Patients' experience of study participation and triggers of myocardial infarction

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DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD) at the Faculty of Medicine at Lund University.
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Abstract

Introduction Myocardial infarction (MI) is one of the most common causes of death globally and affect the individual both physically and mentally. Two overall aims are investigated in this thesis. First, to assess patients' experiences of informed consent and study participating in an acute setting of myocardial infarction. The second aim was to obtain more knowledge about the reason of increased incidence of myocardial infarction during national holidays.

Methods Study I used a four-question telephone survey conducted one week after randomization in a clinical trial that included patients with and without ST-elevation MI (STEMI) in the acute phase upon arrival at coronary catheterisation laboratory. Study II involved semi-structured web interviews approximately three months after randomization in a double-blind clinical trial. Study III and IV utilised a postal questionnaire to investigate potential triggers among all living patients experienced an MI in Sweden with symptom onset on national holidays and predefined dates. Study III also used a control group of patients with stable angina. Study V utilised retrospective device data from patients with cardiac implantable electronic devices over a five-year period, analysing fluid changes and other physiological metrics during national holidays.

Results Most participating patients were positive to enrolment in clinical trials, even in the emergency setting and objected to deferred consent. Four categories in the interview study were identified: *A willingness to contribute*, *The perception of information*, *Be in a vulnerable situation* and *Adaption to a new technology*. Self-reported stress, worry, and depression were the most reported triggers to MI during national holidays, with the most profound effects observed among women. Device data revealed impaired fluid regulation in the heart and lungs during national holidays, as well as reduced physical activity and heart rate variability.

Conclusions Verbal informed consent followed by written consent is considered feasible for STEMI trials. In non-emergency setting, clear verbal explanations and concise written materials are preferred, and patients value contributing to future advancements. The use of a medication dispenser with a wirelessly connected cap to monitor medication adherence was well-received, with no negative feelings of being monitored. Christmas and holiday-related MI may be triggered by increased stress and worry, particularly in women, but not by travels, conflicts, or reduced medication adherence. Transient fluid accumulation, reduced physical activity, and impaired heart rate variability were observed during Christmas and Midsummer in patients with devices, potentially contributing to impaired cardiac health during holidays.

Key words: Myocardial infarction, Informed consent, Heart disease risk factors, Secondary prevention

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To my family

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List of papers

This thesis is based on the following papers, referred to hereafter by their respective Roman numerals. The papers (I–IV) are published open access and are appended at the end of the thesis.

I. **Olsson A**, Ring C, Josefsson J, Eriksson A, Rylance R, Fröbert O, James S, Sparv D, Erlinge D. Patient experience of the informed consent process during acute myocardial infarction: a sub-study of the VALIDATE-SWEDEHEART trial. *Trials*, 2020;21(1):246.

II. Henriksson C, **Olsson A**, Andersen K, Arefalk G, Erlinge D, Hofmann R, Ridderstråle W, Oldgren J, James S. Patients' experience of clinical trial participation involving a product remotely assessing study drug adherence. *Contemporary Clinical Trials Communications.* 2024:101307.

III. **Olsson A**, Thorén I, Mohammad MA, Rylance R, Platonov PG, Sparv D, Erlinge D. Christmas holiday triggers of myocardial infarction. *Scandinavian Cardiovascular Journal,* 2021;55(6) 340–44.

IV. **Olsson A,** Mohammad MA, Rylance R, Platonov PG, Sparv D, Erlinge D. Sex differences in potential triggers of myocardial infarction. *European Heart Journal Open,* 2023 (3), 1–9.

V. **Olsson A**, Rylance R, Mohammad MA, Borgquist R, Erlinge D, Platonov PG. Increased fluid accumulation, reduced physical activity and heart rate variability during national holidays in patients with cardiac implantable electronic devices. *European Journal of Preventive Cardiology,* e-publication ahead of print; https://doi.org/10.1093/eurjpc/zwaf054

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Abbreviations

ACS	Acute Coronary Syndrome
BMI	Body Mass Index
BP	Blood Pressure
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CIED	Cardiac Implantable Electronic Device
CVD	Cardiovascular Disease
CRP	C-reactive protein
ECG	Electrocardiogram
IC	Informed Consent
LDL-C	Low Density Lipoprotein Cholesterol
Lp(a)	Lipoprotein (a)
LVEF	Left Ventricular Ejection Fraction
MI	Myocardial Infarction
NSTEMI	Non-ST-Elevation Myocardial Infarction
OGTT	Oral Glucose Tolerance Test
OVFI	OptiVol Fluid Index
Riks-HIA	Register of Information and Knowledge about Swedish Heart Intensive-Care Admissions
PCSK-9	Proprotein Convertase Subtilisin–Kexin type 9
SCAAR	Swedish Coronary Angiography and Angioplasty Registry
STEMI	ST-Elevation Myocardial Infarction
SWEDEHEART	Swedish Web-system for Enhancement and Develop-ment of Evidence-based care in Heart disease Evaluated According to Recommended Therapies
UA	Unstable Angina
WHO	World Health Organisation

Introduction

Cardiovascular disease

Epidemiology

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide mostly due to a growing and aging population[1], even though a decrease in mortality has been seen the last 30-40 years. The incidence varies by region, age, sex, and socioeconomic status[2]. High-income countries typically report higher incidence rates compared to low-income countries. In Europe, huge inequalities in the disease burden persist between countries, with greater burden of CVD in middle-income nations[3]. In some high-income countries cardiovascular disease is no longer the leading cause of death. Globally, CVD is responsible for an estimated 17.9 million deaths each year. Over 80% of these deaths are due to myocardial infarctions and strokes, with one-third of these deaths occurring prematurely in people under the age of 70[4].

The term CVD refers to diseases that impact the blood vessels of the heart, brain, and peripheral arteries. The most prevalent of these is coronary artery disease (CAD), which is responsible for about 7.4 million deaths worldwide each year.[5]. The primary clinical manifestation of CAD is myocardial infarction (MI), which is the focus of this thesis. In Sweden, the mortality rate in MI has reached a plateau the latest 15 years and 1 year survival has been about 13 % during the recent years[6].

CAD is most often characterized by the narrowing or blockage of coronary arteries due to the buildup of atherosclerotic plaques and a complex pathophysiological process leading to erosion or plaque rupture and formation of a thrombus[7], Figure 1. The thrombus itself can partially or completely occlude the coronary artery, resulting in unstable angina, MI or sudden cardiac death.

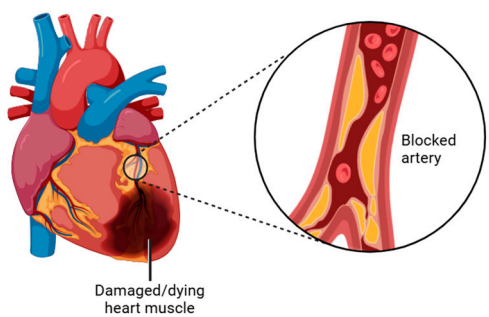


Figure 1. Myocardial infarction due to a thrombus which partially or complete occlude the artery in the heart muscle, resulting in necrosis of muscle cells. Created with BioRender.com.

Risk factors

Non-modifiable risk factors

Some risk factors of CVD or CAD are inherent to an individual's physiology and genetic makeup. They often involve aspects that are difficult to modify through lifestyle changes. The main non-modifiable risk factors are described below.

Age

The risk of CAD increases with age[1]. The start of atherosclerosis begins in teenage and growth with time, Figure 2. With advancing age, the walls of arteries undergo structural and functional changes, leading to increased stiffness and reduced elasticity. This phenomenon is related to both intrinsic and extrinsic vascular mechanisms[9]. During recent years, the term inflamm-aging has been introduced, since chronic low-grade, systemic inflammation accelerate the biological age and progress of atherosclerosis[10].

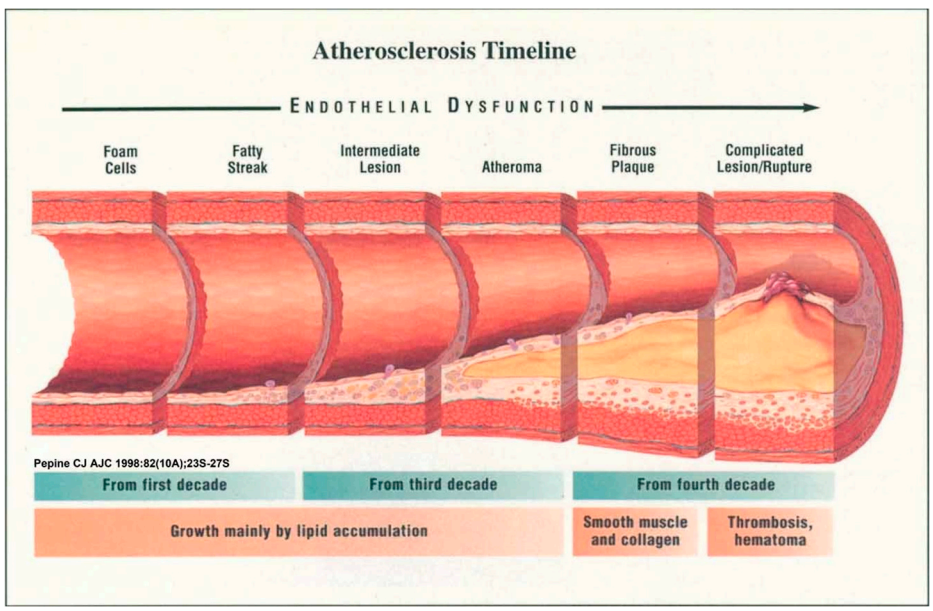


Figure 2. Timeline of development of atherosclerosis. Printed with permission from Elsevier[8].

Sex

Despite being the leading cause of death globally in both sexes, the incidence of CAD is lower in women compared to men in all age groups[3,5]. The differences however become less apparent with age[11]. Women are affected about 5-7 years later and are most likely protected by the oestrogen until post menopause[12]. Sex-specific

risk factors have been increasingly recognised in recent years and some of them are illustrated in Figure 3.

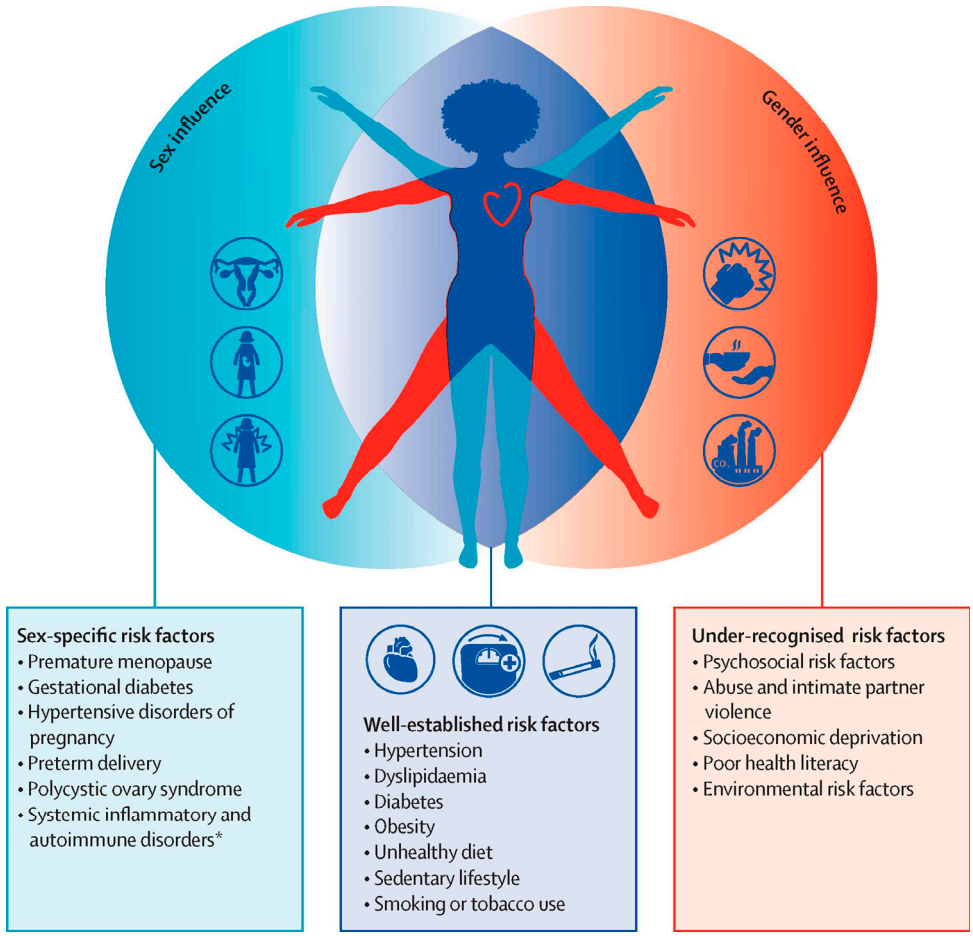


Figure 3. Risk factors for cardiovascular disease in women. Reprinted from Vogel et al, Lancet 2021[13] with permission from Elsevier.

Genetic factors

Specific genetic mutations or inherited conditions can predispose individuals, and the risk of coronary events has been calculated to be 91 % higher among people in the highest quintile of genetic risk compared to those in the lowest quintile[14]. The advances in technology have enabled the discovery of many different DNA-variants that carry a higher risk of CAD[15-17]. Histological data has shown that this genetic predisposition was seen even in ancient mummies[18]. The genetic risk is not age-dependent, and awareness of an elevated genetic risk score can be utilised in primary

prevention long before other modifiable risk factors arise. Polygenic risk score to predict CAD is superior to conventional risk factors in risk stratification for primary prevention of CAD[19,20] but is so far limited to research and not yet used in clinical practice. It is important to note that even with a high genetic risk for cardiovascular disease, a healthy lifestyle can significantly improve prognosis [21].

Ethnicity

There is a significant variability in risk factors between different ethnic groups. Immigrants from South Asia shows the highest CVD rates, independent of the traditional risk factors. The reason for this variation is not sufficiently studied and when dealing with risk score for CAD this must be considered[22].

Modifiable risk factors

The lifetime risk of CAD differs markedly according to modifiable risk factor burden [23]. The Framingham cohort started 1948 in US and few years later demonstrated that hypertension, obesity and cholesterol were strongly associated with CVD[24]. Several decades later, the global INTERHEART case control study showed that about 90 % of the risk for MI could be attributed to nine risk factors[25]. In addition to the ones in the initial Framingham cohort, diabetes mellitus (DM), psychosocial factors, poor diet, low alcohol consumption and inactivity were associated with MI. The prospective global PURE study identified fourteen modifiable risk factors attributed to about 71 % of CVD cases[26]. Low education, household pollution and low grip strength was added to the former known risk factors. The Global Cardiovascular Risk Consortium concluded in 2023 that about 55 % of global CVD could be attributed to the five most important risk factors; BMI, systolic blood pressure, non-HDL cholesterol, current smoking and diabetes[27]. In recent years, there has been increased focus on residual risk to identify new therapeutic targets. The proportion of patients experiencing a first STEMI event without any known risk factors is growing, highlighting the need for a deeper understanding in this area. The following factors are the most common risk factors, modifiers or determinants of CAD and are described below, Figure 4.

Figure 4. Main modifiable risk factors. Created using BioRender.com.

Hypertension

The main modifiable risk factor is elevated arterial systolic blood pressure (BP). This risk factor alone contributes to increased global all-cause mortality and 212 million lost healthy life years (8.5% of the global total) each year[28]. It is a major component, independent of other CVD risk factors in all prediction models for CAD. BP increases continuously with age in most countries worldwide. In isolated, pre-industrial societies with limited intake of dietary sodium and low environmental impact the rise in BP with age is small if exists at all[29,30]. Multifactorial reasons like increased sodium consumption, genetic predisposition, poor sleep quality, alcohol intake, high mental stress and immunological factors plays a significant role in the development of hypertension[31,32]. An elevated BP is affected, among other things, by renal and peripheral vascular resistance, endothelial dysfunction, sympathetic nervous system and contributes to progressive stiffening of the arterial vessels and accelerate the process of atherosclerosis[32]. BP lowering can rapidly reduce the cardiovascular risk[33]. It can be performed through pharmacotherapy and lifestyle modifications[34] and is effective in all ages[35].

Hyperlipidaemia

Elevated levels of blood lipids are well documented risk factors for CAD, in particular increased low-density lipoprotein cholesterol (LDL-C)[36]. Lowering LDL-C with statins, ezetimibe or proprotein convertase subtilisin–kexin type 9 (PCSK-9) inhibitor have been effective to reduce cardiovascular events both in high-risk patients[37] and in patients with intermediate risk without previous CVD[38]. Observational studies have shown that the association between high LDL-C and future cardiovascular events seems to be related to coronary atherosclerosis[39]. The lipid-risk picture is however multifaceted. Among statin-treated patients, the residual risk and prediction for future events have been more linked to levels of high sensitive c-reactive protein (CRP) than levels of LDL-C [40].

Genetically determined familial hypercholesterolemia (FH), characterised by elevated LDL-C, is associated with an increased risk of premature cardiovascular events and affects approximately one in 300 individuals globally[41]. Early identification and treatment are essential to mitigate this risk.

Lipoprotein (a) (Lp(a)) is so far the most common genetically determined risk factor for CVD. The protein is similar to LDL but contains an additional apolipoprotein (a) and the risk factor exists throughout a person's lifetime and remains unaffected by lifestyle changes and currently approved therapies[42]. High levels of Lp(a) are a risk factor independent of LDL-C.

Elevated triglycerides are related to subclinical atherosclerosis and vascular inflammation independent of the LDL-C levels but have also been rediscovered during the last decades as a residual risk factor for CAD-events when LDL-C levels are well treated[43].

The latest European risk score, SCORE2[44], include an estimation of non-HDL cholesterol, which is calculated as total cholesterol minus HDL. This measure accounts for all types of "bad" cholesterol: LDL-C, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and Lp(a). Non-HDL cholesterol is considered a better predictor of cardiovascular risk than LDL-C alonealone[45,46].

Smoking

Following hypertension, smoking is the second leading risk factor for disability adjusted life-years globally and causes over 7 million deaths each year globally. Since 1990, the prevalence of smoking has decreased around the globe. However, as populations have grown, the total number of smokers has increased globally[47].

Smoking even a single cigarette per day is associated with a significantly elevated risk of CAD (RR 1.48 in men and 1.57 in women) compared with never-smokers[48]. In young smoking adults, i.e., those younger than 50 years, the CVD risk is five times higher than in non-smokers[22].

Obesity

Obesity, defined as body mass index (BMI) >30 kg/m^2 directly contributes to the onset of cardiovascular risk factors such as hyperlipidaemia, type 2 DM, hypertension, and sleep disorders[49]. Additionally, obesity independently drives the development of cardiovascular disease and increases cardiovascular mortality, beyond the impact of other risk factors. Genetically driven obesity, however, appears to be less harmful than lifestyle-driven obesity as demonstrated in a Swedish twin study, recently published[50]. Several studies emphasize abdominal obesity, measured by waist circumference, as a significant cardiovascular disease risk marker, independent of body mass index[51,52]. Since BMI has limitations depending on body composition, the recommendation is to add the measure of the abdominal waist in prevention work[53]. Lifestyle changes and subsequent weight loss have been shown to improve metabolic syndrome, as well as reduce associated systemic inflammation and endothelial dysfunction[49].

Diabetes mellitus

Diabetes mellitus (DM) is a disease characterised by abnormally high blood glucose levels caused by insulin resistance (type 2) or insufficient insulin production (type 1). The most common, type 2 DM develops from obesity and physical inactivity in addition to genetic susceptibility. Its prevalence in high-income countries increases, and is mainly related to our lifestyle[54]. The insulin resistance affects the vascular system in multiple molecular pathways[55,56]. When having DM type 2 the risk for CAD is about twofold[54] and in type 1 at least threefold[57] compared to individuals without DM. MI patients with prediabetes have similarly higher risk of future CV events[58]. Oral glucose tolerance test (OGTT) has been important in detection of risk

patients. Therapeutic control of the diabetes, other risk factors and lifestyle management are important to optimize the primary prevention.

Physical inactivity and sedentary lifestyle

Physical inactivity is the fourth leading cause of death worldwide[59]. Several reviews and meta-analyses have shown consistent evidence of the association of increased physical activity with better cardiovascular outcomes both in the primary and secondary prevention settings[60-64]. Physical activity has the potential to modify major risk factors by lowering blood pressure, reducing abdominal waist, improving insulin resistance and lipid profiles[65,66]. Some of the mechanisms are summarized in Figure 5 reproduced from EHJ[67]. In addition, physical activity has been an effective intervention aiming to reduce psychosocial burden, like depression[68].

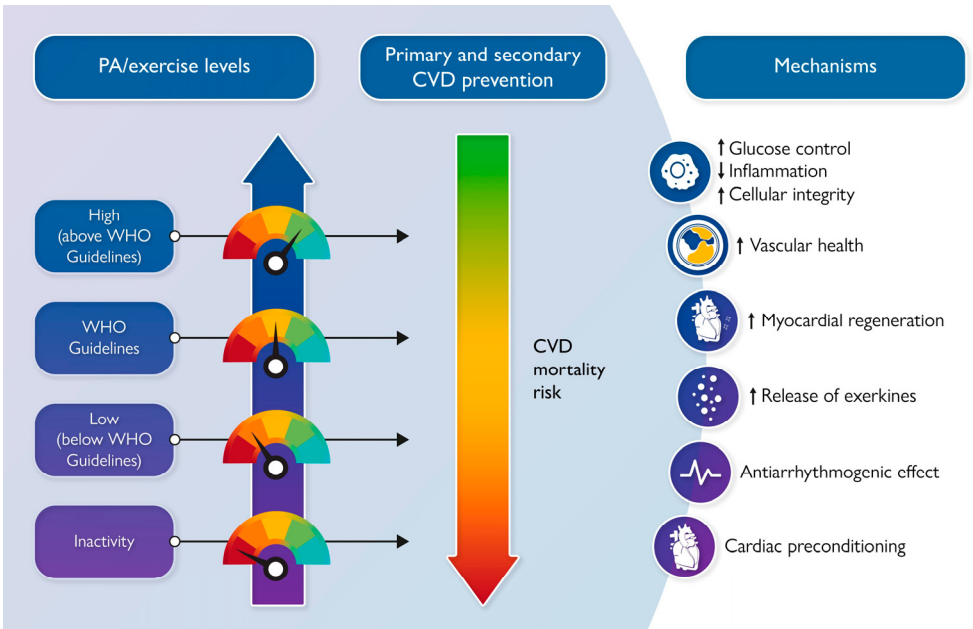


Figure 5. Summary of the main effects of regular physical activity and exercise on cardiovascular disease[67]. Printed with permission of Oxford University Press.

