that it continues to be taken. The absolute benefits of statin therapy depend on an individual's absolute risk of occlusive vascular events and the absolute reduction in LDL cholesterol that is achieved" (p2532).

The Cholesterol Treatment Trialists' Collaboration (2019) reported a meta-analysis of 28 randomised controlled trials (published between 1996 and the beginning of 2018) specifically for older adults (55 years and above). For analysis purposes six age groups were distinguished, and only studies with more than one thousand participants were included. Most trials compared

[9] Technically, HMG-CoA reductase inhibitors.

- Modern medical treatments have great potential to prevent many diseases, pointed out Collins et al (2016), but "their appropriate use relies on the availability of robust data on safety and efficacy, as well as on a sound understanding of the interpretation and application of such evidence. Randomised controlled trials of adequate size are needed to be confident that any moderate benefits and any moderate harms of a treatment have been assessed sufficiently reliably. In certain circumstances, available evidence from randomised trials about the effects of a treatment may be limited (perhaps because it is deemed not possible or too difficult to do adequate trials)" (p2532).

- A great burden is placed upon randomised controlled trials. Their key strength is that "the process of randomisation results in groups of patients who differ from each other only by the play of chance with respect to their risks of having all types of health outcome (ie: the randomised treatment groups are balanced with respect to both known and unknown risk factors, irrespective of whether or not these have been assessed). In addition, masking assignment of study treatment with a placebo minimises the differential assessment of adverse events between the study treatment groups following randomisation. Continued follow-up of all randomised patients (even if some stop taking their assigned treatment) maintains the like-with-like comparison produced by the randomisation process (since, for example, the patients who stop may differ between the randomised groups)" (Collins et al 2016 p2533).

- Large-scale observational studies have the advantages of spotting rare outcomes from many patients, and over a prolonged period of use.

Table 3.1 - Randomised controlled trials as evidence.

statin to a placebo, but five trials compared intensive and standard statin regimen. The average follow-up period was five years.

All 28 trials showed a significant benefit for statin therapy over the comparator in vascular events. Overall, it was calculated that every 1.0 mmol/L reduction in LDL cholesterol reduced the relative risk of major coronary events by 24%. There was a slightly smaller reduction of risk for the oldest age group (75 years plus).

In the period after onset of ACS, there is a high risk of recurrence and death. Statin therapy is an option here. Vale et al (2014) reported some benefits to such treatment in a Cochrane review.

Cochrane reviews are high quality literature reviews. In this case, randomised controlled trials comparing statins with placebo or usual care, where

statins were initiated within fourteen days after the onset of ACS, and lasting at least thirty days were sought. Eighteen relevant studies were found. The conclusion was that "initiation of statin therapy within 14 days following ACS does not reduce death, myocardial infarction, or stroke up to four months, but reduces the occurrence of unstable angina at four months following ACS" (Vale et al 2014 p2).

The researchers, along with other studies, felt that the beneficial effects of statins are cumulative, and longer term (eg: statistically significant after six months (Cannon et al 2004); 1-2 years of use (LIPID Study Group 1998)). This highlights a general issue with the evaluation of treatment - ie: when to set the outcome measure (as well as which outcome measure(s) to use). There is plenty of evidence (eg: Studer et al 2008) to support statins to "effectively reduce low-density lipoprotein (LDL) cholesterol and clinical endpoints such as cardiovascular events and overall mortality in a large spectrum of patients at varying risk of cardiovascular disease" (Vale et al 2014 p5). Vale et al's (2014) review was specific to ACS patients in the 3-6 months after onset.

In terms of side effects, Collins et al's (2016) review reported no excess of memory loss or impact on cognitive function, particularly among older adults, for example. Key studies quoted included the "Heart Protection Study" (Heart Protection Study Collaborative Group 2002) (over 20 000 individuals followed for an average of five years), which compared simvastatin (40 mg daily) to a placebo, and the "PROSPER trial" (eg: Trompet et al 2010) on pravastatin (nearly 6000 70-82 year-olds followed for an average of 3.5 years).

Collins et al (2016) admitted in conclusion: "The only adverse events shown definitely to be caused by statin therapy — ie: are adverse effects of statins — are myopathy (specifically defined as muscle pain or weakness combined with large increases in blood concentrations of creatine kinase) and diabetes, although it is likely that the risk of haemorrhagic stroke is also increased. Typically, treatment of 10 000 patients for 5 years with an effective statin regimen (eg: atorvastatin 40 mg daily) would be expected to cause about 5 extra cases of myopathy (one of which might progress to rhabdomyolysis), 50–100 cases of diabetes, and 5–10 haemorrhagic strokes. Statin therapy may also cause symptomatic adverse events (eg: muscle pain or weakness) in up to 50–100 patients per 10 000 treated for 5 years. The absolute excesses of

adverse events with statin therapy are increased in certain circumstances (eg: with higher statin doses and in combination with certain drugs, or in particular types of patient or population), but they are still small by comparison with the beneficial effects" (p2553).

3.1.1. Lipid-Lowering Agents

Statin therapy is not the only medication or substance available to reduce the risk of high cholesterol (or lipid). Dugre et al (2023) performed an umbrella review of lipid-lowering therapies for cardiovascular disease prevention. An umbrella review is a synthesis of previous systematic reviews (which are analyses of individual studies). Seventy-six reviews published between 2017 and early 2022 were included. Each review focused on a particular therapy, and included only randomised controlled trials. The lipid-lowering agents were bile acid sequestrants (BAS), ezetimibe, fibrates, niacin, omega-3 supplements, statins, and proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors. The main outcome measure was a major adverse cardiovascular event (MACE) (eg: cardiovascular death).