In order to provide health benefits, the World Health Organisation (WHO) have formulate well-defined recommendations about the amount of moderate- and vigorous-intense physical activity as well as recommendations to limit sedentary behaviour [69]. In secondary prevention, physical activity and exercise-based cardiac rehabilitation are fundamental components of the prevention program.

Diet

The EAT-Lancet Commission declared in 2019 that consuming an unhealthy diet contributes considerably to premature death and morbidity worldwide[70]. The highest adherence of EAT-Lancet recommended diet was associated with lower cardiovascular mortality (HR 0.68; 95 % CI 0.54-0.84) when compared to lowest adherence when the index was tested retrospective in a cohort from Sweden with 20 years of follow up[71]. The results in diet trials are often criticised due to several potential bias. Blinding is for several reason not possible and measurements are often subjective. Changing of one´s diet is challenging, and motivation and adherence are often more successful in physically and psychologically healthier persons.

The prospective, randomized CORIOPREV study demonstrated that the Mediterranean diet was superior to low-fat diet in preventing cardiovascular events in a secondary prevention cohort[72]. Similar result was shown in a primary prevention cohort in the PREDIMED trial[73]. In the ESC guidelines there is now a class 1A recommendation for a healthy, Mediterranean or similar diet with unsaturated fat and reduced salt intake[22]. In addition, there are strong recommendations for plant-based diet rich of fibre, fruits, vegetables, fish and restricted sugar and alcohol-consumption.

Alcohol

Although several epidemiological trials suggested that low-moderate consumption may be beneficial for cardiovascular health, the evidence is sparse and inconclusive. Later trials with improved designs to eliminate confounders show no such protective effects[74].

Inflammation

In recent decades, inflammation has been highlighted as a contributor to the development of atherosclerosis in all phases and as an independent predictor of the residual risk of MI [7,40,75,76]. High-sensitive CRP and pro-inflammatory cytokines as IL-6 are the most common investigated biomarkers. Patients with rheumatoid arthritis and other autoimmune disorders have a higher susceptibility to CVD[77] due to systemic chronic inflammation.

Psychosocial risk factors

An increasing body of evidence underscores the interconnectedness of the brain, mind, heart, and body, which can influence cardiovascular health, individual CVD risk factors, and cardiovascular outcomes, both positively and negatively[78]. Both the Framingham study[79] and the INTERHEART study[25] identified psychosocial factors as CVD risk factors several decades ago. The factors assessed in the INTERHEART

using structured questionnaires were depression, locus of control, perceived stress and life events. In the Framingham cohort, type A behaviour, daily stress, aging worries and tension were associated with incidence of MI. In recent years, the prospective Copenhagen City Heart Study stated that vital exhaustion was one of the most important independent predictors for cardiovascular events[80].

Psychosocial risk factors are often linked with socioeconomic status, lifestyle, and behaviour, making it hard to identify clear causes. They are considered key determinants of cardiovascular disease because they shape broader social and environmental conditions, like stress, socioeconomic status, and social support, that impact long-term disease risk[81,82]. In this thesis I use the term risk factor, although I am aware that a more accurate term might be determinants.

Due to the improvement in traditional risk factor management in recent decades in the Western world, the relative importance of psychosocial risk factors is likely to increase. Conventional risk factors have significantly decreased among patients with first STEMI in Sweden from 2006 to 2014. The proportion of patients with no known risk of hypertension, hypercholesterolemia, diabetes and smoking increased from 11% to 27% during this period and women without known risk factors had increased 30 days all-cause mortality[83,84]. Despite this, only a few validated risk assessment tools have included aspect of psychosocial health[85] even if recent guidelines have highlighted the need for screening[22]. Some of the most common psychological risk factors are described below.

Stress

Work stress as well as private-life stress has been associated with increased risk of CVD[86,87]. Being a caregiver to a loved one has been associated with a 63% higher risk of mortality during four years of follow-up. The increased risk was most evident in strained caregivers with known cardiovascular disease[88]. Stress is supposed to accelerate the progression of atherosclerosis, impair recovery as well as being a trigger in people with underlying disease[89]. A case-control study found significantly higher hair cortisol levels one month prior to an MI event compared to controls in middle-aged individuals in Sweden[90]. In the absence of reliable objective stress measurements in relation to onset of MI, hair cortisol levels could play a role, as they can be measured retrospectively[91]. The known complex pathophysiological effects of stress can be visualized in Figure 6. Some cognitive behavioural therapy or stress management interventions included in cardiac rehabilitation have reported large reductions in cardiovascular events with HR ranging from 0.49- 0.59[92,93].

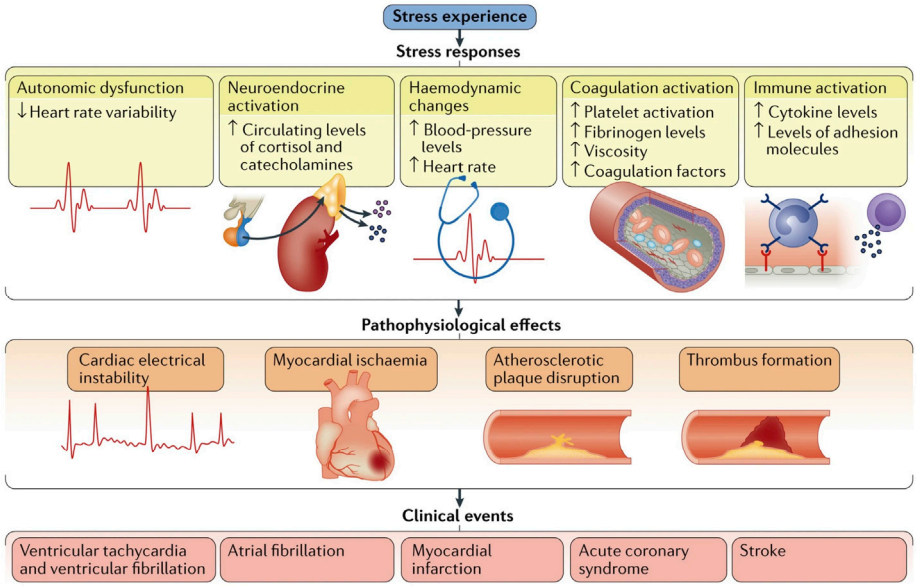


Figure 6. The effects of stress contributing to cardiovascular events. Reprinted with permission from Springer Nature[89].

Depression

The incidence of depression among patients with CVD is three times higher than in the general population[94]. The mechanisms and pathways are not fully examined but are most probably bidirectional with an age-dependent component. Depression diagnosis is associated with 30% increase in the risk of having a CVD event even after adjustment for sociodemographic factors and lifestyle behaviours[95]. The prevalence of depression is twice as common among women and the association between depression and cardiovascular events are most prevalent among younger woman[96].

Sleep disturbances

In the latest version of Life´s Essential[97], see Figure 7, sleep has been added as the 8th metric of the definition of cardiovascular health. Poor sleep quality, insufficient sleep duration and excessive sleep duration have all been associated with increased risk of CVD[98]. The association between sleep duration with CVD seems to be U-shaped and 6-8 hours per night seems to be optimal[99]. Endothelial dysfunction, systemic inflammation, sympathetic tone are supposed to be the pathophysiological explanation. One example of sleep disturbances is the daylight-saving time during spring and autumn which disrupt people's circadian rhythm. Swedish retrospective

data from 15-20 years showed that the incidence of myocardial infarction was increased the days after transition to daylight saving time in the spring and decreased the first day after daylight saving in autumn[100].

Figure 7. Life´s Essentials by AHA[97]. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001078 (fig 1). The figure is not allowed to be published in the online version.

Acute risk factors of coronary thromboembolic events

In addition to these known risk factors, the myth of a trigger for the onset of myocardial infarction has been debated throughout history. In the early 20th century, two Russian physicians Vasily Obraztsov and Nikolay Strazhesko provided the first description of non-fatal myocardial infarctions and their clinical presentation[101]. Along with describing symptoms and cardiac status, they declared:

> "All patients noted an acute, sudden onset of the disease. Direct events often precipitated the disease; the infarct began in one case on climbing a high staircase, in another during an unpleasant conversation and in a third during emotional distress associated with a heated card game".

This proposal of an onset trigger was lively debated the following decades and ended temporarily when Arthur M. Master concluded that a coronary occlusion takes place irrespective of precipitating activity in 1960[102].

Circadian variation

In the 80s several studies reported findings of the circadian variation of the onset of MI, as well as sudden cardiac death and strokes[103-106]. These circadian variations were also seen in the incidence of ventricular arrhythmias[107] and non-obstructive coronary arteries (MINOCA)[108]. In the morning, the natural increase in sympathetic activity, increased elevated blood pressure, heart rate, and blood clotting tendencies affects the arteries and can potentially trigger an event related to a previously damaged or exposed plaque in the coronary artery[109]. The use of beta blockers appear to provide some protection against the circadian trigger by reducing sympathetic activity and the likelihood of plaque rupture in the coronary arteries during the morning surge[110]. A recent study reported that morning-onset MI was

associated with higher odds (OR 1.65 [95% CI 1.19-2.28]) of culprit in the right coronary artery (RCA) compare to left arterial descending artery (LAD)[111].

Physical activity

Similar to the description by Russian physicians in 1910, vigorous physical activity was re-identified as a potential trigger of MI at the beginning of the 1990s. Earlier evidence had been descriptive, and limited conclusions were drawn. A new case-crossover design was introduced, with patients acting as their own controls. In this study, the relative risk (RR) of MI was 5.6 [95% CI 2.7–12.8] if heavy physical activity was performed within one hour before the onset of symptoms compared to a reference period. In usually sedentary individuals, the RR was 107[112]. Similar results were observed in the Stockholm Heart Epidemiology Program (SHEEP),[113] which indicated a significantly higher risk of vigorous physical activity if limited regular physical training (less than once a week) compared to individuals who reported more than four episodes of regular physical activity per week, with a RR of 101 versus 3.3. Other studies have confirmed similar results in other kinds of physical activities like snow shovelling and sexual activities[114-116].

Environmental factors

Association with factors like cold weather[117-119], lower atmospheric air pressure, higher wind velocity, and shorter sunshine duration[119] has been associated with increased risk of MI. Increased concentrations of fine particles of air pollution have in addition been suggested to transiently increase the risk of MI within a day[120].

There is increasing evidence supporting the hypothesis that viral infection, respiratory infections and influenza, can trigger MI[121]. In viral infections, the inflammatory response can destabilize atherosclerotic plaques, composed of inflammatory cells that become activated in a pro-inflammatory state. This condition can result in endothelial dysfunction and injury, leading to a prothrombotic state characterized by increased platelet reactivity and a heightened risk of MI. Influenza vaccination in patients with coronary heart disease has been associated with a 40% relative risk reduction in cardiovascular death and all-cause mortality within 12 months post-MI[122].

Heavy meal

In the Australian Triggers and Modifiers of Acute Myocardial Infarction (TAMAMI) study a heavy meal within 2 hour was associated with a RR of 3.67 [95% CI 1.02-13.14]. Similar results was reported in an Israeli study[123]. Individuals in the Western world spend most of the day in a post-meal, so-called postprandial state. Postprandial lipidaemia and postprandial hyperglycaemia are both associated with increased oxidative stress, endothelial inflammation and hypercoagulability[124,125]. Within healthy individuals the plasma triglycerides

increase significantly after a high-fat meal, peaking around four hours and returning to fasting levels around eight hours afterwards[126].

Psychosocial stress

Acute psychosocial triggers like natural disasters and other stressors have been associated with increased incidence of MI. Several studies have reported higher risks in connection to earthquakes[127-129], hurricanes[130,131] and important fotball-games[132-134]. The risk of MI was 21-fold higher within the first 24 hours after the loss of a significant person and decreased over time, according to the Determinants of Myocardial Infarction Onset Study (MIOS) study[135] highlighting that acute emotions such as grief can significantly trigger cardiovascular events. The MIOS study reported that increased anger within two hours was associated with increased MI as well[136]. Anxiety or emotional stress as a trigger before onset MI has furthermore been reported to be associated with elevated anxiety and poor mental health status at 12 month[137], re-hospitalization[138] and increased 10 year all-cause mortality[139].

National holidays

The terms 'Merry Christmas Coronary' and 'Happy New Year Heart Attack' were coined by Kloner in 2004[140], following several reports describing the phenomenon of increased incidence of cardiac deaths during Christmas and New Year in the US[141,142]. Several potential mechanisms were proposed as delay in seeking care, increased emotional stress, overindulgence in food, fats, salt, alcohol, cold weather, particles from wood-burning fireplaces and reduced level of healthcare staff.

In 2018, Mohammad et al published the Swedish nationwide study covering 16 years of admission for myocardial infarction[143]. More than 280 000 cases were analysed using the SWEDEHEART registry. Christmas and Midsummer holidays were associated with higher risk of myocardial infarction, incidence rate (IR) 1.15 [95% CI 1.12-1.18]. The day with highest observed incidence were Christmas Eve (1.37 [1.29-1.46]). These findings were particularly seen in patients aged over 75 years and in patients with comorbidities like diabetes and previous known CVD.

Acute coronary thromboembolic events

The traditional risk factors contribute to and accelerate the development of atherosclerosis. Severe coronary atherosclerosis itself rarely causes significant symptoms but typically leads to progressively worsening angina, with symptoms arising during physical activity when the heart muscle's oxygen demand exceeds the limited blood flow through the narrowed arteries. The most severe manifestation is when an acute coronary thromboembolic event, or acute coronary syndrome (ACS),

occurs when a thrombus partially or completely occludes the coronary artery. This can occur following the presence of an evident trigger or happen entirely at random.

ACS is defined as encompassing ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA)[144]. ACS is often the first clinical manifestation of CAD, with symptoms ranging from the absence of clear clinical signs to the loss of consciousness and cardiac arrest. Along with the symptoms, ECG findings and high-sensitivity troponin levels guide the final diagnosis, Figure 8.

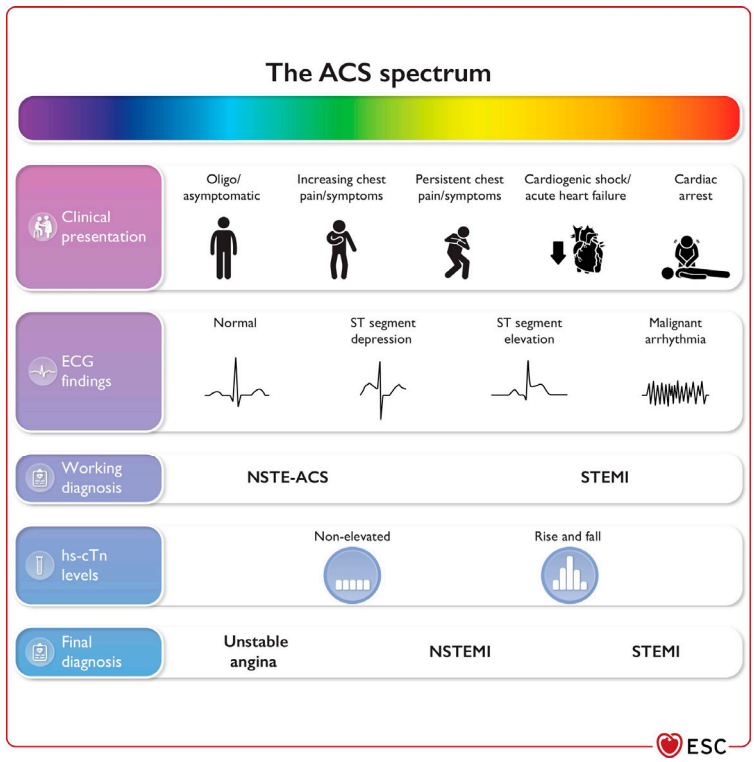


Figure 8. The spectrum of clinical presentations, electrocardiographic findings, and high-sensitivity cardiac troponin levels in patients with acute coronary syndrome [144]. Printed with permission of Oxford University Press.

Myocardial infarction is defined as necrosis of cardiomyocytes due to acute myocardial ischaemia and can be measured by cardiac specific enzymes or troponins. The diagnosis is associated with rise and fall of troponins in combination with symptoms, ECG changes and any evidence of myocardial death by imaging or findings of coronary artery thrombus by angiography[145].

Acute thromboembolic events are most commonly caused by one of three pathogenetic mechanisms[146]. The most frequent cause is the rupture of a thin fibrous cap, which triggers thrombus formation, leading to a partial or complete occlusion of the artery. This is often referred to as vulnerable plaque rupture. The second most common cause of MI is endothelial damage and thrombus formation associated with erosion of the arterial plaque, while the plaque itself remains intact. The characteristics of these two primary causes are illustrated in Figure 9. A third, less common cause of coronary thrombosis is in the presence of a calcified nodule, typically observed in elderly patients with heavily calcified arteries.

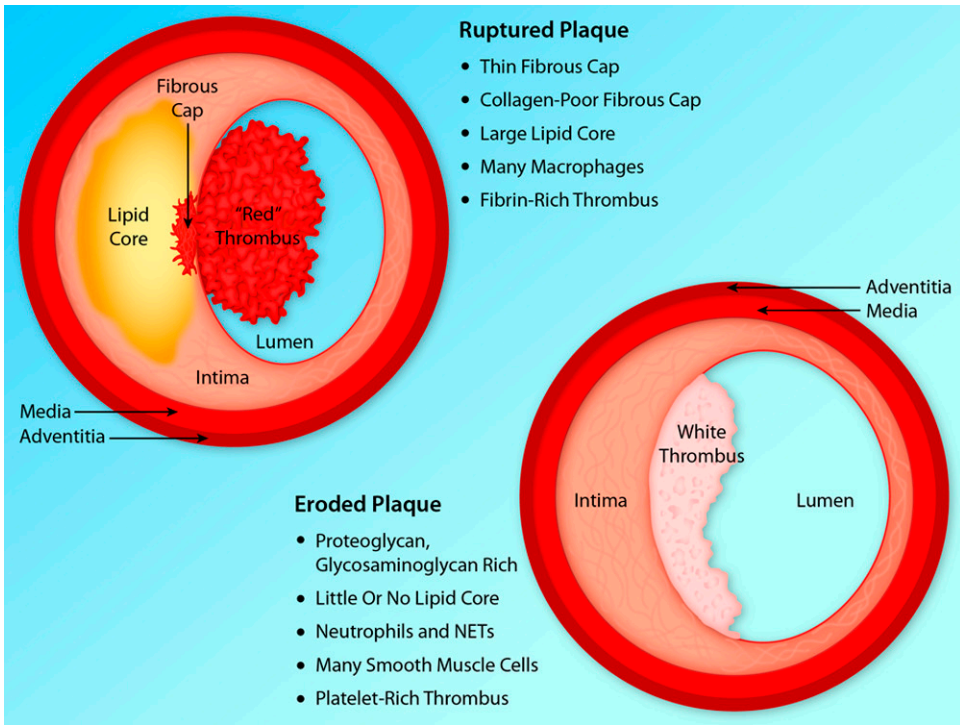


Figure 9. **The two main causes for an ACS, rupture of a vulnerable plaque and a plaque erosion**[147]. Printed with permission from Wolters Kluwer Health, Inc.

The pathophysiological causes of MI have advanced with improvements in intravascular imaging, alongside autopsy studies. Eroded plaques are now increasingly recognized as a common characteristic of culprit lesions in ACS[148,149], Figure 10. This is likely driven by the statin effects on lipid levels and reduced vascular inflammation. These plaque erosions are associated with a better risk profile and outcomes than plaque rupture[148]. Since the fibrous cap still is intact in a scenario of this, a future non-invasive treatment approach has been proposed and a proof-of-concept strategy without stenting is tested in a pilot study[150].

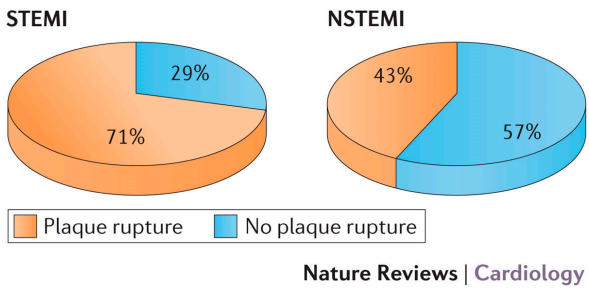


Figure 10. **Distribution of different pathogenesis in STEMI vs NSTEMI**. Data from pathology and OCT studies[151]. Printed with permission of Springer Nature.

The rupture of a vulnerable plaque is considered a high-risk event, and numerous efforts are underway to identify these plaques before clinical symptoms arise. The challenge lies in the fact that less than 5% of vulnerable plaques rupture over a three-year period.[152]. Improved prediction could be achieved through intravascular imaging measurements like large plaque burden, smaller lumen area, thin-cap fibroatheroma, low endothelial shear stress, and high lipid core burden[152-154]. Current evidence suggests that clinically silent plaque ruptures can occur, and that the combination of "vulnerable plaques" in a "vulnerable patient" - along with the prothrombotic environment of circulating blood - appears to be a key factor in triggering acute coronary events[155].

Medical treatment

The acute reperfusion therapy of today, regardless of the pathophysiology, depends on the initial assessment of the ECG and the presence of any ST elevation. If a STEMI is suspected, a percutaneous coronary intervention (PCI) is the evidence-based first-choice strategy, provided it is available within 120 minutes[156]. The focus is to open the coronary artery as soon as possible to restore the oxygen supply to the heart muscle cells to minimize necrosis of cardiomyocytes. If not possible to attain a PCI intervention within mentioned time frame, thrombolysis should be given instead[157,158]. In a patient with a diagnosis of NSTEMI, a coronary angiography is recommended within the time frame that depends on the clinical presentations, hemodynamic instability, arrythmias and selected risk scores[144]. The benefit of early revascularization in this group is primarily the decreased recurrence of ischaemia but its effect on the reduced mortality has not been proven[159]. In the case of multivessel-disease, coronary artery bypass grafting (CABG) may be a better strategy than PCI in selected cases[160]. Expected outcome differences should be discussed in a multidisciplinary team and guide the patient in choice of treatment[161].

Besides revascularization as the primary treatment strategy, the acute treatment of MI includes oxygen if needed to compensate decreased saturation[162], opioids to

relieve pain, lipid lowering therapy and antithrombotic therapy[144]. The length of hospitalization for an MI has been shortened over the last decades and low-risk STEMI patients could be discharged after 48 hours[163] without increased risk of subsequent events.

Secondary prevention

Secondary prevention with long-term medical therapy, smoking cessation and lifestyle changes should begin in the acute phase and the significance of this part is highlighted in the latest guidelines[22,144], Figure 11.

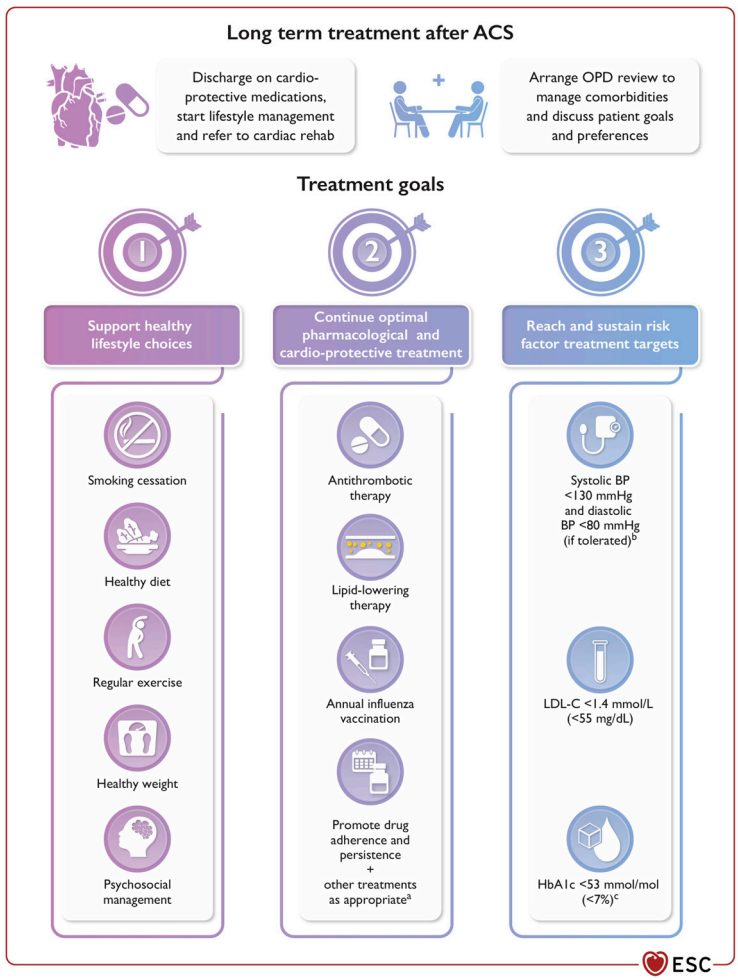


Figure 11. Long-term management after ACS.
OPD, outpatient department.[144] Printed with permission.

Preventing the more acute triggers of MI is challenging and depends on the specific trigger. Some triggers, such as environmental factors, are unavoidable, while others may be mitigated through behavioural changes and stress management programs. Triggers that pose greater risk, particularly in older patients, such as heavy meals and snow shovelling, may be avoidable.

Patient perspective and person-centred care

Myocardial infarction is a severe and often life-threatening event that many patients closely associate with the threat of death, leading to emotional responses such as anxiety, shock, denial or despair. The psychosocial consequences of this experience can be profound, with patients often struggling to access adequate emotional support. Beyond managing the physical illness, patients face the challenge of adapting to a new reality and uncertain future, which can be psychologically challenging[164]. Coping with lifestyle changes, medical treatments, and the emotional burden can complicate recovery. Education level, marital status, social support and a sense of coherence has been positive predictors of good health-related quality of life after newly diagnosed CAD[165]. One review reported that post traumatic stress disorder was prevalent in about 15 % of MI patients[166].

Person-centred care with three main core components consisting of patient's narrative, shared decision-making and documentation of the partnership have been beneficial in the care of patients with myocardial infarction[167]. Patients who actively engage in their own care, receive self-management support, and regular follow-up within coordinated systems, experience better outcomes and higher satisfaction with their care[168].

Study participation

To be invited to participate in a clinical trial during acute illness like MI is challenging, both for the patient and the physician who is responsible for obtaining the inform consent. Ågård et al[169] reported that out of over 700 Swedish physicians in cardiology with experience of including MI patients in trial, 44 percent did not feel that it should be possible to include acute MI patients in clinical trials. Mostly due to the amount of information needed to include and the cognitive capability of the patient.

According to international ethical guidelines[170] the researchers have a duty to:

- Seek and obtain consent, but only after providing relevant information about the research and ascertaining that the potential participant has adequate understanding of the material facts;
- Refrain from unjustified deception or withholding of relevant information, undue influence, or coercion;
- Ensure that the potential participant has been given sufficient opportunity and time to consider whether to participate; and
- As a general rule, obtain from each potential participant a signed form as evidence of informed consent. Researchers must justify any exceptions to this general rule and seek the approval of the research ethics committee.

A patients' participation in a clinical trial has been described as both beneficial and challenging[171-174]. Facilitating factors include trust in healthcare professionals, hope for better treatment, increased care and monitoring, and the opportunity to contribute to research. However, barriers such as lengthy trial duration, intensive testing, significant time commitment, concerns about the investigational drug or device, and lack of confidence in study personnel can hinder participation.

Emergency consent and ethical guidelines

The informed consent process in emergency settings poses additional challenges. Barriers include time constraints due to urgent, life-saving treatments and the severity of illness symptoms, which can hinder the ability to provide or comprehend detailed information.

Informed consent in emergency settings is guided by ethical frameworks such as the Declaration of Helsinki and the Belmont Report, both emphasizing respect for autonomy, beneficence, and justice[175,176]. These guidelines advocate for voluntary, informed participation, but their application is complicated in emergencies where patients may lack the capacity to consent. In such cases, alternatives like obtaining consent from a legally authorized representative (LAR) or using deferred consent may be necessary. In Sweden, legal restrictions prevent certain elements of these frameworks from being fully applicable, especially regarding the designation of a legally authorized representative (LAR), which is a critical consideration in emergency research.

The Council of International Organizations of medical sciences (CIOMS) guidelines[170] , based on recommendations from the Declaration of Helsinki, recommend ethics committee to approve a modification or deferred informed consent to research if following criteria is fulfilled:

- the research would not be feasible or practicable to carry out without the waiver or modification
- the research has important social value
- the research poses no more than minimal risks to participants

There is however only a limited number of trials having the potential for this exception[177] and local ethics committees may interpret guidelines differently, even in similar clinical settings and for the same medical issues.

Traditionally, MI trials have used written prospective consent; however, several studies from the early 2000s highlighted that MI patients enrolled in various trials often had a limited understanding of key research components[178-180] and only a minority of patients read the written information before randomization[179,181,182]. This question gained further attention when the HEAT-PPCI[183] trial was presented in 2014, where deferred consent was used, and no patients were asked about participation prior to randomization. When consent was obtained the day after randomization, only 4 out of 1,829 patients declined participation.

Aims

Overall aims

The first aim of this thesis was to assess patient's experiences of informed consent and study participating in an acute setting to guide future design of studies in this population. The second aim of this thesis was to obtain more knowledge about the reason of increased incidence of myocardial infarction during national holidays.

Specific aims

I. The aim was to study patient experience in relation to the informed consent process in the VALIDATE-SWEDEHEART trial.

II. The aim was to obtain better knowledge and understanding of patients experience of participating in the DAPA-MI trial.

III. The aim was to identify the primary triggers of MI during Christmas, hypothesising that an increased incidence of MI during the Christmas holidays is triggered by emotional stressors, physical activity, and excessive food and alcohol consumption.

IV. The aim was to identify self-experienced triggers of MI and discern potential sex differences.

V. The aim was to remotely assess changes in cardiac and activity metrics in patients with CIED during three major national holidays in Sweden over a five-year period.

Methods

Overview

A summary of the methods used in the papers included in this thesis, Table 1.

Table 1. Overview of methods used in the papers.

Paper	I	II	III	IV	V
Design	Cross-sectional	Qualitative	Case-control	Cross-sectional	Retrospective cohort
Data	Structured telephone interview, four questions	Semi-structured interviews	Postal questionnaire Swedeheart-Scaar+Riks-HIA	Postal questionnaire Swedeheart Riks-HIA	CareLink database (Medtronic) Med. records
Study population	414 participants in the VALIDATE- trial from three sites	21 participants in the DAPA-MI trial from four sites	189 participants with MI during Christmas and 157 controls	451 MI patients	96 patients with CIED, 645 holiday observations
Setting	Lund, Örebro, Umeå	Centralized web-interviews	Nationwide	Nationwide	Lund
Data-collection	2015-2016	2021-2022	2018-2020	2018-2020	2015-2020
Purpose	Patient experience of IC process	Experience of study-participation and remote monitoring adherence	Identify potential triggers of MI during Christmas	Identify potential triggers of MI and discern potential sex differences	Assess the relationship between cardiac and activity measurements and national holidays
Analysis/statistic	Descriptive, Chi-square test	Qualitative content analysis	Chi-square, summative content analysis	Logistic regression	Linear mixed model
Clinical Trial.gov /Ethical permission	NCT02311231	NCT04564742 (Dapa-MI) 2021-02963	2019/01586	2019/ 01586	2020-05843, 2021-05826-01

National quality registry

In **paper I- IV** The Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART)[184] is involved, either as part of the main trial or as the source for population recruitment. This is a national quality register and today merger of seven different registries including patients with MI during hospitalization (Riks-HIA) and follow-up (SEPHIA), patients undergoing coronary interventions (SCAAR) and aortic valve interventions (SWENTRY). Recent years patients with heart failure (SwedeHF) and cardiac surgery (Swedisch Cardiac Surgery Registry) are added to SWEDEHEART as well as an initiation of a cardiogenetic registry. Since all residents in Sweden have a unique personal identification number, data in SWEDEHEART could be linked to other registries. The unique contribution to high quality care using quality indicators and in addition the possibility to perform randomized, double-blind trials have made the registry to one of the most valuable registries worldwide.

Paper I and II were related to two different randomized registry clinical trials (RRCT) performed within the SWEDEHEART-registry.

In paper III and IV the population was retrieved from the Riks-HIA and matched controls used in paper III were taken from the SCAAR-registry.

Paper I

Main trial

The VALIDATE-SWEDEHEART trial (Bivalirudin versus Heparin in ST-Segment and Non–ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy in the Swedish Web System for Enhancement and Development of Evidence-based Care in Heart Disease Evaluated according to Recommended Therapies Registry Trial)[185] was a multicentre, registry-based, open-label, randomized controlled clinical trial. When admitted to hospital with a diagnosis of STEMI or NSTEMI and urgent PCI was planned, patients were screened for eligibility criteria. Informed consent (IC) was obtained in the coronary catheterization laboratory. For the STEMI group, patients provided witnessed oral consent prior to undergoing PCI, which was later supplemented with a written confirmation. In the NSTEMI group, written IC was required before randomization.

Sub study; population, procedure and statistics

This sub study was conducted at three of the hospitals involved in the main trial. During the telephone follow-up call one week after inclusion, as per the main study protocol, patients who had already consented to the primary trial were consecutively recruited for this sub study. They were asked to respond to a survey consisting of four questions:

- Do you remember being asked to participate in a study?
- How was your experience of being asked to participate; do you remember it being positive or negative?
- Would you have liked more information about the study?
- Do you think it would have been better if you were included in the study without being informed until a later time?

Study-specific research nurses conducted the telephone follow-up calls. Data were collected using a predefined matrix, and the responses were subsequently compiled and analysed.

Categorical variables were analysed using the chi-square test to assess differences in proportions between groups. If the number of observations was too low, Fisher's exact test was applied. A p-value of <0.05 was considered statistically significant. The subgroup analysed were STEMI/NSTEMI diagnosis, sex and age and these were performed using the same statistical methods.

Paper II

Main trial

The DAPA-MI (Dapagliflozin in Patients without Diabetes Mellitus with Acute Myocardial Infarction) was a registry-based, double-blind, randomized controlled clinical trial. The protocol permitted inclusion and randomization within 10 days of admission for MI (index hospitalization). The first follow-up visit was scheduled 6 to 10 weeks after randomization, with subsequent visits planned at 10-month intervals.

The DAPA-MI trial utilized a smart cap attached to study drug bottles, equipped with wireless technology (CleverCap Lite; Compliance Meds Technologies, Ives

Estates, FL, USA) to monitor medication adherence, Figure 12. When the cap was opened, a wireless signal was transmitted to a central portal via the 3G network. This real-time monitoring allowed for fewer trial visits for participants. If unexpected usage patterns were detected, an automated email notification was sent to research nurses to follow up with the patient. The cap featured an integrated audio notification system that emitted a sound when opened and could also alert patients to low battery status.

Figure 12. The smart cap used in the DAPA-MI trial, CleverCap Lite. Copyright Compliance Meds Technologies LLC, Miami, FL, USA. Printed with permission.

Interview study; population, procedure and analysis

The ten top-recruiting sites in Sweden to the main trial were asked to recruit patients to the interview study. Four out of these ten sites accepted the invitation and recruited patients during their first follow-up visit. Eligible patients were those with access and ability to use a web-based communication platform. Digitally semi-structured interviews were performed using zoom-application and verbal consent was obtained in the beginning of the interview. Four main questions formed the basis of the interview:

- How did you experience being asked to participate in a clinical trial?
- How did you experience the information about the DAPA-MI trial?
- What is your experience using the bottle cap?
- What is your experience with the technology around the bottle cap?

Recruiting process continued until no substantial content was acquired according to first author who performed the interviews. The semi-structured interviews were analysed using manifest qualitative content analysis, following the approach outlined by Graneheim and Lundman[186]. Each step of the analysis was discussed, revised, and conducted in collaboration with the author of this thesis.

Paper III and IV

Population, questionnaire and design

In these studies, we identified patients with MI on specific dates through the Riks-HIA registry, while controls for **Paper III** were retrieved from the SCAAR registry. In both studies, we used a self-designed questionnaire to assess the experience of potential triggers. The questionnaires consisted of 27 potential triggers with additional questions about tobacco use, symptoms, social activities and a possibility to describe any potential trigger or reason for increased stress. The questionnaire was slightly modified depending on the target group. It was sent out together with an information letter and an informed consent form. Attached on the following two sides is the translated version of the questionnaire sent to patients who experienced an MI during Christmas.

The last 24 hours before your myocardial infarction consisted of:

Tick the appropriate box.

1=much less than usual, 2=a little less than usual, 3=as usual, 4=a little more than usual, 5=much more than usual and "Not at all/not applicable"

Activities

To what extent did you engage in following activities?	1 Much less than usual	2 A little less than usual	3 As usual	4 A little more than usual	5 Much more than usual	Not at all/ Not applicable
1. Physical activities	☐	☐	☐	☐	☐	☐
2. Longer trip (car/train/flight)	☐	☐	☐	☐	☐	☐
3. Snow shoveling	☐	☐	☐	☐	☐	☐
4. Cleaning	☐	☐	☐	☐	☐	☐
5. Cooking	☐	☐	☐	☐	☐	☐
6. Outdoor activities	☐	☐	☐	☐	☐	☐
7. Insomnia	☐	☐	☐	☐	☐	☐
8. Sexual activity	☐	☐	☐	☐	☐	☐
9. Compliance to prescribed medication	☐	☐	☐	☐	☐	☐

Emotion

To what extent did you experience following emotions?	1 Much less than usual	2 A little less than usual	3 As usual	4 A little more than usual	5 Much more than usual	Not at all/ Not applicable
10. Joy	☐	☐	☐	☐	☐	☐
11. Happiness	☐	☐	☐	☐	☐	☐
12. Stress	☐	☐	☐	☐	☐	☐
13. Exhilaration	☐	☐	☐	☐	☐	☐
14. Anxiety	☐	☐	☐	☐	☐	☐
15. Depression	☐	☐	☐	☐	☐	☐

Emotion

To what extent did you experience following emotions?	1 Much less than usual	2 A little less than usual	3 As usual	4 A little more than usual	5 Much more than usual	Not at all/ Not applicable
16. Loneliness	☐	☐	☐	☐	☐	☐
17. Sadness	☐	☐	☐	☐	☐	☐
18. Worry	☐	☐	☐	☐	☐	☐
19. Anger	☐	☐	☐	☐	☐	☐
20. Feeling upset	☐	☐	☐	☐	☐	☐
21. Troubles	☐	☐	☐	☐	☐	☐
22. Quarrel/conflicts	☐	☐	☐	☐	☐	☐
23. Financial worries	☐	☐	☐	☐	☐	☐

Food and drinks

To what extent did you eat and drink the current day?	1 Much less than usual	2 A little less than usual	3 As usual	4 A little more than usual	5 Much more than usual	Not at all/ Not applicable
24. Food	☐	☐	☐	☐	☐	☐
25. Fatty food	☐	☐	☐	☐	☐	☐
26. Sweets	☐	☐	☐	☐	☐	☐
27. Alcohol	☐	☐	☐	☐	☐	☐

28. How many standard alcoholic drinks did you drink the current day?

- ☐ Less than one
- ☐ 1-4 standard drinks
- ☐ 5-9 standard drinks
- ☐ 10-14 standard drinks
- ☐ 15 or more standard drinks

One standard drink (12 g) corresponds to:

The last 24 hours before your myocardial infarction

General

29. Did you smoke tobacco the current day? ☐ Yes → Number of cigarettes/cigars or equivalent ☐☐
☐ No

30. Du you usually smoke? ☐ Yes → Number of cigarettes/cigars or equivalent per day ☐☐
☐ No

31. Who did you socialize with the current day?
Several choices are possible

- ☐ Closest family (children, siblings, parents, partner)
- ☐ Larger family gathering
- ☐ Neighbours
- ☐ Friends
- ☐ Nobody

32. Which of the following best matches your physical activity normally?
Only one answer is possible

- ☐ Hardly any physical activity
- ☐ Mostly sitting, sometimes a walk, light household activities
- ☐ Light physical exercise around 2- 4 h a week, such as walks, ordinary gardening, cleaning
- ☐ Moderate exercise 1- 2 h a week, such as jogging, heavy gardening, cleaning or light physical activities more than 4 h a week
- ☐ Moderate exercise as least 3 h a week, such as tennis, swimming
- ☐ Hard or very hard exercise regularly and several times a week

Symptoms 24 hours before up to your myocardial infarction

To what extent did you have the following symptoms?	1 Muck less than usual	2 A little less than usual	3 As usual	4 A little more than usual	5 Much more than usual	Not at all/ Not applicable
33. Fatigue	☐	☐	☐	☐	☐	☐
34. Dyspnea	☐	☐	☐	☐	☐	☐
35. Chestpain	☐	☐	☐	☐	☐	☐
36. Chestpain/dyspnea on slight exertion	☐	☐	☐	☐	☐	☐

37. When did your symptoms begin?

- ☐ Just before Christmas festivities
- ☐ During Christmas festivities
- ☐ Shortly after the festivities
- ☐ During the evening several hours after the Christmas festivities
- ☐ Other occasion: ☐
- ☐ Did not celebrate Christmas

Did you have any of the following symptoms in the last 24 hours before having your heart attack?

	Yes	No
38. Current infection	☐	☐
39. Nausea	☐	☐
40. General sense of illness	☐	☐
41. Syncope/sense of syncope	☐	☐
42. Cardiac arrest	☐	☐

43. Which was your main symptom? ☐

44. On whose initiative was contact with health care made? ☐ My own ☐ Relative/friends ☐ Other

45. How did you get to the hospital? ☐ Ambulance ☐ Other (by your own or got a ride)

46. Can you relate to something else that happened close to your infarction:

47. If you felt stressed, please specify the cause, internal or external circumstanses.

Thank you for your participation!

The responses to the questionnaire consisted of six selectable options. Two of them (not at all/not applicable and as usual) did not represent any changes from baseline. Since we hypothesized that only an increase in any category could act as a trigger, we recoded the answers to 1 for experienced the category more than usual ("a little more than usual" and "much more than usual") and all other answers as 0.

Paper III was a case control study where we compared the responses of MI patients, experienced symptom onset during Christmas (24-26 Dec), to the responses of a control group. The controls were matched 2:1 (Christmas 2018) according to age and sex and were inquired to answer questions about habits and behaviour during Christmas holiday. **Paper IV** was a cross-sectional study of MI patients with symptom onset during both holiday and weekdays and the prevalence of potential trigger was analysed based on sex disparities.