A significant reduction in MACE was found with statins, and ezetimibe, but less so with PCSK9 inhibitors, fibrates, and omega-3 supplements. No effect for niacin, and BAS. Statins produced the "most consistent evidence" compared to placebo, and there were benefits when combined with ezetimibe, or PCSK9 inhibitors, for instance (table 3.2). A relative risk reduction of about 25% was calculated for statins overall.

The studies varied in their MACE definition, which accounted in part for differences between the agents. For example, omega-3 supplements reduced cardiovascular mortality, but not other MACE (eg: non-fatal myocardial infarction). The size of the sample and their characteristics varied also in studies. Some agents were studied more than others (eg: fourteen reviews for PCSK9 inhibitors versus two for fibrates).

On the plus side, Dugre et al (2023) included only reviews "reporting patient-oriented outcomes, excluding studies reporting only surrogate markers" (p709).

- Wu et al (2024) reported a meta-analysis of randomised controlled trials of combined statin and non-statin therapies for reducing cholesterol in patients with acute coronary syndrome. Nine trials were found (published before mid-2023).

- Risks were significantly reduced for MACE, recurrent acute coronary syndrome, non-fatal myocardial infarction, and stroke, for instance, compared to statins only, but not all-cause or cardiovascular-related mortality.

- The studies in the meta-analysis varied in statin type and dose, and in non-statin treatment used (ezetimibe or PCSK9 inhibitors).

- In total, nearly 40 000 patients were included in the studies, of which one-quarter were female, and the mean age was 61 years. Follow-up duration ranged from eight weeks to seven years, and baseline low-density lipoprotein cholesterol (LDL-C) levels varied between individuals. Some studies did not provide enough information about demographic characteristics and co-morbidities of participants.

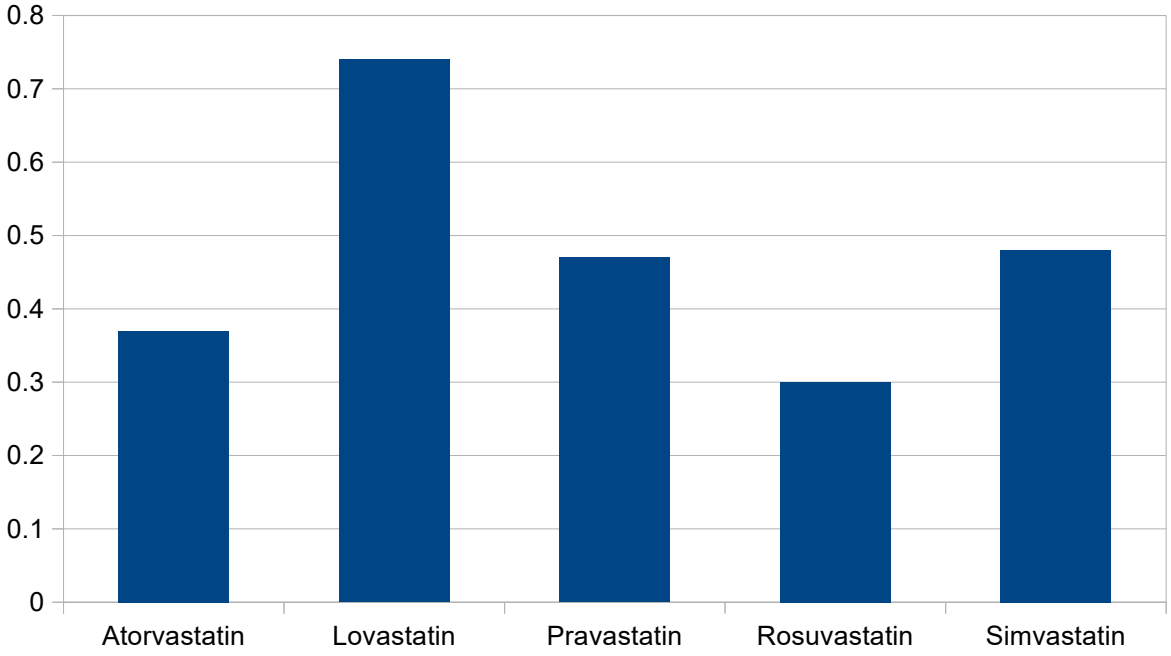
Table 3.2 - Statin and non-statin combined therapy.

3.1.2. Statin and Aspirin

Aspirin has been found to reduce the risk of major vascular events by 15-20%, and so "the role of aspirin in the prevention and treatment of cardiovascular disease is widely acknowledged in the medical community" (Liu et al 2023 p1). Similarly, statins alone are beneficial, but what about the combination of aspirin and statins?

Liu et al (2023) provided positive data from the National Health and Nutrition Examination Surveys 2011 to 2018 in the USA. The use of aspirin, and/or statin for preventive purposes were self-reported by over 3300 adults.

Compared to aspirin alone, the risk of cardiovascular disease was significantly reduced for participants taking daily aspirin and one of five types of statin (atorvastatin (table 3.3), lovastatin, pravastatin, rosuvastatin, and simvastatin) (figure 3.1). The combination of aspirin and rosuvastatin was most beneficial, after controlling for sex, age, fitness level, and diabetes.