Statistics

In **paper III** the binary outcome of the trigger prevalence between the groups was analysed using chi-square test and Fisher´s exact test if too few observations. The free text was summarized by content and divided into themes. In **paper IV** the outcome of every specific trigger was analysed with multivariate logistic regression and reported as odds ratios (OR). Adjustments for age, infarct-type, history of MI, hypertension, diabetes and smoking were performed. Missing data were less than five percent in all triggers except symptoms. A complete case analysis was conducted in both papers. The analysis of both papers was performed using SPSS version 26.

Paper V

Population, design and variables of interest

This was a retrospective, longitudinal, cohort study. The source for the study population in paper V was the CareLink remote device monitoring database (Medtronic, Inc., Minneapolis, MN) which consist of all patients with cardiac implantable electronic devices (CIED) in Lund using Medtronic´s device. The total sample of this cohort during 2015 and 2020 were 800 individual patients. Within this cohort we were specifically interested in those who had a measurement of intrathoracic impedance during at least one holiday; Christmas, New Year or Midsummer. Midsummer and Christmas holiday 2020 were excluded from analyse due to Covid-19 restrictions and possible bias related to that. The remote database consists of daily measurements of arrhythmias variables, activity variables and fluid measurements. The variables of interest in our study are visualized in Figure 13 and 14. *Daily impedance* is one average value per day of the intrathoracic impedance,

measured in Ohm, based on regular measurements between 12 AM to 5 PM. A decrease in daily impedance indicates an increased intrathoracic fluid retention[187].

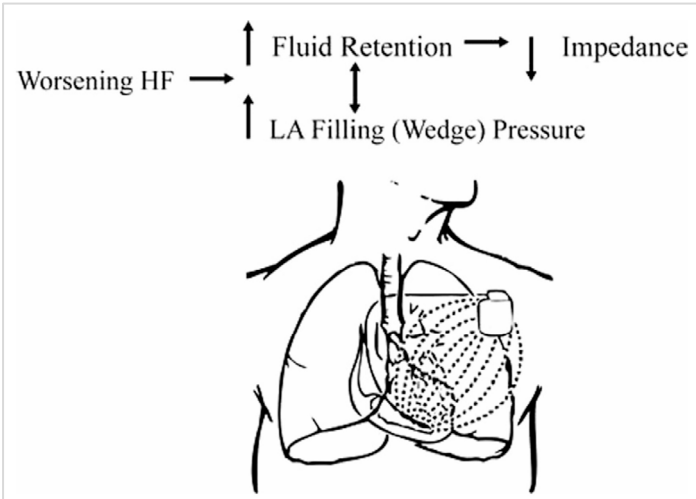


Figure 13. The intrathoracic impedance is measured about 60 times a day between noon and 5 PM using the vector between the device case and the right ventricular lead. A mean value per day is derived. As fluid is retained in the lungs because of worsening heart failure (HF), the impedance decreases. LA = left atrial; ↑ = increase; ↓ = decrease. Printed with permission from Elsevier[187]

The Accumulated difference in Ohm or the *OptiVol fluid index* (OVFI) is derived from the accumulated negative difference between the daily impedance and a running average impedance. The *Threshold crossing* is a binary variable displayed if the OVFI crosses the predeterminate threshold. The threshold for all patients was 60 Ohm, Figure 14.

Day Heart Rate is defined as average heart rate in the 12 h period from 8 AM to 8 PM. *Heart Rate Variability* is defined as the variability value from median ventricular heart rate determined every 5 minutes. Activities of daily living are defined as active minutes per day derived from the rate response accelerometer. In addition to the CareLink database we used medical records to obtain relevant diagnosis, medications and measurements of left ventricular ejection fraction (LVEF), updated for every year of observation.

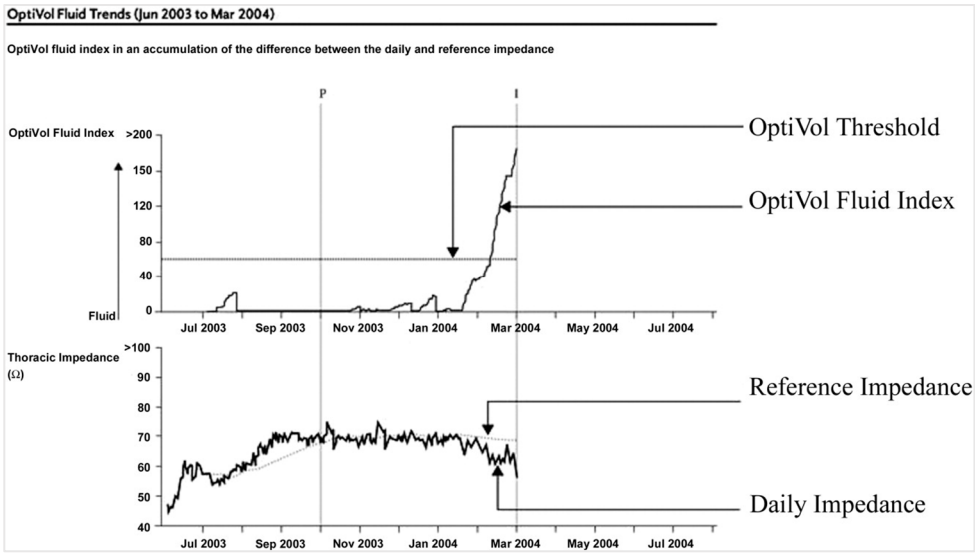


Figure 14. Visual explanation of Optivol Fluid Index (OVFI), threshold and daily intrathoracic impedance. The predefined threshold was 60 for all patients. When the daily impedance decreases for several consecutive days, the OVFI increases accordingly. Printed with permission from Elsevier[187].

The outcome estimate in this study was the difference between baseline period and the holiday in intrathoracic impedance, physical activity, day heart rate, heart rate variability and OVFI. The baseline period for Christmas and New Year was defined as mean value of 21, 22 and 23 of December. The baseline period for Midsummer holiday was three days preceding Midsummer Eve. The holidays were analysed individually with regard to daily impedance and combined for all outcomes. Subgroup analysis of intrathoracic impedance was performed in groups categorized by LVEF above or less than 40 %, previous medical history, activity level and decrease in activity.

Statistics

Baseline characteristics were presented as counts and percentages for categorical data and as means and standard deviations for continuous data. The normality of the outcome variables was assessed visually using histograms. The outcome estimate, the difference between baseline and holiday, was analysed using a linear mixed-effect model, accounting for repeated measurements from patients with a random effect at the patient level. Fixed effects included time (baseline vs. holiday), sex, age, and selected subgroups in the secondary analysis. Due to significant variability in individual baseline impedance values, graphs were generated using percentage differences. A two-sided p-value of less than 0.05 was considered statistically

significant. The distribution of the OVFI was highly right skewed, necessitating the use of median values in the graphs. Since the residuals were normally distributed, no transformation was required in the model estimation. STATA version 18.0 for Windows was used.

Ethical considerations

All studies were conducted in accordance with the Declaration of Helsinki[188] and approval was given by the ethical review board of Lund or the Swedish ethical review authority. All ethical approval diary numbers are included in Table 1.

The SWEDEHEART registry does not require mandatory written consent. All patients are informed about the registry upon admission or during hospitalization, with the option to opt out. Written consent was obtained for the clinical trials referenced in **papers I and II**, from which patients were selected, and verbal consent was secured prior to their inclusion in the interview studies. In **papers III and IV**, written consent was obtained and was sent along with the postal questionnaire. **Paper V** was a retrospective study, with ethical approval permitting research in patients with ICD/CRT devices using data from the CareLink database, along with relevant diagnoses and imaging from medical records, without requiring written consent from the patients. Given that many of the patients were deceased at the time of the study, obtaining consent through other means would have been challenging.

All studies in this thesis, except for Paper V, focus on patient perspectives related to myocardial infarction or chronic coronary artery disease. While these experiences are invaluable for understanding the patient journey, they are difficult to quantify, as they reflect individuals during a critical and vulnerable period in their lives. These patients, having recently experienced a myocardial infarction, are impacted in multiple ways—physically, emotionally, and psychologically. Data on their experiences is collected at different time points and contexts following the infarction, capturing their perceptions before, during, and after hospitalization. Ensuring that these sensitive perspectives are gathered ethically and respectfully is a core consideration throughout the research.

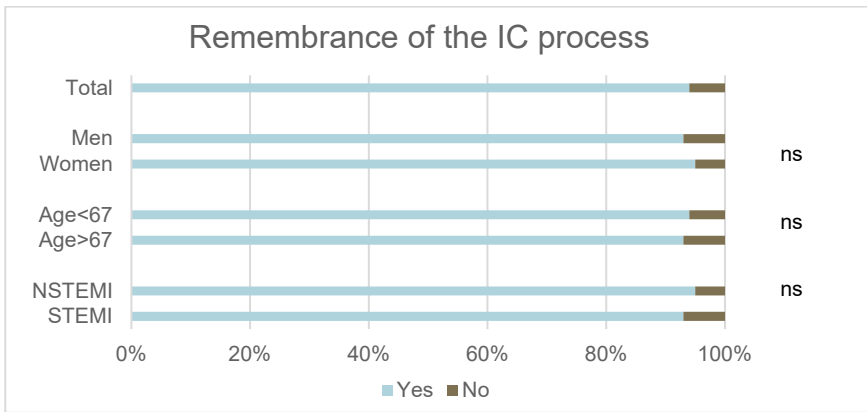
All studies included extensive data sets with sensitive personal data and careful handling, including secure data system, was required to ensure that potential harm was avoided.

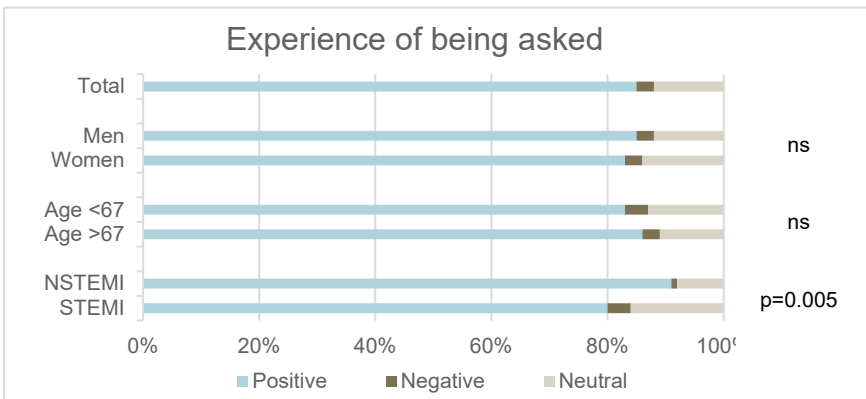
Results

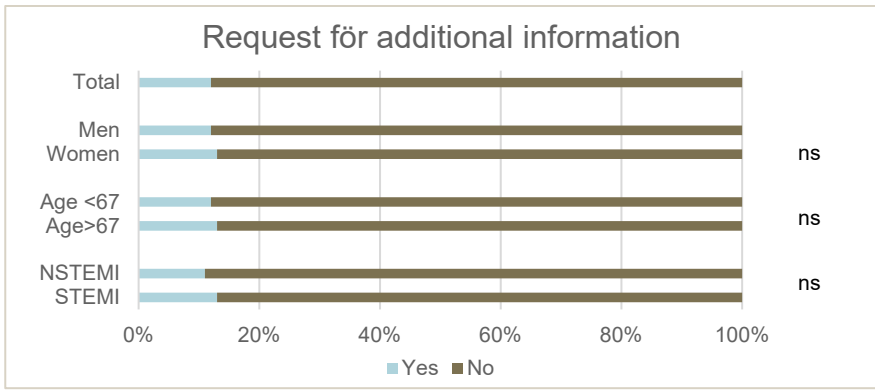
Paper I

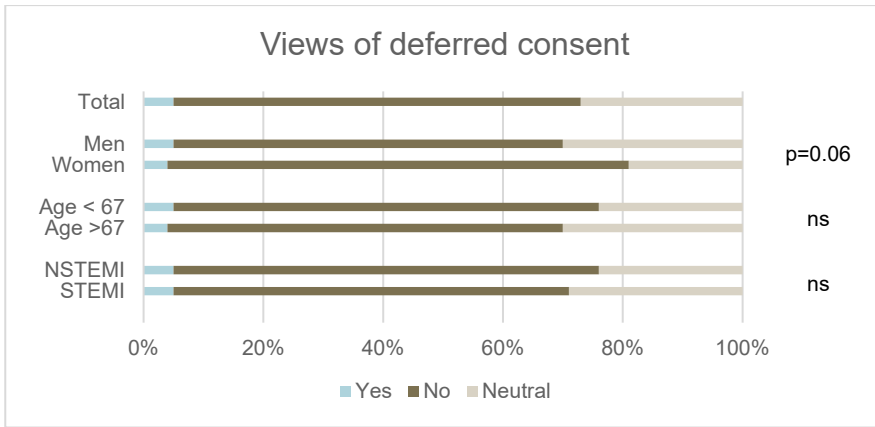
A total number of 414 patient were included in the study. Of these, 25 % were women, 56 % had STEMI, 23 % current and 37 % former smokers, 15 % with previous MI and 1.5 % had cardiopulmonary resuscitation before arrival at the catheterization laboratory. Median age was 67 years (IQR 59-73).

Below are the results derived from the four questions, visualized in bar graphs.









In total 94 % remembered the IC process and being included in a study. Of those, 85% experienced this as positive and 88 % did not request additional information. Five percent thought it would have been better to be included without any consent until a later timepoint. No significant differences were seen between the groups except that the STEMI population were less positive to be asked in the emergency setting.

Paper II

In the semi-structured interview study, 25 patients included in the main trial DAPA-MI initially accepted being contacted by the main researcher for interviews. Four of these were later excluded due to lack of response when the main researcher attempted to make contact or because they later declined participation in the interview. Seventeen of the participants were men and four were women, with a median age of 59 years, ranging from 44 to 80 years.

The analysis resulted in four categories: *A willingness to contribute*, *The perception of information*, *Be in a vulnerable situation* and *Adaption to a new technology,* Figure 15.

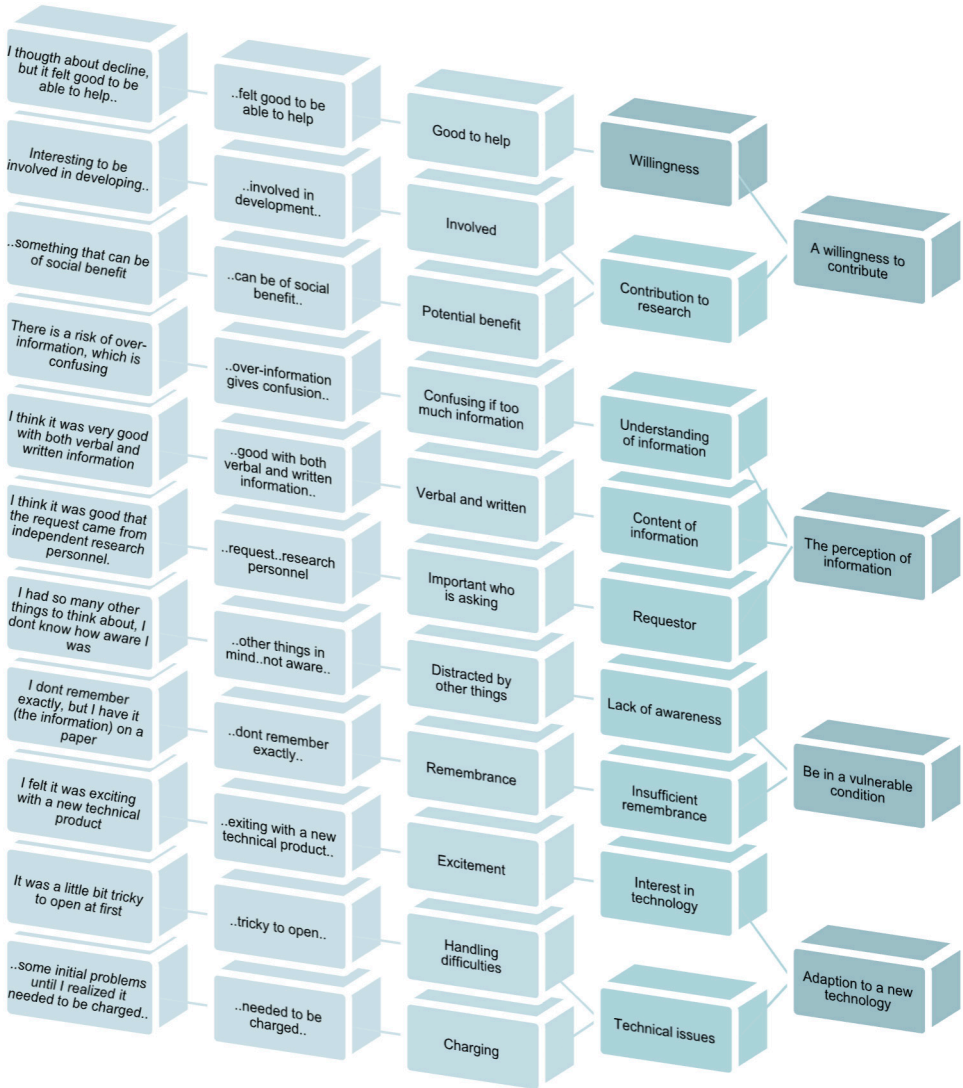


Figure 15. Examples of meaning units, condensed meaning units, codes, sub-categories and the main categories.

Paper III

A total of 542 patients were identified in the SWEDEHEART registry and received a postal questionnaire along with informed consent forms. This included 287 patients who experienced a myocardial infarction during Christmas in 2018 or 2019, and 255 patients in the matched control group. The overall response rate was 64%. In the MI-Christmas group, 189 patients (66%) completed the questionnaire, while 157 patients (62%) from the control group responded. Baseline demographic information is shown in Table 2. In the MI population, 30% had STEMI, and 70% had NSTEMI.

Table 2. Baseline demographics of study groups. Presented as numbers (%) unless otherwise stated.

	MI-Christmas		Control-group	
Characteristics	**Responders**	**Non-responders**	**Responders**	**Non-responders**
Number (%)	189 (65.9)	98 (34.1)	157 (61.6)	98 (38.4)
Mean (SD) age (years)	72.8 (10.3)	72.3 (12.3)	73.3 (9.5)	72.4 (12.6)
Male	130 (68.8)	64 (65.3)	110 (70.0)	67 (68.4)
Mean (SD) BMI	27.3 (4.6)	27.1 (4.9)	27.1 (4.1)	27.6 (4.4)
Current smoker	28 (14.8)	24 (24.5)	11 (7.0)	9 (9.2)
Medical history				
Diabetes	46 (24.3)	36 (36.7)	23 (14.6)	22 (22.4)
Hypertension	117 (61.9)	74 (75.5)	131 (83.4)	82 (83.7)
Myocardial infarction	53 (28.0)	41 (41.8)	55 (35.0)	34 (34.7)
PCI	38 (20.1)	29 (29.6)	66 (42.0)	38 (38.8)
CABG	19 (10.1)	8 (8.2)	15 (9.6)	12 (12.2)
Chronic heart failure	11 (5.8)	11 (11.2)		
Stroke	9 (4.8)	4 (4.1)		

Activity

No activity, reported as more than usual, was more frequently expressed by patients with MI during Christmas compared to the control group. Cleaning (9% vs. 21%, p=0.001) and outdoor activity (5% vs 12%, p=0.03) were more commonly reported by responders in the control group. All activities are illustrated in Figure 16. Both groups reported decreased physical activity during Christmas, 25% in MI group versus 31% in the control group. Lower medication adherence than usual was reported by 1.6% of the MI group compared to 0.6% of the control group. The complete percentage distribution of responses from both groups is included in supplementary material, Table 1.

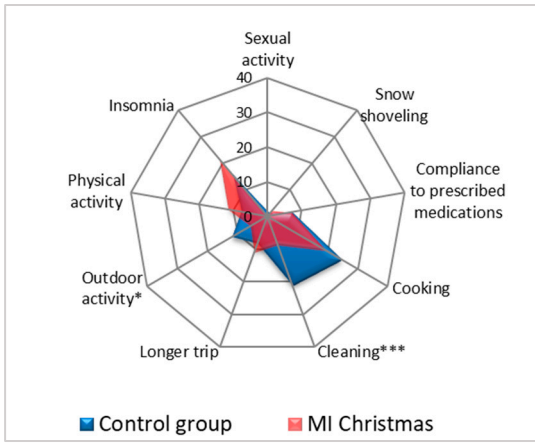


Figure 16. Report of a little more or much more of activities than usual in the 24 h pre-MI or 24–26 Dec in the control-group. Values represent the percentage of responders. *p < .05, **p < .01, ***p < .001.

Emotions

Stress (37% vs. 21%, p=0.002), depression (21% vs. 11%, p=0.02) and worry (26% vs. 10%, p <0.001) were more frequently reported by patients with MI during Christmas compared to the control group. The distribution of increased emotions in MI group and the control group is illustrated in Figure 17. Detailed responses are presented in the supplementary material, Table 2.

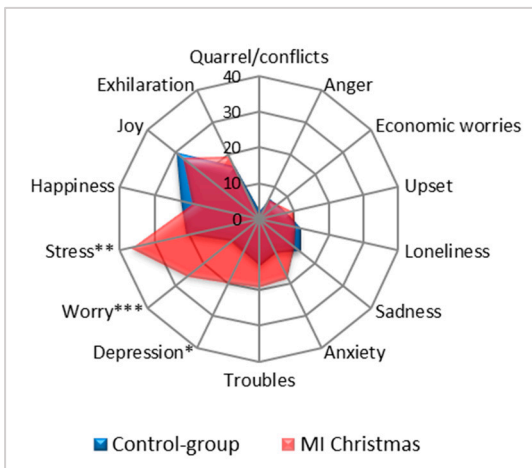


Figure 17. Report of a little more or much more of emotions than usual in the 24 h pre-MI or 24–26 Dec in the control-group. Values represent the percentage of responders. *p < .05, **p < .01, ***p < .001.