(Data from Liu et al 2023 table 3)

Figure 3.1 - Risk of heart attack based on aspirin and type of statin (where aspirin alone = 1.00).

- Atorvastatin, by reducing the level of cholesterol and its impact on the steroidogenesis pathway, has the potential to reduce levels of testosterone and other androgens.
- In a Cochrane Review, Shawish et al (2021) found no reduction in total testosterone in men, but a reduction in the case of females with polycystic ovary syndrome (PCOS) (ie: higher than normal levels of androgens).
- The review was based on six randomised controlled trials (four involving women with PCOS and two with male participants). The certainty of the evidence, however, was rated "low to very low".

Table 3.3 - Atorvastatin and testosterone levels.

3.2. BETA-BLOCKERS

Beta-blockers as medication for patients with heart failure after acute myocardial infarction (AMI) is well established (eg: Chatterjee et al 2013), but less so for patients without heart failure after AMI (Safi et al

2021) [10].

Safi et al (2021) reviewed the evidence on the latter. Twenty-five randomised controlled trials were found in the literature search. Meta-analysis showed that beta-blockers "probably" reduced the risks of all-cause mortality, MI, and major cardiovascular events when compared to placebo or no treatment, but "may not affect the risk of angina" (p2). Overall, a reduction of relative risk of at least 10% was calculated for patients younger than 75 years old without heart failure after AMI.

The authors concluded: "The evidence should be interpreted with caution, as certainty was judged to be moderate to low for all outcomes" (Safi et al 2021 p3). This was because the methodological quality of the studies was variable. For example, mixed groups of participants in terms of heart problems, different types of beta-blocker studied, and exclusion criteria varied, as did outcome measures used.

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4. HOSPITAL EXPERIENCE IATROGENIC CONDITION

4.1. INTRODUCTION

I want to introduce the idea of "hospital experience iatrogenic condition" (HEIC) to describe how the experience of being in hospital works against getting better in many ways. It is not that the medical staff are deliberately working to make the patient worse, but that the nature of the environment is the opposite to what would be ideal for a sick individual. Put simply, the environment is stressful, and high levels of stress are detrimental to healing.

The key factors in HEIC are:

i) The environmental stressors of the hospital, particularly in intensive care units (ICUs) - eg: noise [11], and constant bright lighting which limit sleep and rest (table 4.1).

ii) Systems and schedules that force the individual to fit into a "round hole", whatever their shape of "peg". It could be called "factory healthcare" or a "conveyor belt of care" that predominates over individual differences. In a large hospital, it is important to have routines etc, but these may not be best for the individual. For example, breakfast is set for 6 am, and the patient, who after a troubled night of sleep, is woken to give them breakfast.

These two factors are irrelevant of the quality of medical care, which may be excellent.

[11] "It has been reported that noise levels in ICUs are higher than recommended by the World Health Organisation. Activities of health staff and alarms are the main sources of noise causing stress in ICUs, and voices from other patients and the infrastructure also contribute to noise. While alarms go off, staff and patients can be continuously awake. Alarms create the same perception as a human scream and tend to activate brain regions recognising threats. Noise
causes sleep disturbances, has negative psychological effects, and can cause stress. This indicates that there is too much noise in the ICU environment, and it has a severe effect on patients" (Zengin et al 2020 pp112-113).

1. Noise
2. Light
3. Hearing other patients talk
4. Limited freedom of movement as attached to machine
5. Urination in a bottle
6. "People" (simply, the presence of other people around)
7. Staff talking
8. Snoring of others
9. Hunger etc
10. Bed

Overall, so different to the home experience

Table 4.1 - Stressors experienced on first night in High Dependency Unit (HDU).

4.2. IATROGENIC DISEASE

Madeira et al (2007) began thus: "From the Greek words iatrós, meaning 'medical', and geneá, meaning 'origin', iatrogenic means the occurrence of negative effects caused by a medical procedure. It is frequently thought that iatrogenic means 'error' or 'neglect', but iatrogenic effects and medical errors are opposite terms, not synonymous ones. An error is a mistake or the result of ignorance and, thus, opposes the concept of medical attitude, whereas an iatrogenic effect is the consequence of an accurate action based on a correct indication and adequate criteria and can be predicted by the physician. When, in trying to heal, relieve, or treat a patient, the physician (like any other health care worker) generates psychological, functional, or organic illness that takes the from of pain, disease, or disturbance, he is being iatrogenic. The diagnosis may be difficult, delayed, or initially missed as iatrogenic illness can be generated directly from the doctor–patient relationship or by means of agents used in the diagnostic search, or as a consequence of a therapeutic, instrumental (technical), or drug-related measure" (pp391-392) [12].

Preferring the term "iatrogenic conditions", Boltz (2013) divided them into preventable (eg: medical errors [13]) and unpreventable (eg: side effects of chemotherapy).

[12] Tamarelli et al (2024) conceptualised "iatrogenic harm" as "a medical intervention that reduces a person's health or well-being or hinders their recovery. This harm can be either psychological (eg: by causing distress) or physical (eg: by causing pain or impairing functioning)" (p220). While Boltz (2013) emphasised "any unintended adverse patient outcome due to a health-care intervention not related to the natural course of an illness or injury" (p1023).

[13] Error due to lack of clinical standardisation (ie: "unnecessary variation in practice") is a sub-set of iatrogenic conditions (Morris 2004). "Many clinicians respond openly that such standardisation interferes with individualisation or tailoring of treatment to the needs of a specific patient" (Morris

There has been more focus on the former for the reason that something can be done. For example, the Institute of Medicine (2001) in the USA produced a report that advocated re-engineering health-care delivery, and proposed six aims - for care to be safe, effective, patient-centred, timely, efficient, and equitable (Boltz 2013).

The medical literature tends to focus on physical illness caused by medical treatment, and adverse drug reactions (ADRs) or events; ADEs) are a common example (table 4.2). Put simply, an individual with "disease A" is given a medication as treatment, but this medication causes side effects or reactions that produce "disease B". Likewise, while in hospital for "infection C", the patient picks up "infection D".

My use of iatrogenic in HIC is psychological rather than physical as in the traditional use, though that distinction may not be clear cut.

- Medications - eg: ADRs.
- Therapeutic or diagnostic interventions - eg: venipuncture (taking a blood sample) increases the risk of infection; misdiagnosis.
- Nosocomial or facility-acquired infections - eg: anti-biotic-resistant infections in hospitals.
- Environmental factors - eg: environment-related injuries sustained while in hospital.

Table 4.2 - Types of iatrogenic complications (Boltz 2013).

In a classic US study, Steel et al (1981) found that one-third of over 800 patients at one hospital in five months in 1979 had an iatrogenic illness (defined as "any illness that resulted from a diagnostic procedure or from any form of therapy"). Three categories of iatrogenic complications were noted - medication-related, diagnostic and therapeutic procedures, and miscellaneous (eg: falls). Complications were associated with the patient being older, taking more medications simultaneously, and

2004 p80). Okkenhaug et al (2024) preferred the wider term "adverse events", which they defined in a psychiatric context as "an unintended injury caused by medical management resulting in the prolongation of a hospital stay or in diminished function/disability" (p406).

a longer stay in hospital [14].

The study included new patients admitted to a variety of wards including an ICU, a coronary care unit, and two general medical wards. "As expected, the intensive care settings accounted for more of the iatrogenic illness than did the others. However, when subjected to a logistic analysis, the unit in which the patient received care was not a determinant of iatrogenic illness; only the referring site (home, hospital, nursing home etc) and the assessment of the patient's condition on admission by the house officer were important determinants. This suggests that both patient and system (environment and clinician) attributes contributed to iatrogenic illness" (Morris 2004 p80).

Steel et al (1981) showed "a lack of progress" since a similar study (Schimmel 1964): "The many advances in diagnostic and therapeutic interventions that had appeared during those 15 years were not matched by a reduction in iatrogenic illness suffered by patients in hospital" (Morris 2004 p80).

The hospital experience involves long periods of waiting, which can translate into boredom. "Boredom is commonly reported in hospitals, where patients may sense that 'time stands still' [Radley and Taylor 2003]" (Tamarelli et al 2024 p220).

Tamarelli et al (2024) asked whether boredom could be seen as an iatrogenic harm in locked psychiatric units in particular. "Several aspects of inpatient psychiatric wards clearly contribute to patients' experience of boredom. Despite staff perceiving units as 'busy', given their own job duties and group programming offered to patients, as much as 90% (weekdays) to 96% (weekends) of patients' time (as measured in one secure Australian forensic unit) comprises passive activities [Farnworth et al 2004]. Patients spend many unstructured hours without access to activities they can typically do at home, including chores, media consumption, or professional labours. Visiting hours with loved ones and time outdoors are restricted, if available at all" (Tamarelli et al 2024 p220).

On the positive side, individual without things to do have time to think and reflect, may be stimulated to creativity or curiosity, or socialising opportunities.

Tamarelli et al (2024) concluded: "Boredom is justified in situations in which the likely harms of the alternatives to hospitalisation are more severe than the

[14] Barr (1956) is viewed as one of the first studies.

harm caused by boredom. On the other hand, boredom is not a justifiable iatrogenic harm if the reduction in psychological well-being induced by boredom outweighs the benefit of hospitalisation" (pp222-223).

4.3. EXPERIENCES OF ICU

Zengin et al (2020) divided the stressors in ICUs into the categories of physical/environmental, and psychological. The stressors "can be because of surgery or medical treatment, relationships with health staff, or the ICU environment. They can be of different origins (eg: somatic, social, or mechanical). Sleep deprivation, loneliness, fear, difficulty experienced by relatives, impersonal treatment, not feeling safe, and dependency on health care staff are psychological stressors causing anxiety and stress. Environmental stressors include being in an unfamiliar environment and noise resulting from people and other factors in the environment. In general, these stressors include the presence of a tube in the mouth or nose, pain, inability to sleep and speak, thirst, fear of death, longing for family, urinary and faecal incontinence, and alarm sounds" (Zengin et al 2020 p110).

Alasad et al (2015) listed these stressors from their summary of four studies: the presence of invasive procedures, lack of privacy, separation of family, immobility, pain, often need of mechanical ventilation, constant noise, frequent sleep interruptions, and unfamiliar people. While the sleep disruption impacts the immune system and resistance to disease, and potentially delays wound healing (Alasad et al 2015).

There can be an impact post-discharge (eg: psychological problems) [15]. The individual's perception of the stressors, and their coping strategies are key mediators of the experience. Also duration of stay, treatment during ICU stay, and communication by staff are relevant (Zengin et al 2020).