Food, sweets, alcohol consumption and symptoms

In the MI group, 33% reported increased food consumption compared to 43% in the control group (p=0.002). A similar pattern was observed for sweet consumption, with 32% in the MI group versus 43% in the control group (p=0.03). No significant differences were found in fatty-food or alcohol consumption between the two groups, Figure 18.

Symptoms were more frequently reported by the MI group, both fatigue, dyspnoea and chest pain were significantly more reported among the MI population, illustrated in Figure 18. Detailed responses about food, alcohol and symptoms are presented in the supplementary material, Table 3.

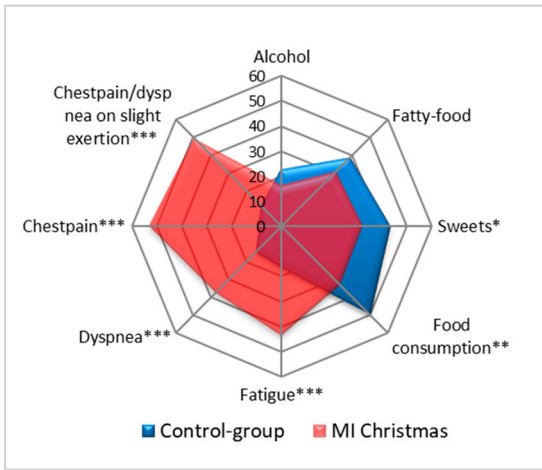


Figure 18. Report of a little more or much more of food, alcohol and symptoms than usual in the 24 h pre-MI or 24–26 Dec in the control-group. Values represent the percentage of responders. *p < 0.05, **p < 0.01, ***p < 0.001.

Paper IV

The population in this study consisted of patients diagnosed with type I MI, with symptom onset occurring on pre-defined days, covering both weekdays and holidays (5–7 December, 24–26 December 2018, 14–16 January, 30–31 May, 21–22 June, 8–9 July, and 24–26 December 2019). A total of 765 patients were identified in the SWEDEHEART registry and received a postal questionnaire along with informed consent forms. Baseline demographics and differences between responders and non-responders, as well as differences between men and women, are presented in Table 3.

Table 3. Baseline demographics of responders and non-responders. Presented as numbers (%) unless otherwise stated.

Characteristics	Responders	Non-responders	p-value	Female responders	Male responders	p-value
Number (%)	451 (59.0)	314 (41)		134 (29.7)	317 (70.3)	
Mean (SD) age (years)	71.6 (10.5)	71.1 (12.6)	0.58	73.9 (10.6)	70.6 (10.3)	**<0.01**
Mean (SD) BMI	27.1 (4.4)	27.8 (5.1)	0.05	26.3 (4.8)	27.4 (4.1)	**0.02**
Current smoker	62 (13.7)	70 (22.3)	**<0.01**	21 (15.7)	41 (12.9)	0.44
STEMI	145 (32.1)	104 (33.1)	0.78	30 (22.4)	115 (36.3)	**<0.01**
Medical history						
Diabetes	97 (21.5)	106 (33.8)	**<0.001**	23 (17.2)	74 (23.3)	0.30
Hypertension	262 (58.1)	227 (72.3)	**<0.001**	88 (65.7)	174 (54.9)	0.08
Myocardial infarction	114 (25.3)	120 (38.2)	**<0.001**	29 (21.6)	85 (26.8)	0.46
PCI	92 (20.4)	91 (29.0)	**0.02**	16 (11.9)	76 (24.0)	**0.02**
CABG	43 (9.5)	27 (8.6)	0.66	6 (4.5)	37 (11.7)	**0.02**
Chronic heart failure	30 (6.7)	40 (12.7)	**<0.01**	3 (2.2)	27 (8.5)	**0.01**
Stroke	27 (6.0)	17 (5.4)	0.27	8 (6.0)	19 (6.0)	0.98

Values are numbers and percentages unless stated otherwise. Significant differences between groups in bold. BMI, body mass index; SD, standard deviation. PCI, percutaneous coronary intervention. CABG, coronary artery bypass grafting.

Sex perspectives

Of the three main categories, 64% of women reported experiencing at least one emotional trigger more than usual, compared to 53% of men (p=0.03), Table 4.

Table 4. Sex differences in reported trigger on group-level.
*Adjusted for age, previous MI, hypertension, diabetes, smoking, and NSTEMI/STEMI.

Reported trigger	Male, n (%)	Female, n (%)	Crude female: male OR			Adjusted* female: male OR		
			OR	95 % CI	p-value	OR	95 % CI	p-value
Activities	140 (44.2)	64 (47.8)	1,16	0,77-1,73	0,483	1,27	0,83-1,96	0,273
Emotions	168 (53.0)	86 (64.2)	1,59	1,05-2,41	0,029	1,71	1,1-2,69	0,017
Food and alcohol	91 (28.7)	32 (23.9)	0,78	0,49-1,24	0,294	0,92	0,56-1,49	0,725

The most commonly reported individual trigger was stress, reported by 50% of women compared to 30% of men, with an OR of 2.33 (95% CI: 1.53–3.55, p<0.001). Other emotional triggers were also reported more frequently by women than men, including sadness (OR 3.52, 1.92–6.45), feeling upset (OR 2.69, 1.47–4.95), anger (OR 2.49, 1.20–5.16), loneliness (OR 2.33, 1.24–4.40), anxiety (OR 2.21, 1.33–3.67), worry (OR 2.17, 1.36–3.46), and depression (OR 2.06, 1.26–3.36), Figure 19.

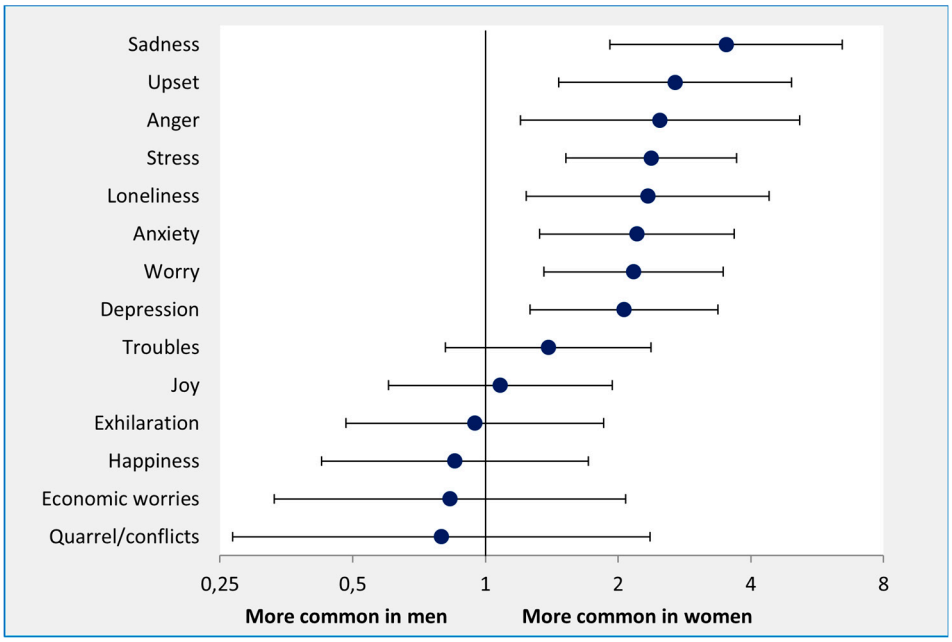


Figure 19. Odds ratio female: male. Emotions. Adjusted for age, previous myocardial infarction, hypertension, diabetes, smoking, and STEMI/NSTEMI.

Outdoor activity was reported more frequently in men, (OR 0.35, 0.14–0.87) while cooking (OR 2.77, 1.45–5.27), cleaning (OR 2.39, 1.01–5.67), and insomnia (OR 2.31, 1.39–3.82) were reported more often by women, Figure 20.

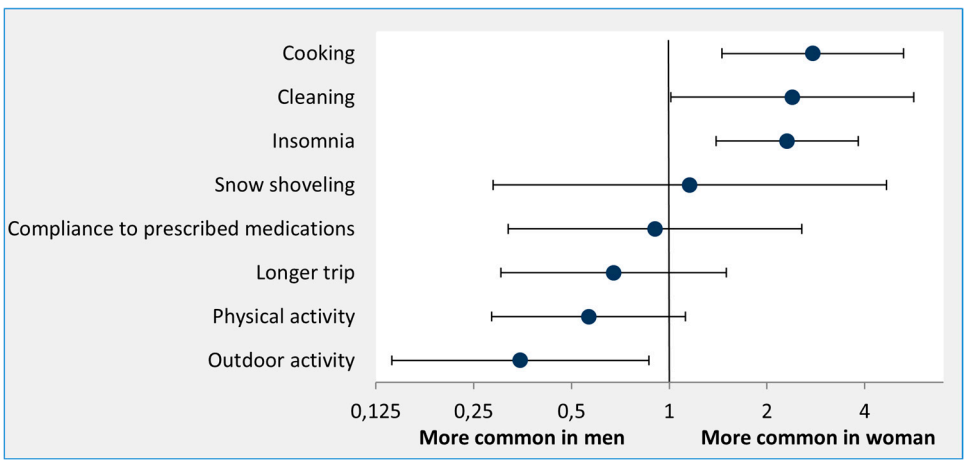


Figure 20. Odds ratio female: male. Activities. Adjusted for age, previous myocardial infarction, hypertension, diabetes, smoking, and STEMI/NSTEMI.

No sex differences were observed in food consumption (OR 0.70, 0.38–1.28) or alcohol intake (OR 1.02, 0.51–2.06), Figure 21.

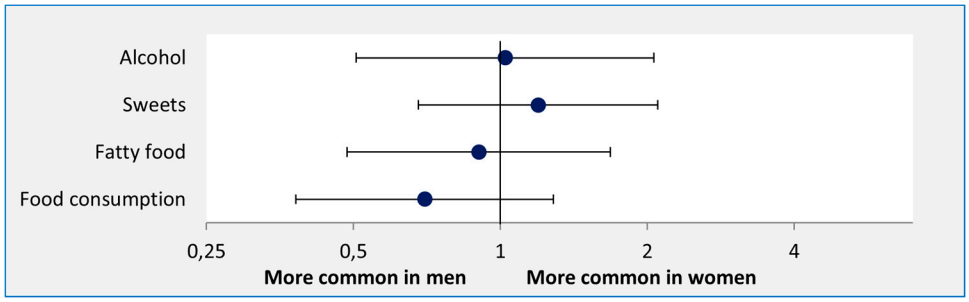


Figure 21. Odds ratio female: male. Food and drink. Adjusted for age, previous myocardial infarction, hypertension, diabetes, smoking, and STEMI/NSTEMI.

Women reported increased symptoms of fatigue (OR 1.74, 1.12-2.69), general sense of illness (OR 2.12, 1.30-3.43) and nausea (OR 2.55, 1.26-4.11) more often than men, Figure 22. The total distribution of answers for all categories is provided in the supplementary material, Tables 5–7.

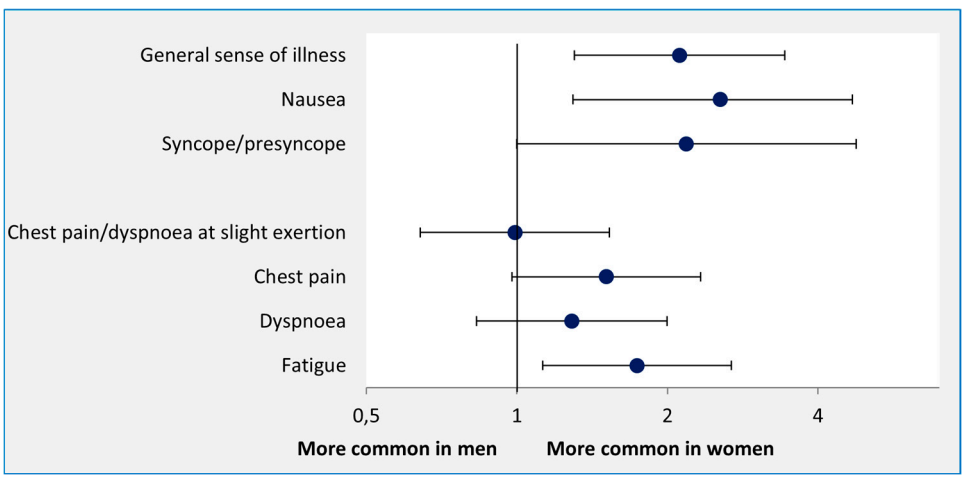


Figure 22. Odds ratio female: male. Emotions. Adjusted for age, previous myocardial infarction, hypertension, diabetes, smoking, and STEMI/NSTEMI.

Paper V

In total 96 patients had thoracic impedance monitoring and fulfilled the inclusion criteria for further analysis. The monitoring data covered an average of 2.2 years per patient, contributing to a total of 245 patient-years and 649 patient-holidays. Baseline demographics are shown in Table 5. In summary, the cohort exhibited a mean age of 69 years, predominantly comprising of males. About four out of five patients had a CRT device, and over two-thirds of the patients had an LVEF below 40% at baseline. Patients with LVEF more than 40% had more often a history of arrythmias and a secondary prevention ICD compared with patients with lower LVEF. In patients with normal LVEF, 85% of the observations had a secondary prevention ICD.

Table 5. Patient and observation characteristics.

	Patients, upon inclusion	Christmas, observations	New Year, observations	Midsummer, observations	In total observations
Number of patients/observations	96	217	213	219	649
Age, years (SD)	69 (10)	69 (11)	69 (11)	70 (10)	69 (10)
Male gender, n (%)	79 (82)	177 (82)	173 (81)	177 (81)	527 (81)
CRT, n (%)	75 (78)	149 (69)	146 (69)	149 (68)	444 (68)
ICD, n (%)	88 (92)				
- primary	64 (67)	143 (66)	140 (66)	138 (63)	419 (65)
- secondary	24 (25)	61 (28)	60 (28)	71 (32)	194 (30)
Hypertension, n (%)	59 (61)	126 (58)	123 (58)	129 (59)	380 (59)
Diabetes, n (%)	31 (32)	67 (31)	66 (31)	64 (29)	199 (31)
Cardiomyopathy, n (%)	91 (94)				
- ischemic	35 (36)	75 (35)	75 (35)	81 (37)	223 (36)
- non-ischemic	56 (58)	125 (58)	122 (57)	119 (54)	364 (56)
Atrial fibrillation, n (%)	49 (51)				
- paroxysmal	23 (24)	47 (22)	47 (22)	50 (23)	144 (22)
- persistent	26 (27)	62 (29)	61 (29)	62 (28)	185 (29)
Kidney failure, n (%)	33 (34)	64 (29)	63 (30)	69 (32)	198 (31)
Ejection fraction, n (%)					
>50%	5 (5)	20 (9)	18 (8)	22 (10)	60 (9)
40-49 %	13 (14)	40 (18)	40 (19)	41(19)	121 (19)
30-39%	21 (22)	48 (22)	46 (21)	49 (22)	145 (22)
<30 %	54 (56)	97 (45)	97 (46)	90 (41)	282 (43)
missing	3 (3)	12 (6)	12 (6)	17 (8)	41 (6)
Medical treatment (cardiac), n (%)					
Betablockers	92 (96)	207 (96)	204 (96)	209 (95)	621 (96)
ACE-i/ARB/Nepr	87 (91)	189 (88)	186 (87)	187 (85)	561 (86)
MRA	56 (58)	110 (51)	107 (50)	107 (49)	324 (50)
Diuretics	65 (68)	151 (70)	150 (70)	156 (71)	459 (71)
SGLT 2-inh	2 (2)	5 (2)	5 (2)	6 (3)	16 (2)
Statins	59 (61)	134 (62)	134 (62)	137 (63)	406 (63)

Intrathoracic impedance

When Christmas, New Year and Midsummer Day were combined the daily intrathoracic impedance decreased with 1.1 Ohm, 95% CI [-1.6, -0.7], p<0.001 compared to baseline. A non-significant decrease in impedance was observed during Christmas, New Year and Midsummer Eve compared to baseline, -0.2 Ohm, 95% CI [-0.6, 0.3], p=0.47. The percentage change during the combined holiday related to baseline period is visualized in Figure 23.

The decrease in daily intrathoracic impedance remained statistically significant when Christmas and Midsummer Day holidays were analysed individually with a decrease during Christmas Day (- 1.3 Ohm, 95% CI [-2.0, -0.6], p< 0.001), and on Midsummer Day (-1.3 Ohm, 95% CI [-2.0, -0.6], p<0.001). On New Years Day a non-statistically significant trend was observed; -0.6 Ohm, 95% CI [-1.3, 0.1], p = 0.08. The percentage change of impedance for each holiday individually is shown in Figure 23. Twenty five percent of the observations had an impedance drop of 3.2 ohms or more consistently between time periods and ten percent of observations showed an impedance drop of 5.2 ohms or more. The average mean of the daily intrathoracic impedance was normalized within two days after the holiday.

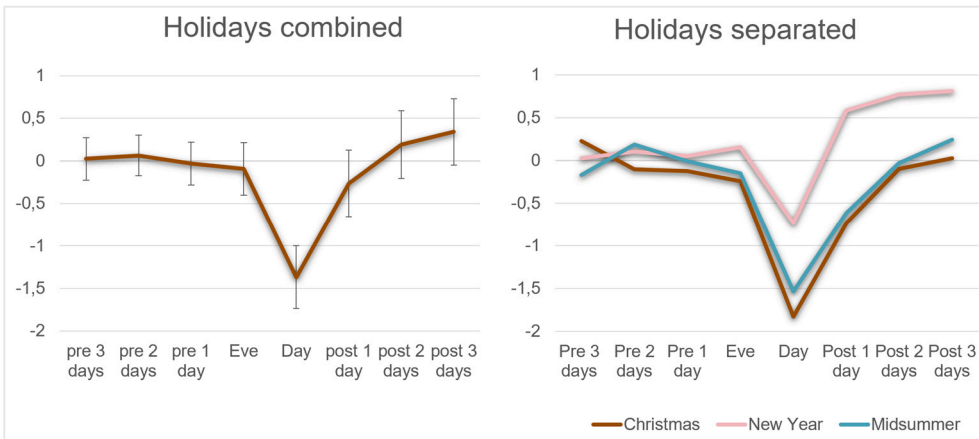


Figure 23. Intrathoracic impedance. Percent change from baseline. Holidays combined including 95% CI.

The daily impedance changes between baseline and Christmas, New Year and Midsummer Day were observed in patients with reduced LVEF (<40%); -1.0 Ohm, 95% CI [-1.6, -0.4], p=0.001 as well as in patients with normal or mildly reduced LVEF (≥40%); -1.1 Ohm, 95% CI [-1.7,-0.4], p=0.003. P for interaction was 0.9. Figure 24.

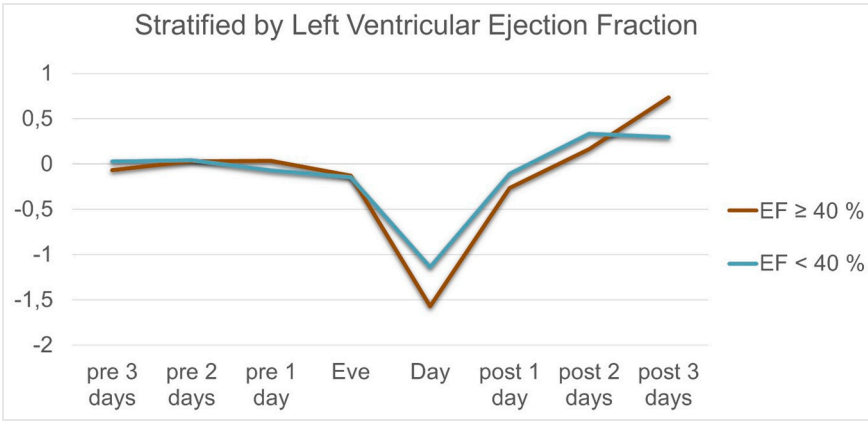


Figure 24. Intrathoracic impedance. Percent change from baseline, stratified by LVEF.

A similar impedance drop was observed regardless of diabetes diagnosis (p for interaction 0.24), hypertension (p for interaction 0.35), kidney disease (p for interaction 0.61), ischemic or non-ischemic cardiomyopathy (p for interaction 0.51 vs 0.71).

OptiVol Fluid Index and threshold crossings

The OptiVol Fluid Index (OVFI) increased after the holidays compared to baseline, reached maximum 1 and 2 days after (a mean of 2.9 Ohm/day, 95% CI [0.1, 5.8], p=0.04) and returned to baseline within a week. Seventeen alerts of crossed threshold of 60 Ohm were detected within one week after or during the holidays in relation to eight alerts during the week before the holidays. Of these in total twenty-five alerts, only two were observed in patients with LVEF >40%. Graph showing OVFI, daily impedance and threshold crossing distributions during Christmas, New Year and Midsummer holidays are illustrated in Figure 25.