In terms of specific studies, Soh et al (2008), for example, found that the five most reported ICU stressors were inability to move because of needles, pain, feeling bored, missing spouse, and temperature (ie: too hot or cold).

Rattray et al (2004) examined ICU experiences based on four categories - awareness of surroundings, recall of experiences, frightening experiences, and satisfaction

[15] Long-term effects have been reported up to two years after the ICU experience (Alasad et al 2015).

with care - which were the basis of their "Intensive Care Experience Scale (or Questionnaire)" (ICES; ICEQ) (table 4.3) (appendix 4A). McKinley et al (2016) found a relationship between ICU experiences and quality of life six months after discharge. Specifically, "a positive relation between the physical component of the quality of life and awareness of surroundings and a negative relation between the quality of life and frightening experiences. They also reported a negative relation between the mental component of the quality of life and ICU experiences and a positive relation between awareness of surroundings, recall of experiences, and satisfaction with care and ICU experiences" (Zengin et al 2020 p110).

- Awareness of surroundings: "I recognised my relatives"; "I felt safe"; "I felt in control".
- Frightening experiences: "I felt scared"; "I thought I would die"; "I saw strange things".
- Recall of experiences: "I wish I remembered more about it"; "I seemed to sleep too much"; "I never knew whether it was night or day".
- Satisfaction with care: "My care could have been better"; "I was constantly disturbed"; "It was always too noisy".

(Source: Rattray et al 2004 table 4 p69)

Table 4.3 - Example of items from ICES/ICEQ.

Zengin et al (2020) investigated stressors and the ICU experiences in a hospital in Istanbul in 2014-2015. A questionnaire including the ICES was the method of data collection. In total, 116 patients were interviewed by nurses at the point of departure from ICU.

The level of stress was categorised as "lot", "some", or "never". Concentrating on the first group, the most common stressors were thirst, separation from family, tracheal tube aspiration, pain, and inability to speak.

Stressors were positively correlated with the "frightening experiences" sub-scale of the ICES, and negatively with "satisfactory with care", but no clear relationship for the other two sub-scales. Noise was linked to "frightening experiences".

Alasad et al (2015) had used the ICES with 98 patients in ICUs in three hospitals in Amman, Jordan.

Interviews were performed by trained research assistants within 72 hours after leaving ICU. Convenience sampling was used. The vast majority of the participants reported "care was as good as it should be", but a similar number (over 80%) agreed that "I was glad to transfer out of intensive care unit". Only one-third of respondents found the ICU too noisy. Female patients reported significantly more frightening experiences and less satisfaction than male patients.

Halvorsen et al (2022) reviewed the evidence on the factors that enhance the well-being of patients in an ICU. They defined well-being as more than the absence of disease, and as "a holistic view comprising physical, mental and social determinants of health... This reflects personal meanings, strengths and interactions of individuals, families and communities, with individual levels of importance and impact based on a subjective evaluation according to the context of the culture and settings in which it is used" (Halvorsen et al 2022 p4).

The "fundamentals of care" (FOC) framework was also used, which includes physical, psychological and relational dimensions. "Thus, there is an interplay between how practical tasks are performed, how they physically and psychologically affect patients and the relationship between patients and nurses. The interconnection of these dimensions aligns with the extensive caring needs of ICU patients, and how these should be met to potentially enhance well-being, when well-being is understood holistically to include physical, psychological and relational aspects of being" (Halvorsen et al 2022 p5).

A literature search of peer-reviewed empirical studies published between January 2000 and September 2019 in English, Danish, Swedish, and Norwegian was made. Initially, 66 studies were found, but twelve of them were finally included as relevant. The factors for well-being were classed as facilitators or barriers.

The barriers to well-being while being cared for in an ICU included:

a) Physical stressors and conditions (eg: pain; discomfort).

b) Emotional stressors (eg: anxiety).

c) Missing close family.

d) Environmental disturbances (eg: noise, lights).

e) Insecurity of time and space - One study (Olausson et al 2013) examined this issue. Halvorsen et al (2022) explained: "The findings demonstrate how important it is to understand the multi-dimensional meaning of the ICU room as an existential place when a person is critically ill. The room reflects vulnerability in the tension between life and death. It mirrors suffering from neighbouring patients, extending the burden beyond oneself and escalating fear. Furthermore, the absence of sound and silence was just as alarming. The ICU room was experienced as a place that impeded the maintenance of integrity, due to its design and impersonality. Patients expressed the feeling of being in a place 'in between' and that they felt bodily extensions to other places and situations, in and outside the hospital. These feelings could be very frightening, creating feelings of loss of control and loneliness, as well as being barriers to well-being. As described by Olausson et al (2013...), the critically ill patients were 'homeless' in the room and obedient, with a weak voice that was barely heard" (p13).

The facilitators of well-being were summed up in the theme of "meeting physical needs and activities". But also the relationship with staff. "Patients described the intensive care room as a place of trust and security due to positive interaction with the staff. Trust was manifested by caring activities, and by being touched and spoken to in a kind manner. Activities that gave patients a sense of being taken care of, being in good hands and having ICU staff around were important for patients to feel safe and calm, which increased their emotional well-being" (Halvorsen et al 2022 p13).

Overall, the experiences of the ICU and well-being can be described as multi-dimensional - physical, emotional, relational, and environmental (table 4.4).