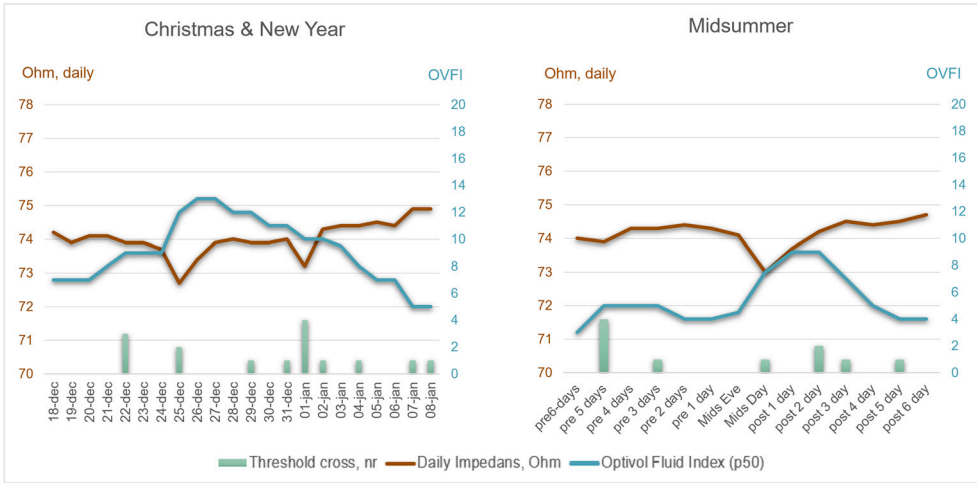


Figure 25. Thresholds crossings (nr, secondary vertical axis), mean daily impedance and median of Optivol Fluid Index (OVFI) during the holidays.

Activity

Daily activities decreased during Christmas, New Year and Midsummer Day by a mean of 40 minutes, 95% CI [35-45], p<0.001. We categorized the patients in quartiles based on activity level during baseline period. No statistically significant changes in impedance drop were seen between the groups. We then categorized the patients in quartiles based on change in activity level between the baseline and the Day. The impedance drop was larger in patients who decreased their activity level most, Table 6.

Table 6. Impedance drop in relation to change in activity. Change between baseline and Christmas, New Year and Midsummer Day combined.

	Impedance drop, Ohm	95% CI	P-value	Nr of observations
Increased activity, Q1	0.3	-0.6, 1.1	0.5	162
< 24 min decrease in activity, Q2	0.6	-0.5, 1.7	0.3	163
25-54 min decrease in activity, Q3	2.3	1.0, 3.5	**<0.001**	160
>55 min decrease in activity, Q4	2.0	0.7, 3.6	**0.002**	164

Heart rate and arrhythmia

Heart rate decreased by an average of 1.4 beats per minute (95% CI [0.8-2.0], p<0.001) during Christmas, New Year, and Midsummer Day compared to the baseline period. Similarly, heart rate variability decreased by an average of 8.0 ms

(95% CI [4.8-11.2], p<0.001) during these same holidays, Table 7. Only one patient had an appropriate ICD shock in relation to the holiday period. The patient had several episodes of ventricular tachycardia (VT) with adequate shock therapy during the night between Christmas Eve and Christmas Day. The day afterwards the daily thoracic impedance had decreased by 12 Ohm or 17 percent.

Half of the patients had persistent or paroxysmal atrial fibrillation upon inclusion. No episodes of new-onset atrial fibrillation were detected during the holidays. Within the group of patients with paroxysmal atrial fibrillation there were only minor changes in total burden of atrial fibrillation during the holidays.

Table 7. Linear mixed-effect model, outcome estimates, difference in baseline versus holiday Christmas, New Year and Midsummer combined.

		Holiday Eve (95 % CI, p-value)			Holiday Day (95 % CI, p-value)			Nr patients /obs
Daily thoracic impedance, Ohm	Crude	-0.2	-0.6, 0.3	p=0.47	-1.1	-1.6, -0.7	**p<0.001**	96/649
	Adjusted age, sex	-0.1	-0.6, 0.3	p=0.55	-1.1	-1.6, -0.7	**p<0.001**	
Daily activity, minutes	Crude	-22.9	-28.3, -17.5	**p<0.001**	-39.8	-45.2, -34.5	**p<0.001**	96/649
	Adjusted age, sex	-23.2	-28.5, -17.8	**p<0.001**	-40.1	-45.4, -34.8	**p<0.001**	
Day heart rate, bpm	Crude	-0.3	-0.9, 0.4	p=0.43	-1.4	-2.0, -0.8	**p<0.001**	87/607
	Adjusted age, sex	-0.3	-0.9, 0.4	p=0.42	-1.4	-2.0, -0.8	**p<0.001**	
Heart rate variability, ms	Crude	-1.3	-4.6, 2.0	p=0.44	-7.9	-11.2, -4.7	**p<0.001**	58/358
	Adjusted age, sex	-1.3	-4.6, 1.9	p=0.41	-8.0	-11.2, -4.9	**p<0.001**	

During the holidays and the subsequent week, none of the patients sought medical attention for symptoms of heart failure or MI. However, the patient who received shock therapy for VT was admitted to the hospital and required further hospitalization.

Discussion

Informed consent in relation to acute myocardial infarction

Inclusion in clinical trials during an acute myocardial infarction presents complex ethical and practical challenges. First, patients experiencing a myocardial infarction may have impaired cognitive function due to stress or medication, complicating their ability to make fully informed decisions. Second, ethical guidelines mandate that informed consent must be obtained voluntarily, ensuring that the patient understands the trial's aims, risks, and procedures. Third, the urgent nature of myocardial infarction treatment limits the time available for lengthy consent processes, as delays could worsen patient outcomes. Balancing these factors - patient understanding, ethical consent and the need for rapid intervention - creates a dilemma that challenges standard protocols in clinical research. Certain diagnoses, such as sepsis, severe brain injuries, and conditions requiring acute intubation, are included in emergency care settings where deferred consent is permitted in most countries. However, patients with myocardial infarction, stroke, and other similar conditions fall into a "grey area" within emergency care. Our studies investigate patient attitudes and experiences of informed consent in two different settings during the MI hospitalization.

Main findings paper I

The first study incorporated patients' attitudes to informed consent obtained in the VALIDATE-SWEDEHEART trial[189]. This multicentre trial was performed in the coronary catheterization laboratory, including a single intervention randomization during PCI with an assumed minimal risk to patients. In opposite to the HEAT PPCI trial performed in UK a few years before with deferred consent, the ethical committee in Sweden approved a verbal consent in the STEMI population before randomization followed by a written informed consent as soon as possible. Our study highlighted the patient's perspective upon this approach and some aspects could be discussed. The vast majority (94%) remembered that they had been included in a study. Of those who remembered the inclusion 88% were satisfied with the information provided and only 3% experienced the asking as negative. When asked about deferred consent 68% dismissed that and wanted to be involved

in the decision, 5% had preferred deferred consent and 27% were neutral, stating that either approach would have been acceptable to them.

Recall and understanding

Previous studies have attempted to address this dilemma in acute myocardial infarction patients from various perspectives. Similar results regarding patient recall were observed in the HERO-2 consent study[179]. Patients were interviewed before discharge, and 94% of those who gave consent remembered their inclusion. In our study, interviews were conducted by phone approximately seven days after discharge, yielding comparable results. However, fragmentary recall and limited understanding of the trial have been observed in other studies[178,180,181], and similar experiences likely appeared in our study population, but were not captured by our structured questions. In our study, 12% indicated they would have wanted additional information about the study. Reviews have shown that a large proportion (50-80%) of trial participants across various conditions did not fully understand important aspects of the study such as the experimental design, randomization, risks and potential harms[190-192]. This understanding appears to be lower in acute myocardial infarction trials compared to non-emergency trials[178]. It seems however that detailed understanding is not asked for by the patients. They are often satisfied with having gained an understanding of potential risks and obligations required after inclusion. Specific details about randomization are often difficult to comprehend, and therefore, they are not typically requested by the patients[193,194]. The recent ESC guidelines recommend the "teach-back" technique to assess patients´ understanding[144]. A shorter version of this strategy may be useful even in emergency settings.

Deferred consent

The use of deferred consent has been proposed both in low-risk pragmatic trials[195] and among myocardial infarction patients following the HEAT-PPCI trial[196,197], due to the low level of comprehended information and the questioned ability to make an autonomous decision within the narrow time frame. However, in our study, 68% disapproved of using deferred consent as an alternative. A review[198] aimed at understanding the attitudes of various stakeholders toward deferred consent; out of 27 studies, three reported negative patient views on deferred consent, two involving myocardial infarction patients and one involving stroke patients. Positive attitudes were mostly observed in low-risk trials with a narrow therapeutic window and a potential benefit occurred. The views of enrolled patients from the HEAT-PPCI trial are unknown, but such insights would have been valuable in providing a broader perspective on this complex ethical dilemma. In the ESCAPE study, which included stroke patients without prospective consent, most enrolled patients opposed the deferred consent strategy afterward, though the majority did not withdraw their consent[199].

Dickert et al[200] interviewed 30 myocardial infarction patients and presented three hypothetical trial scenarios: first, a comparative effectiveness trial with an antiplatelet agent; second, a placebo-controlled trial with a novel agent; and third, a comparative effectiveness trial involving different uses of an intra-aortic balloon pump. Nineteen of these patients felt it would be unacceptable to be enrolled in any of these trials without prospective consent. The two main reasons given for opposing deferred consent were the desire to be the decision-maker and the need for transparency of information. Some participants expressed that transparency increased their trust in the physician.

After the DANAMI-2 study in Denmark, which compared a medical strategy (fibrinolysis) with an interventional approach (primary angioplasty), the informed consent process was investigated both qualitative[201] and quantitatively[182] among enrolled patients as well as those who refused consent. The most common reason for refusal was the limited timeframe and the difficulty in making a decision. Despite the complexity of this trial, most patients (78% of 103) agreed or mostly agreed that they were capable of participating in the decision about enrolment. Most patients (72-79%) understood the primary purpose and concept of randomization in the clinical trial, and 89% perceived their participation as voluntary. However, only 50% felt it was acceptable that patients in their situation should have to decide whether to participate in a clinical trial. Among those who did not find this acceptable, only two stated that the doctor should randomize and decide for the patients. Those who found this acceptable expressed support for the patient's right to make their own decision, the value of research for future patients, and the belief that as long as patients feel capable of making a decision, they should do so. This is in line with our results and others[202]. Most patients feel capable despite the emergency situation and want to take part in the decision-making process.

Implications for future research

A majority of the patients opposed deferred consent, and our results therefore confirm those of other studies involving MI patients. As long as most patients disagree with being randomized without the option to refuse, excluding prospective consent would be unethical. Efforts to simplify the informed consent process are in the interest of both patients and clinics. Written informed consent has been considered too complex, too lengthy, and impractical in emergency contexts[169,181,182,201,203]. Verbal information is considered most important by patients, and instead of allocating time for reading, more time should be devoted to providing patients with clear and concise explanations. Written informed consent afterwards has however been seen as a valuable complement, in order to give the study legitimacy, provide legal protection for the patient and the hospital[194]. Future research should focus on ensuring that relevant verbal information is communicated to the patient, regardless of the person provides it. Ethical committees could

streamline this process through education, such as providing physicians with standardised help texts to enhance oral communication. Refining graphical aids to better communicate trial design and purpose could also be beneficial, especially in complex trials. Focus groups and patient involvement are necessary and could result in a shortened person-centred consent form for emergency consent, similar to those currently being evaluated for stroke trials[204].

Limitations and methodological considerations

The structured telephone survey, which included four questions, did not allow for a deeper exploration of participants' attitudes, their understanding of various aspects of the clinical trial, or their preferences regarding the opposed deferred consent. A number of validated patient-reported measures assessing informed consent in clinical trials are available[205]. However, these mainly focus on understanding and voluntary aspects, and do not address the emergency context or the different approaches to consent. The advantage may have been that this brief approach, with four simple questions, likely resulted in a larger sample size than if we had used a more detailed questionnaire.

The wording of the questions may have influenced the results. Additionally, independent interviewers were not utilised; instead, study-specific research nurses involved in the main trial collected the sub-study data. However, the use of a standardised interview matrix likely minimised the risk of interviewer bias. Importantly, we were unable to include patients who declined participation in the main trial, so these findings reflect only the perspectives of those who agreed to participate. Non-Swedish speakers were also excluded from the main trial due to the written consent being available exclusively in Swedish, leaving their perspectives unrepresented and decrease the external validity. The results were, however, comparable across the three participating sites, which increases the internal validity, and the findings could be generalized to a Swedish-speaking study population. However, no power calculation was performed, increasing the risk of Type II errors. Nonetheless, the differences in experience between the STEMI and NSTEMI groups were significant, and the results align with previous studies. Furthermore, the groups were of similar size, which adds robustness to the findings. To identify potential significant differences between sex regarding preferences for deferred consent, a larger patient sample would be needed, especially since women were underrepresented in the study.

Main findings, paper II

This study provides insight into the perspective of trial participation and informed consent obtained during hospitalization for MI, but not in the emergency setting. As hospital stays for MI continue to shorten, a patient’s time for reflection is, in the

best cases, overnight, allowing for the possibility to discuss the study invitation with family. However, this period could be limited to just a few hours, depending on the time needed for patient's decision. The interviews were performed in about three months after the inclusion in the trial. The study identified four main categories of patients' experience: *a willingness to contribute*, *the perception of information, be in a vulnerable situation* and *adaptation to a new technology*[206].

Previous studies have in part shown similar findings in interviews with patients after a myocardial infarction. The positive attitude towards being part of research, being able to "help", contributing to future progress, and facilitating outcomes for future patients has been explored in other studies[181,182,202] and aligns with the ethical concept of beneficence. None of the interviewees in our study felt any pressure to participate. In other trials, however, a minor issue in clinical trials conducted in emergency settings was that a few patients recalled feeling coerced into participation. "-If you just sign here, we can proceed..."[194]. The perception of information is strongly influenced by the individual delivering it. Both in our study and in others, the importance of a professional approach is evident. Clear and concise information delivered by someone able to instil a sense of confidence and trust was highly valued both in our study and other[194,201]. Scicluna et al[194] highlighted not only the professional manner in which the information was delivered but also the way patients were acknowledged as individuals. One participant noted, "They took the time to let you know…you were somebody to them." Another remarked, "They talked to me like an adult...don't use too big of words…and don't try to use baby words". Communication skills has been proven to be important in recruiting patients[207] and physicians' tone of voice, ability to build trust, and clarity in explanations play a crucial role[208].

A somewhat surprising aspect revealed from our study was that at least two patients emphasized and appreciated that the question came from dedicated study personal and not the personal or the physician involved in their usual care. The procedure of who asks for consent likely varies between countries, hospitals, and depending on the type of study and this question is therefore not easy to distinguish from previous studies. The advantage of having someone who is not responsible for the regular care is that the research information is clearly separated, as previous research has shown a lack of understanding of the specific aspects of the study. This approach is however more difficult to implement in emergency settings when inclusion takes place around the clock.

The vulnerable situation of patients has been previously discussed, and similar findings seem to apply both in the emergency setting and in the subsequent days. Most patients are profoundly affected by their illness, grappling with both the new diagnosis and the emotions that accompany it. An advantage of recruiting patients for clinical trials after the initial hours is that it provides them with time to reflect on their decision and, if needed, the possibility to consult with family members.

One purpose of the study was to evaluate patients' experiences with a new technological product that involved monitoring their medication intake through a wirelessly connected cap on their medication bottle. Some struggling with handling was described but possibly the most important finding was that the device did not give any negative feelings of being controlled. Technical and handling-related issues are relatively easy to address, but infringements on personal integrity and feelings of being monitored are significantly more serious.

Implications for future research

It is still unclear what impact it has when specific study personnel are the ones asking for consent. Perhaps the time commitment, often limited by the primary physician involved in usual care, plays a significant role. It could also be the imbalance of power between the patient and the doctor that might negatively affect the level of voluntariness. Patients may feel they don't want to disappoint the physician. This area needs to be further evaluated. Therapeutic misconception is common and maybe this could be limited if the disclosure of study information is given by dedicated study personal not integrated into the usual care. Furthermore, it is important to ensure in a larger sample of patient, that remote monitoring does not have any negative impact on patients feeling of integrity. A questionnaire that includes some of these aspects, distributed to significantly more participants, would be of great interest to confirm these findings.

Interventions to simplify patients' participation in clinical trials are important. Future strategies should encourage the integration of various devices or artificial intelligence to promote follow-up schedules and adherence to study medications.

Limitations and methodological considerations

One purpose of the study was to evaluate the new bottle cap used in the DAPA-MI trial. Since the interviews were conducted approximately three months after enrolment, there was limited time for patients to fully recognise the advantages or disadvantages of the device. The qualitative design does not allow for generalisation but provides deeper insights into the patients' thoughts. Some aspects are commonly used to determine the trustworthiness of a qualitative study, namely credibility, transferability, dependability and the conformability[209]. The digital interview format, necessitated by geographic distance and the ongoing pandemic, limited the ability to interpret non-verbal cues such as body language. This may have affected the richness of the data and, consequently, the credibility of the findings. The fact that both the interviewer and the second author were experienced in working with heart patients likely influenced the results as well. Using a neutral interviewer and conducting member checking with participants could have further strengthened the

credibility and confirmability of the study. Important details may have been overlooked, and alternative observations might have emerged.

The inclusion of participants of both sexes, representing a range of ages and from four geographically diverse sites, enhances the transferability of the findings. While the documentation of some codes and categories improves the dependability of the study, more comprehensive documentation could have increased this further. Additionally, direct quotes from participants strengthen the authenticity of the findings by giving voice to their experiences.

Triggers of myocardial infarction during national holidays

The second aim of this thesis was to identify potential triggers for myocardial infarctions during national holidays. This aim was explored through three distinct studies. Two of these studies focused on the subjective experiences of potential triggers prior to the MI, while the third study relied on objective observations of a variety of heart metrics during national holidays.

Stress and psychosocial aspects

The major findings in **paper III and IV** exploring self-experienced trigger were stress, worry and depression as potential triggers of myocardial infarction during Christmas[210,211]. This was most common in women but even 30% of men experienced more stress than usual in the previous 24 hours before symptom onset of MI. Troubles and anxiety were reported by numerically more individuals with MI than the controls, but the differences were not significant. In the INTERHEART study a psychosocial index were used, which included stress, depression, life event and low locus of control[25]. The OR for the psychosocial factors was 2.51 [95% CI 2.15-2.93]. In the data from our case-control study the OR for stress was 2.23 (manually calculated) and the OR for worry and depression were 3.18 respective 2.12. As in our study, the psychosocial factors were reported by more women than men in the population of the INTERHEART study. In a review by Nawroth et al[212] covering 36 different studies about triggers to MI, negative feelings had an OR of 4.46 [95% CI 1.85-10.77].

Previous studies have highlighted the stress associated with being a caregiver[88]. In our study, participants' descriptions of stress-inducing events prior to the onset of MI often involved caregiving responsibilities during Christmas or concerns about family members, which confirms previous results. Job strain, a frequently reported risk factor for MI[213,214] was also evident. Several participants described periods of

increased work-related stress, while one, somewhat unexpectedly, identified the stress of being off work during the Christmas holiday as a contributing factor.

Major holidays, particularly Christmas, are commonly associated with family gatherings and social events. In our study, 77% of MI patients had socialized with close family members within the past 24 hours, while 7% attended larger family gatherings. While these events can bring great joy, they may also cause stress and anxiety for some individuals. Notably, conflicts were rare in our population.

Feelings of loneliness and sadness, often heightened during holidays, were similarly prevalent across both groups in our study.

Food and alcohol beverage

Food consumption more than usual, including fatty foods and sweets, was more frequently reported by the control group, though around 30% of MI patients also reported this behaviour. Among these MI patients, only 3.8% reported consuming "much more" food than usual, indicating that the increase was generally modest for most. This suggests that while indulgence during holidays was present, it was not excessive in the majority of MI patients. Based on the study's design, these factors appear to offer a protective effect rather than posing a risk. However, design limitations discussed later, likely contributed to this unexpected finding. Previous research indicates that heavy meals can act as triggers. The increased consumption of fat- and salt-rich foods during major holidays likely impacts patients with coronary artery disease negatively, given the heightened population exposure.

An increased alcohol intake was reported during the Christmas holiday by about one-fifth of the participants. Among MI patients, 16.3% noted higher consumption than usual, compared to 22.9% in the control group. Only 1.6% versus 1.3% described their intake as "much more than usual," likely indicating moderate drinking habits. The negative effects of increased alcohol consumption on morbidity and mortality associated with other diseases have been contradictory in research related to MI. While moderate consumption can positively influence biomarkers like apolipoprotein A1 and fibrinogen, lowering MI risk[215], heavy drinking adversely affects blood lipids, promotes coagulation, and increases thrombosis risk[216].

The potential effects of cardiovascular fluid retention from food and drink during holidays were evident in **Paper V**. When analysing the holidays separately, a significant decrease in daily impedance was observed on both Christmas Day and Midsummer Day. These findings align with previous research in a smaller heart failure cohort during Midsummer[217]. Unlike that study, this research included patients with preserved LVEF and we found that daily impedance was sensitive enough to detect changes even in individuals with normal heart function. While the exact relationship between these changes, LVEF and food or drink intake remains unclear, it raises the possibility that individuals with normal cardiac function,

potentially less mindful of their heart health, may have consumed larger quantities during the holidays. Similarly, heart rate variability (HRV) decreased during the holidays, a pattern that has also been observed following high-fat meals. This suggests that dietary factors may contribute to these findings.

The low incidence of adverse events in the CIED population, despite significant changes in physiological metrics, calls into question the clinical relevance of these findings. The advice to a vulnerable patient should be, at the very least, to eat and drink in moderation to avoid placing excessive strain on the heart.

Sedentary lifestyle

The self-reported habits during Christmas and the objectively measured daily activities from the CIED both demonstrated a pronounced sedentary lifestyle during the holidays. While its contribution to the incidence of MI is unclear, it may potentially exacerbate other triggers, such as increased food consumption. Notably, fluid retention was most pronounced in individuals who reduced their activity levels the most. This finding suggests that taking a walk between meals could help alleviate the strain on the heart and support cardiovascular health during the holidays.

Travel, conflicts, economic worries

Other potential holiday triggers like travels, conflicts, economic worries and reduced compliance to prescribed medication did not seem to contribute to the increased incidence of MI during holidays. The prevalence of these categories was low in both groups.