Any review depends on the studies available, and particularly on their methodological quality. Relevant issues here included:

i) Research method type - quantitative (seven studies), qualitative (4 studies) or mixed (one study).

ii) Country of study - North and Western Europe (10 studies; three from Sweden), and North America (two studies). Differences in care and/or ICU protocols.

iii) Measurement of well-being - directly (eg: "WHO

[World Health Organisation] Well-Being Index") or indirectly (eg: "Environmental Stressor Questionnaire"). The researchers admitted that "most of the included articles did not investigate well-being per se, and we might therefore not have recognised or identified some aspects that enhance well-being. It was a challenge that well-being was mainly found in terms of what inhibits well-being, rather than what enhances it. This constituted an analytical challenge and may have resulted in erroneous interpretations" (Halvorsen et al 2022 p15).

iv) Sample size - 27 patients in one ICU to 168 patients in sixteen ICUs in quantitative studies, and nine to 250 qualitative interviews.

v) How long after leaving the ICU before the patient was interviewed.

- "Nurses need to think and act holistically to provide patient well-being.
- Well-being can be provided by focussing on all aspects of care ranging from mouth care to advanced technological procedures, and relational care involving family and staff.
- Focus on the patient's relationship with the ICU team to provide a safe and trustful environment is imperative to well-being.
- Considerations of bed position, views of nature, and sounds and light in the environment are highly relevant to enhancing patient well-being.
- An individual approach to family presence is needed as a balanced act of caring.
- ICU nurses have to be aware of the fact that family presence may be very comforting but may also cause worries and concern.
- Providing diaries to patients, in particular in post-discharge recovery, has proven very valuable for many patients" (p16).

Table 4.4 - Clinical practice recommendations made by Halvorsen et al (2022).

4.4. APPENDIX 4A - DESIGNING MEASUREMENT SCALES

There are a number of scales specially developed for use with patients who have been in an ICU, including the

ICES/ICEQ, and the "Family Satisfaction in Intensive Care Unit" (FS-ICU) survey (Wall et al 2007).

Tao et al (2025) performed a systematic review of the research that developed such scales, and found seventeen relevant studies published before November 2022. The search terms included "patient satisfaction", "patient experience", and "patients' perception of quality", and their synonyms in five academic databases. The methodological quality of each study was assessed on ten dimensions of the "COnsensus-based Standards for the selection of health Measurement Instruments risk of bias checklist" (COSMIN-RoB-Checklist) (Terwee et al 2018) (table 4.5). None of the scales reported all ten dimensions of information.

Fifteen scales were found in the 17 studies in the review. Looking at the individual items in the different scales, they assessed the following categories most commonly - "Respect for patient-centred values, preferences and expressed needs", "Information, communication and education", and "Physical comfort" [16].

The scales were designed for use with patients (5 of 15), family members as proxies (7), or both (3), and tended to use five-point Likert scales (eg: "strongly agree" to "strongly disagree"), or satisfaction scores (eg: "strongly satisfied" to "strongly dissatisfied"). Postal surveys were the most common mode of administration, followed by face-to-face interviews.

The researchers end thus: "After an overview of all patient experience scales, it can be carefully concluded that the ICU Experience scales have significant room for improvement" (Tao et al 2025 p11).

The "Global Trigger Tool - Psychiatry" (GTT-P) [17] (Nilsson et al 2020) (table 4.6) was developed in Sweden to measure iatrogenic adverse events (AEs) in psychiatric services [18]. "Triggers" are factors identifiable in patient records that are associated with potential AEs (Okkenhaug et al 2024). During the process of adapting the GTT-P to Norwegian psychiatric services, Okkenhaug et al (2024) undertook focus groups with service users and

[16] The other categories were "Access to care", "Co-ordination and integration of care", "Emotional support", "Welcoming the involvement of family and friends", and "Transition and continuity". The categories came from the "National Health Service (NHS) Patient Experience Framework".

[17] The GTT-P was developed from the "Global Trigger Tool" (GTT) (eg: Griffin and Resar 2009) which covered hospital treatment generally. Reviewing studies using the GTT, rates of AEs varied in general inpatients between 7% and 40%, with infections, problems with surgical procedures and medication being most common (Hibbert et al 2016).

[18] In 2552 medical records involving psychiatric hospital care in Sweden in 2017, 438 (17.2%) had a total of 720 identified AEs (Nilsson et al 2020).

- 1. Scale development - 3 scales lacked information about item development.
- 2. Content validity.
- 3. Structural validity - reported for 12 scales.
- 4. Internal consistency - 12 scales.
- 5. Cross-cultural validity - no scales [19].
- 6. Reliability - 5 scales.
- 7. Measurement error - reported for 3 scales.
- 8. Criterion validity.
- 9. Hypothesis testing for construct validity.
- 10. Responsiveness - 4 scales.

Table 4.5 - COSMIN-RoB-Checklist dimensions.

staff. The following themes emerged from analysis of the three focus groups:

i) Mental injury - eg: the impact on a patient of observing an emergency event with other patients.

ii) Physical injury - eg: "overlook somatic illness in diagnosis" (p410), as one health professional pointed out.

iii) Trigger: coercion - eg: one health professional explained: "I think of the trauma that we can inflict on them [service users] because they are hospitalised because of risks of self-harm or suicidal thoughts and to protect them from it, then we may need to use mechanical coercive instruments that we subsequently hear create problems for them like PTSD, trauma" (p410).