Implications for future research

Further research is needed regarding the role of food as an acute trigger for myocardial infarction. There is limited existing research on this topic, and our studies did not provide clear results. Future studies should also focus on tracking impedance data while simultaneously collecting exposure data, such as food and drink intake, in patient groups with varying heart function (LVEF).

Limitations and methodological considerations

Causality

None of the studies were designed to establish causal relationships. While we cannot definitively state what triggers a myocardial infarction during Christmas, we can

highlight associations and offer hypotheses. This means that our findings should be interpreted as indicative of potential relationships rather than causal explanations.

Recall bias

The primary limitation of the two first studies are the potential for recall bias, especially given that participants retrospectively reported their habits and emotions around Christmas through questionnaires. This bias is further complicated by the tendency to attribute psychological stress or illness to physical health events, such as an MI. Participants may remember experiences as more intense or closer in time to the MI than they actually were. Research suggests that while positive emotions are often overestimated retrospectively, negative emotions are generally recalled with greater accuracy, which may influence the reported results[218].

To evaluate potential differences based on the timing of the surveys, we compared data from the first year, where participants completed the questionnaires approximately 10 months after the Christmas holidays, with data from the second year, where the questionnaires were distributed in January and February. A visual review of the reported triggers showed a high degree of consistency between the two groups. However, no statistical comparisons were performed to confirm these observations.

Questionnaire, construction and analysis

To explore various potential triggers, we developed a questionnaire, which, while tailored to our study, has limitations in terms of validation and comparability with other research. To enhance validity and reliability, the questionnaire was pilot-tested on a subset of MI patients, leading to revisions based on patient feedback. However, since the pilot study involved hospitalized patients shortly after their MI, it did not reveal issues related to the longer timeframe between the MI event and questionnaire completion. In retrospect, questions about smoking and activity levels were ambiguously phrased and thus unsuitable for analysis, as they could have led to misleading conclusions.

A different approach could have involved using validated patient reported outcome measurement (PROM), each targeting a specific aspect of potential triggers, such as diet, stress and activity, combined with a common case-crossover design. Participants could then compare habits during Christmas to another pre-specified date. However, such a method might require a large number of questionnaires, which could be burdensome for participants and limit the inclusion of factors like travel, medication adherence, or snow shovelling - issues specific to the holiday season. Additionally, the long timeframe between the MI and completing the questionnaires could make recall of an ordinary day irrelevant, whereas memory of Christmas habits or pre-event behaviours seemed more pertinent.

Respondents were asked to assess behaviours, emotions, or food consumption relative to their "usual" habits. The subjective interpretation of response categories in the study could impact validity in several ways. On the positive side, it allows participants to provide personalised and nuanced responses, enriching the data and capturing individual experiences more effectively. However, this subjectivity introduces inconsistency, as participants might interpret similar behaviours differently, reducing comparability and internal validity.

The recoding of response categories, where only the two "increased experience" options were assigned a value of 1, simplifies data analysis by focusing on responses likely to identify potential triggers. This approach enhances the ability to identify specific behaviours or experiences related to acute events. However, it risks excluding nuanced information from other responses, such as minor deviations or neutral answers, potentially limiting the depth of interpretation and failing to capture subtle patterns that might also play a role in triggering events.

To ensure transparency, all categories of responses were presented in our study. However, we considered it clinically irrelevant to analyse neutral or decreased responses. Therefore, dichotomizing the responses was deemed more appropriate for addressing the study's specific aim. This approach helped focus on the most meaningful differences related to the potential triggers being investigated.

Paper V

The observational design and objective outcomes of Paper V offers a different perspective on the potential triggers during the holidays. A key limitation is the lack of data on actual consumption of food and drinks, which prevents analysis of how the amount consumed relates to the measured physiological metrics. This gap limits the ability to make definitive connections between consumption patterns and the observed physiological changes.

The strength of this study lies in the use of five years of measurements combined with a mixed-effects regression model, which effectively minimizes potential biases from repeated measurements and individual habits.

Conclusions

This thesis assessed patient's experiences of informed consent and study participating in the acute setting of MI and in addition tried to identify possible triggers to MI during holidays. The following conclusions were drawn:

- Most patients have a positive view of being asked for informed consent in an emergency setting and understand they were part of a clinical trial. They disapprove of an alternative approach involving deferred consent. Verbal consent followed by written consent as soon as possible appears feasible for trials involving STEMI patients recruited in the catheterization laboratory.

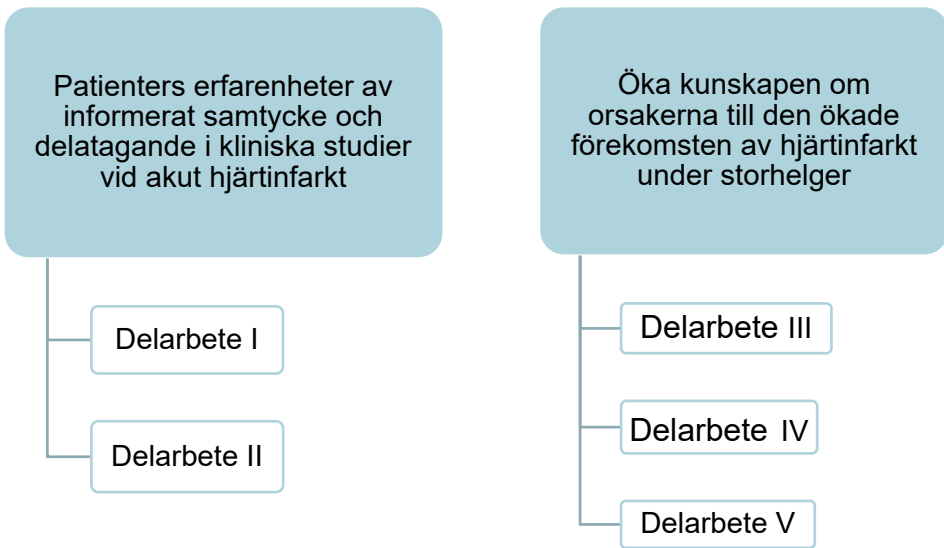
  Interviews with patients recruited later during hospitalization identify that concise and clear verbal explanations accompanying written information are preferred. Despite coping with their new diagnosis and fragmented memories of the initial days, patients express a positive attitude toward participating in clinical trials. A common motivation is the desire to contribute to future advancements and help others. Patients also responds favourably to the tested wireless bottle cap designed to remotely assess study drug adherence, reporting no feelings of being overly monitored or controlled.

- Self-reported experiences indicate increased stress and impaired psychological well-being as potential triggers for Christmas-related MI, particularly among women. While triggers such as food, sweets, and alcohol consumption were relatively common, they were reported even more frequently in the control group. Factors such as quarrels, long-distance travel, decreased adherence to prescribed medications, and economic worries are not identified as major contributors. Outdoor activities were significantly more commonly reported by men.

  In retrospective observational data from patients with cardiac implantable electronic devices, Christmas and Midsummer holidays are associated with a transient decrease in intrathoracic impedance, indicating increased fluid accumulation. This is not linked to underlying systolic ventricular dysfunction and coincides with reduced physical activity and diminished heart rate variability. These factors may contribute to the previously reported negative impact of national holidays on cardiac health.

Summary in Swedish (populärvetenskaplig sammanfattning)

Hjärtinfarkt är en av de vanligaste dödsorsakerna globalt och påverkar den enskilde individen både fysiskt och psykiskt. Denna avhandling innefattar två övergripande syften. Det första syftet var att undersöka patienters erfarenheter av informerat samtycke och deltagande i kliniska studier vid en akut hjärtinfarktsituation. Det andra syftet var att öka kunskapen om orsakerna till den ökade incidensen av hjärtinfarkt under storhelger.



Metoder

I delarbete I användes en telefonenkät med fyra frågor som genomfördes en vecka efter randomisering i en forskningsstudie som inkluderade patienter i akutskedet i samband med ankomst till laboratoriet för kranskärlsröntgen. Delarbete II innefattade semi-strukturerade webintervjuer cirka tre månader efter randomisering i en dubbelblind klinisk studie.

Delarbete III och IV använde en enkät för att undersöka potentiella triggerfaktorer bland alla levande personer som upplevt en hjärtinfarkt under julhelgen och andra förutbestämde datum i Sverige under två års tid. Delarbete III inkluderade även en kontrollgrupp av patienter med stabil kranskärlssjukdom. Delarbete V använde retrospektiva femårsdata från patienter med ICD och CRT och analyserade vätskeförändringar och andra fysiologiska parametrar under jul, nyår och midsommarhelg.

Resultat

De flesta inkluderade patienter var positiva till att delta i kliniska forskningsstudier, även i akutskedet, och motsatte sig att bli inkluderad i forskningsstudie utan att bli tillfrågad. Fyra huvudkategorier identifierades i intervjustudien: *Viljan att bidra*, *Uppfattning om information*, *Att vara i en utsatt situation* och *Anpassning till ny teknik*.

Självrapporterad stress, oro och depression var de mest förekommande rapporterade triggerfaktorerna innan hjärtinfarkt under julhelgen. Ökat mat och dryckesintag var också vanligt men det var än vanligare i kontrollgruppen. Längre resor, slarv med läkemedelsintag samt konflikter rapporterades i mycket låg grad. Psykosociala triggers inklusive stress rapporterades i högre utsträckning av kvinnor. Utomhusaktiviteter var vanligare bland män. Data från personer med ICD samt CRT visade på sjunkande intra-torakal impedans i hjärta och lungor under storhelger, vilket kan tyda på ökad vätskeansamling. Detta var mest uttalat under jul- och midsommarhelgen tillsammans med minskad fysisk aktivitet och lägre hjärtfrekvensvariabilitet.

Slutsatser

Muntligt informerat samtycke, följt av skriftligt samtycke i ett lugnare skede, får anses vara ett lämpligt tillvägagångssätt vid STEMI-studier. I icke-akuta situationer föredrar patienterna tydlig muntlig information tillsammans med skriftlig, och de som samtyckt till deltagande värdesätter möjligheten att få bidra till forskning och framtida utveckling. Användningen av ett digitalt lock på läkemedelsburken för att på distans kunna följa medicinintaget mottogs väl, utan att orsaka negativa upplevelser av övervakning.

Hjärtinfarkt under jul och andra storhelger är associerat med en ökad stress och oro, särskilt hos kvinnor, men orsakas sannolikt inte av ökad frekvens av resor, konflikter eller slarv med medicinering. Tillfällig vätskeansamling, minskad fysisk aktivitet och försämrad hjärtfrekvensvariabilitet observerades under jul och midsommar hos patienter med ICD och CRT, vilket potentiellt kan bidra till försämrad hjärthälsa under storhelger.

Tack

Den här avhandlingen hade aldrig blivit varken påtänkt, genomförd eller avklarad utan inspiration och stöd från ett stort antal personer runt omkring mig. Många har också bidragit till att den här resan blev en rolig och mycket lärorik erfarenhet.

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References

1. Roth GA, Abate D, Abate KH*, et al.* Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2018;**392**:1736-1788. doi: 10.1016/S0140-6736(18)32203-7
2. Stringhini S, Carmeli C, Jokela M*, et al.* Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. *Lancet* 2017;**389**:1229-1237. doi: 10.1016/s0140-6736(16)32380-7
3. Timmis A, Vardas P, Townsend N*, et al.* European Society of Cardiology: cardiovascular disease statistics 2021. *European Heart Journal* 2022;**43**:716-799. doi: 10.1093/eurheartj/ehab892
4. Organization WH. Global Health Estimates: Life expectancy and leading causes of death and disability. In; 2019.
5. Tsao CW, Aday AW, Almarzooq ZI*, et al.* Heart Disease and Stroke Statistics—2023 Update: A Report From the American Heart Association. *Circulation* 2023;**147**:e93-e621. doi: doi:10.1161/CIR.0000000000001123
6. SWEDEHEART. Annual report. In; 2023.
7. Hansson GK. Inflammation, Atherosclerosis, and Coronary Artery Disease. *New England Journal of Medicine* 2005;**352**:1685-1695. doi: doi:10.1056/NEJMra043430
8. Pepine CJ. The effects of angiotensin-converting enzyme inhibition on endothelial dysfunction: potential role in myocardial ischemia. *American Journal of Cardiology* 1998;**82**:23S-27S. doi: 10.1016/S0002-9149(98)00805-4
9. Tyrrell DJ, Goldstein DR. Ageing and atherosclerosis: vascular intrinsic and extrinsic factors and potential role of IL-6. *Nature Reviews Cardiology* 2021;**18**:58-68. doi: 10.1038/s41569-020-0431-7
10. Maidana D, Arroyo-Álvarez A, Arenas-Loriente A*, et al.* Inflammation as a New Therapeutic Target among Older Patients with Ischemic Heart Disease. *J Clin Med* 2024;**13**. doi: 10.3390/jcm13020363
11. Albrektsen G, Heuch I, Løchen M-L*, et al.* Lifelong Gender Gap in Risk of Incident Myocardial Infarction: The Tromsø Study. *JAMA Internal Medicine* 2016;**176**:1673-1679. doi: 10.1001/jamainternmed.2016.5451
12. Vitale C, Mendelsohn ME, Rosano GMC. Gender differences in the cardiovascular effect of sex hormones. *Nature Reviews Cardiology* 2009;**6**:532-542. doi: 10.1038/nrcardio.2009.105

13. Vogel B, Acevedo M, Appelman Y*, et al.* The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030. *The Lancet* 2021;**397**:2385-2438. doi: https://doi.org/10.1016/S0140-6736(21)00684-X
14. Khera AV, Emdin CA, Drake I*, et al.* Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *N Engl J Med* 2016;**375**:2349-2358. doi: 10.1056/NEJMoa1605086
15. Lander ES, Linton LM, Birren B*, et al.* Initial sequencing and analysis of the human genome. *Nature* 2001;**409**:860-921. doi: 10.1038/35057062
16. Deloukas P, Kanoni S, Willenborg C*, et al.* Large-scale association analysis identifies new risk loci for coronary artery disease. *Nat Genet* 2013;**45**:25-33. doi: 10.1038/ng.2480
17. Khera AV, Chaffin M, Aragam KG*, et al.* Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. *Nat Genet* 2018;**50**:1219-1224. doi: 10.1038/s41588-018-0183-z
18. Zink A, Wann LS, Thompson RC*, et al.* Genomic correlates of atherosclerosis in ancient humans. *Glob Heart* 2014;**9**:203-209. doi: 10.1016/j.gheart.2014.03.2453
19. Roberts R, Fair J. Genetics, its role in preventing the pandemic of coronary artery disease. *Clinical Cardiology* 2021;**44**:771-779. doi: https://doi.org/10.1002/clc.23627
20. Abraham G, Havulinna AS, Bhalala OG*, et al.* Genomic prediction of coronary heart disease. *Eur Heart J* 2016;**37**:3267-3278. doi: 10.1093/eurheartj/ehw450
21. Said MA, Verweij N, van der Harst P. Associations of Combined Genetic and Lifestyle Risks With Incident Cardiovascular Disease and Diabetes in the UK Biobank Study. *JAMA Cardiology* 2018;**3**:693-702. doi: 10.1001/jamacardio.2018.1717
22. Visseren FLJ, Mach F, Smulders YM*, et al.* 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). *European Heart Journal* 2021;**42**:3227-3337. doi: 10.1093/eurheartj/ehab484
23. Berry JD, Dyer A, Cai X*, et al.* Lifetime Risks of Cardiovascular Disease. *New England Journal of Medicine* 2012;**366**:321-329. doi: doi:10.1056/NEJMoa1012848
24. Dawber TR, Moore FE, Mann GV. Coronary heart disease in the Framingham study. *Am J Public Health Nations Health* 1957;**47**:4-24. doi: 10.2105/ajph.47.4_pt_2.4
25. Yusuf S, Hawken S, Ôunpuu S*, et al.* Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *The Lancet* 2004;**364**:937-952. doi: 10.1016/S0140-6736(04)17018-9
26. Yusuf S, Joseph P, Rangarajan S*, et al.* Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet* 2020;**395**:795-808. doi: 10.1016/s0140-6736(19)32008-2

27. Global Effect of Modifiable Risk Factors on Cardiovascular Disease and Mortality. *New England Journal of Medicine* 2023;**389**:1273-1285. doi: doi:10.1056/NEJMoa2206916
28. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;**388**:1659-1724. doi: 10.1016/s0140-6736(16)31679-8
29. Carvalho JJ, Baruzzi RG, Howard PF*, et al.* Blood pressure in four remote populations in the INTERSALT Study. *Hypertension* 1989;**14**:238-246. doi: 10.1161/01.hyp.14.3.238
30. Page LB, Damon A, Moellering RC, Jr. Antecedents of cardiovascular disease in six Solomon Islands societies. *Circulation* 1974;**49**:1132-1146. doi: 10.1161/01.cir.49.6.1132
31. Grillo A, Salvi L, Coruzzi P, Salvi P, Parati G. Sodium Intake and Hypertension. *Nutrients* 2019;**11**:1970. doi:
32. Oparil S, Acelajado MC, Bakris GL*, et al.* Hypertension. *Nature Reviews Disease Primers* 2018;**4**:18014. doi: 10.1038/nrdp.2018.14
33. Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet* 2000;**356**:1955-1964. doi: 10.1016/s0140-6736(00)03307-9
34. Rosendorff C, Black HR, Cannon CP*, et al.* Treatment of Hypertension in the Prevention and Management of Ischemic Heart Disease. *Circulation* 2007;**115**:2761-2788. doi: doi:10.1161/CIRCULATIONAHA.107.183885
35. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis. *Lancet* 2021;**398**:1053-1064. doi: 10.1016/s0140-6736(21)01921-8
36. Ference BA, Ginsberg HN, Graham I*, et al.* Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 2017;**38**:2459-2472. doi: 10.1093/eurheartj/ehx144
37. Sabatine MS, Giugliano RP, Keech AC*, et al.* Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. *New England Journal of Medicine* 2017;**376**:1713-1722. doi: doi:10.1056/NEJMoa1615664
38. Yusuf S, Bosch J, Dagenais G*, et al.* Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *New England Journal of Medicine* 2016;**374**:2021-2031. doi: doi:10.1056/NEJMoa1600176
39. Mortensen MB, Dzaye O, Bøtker HE*, et al.* Low-Density Lipoprotein Cholesterol Is Predominantly Associated With Atherosclerotic Cardiovascular Disease Events in Patients With Evidence of Coronary Atherosclerosis: The Western Denmark Heart Registry. *Circulation* 2023;**147**:1053-1063. doi: doi:10.1161/CIRCULATIONAHA.122.061010

40. Ridker PM, Bhatt DL, Pradhan AD*, et al.* Inflammation and cholesterol as predictors of cardiovascular events among patients receiving statin therapy: a collaborative analysis of three hospitalid trials. *The Lancet* 2023;**401**:1293-1301. doi: https://doi.org/10.1016/S0140-6736(23)00215-5
41. Vallejo-Vaz AJ, Stevens CAT, Lyons ARM*, et al.* Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). *The Lancet* 2021;**398**:1713-1725. doi: https://doi.org/10.1016/S0140-6736(21)01122-3
42. Kamstrup PR, Neely RDG, Nissen S*, et al.* Lipoprotein(a) and cardiovascular disease: sifting the evidence to guide future research. *European Journal of Preventive Cardiology* 2024;**31**:903-914. doi: 10.1093/eurjpc/zwae032
43. Ginsberg HN, Packard CJ, Chapman MJ*, et al.* Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies—a consensus statement from the European Atherosclerosis Society. *European Heart Journal* 2021;**42**:4791-4806. doi: 10.1093/eurheartj/ehab551
44. group Sw, collaboration ECr. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. *European Heart Journal* 2021;**42**:2439-2454. doi: 10.1093/eurheartj/ehab309
45. Hansen MK, Mortensen MB, Warnakula Olesen KK, Thrane PG, Maeng M. Non-HDL cholesterol and residual risk of cardiovascular events in patients with ischemic heart disease and well-controlled LDL cholesterol: a cohort study. *Lancet Reg Health Eur* 2024;**36**:100774. doi: 10.1016/j.lanepe.2023.100774
46. Wu F, Juonala M, Jacobs DR*, et al.* Childhood Non-HDL Cholesterol and LDL Cholesterol and Adult Atherosclerotic Cardiovascular Events. *Circulation* 2024;**149**:217-226. doi: doi:10.1161/CIRCULATIONAHA.123.064296
47. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019. *Lancet* 2021;**397**:2337-2360. doi: 10.1016/s0140-6736(21)01169-7
48. Hackshaw A, Morris JK, Boniface S, Tang JL, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. *Bmj* 2018;**360**:j5855. doi: 10.1136/bmj.j5855
49. Powell-Wiley TM, Poirier P, Burke LE*, et al.* Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation* 2021;**143**:e984-e1010. doi: doi:10.1161/CIR.0000000000000973
50. Ojalehto E, Zhan Y, Jylhävä J*, et al.* Genetically and environmentally predicted obesity in relation to cardiovascular disease: a nationwide cohort study. *eClinicalMedicine* 2023;**58**. doi: 10.1016/j.eclinm.2023.101943
51. Tatsumi Y, Nakao YM, Masuda I*, et al.* Risk for metabolic diseases in normal weight individuals with visceral fat accumulation: a cross-sectional study in Japan. *BMJ Open* 2017;**7**:e013831. doi: 10.1136/bmjopen-2016-013831

52. Abraham TM, Pedley A, Massaro JM, Hoffmann U, Fox CS. Association between visceral and subcutaneous adipose depots and incident cardiovascular disease risk factors. *Circulation* 2015;**132**:1639-1647. doi: 10.1161/circulationaha.114.015000

53. Rao G, Powell-Wiley TM, Ancheta I*, et al.* Identification of Obesity and Cardiovascular Risk in Ethnically and Racially Diverse Populations: A Scientific Statement From the American Heart Association. *Circulation* 2015;**132**:457-472. doi: 10.1161/cir.0000000000000223