[19] Okkenhaug et al (2024) stated: "A research instrument is only valid if the instrument measures the same thing in all contexts.... There is a challenge in translating that goes beyond language to acknowledge different policy, organisational and historical contexts... International studies rely on common indicators and tools developed in one cultural and healthcare context and adapted to permit cross-national comparisons... The process of adaptation is rarely made explicit, potentially undermining both the validity and replicability of such studies... There is a clear distinction between translation and cross-cultural adaption (CCA) and the latter also considers the difference 'between the source and the target culture so as to maintaining equivalence in meaning' (Epstein et al 2015...). The challenges of CCA of research tools are increasingly acknowledged in the literature, but there is little consensus on the best approach" (p406).

iv) Trigger: inadequate treatment - "Service user concerns about inadequate treatment related to limited information and scope for shared decision-making, while for health professionals this related to insufficient attention to formal diagnostic procedures and care planning" (Okkenhaug et al 2024 p411).

v) Trigger: insufficient continuity of care and transition - "For the service users the lack of follow-up and support in managing the transition from the security of the hospital ward the relative isolation of 'outside' held the potential for generating AEs more than shifts between settings within the hospital" (Okkenhaug et al 2024 p411).

- Treatment (15 triggers) - eg: absence of a care plan; undesired effect of treatment other than medication; absence of family contact.
- Drugs (4 triggers) - eg: absence of the alcohol use disorder identification test (AUDIT).
- Coercive treatment (4 triggers) - eg: coercion; police assistance.
- Medicine (7 triggers) - eg: use of more than five different psychotropic drugs; faults in screening for metabolic risk factors during anti-psychotic treatment.
- Continuity and transition (6 triggers) - eg: change in treatment unit; unplanned discharge.

(Source: Nilsson et al 2020 table 3)

Table 4.6 - Global Trigger Tool - Psychiatry.

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5. MISCELLANEOUS

5.1. GEOMAGNETIC DISTURBANCES

Cardiovascular mortality and morbidity has been found to be associated with greater disturbances of the Earth's magnetic field (EMF) (Vieira et al 2022). "Earth's magnetosphere, encircling a region of space around our planet, is subject to complex interactions between the EMF, solar system, and interplanetary space. Solar activity exerts a dominant influence in the short-term EMF disturbances [geomagnetic disturbances (GMD)] through the injection of high-energy plasma and magnetised emissions, such as solar flares and coronal mass ejections, into the Earth's space environment. These phenomena range in intensity largely according to quasi-periodic 11-year solar cycles" (Vieira et al 2022 p2).

In terms of research studies, Cornelissen et al (2002), for example, reported an increase in risk of myocardial infarction mortality during years of high solar activity compared to low activity in one state in the USA. While in a study of 263 US cities, Vieira et al (2019) found an association between GMD and cardiovascular mortality risk. In Lithuania, Vencloviene et al (2014) found reduced survival of patients hospitalised for acute coronary syndrome on active GMD days.

Vieira et al (2022) analysed data from the "Veterans Affairs Normative Ageing Study" (NAS) in the USA on heart rate variability (HRV), and compared it with GMD data. The NAS cohort consisted of men (aged 21-80 years at baseline) from the Boston area recruited since 1963. HRV was measured for 809 participants between 2000 and 2017. GMD activity was rated daily from 0 to 9 based on official data.

Reduced HRV was significantly associated with greater GMD. "In periods of intense GMD, the reduction of HRV was even stronger in patients with CHD [coronary heart diseasse] and no diabetes" (Vieira et al 2022 p7). Reduced HRV is a known risk factor for adverse cardiovascular events (Vieira et al 2022).

It is suggested that GMD impacts the autonomic

nervous system (ANS). "Studies show that magneto-reception systems composed by photosensitive retinal proteins called cryptochromes detect GMD-related electromagnetic field variations from the environment... The overstimulation of these systems over-activates the functions of the central nervous system, unbalancing standard circadian rhythm processes and the ANS activity... It is well known that sympathetic and parasympathetic nervous system activities of the ANS regulate core functions such as HRV, breathing, and metabolic processes in the body" (Vieira et al 2022 p6).

The NAS cohort was well studied with regular medical tests and collection of data. HRV was measured regularly in controlled conditions between 7 am and 9 am (eg: after an overnight fast). The mean age of the participants was 75 years in the year 2000, and 98% of the sample were White.

The GMD data came from the "National Oceanic and Atmospheric Agency's (NOAA) Space Weather Prediction Centre".

Air pollution exposure, and individual health information (eg: diabetes) were controlled for in the analysis.

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5.2. EYTHRITOL CONSUMPTION

There is evidence emerging that consumption of artificial sweeteners is associated with cardiovascular disease risk (eg: Malik et al 2019). But these epidemiological studies are "limited by potential unmodelled confounding, including reverse causation.

Further, due to current limitations in food labelling requirements, epidemiology studies generally do not quantify individual sweeteners but instead use food questionnaires to estimate consumption in broad categories (eg: natural sweeteners or sugar alcohols)" (Witkowski et al 2024 pp2136-2137).

Specifically, Witkowski et al (2023) found an association between the non-nutritive sweetener erythritol and cardiovascular events in the following three years. Witkowski et al (2024) developed upon this study by comparing erythritol and the equivalent amount of glucose.

This was an intervention study focused on the effect of ingestion of the substance and platelet aggregation (used as a marker of thrombosis risk). US volunteers gave a blood sample before and thirty minutes after ingestion of erythritol or glucose in water after an overnight fast. The level of erythritol was equivalent to that found in foods.

It was found that the sweetener, but not glucose, "enhances platelet reactivity in healthy volunteers, raising concerns that erythritol consumption may enhance thrombosis potential" (Witkowski et al 2024 p2136).

This study involved only twenty volunteers, and measured short-term changes only.

References

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5.3. EMERGENCY RESPONSE TIMES

"Out-of-hospital cardiac arrest" (OHCA) is "the termination of cardiac mechanical activity and subsequent cessation of blood circulation in a patient outside of a hospital" (Huang et al 2021 p1). Survival of such events is low (eg: 10-20% survive to hospital discharge), and this depends on factors like "location of OHCA, witnessed arrest, bystander cardio-pulmonary resuscitation (CPR),

initial cardiac rhythm, and level of post-resuscitation care" (Huang et al 2021 p1). Emergency medical service (EMS) response time is also important, as well as patient characteristics (eg: age; other health problems) [20].

Huang et al (2021) analysed data from Kaohsiung in Taiwan collected from 2015 to 2019 about the latter two factors in particular. The EMS database maintained by the national government keeps details of the event (eg: patient details; EMS management), and the outcome. The total was 6742 relevant OHCA cases.

Overall, 224 patients survived to hospital discharge (3.3%). This group was significantly more likely to be younger, male, have a witness and bystander CPR, and EMS shorter response time, for example, than non-survivors. After adjusting for confounders, EMS response time, younger age, and bystander CPR were key significant factors associated with survival to hospital discharge.

The optimal EMS response time for survival to hospital discharge was 6.2 minutes (or less), but this was shorter for older patients (80 years and above), and/or those without bystander response (eg: OHCA not in a public area).

How does this compare to other studies in a similar part of the world? For example, Ono et al (2016) found the optimal response time was 6.5 minutes in an analysis of over two million bystander-witnessed OHCA cases in Japan 2006-2012, while Lee et al (2019) in South Korea calculated a figure of 7.5 minutes. The differences in time may have been due to patient characteristics and/or emergency services (and their procedures) in the different countries.

Huang et al (2021) found no difference in survival based on the other health problems (co-morbidities) of patients, which was contrary to previous research (eg: a review by Majewski et al 2019).

Huang et al (2021) were not able to assess the quality of bystander CPR, and the study did not include OHCA cases not involving EMS services (eg: taken directly to hospital by family).

Berglund et al (2022) analysed Swedish data on response times of EMS, fire fighters, and smartphone-aided voluntary responders to suspected OHCA cases. The

[20] Nolan et al (2006) talked of the "chain of survival", which had four links, and time was a crucial element. "The original four links of the chain of survival comprised: (1) early access - to activate the emergency medical services (EMS); (2) early basic life support (BLS) to slow the rate of deterioration of the brain and heart, and buy time to enable defibrillation; (3) early defibrillation - to restore a perfusing rhythm; (4) early advanced life support (ALS) - to stabilise the patient" (Nolan et al 2006 p270).

data covered May 2018 to February 2020 in the Stockholm and Gothenberg areas. The EMS involved ambulances with appropriately skilled staff, the fire fighters were on-duty and appropriately trained and equipped, and the volunteers had learned basic CPR and/or had information on nearby automated external defibrillators (AEDs) to bring to the scene.

The dataset included 2631 OHCA cases. The response time (from emergency call received to arrival at patient) was 10.4 minutes for EMS, 10.2 minutes for fire-fighters, 9.6 minutes for AED collecting volunteers, and 6.2 minutes for CPR-trained volunteers. Emergency call centres, however, were slower to inform non-EMS groups.

The researchers recommended an automated system that informed all groups simultaneously rather than manually by staff at call centre which had an order of priority with EMS first.

References

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5.4. ERGOTHIONEINE

Golden oyster mushrooms are rich in an anti-oxidant called ergothioneine, and observation studies have found that eating them regularly is associated with a lower risk of heart disease and premature death (Wade 2025).

In an experiment with mice, Sato et al (2025) fed ten middle-aged individuals with powdered golden oyster

mushrooms daily. After one year, these mice had better heart function as compared to controls (eg: heart pumped more blood).

Ergothioneine has been called "a longevity vitamin" (Robert Beecham of Pennsylvania State University in Wade 2025).

References

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Wade, G (2025) Golden oyster mushrooms may aid heart health New Scientist 25th January, p21

5.5. SLEEP DISORDERS

Sleep disorders are associated with cardiovascular diseases (CVDs), particularly sleep deprivation (for example, through insomnia), but also poor sleep quality, and long sleep duration (Rostamzadeh et al 2024).

The mechanisms of the relationship include hypertension, and inflammation, and in older adults, Klotho and sirtuins ("silencing information regulator 2 (Sir2) proteins") levels. Klotho is a protein, and the level decreases with age, while sirtuins regulate different pathways in the cell (Rostamzadeh et al 2024).

In a review of the evidence on the latter, Rostamzadeh et al (2024) found "a bidirectional relationship between sleep disorders and the serum and tissue levels of Klotho and sirtuins and sleep-related CVDs" (p1).

Reference

Rostamzadeh, F et al (2024) The role of Klotho and sirtuins in sleep-related cardiovascular diseases: A review study npj aging 10, article 43