54. Sarwar N, Gao P, Seshasai SR*, et al.* Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 2010;**375**:2215-2222. doi: 10.1016/s0140-6736(10)60484-9

55. Grundy SM, Benjamin IJ, Burke GL*, et al.* Diabetes and Cardiovascular Disease. *Circulation* 1999;**100**:1134-1146. doi: doi:10.1161/01.CIR.100.10.1134

56. Rodriguez-Araujo G, Nakagami H. Pathophysiology of cardiovascular disease in diabetes mellitus. *Cardiovasc Endocrinol Metab* 2018;**7**:4-9. doi: 10.1097/xce.0000000000000141

57. Hippisley-Cox J, Coupland CAC, Bafadhel M*, et al.* Development and validation of a new algorithm for improved cardiovascular risk prediction. *Nature Medicine* 2024;**30**:1440-1447. doi: 10.1038/s41591-024-02905-y

58. Zeng M, Sun E, Zhu L, Deng L. Influence of prediabetes on the prognosis of patients with myocardial infarction: a meta-analysis. *Diabetology & Metabolic Syndrome* 2024;**16**:160. doi: 10.1186/s13098-024-01381-1

59. Kohl HW, 3rd, Craig CL, Lambert EV*, et al.* The pandemic of physical inactivity: global action for public health. *Lancet* 2012;**380**:294-305. doi: 10.1016/s0140-6736(12)60898-8

60. Ekelund U, Tarp J, Steene-Johannessen J*, et al.* Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ* 2019;**366**:l4570. doi: 10.1136/bmj.l4570

61. Sattelmair J, Pertman J, Ding EL*, et al.* Dose response between physical activity and risk of coronary heart disease: a meta-analysis. *Circulation* 2011;**124**:789-795. doi: 10.1161/circulationaha.110.010710

62. Lee IM, Shiroma EJ, Lobelo F*, et al.* Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012;**380**:219-229. doi: 10.1016/s0140-6736(12)61031-9

63. Lang JJ, Prince SA, Merucci K*, et al.* Cardiorespiratory fitness is a strong and consistent predictor of morbidity and mortality among adults: an overview of meta-analyses representing over 20.9 million observations from 199 unique cohort studies. *British Journal of Sports Medicine* 2024;**58**:556-566. doi: 10.1136/bjsports-2023-107849

64. Dibben GO, Faulkner J, Oldridge N*, et al.* Exercise-based cardiac rehabilitation for coronary heart disease: a meta-analysis. *Eur Heart J* 2023;**44**:452-469. doi: 10.1093/eurheartj/ehac747

65. Silverman MN, Deuster PA. Biological mechanisms underlying the role of physical fitness in health and resilience. *Interface Focus* 2014;**4**:20140040. doi: 10.1098/rsfs.2014.0040
66. Mann S, Beedie C, Jimenez A. Differential effects of aerobic exercise, resistance training and combined exercise modalities on cholesterol and the lipid profile: review, synthesis and recommendations. *Sports Med* 2014;**44**:211-221. doi: 10.1007/s40279-013-0110-5
67. Valenzuela PL, Ruilope LM, Santos-Lozano A*, et al.* Exercise benefits in cardiovascular diseases: from mechanisms to clinical implementation. *European Heart Journal* 2023;**44**:1874-1889. doi: 10.1093/eurheartj/ehad170
68. Noetel M, Sanders T, Gallardo-Gómez D*, et al.* Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials. *BMJ* 2024;**384**:e075847. doi: 10.1136/bmj-2023-075847
69. Bull FC, Al-Ansari SS, Biddle S*, et al.* World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine* 2020;**54**:1451-1462. doi: 10.1136/bjsports-2020-102955
70. Willett W, Rockström J, Loken B*, et al.* Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019;**393**:447-492. doi: 10.1016/s0140-6736(18)31788-4
71. Stubbendorff A, Sonestedt E, Ramne S*, et al.* Development of an EAT-Lancet index and its relation to mortality in a Swedish population. *The American Journal of Clinical Nutrition* 2022;**115**:705-716. doi: https://doi.org/10.1093/ajcn/nqab369
72. Delgado-Lista J, Alcala-Diaz JF, Torres-Peña JD*, et al.* Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial. *The Lancet* 2022;**399**:1876-1885. doi: https://doi.org/10.1016/S0140-6736(22)00122-2
73. Estruch R, Ros E, Salas-Salvadó J*, et al.* Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *New England Journal of Medicine* 2018;**378**:e34. doi: doi:10.1056/NEJMoa1800389
74. Carr S, Bryazka D, McLaughlin SA*, et al.* A burden of proof study on alcohol consumption and ischemic heart disease. *Nat Commun* 2024;**15**:4082. doi: 10.1038/s41467-024-47632-7
75. Libby P, Ridker PM, Maseri A. Inflammation and Atherosclerosis. *Circulation* 2002;**105**:1135-1143. doi: doi:10.1161/hc0902.104353
76. Maidana D, Arroyo-Álvarez A, Arenas-Loriente A*, et al.* Inflammation as a New Therapeutic Target among Older Patients with Ischemic Heart Disease. *Journal of Clinical Medicine* 2024;**13**:363. doi:
77. Johri N, Varshney S, Gandha S*, et al.* Association of cardiovascular risks in rheumatoid arthritis patients: Management, treatment and future perspectives. *Health Sciences Review* 2023;**8**:100108. doi: https://doi.org/10.1016/j.hsr.2023.100108

78. Levine GN, Cohen BE, Commodore-Mensah Y*, et al.* Psychological Health, Well-Being, and the Mind-Heart-Body Connection: A Scientific Statement From the American Heart Association. *Circulation* 2021;**143**:e763-e783. doi: 10.1161/CIR.0000000000000947
79. Haynes SG, Feinleib M, Levine S, Scotch N, Kannel WB. The relationship of psychosocial factors to coronary heart disease in the Framingham study. II. Prevalence of coronary heart disease. *Am J Epidemiol* 1978;**107**:384-402. doi: 10.1093/oxfordjournals.aje.a112557
80. Schnohr P, Marott JL, Kristensen TS*, et al.* Ranking of psychosocial and traditional risk factors by importance for coronary heart disease: the Copenhagen City Heart Study. *European Heart Journal* 2015;**36**:1385-1393. doi: 10.1093/eurheartj/ehv027
81. Foster HME, Celis-Morales CA, Nicholl BI*, et al.* The effect of socioeconomic deprivation on the association between an extended measurement of unhealthy lifestyle factors and health outcomes: a prospective analysis of the UK Biobank cohort. *The Lancet Public Health* 2018;**3**:e576-e585. doi: 10.1016/S2468-2667(18)30200-7
82. Powell-Wiley TM, Baumer Y, Baah FO*, et al.* Social Determinants of Cardiovascular Disease. *Circulation Research* 2022;**130**:782-799. doi: doi:10.1161/CIRCRESAHA.121.319811
83. Figtree GA, Vernon ST, Hadziosmanovic N*, et al.* Mortality in STEMI patients without standard modifiable risk factors: a sex-disaggregated analysis of SWEDEHEART registry data. *The Lancet* 2021;**397**:1085-1094. doi: https://doi.org/10.1016/S0140-6736(21)00272-5
84. Vernon ST, Coffey S, Bhindi R*, et al.* Increasing proportion of ST elevation myocardial infarction patients with coronary atherosclerosis poorly explained by standard modifiable risk factors. *Eur J Prev Cardiol* 2017;**24**:1824-1830. doi: 10.1177/2047487317720287
85. Rout A, Duhan S, Umer M, Li M, Kalra D. Atherosclerotic cardiovascular disease risk prediction: current state-of-the-art. *Heart* 2024;**110**:1005-1014. doi: 10.1136/heartjnl-2023-322928
86. Kivimäki M, Leino-Arjas P, Luukkonen R*, et al.* Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *Bmj* 2002;**325**:857. doi: 10.1136/bmj.325.7369.857
87. Santosa A, Rosengren A, Ramasundarahettige C*, et al.* Psychosocial Risk Factors and Cardiovascular Disease and Death in a Population-Based Cohort From 21 Low-, Middle-, and High-Income Countries. *JAMA Network Open* 2021;**4**:e2138920-e2138920. doi: 10.1001/jamanetworkopen.2021.38920
88. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *Jama* 1999;**282**:2215-2219. doi: 10.1001/jama.282.23.2215
89. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. *Nat Rev Cardiol* 2018;**15**:215-229. doi: 10.1038/nrcardio.2017.189

90. Faresjö T, Strömberg S, Jones M*, et al.* Elevated levels of cortisol in hair precede acute myocardial infarction. *Sci Rep* 2020;**10**:22456. doi: 10.1038/s41598-020-80559-9

91. Iob E, Steptoe A. Cardiovascular Disease and Hair Cortisol: a Novel Biomarker of Chronic Stress. *Curr Cardiol Rep* 2019;**21**:116. doi: 10.1007/s11886-019-1208-7

92. Gulliksson M, Burell G, Vessby B*, et al.* Randomized Controlled Trial of Cognitive Behavioral Therapy vs Standard Treatment to Prevent Recurrent Cardiovascular Events in Patients With Coronary Heart Disease: Secondary Prevention in Uppsala Primary Health Care Project (SUPRIM). *Archives of Internal Medicine* 2011;**171**:134-140. doi: 10.1001/archinternmed.2010.510

93. Blumenthal JA, Sherwood A, Smith PJ*, et al.* Enhancing Cardiac Rehabilitation With Stress Management Training. *Circulation* 2016;**133**:1341-1350. doi: doi:10.1161/CIRCULATIONAHA.115.018926

94. Vaccarino V, Badimon L, Bremner JD*, et al.* Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. *Eur Heart J* 2020;**41**:1687-1696. doi: 10.1093/eurheartj/ehy913

95. Gan Y, Gong Y, Tong X*, et al.* Depression and the risk of coronary heart disease: a meta-analysis of prospective cohort studies. *BMC Psychiatry* 2014;**14**:371. doi: 10.1186/s12888-014-0371-z

96. Smolderen KG, Strait KM, Dreyer RP*, et al.* Depressive symptoms in younger women and men with acute myocardial infarction: insights from the VIRGO study. *J Am Heart Assoc* 2015;**4**. doi: 10.1161/jaha.114.001424

97. Lloyd-Jones DM, Allen NB, Anderson CAM*, et al.* Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association. *Circulation* 2022;**146**:e18-e43. doi: 10.1161/cir.0000000000001078

98. Jaspan VN, Greenberg GS, Parihar S*, et al.* The Role of Sleep in Cardiovascular Disease. *Current Atherosclerosis Reports* 2024;**26**:249-262. doi: 10.1007/s11883-024-01207-5

99. Yin J, Jin X, Shan Z*, et al.* Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. *J Am Heart Assoc* 2017;**6**. doi: 10.1161/jaha.117.005947

100. Janszky I, Ljung R. Shifts to and from Daylight Saving Time and Incidence of Myocardial Infarction. *New England Journal of Medicine* 2008;**359**:1966-1968. doi: doi:10.1056/NEJMc0807104

101. Muller JE. Diagnosis of myocardial infarction: Historical notes from the Soviet Union and the United States. *American Journal of Cardiology* 1977;**40**:269-271. doi: 10.1016/0002-9149(77)90018-2

102. Master AM. The Role of Effort and Occupation (Including Physicians) in Coronary Occlusion. *JAMA* 1960;**174**:942-948. doi: 10.1001/jama.1960.03030080004002

103. Muller JE, Stone PH, Turi ZG*, et al.* Circadian Variation in the Frequency of Onset of Acute Myocardial Infarction. *New England Journal of Medicine* 1985;**313**:1315-1322. doi: doi:10.1056/NEJM198511213132103

104. Willich SN, Linderer T, Wegscheider K*, et al.* Increased morning incidence of myocardial infarction in the ISAM Study: absence with prior beta-adrenergic blockade. ISAM Study Group. *Circulation* 1989;**80**:853-858. doi: 10.1161/01.cir.80.4.853
105. Willich SN, Levy D, Rocco MB*, et al.* Circadian variation in the incidence of sudden cardiac death in the framingham heart study population. *The American Journal of Cardiology* 1987;**60**:801-806. doi: 10.1016/0002-9149(87)91027-7
106. Marler JR, Price TR, Clark GL*, et al.* Morning increase in onset of ischemic stroke. *Stroke* 1989;**20**:473-476. doi: 10.1161/01.str.20.4.473
107. Siegel D, Black DM, Seeley DG, Hulley SB. Circadian variation in ventricular arrhythmias in hypertensive men. *Am J Cardiol* 1992;**69**:344-347. doi: 10.1016/0002-9149(92)90231-m
108. Nordenskjöld AM, Eggers KM, Jernberg T*, et al.* Circadian onset and prognosis of myocardial infarction with non-obstructive coronary arteries (MINOCA). *PLoS One* 2019;**14**:e0216073. doi: 10.1371/journal.pone.0216073
109. Muller JE. Circadian variation and triggering of acute coronary events. *American Heart Journal* 1999;**137**:S1-S8. doi: https://doi.org/10.1016/S0002-8703(99)70390-X
110. Muller JE, Stone PH, Turi ZG*, et al.* Circadian variation in the frequency of onset of acute myocardial infarction. *The New England journal of medicine* 1985;**313**:1315-1322. doi:
111. Chan B, Buckley T, Hansen P, Shaw E, Tofler GH. Circadian variation in acute myocardial infarction and modification by coronary artery disease: a prospective observational study. *Eur Heart J Open* 2023;**3**:oead068. doi: 10.1093/ehjopen/oead068
112. Mittleman MA, Maclure M, Tofler GH*, et al.* Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of Myocardial Infarction Onset Study Investigators. *N Engl J Med* 1993;**329**:1677-1683. doi: 10.1056/nejm199312023292301
113. Hallqvist J, Möller J, Ahlbom A*, et al.* Does heavy physical exertion trigger myocardial infarction? A case-crossover analysis nested in a population-based case-referent study. *Am J Epidemiol* 2000;**151**:459-467. doi: 10.1093/oxfordjournals.aje.a010231
114. Hammoudeh AJ, Haft JI. Coronary-Plaque Rupture in Acute Coronary Syndromes Triggered by Snow Shoveling. *New England Journal of Medicine* 1996;**335**:2001-2002. doi: doi:10.1056/NEJM199612263352617
115. Heppell R, Hawley SK, Channer KS. Snow shoveller's infarction. *Bmj* 1991;**302**:469-470. doi: 10.1136/bmj.302.6774.469-c
116. Muller JE, Mittleman MA, Maclure M, Sherwood JB, Tofler GH. Triggering myocardial infarction by sexual activity. Low absolute risk and prevention by regular physical exertion. Determinants of Myocardial Infarction Onset Study Investigators. *Jama* 1996;**275**:1405-1409. doi: 10.1001/jama.275.18.1405

117. Bhaskaran K, Hajat S, Haines A*, et al.* Short term effects of temperature on risk of myocardial infarction in England and Wales: time series regression analysis of the Myocardial Ischaemia National Audit Project (MINAP) registry. *BMJ* 2010;**341**:c3823. doi: 10.1136/bmj.c3823
118. Ni W, Stafoggia M, Zhang S*, et al.* Short-Term Effects of Lower Air Temperature and Cold Spells on Myocardial Infarction Hospitalizations in Sweden. *Journal of the American College of Cardiology* 2024;**84**:1149-1159. doi: doi:10.1016/j.jacc.2024.07.006
119. Mohammad MA, Koul S, Rylance R*, et al.* Association of Weather With Day-to-Day Incidence of Myocardial Infarction: A SWEDEHEART Nationwide Observational Study. *JAMA Cardiology* 2018;**3**:1081-1089. doi: 10.1001/jamacardio.2018.3466
120. Peters A, Dockery DW, Muller JE, Mittleman MA. Increased Particulate Air Pollution and the Triggering of Myocardial Infarction. *Circulation* 2001;**103**:2810-2815. doi: doi:10.1161/01.CIR.103.23.2810
121. Caldeira D, Nogueira-Garcia B. Myocardial infarction and viral triggers: what do we know by now? *Eur Heart J Suppl* 2023;**25**:A12-a16. doi: 10.1093/eurheartjsupp/suac122
122. Fröbert O, Götberg M, Erlinge D*, et al.* Influenza Vaccination After Myocardial Infarction: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. *Circulation* 2021;**144**:1476-1484. doi: 10.1161/circulationaha.121.057042
123. Lipovetzky N, Hod H, Roth A*, et al.* Heavy meals as a trigger for a first event of the acute coronary syndrome: a case-crossover study. *Isr Med Assoc J* 2004;**6**:728-731. doi:
124. O'Keefe JH, Bell DS. Postprandial hyperglycemia/hyperlipidemia (postprandial dysmetabolism) is a cardiovascular risk factor. *Am J Cardiol* 2007;**100**:899-904. doi: 10.1016/j.amjcard.2007.03.107
125. Esposito K, Nappo F, Marfella R*, et al.* Inflammatory Cytokine Concentrations Are Acutely Increased by Hyperglycemia in Humans. *Circulation* 2002;**106**:2067-2072. doi: doi:10.1161/01.CIR.0000034509.14906.AE
126. Cianflone K, Zakarian R, Couillard C*, et al.* Fasting acylation-stimulating protein is predictive of postprandial triglyceride clearance. *Journal of Lipid Research* 2004;**45**:124-131. doi: 10.1194/jlr.M300214-JLR200
127. Kloner RA. Lessons learned about stress and the heart after major earthquakes. *Am Heart J* 2019;**215**:20-26. doi: 10.1016/j.ahj.2019.05.017
128. Suzuki H, Yamada S, Kamioka M*, et al.* The enormous earthquake hit Japan on March 11 increased acute heart failure -analysis of remote monitoring of intrathoracic impedance. *European Heart Journal* 2012;**33**:172. doi: 10.1093/eurheartj/ehs281
129. Suzuki S, Sakamoto S, Koide M*, et al.* Hanshin-Awaji earthquake as a trigger for acute myocardial infarction. *American Heart Journal* 1997;**134**:974-977. doi: 10.1016/S0002-8703(97)80023-3

130. Gautam S, Menachem J, Srivastav SK, Delafontaine P, Irimpen A. Effect of Hurricane Katrina on the Incidence of Acute Coronary Syndrome at a Primary Angioplasty Center in New Orleans. *Disaster Medicine and Public Health Preparedness* 2009;**3**:144-150. doi: 10.1097/DMP.0b013e3181b9db91
131. Swerdel JN, Janevic TM, Cosgrove NM, Kostis JB. The effect of Hurricane Sandy on cardiovascular events in New Jersey. *J Am Heart Assoc* 2014;**3**:e001354. doi: 10.1161/jaha.114.001354
132. Carroll D, Ebrahim S, Tilling K, Macleod J, Smith GD. Admissions for myocardial infarction and World Cup football: database survey. *Bmj* 2002;**325**:1439-1442. doi: 10.1136/bmj.325.7378.1439
133. Witte DR, Bots ML, Hoes AW, Grobbee DE. Cardiovascular mortality in Dutch men during 1996 European football championship: longitudinal population study. *Bmj* 2000;**321**:1552-1554. doi: 10.1136/bmj.321.7276.1552
134. Wilbert-Lampen U, Leistner D, Greven S*, et al.* Cardiovascular events during World Cup soccer. *N Engl J Med* 2008;**358**:475-483. doi: 10.1056/NEJMoa0707427
135. Mostofsky E, Maclure M, Sherwood JB*, et al.* Risk of acute myocardial infarction after the death of a significant person in one's life: the Determinants of Myocardial Infarction Onset Study. *Circulation* 2012;**125**:491-496. doi: 10.1161/circulationaha.111.061770
136. Mostofsky E, Maclure M, Tofler GH, Muller JE, Mittleman MA. Relation of outbursts of anger and risk of acute myocardial infarction. *Am J Cardiol* 2013;**112**:343-348. doi: 10.1016/j.amjcard.2013.03.035
137. Bhattacharyya MR, Perkins-Porras L, Wikman A, Steptoe A. The long-term effects of acute triggers of acute coronary syndromes on adaptation and quality of life. *International Journal of Cardiology* 2010;**138**:246-252. doi: https://doi.org/10.1016/j.ijcard.2008.08.014
138. Tofler GH, Kopel E, Klempfner R*, et al.* Triggers and Timing of Acute Coronary Syndromes. *The American Journal of Cardiology* 2017;**119**:1560-1565. doi: https://doi.org/10.1016/j.amjcard.2017.02.022
139. Smeijers L, Mostofsky E, Tofler GH*, et al.* Association Between High Levels of Physical Exertion, Anger, and Anxiety Immediately Before Myocardial Infarction With Mortality During 10-Year Follow-Up. *Journal of the American College of Cardiology* 2015;**66**:1083-1084. doi: https://doi.org/10.1016/j.jacc.2015.06.1317
140. Kloner Robert A. The "Merry Christmas Coronary" and "Happy New Year Heart Attack" Phenomenon. *Circulation* 2004;**110**:3744-3745. doi: 10.1161/01.CIR.0000151786.03797.18
141. Kloner RA, Poole WK, Perritt RL. When throughout the year is coronary death most likely to occur? A 12-year population-based analysis of more than 220 000 cases. *Circulation* 1999;**100**:1630-1634. doi: 10.1161/01.cir.100.15.1630
142. Phillips DP, Jarvinen JR, Abramson IS, Phillips RR. Cardiac mortality is higher around Christmas and New Year's than at any other time: the holidays as a risk factor for death. *Circulation* 2004;**110**:3781-3788. doi:

143. Mohammad MA, Karlsson S, Haddad J*, et al.* Christmas, national holidays, sport events, and time factors as triggers of acute myocardial infarction: SWEDEHEART observational study 1998-2013. *Bmj* 2018;**363**:k4811. doi: 10.1136/bmj.k4811
144. Byrne RA, Rossello X, Coughlan JJ*, et al.* 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). *European Heart Journal* 2023;**44**:3720-3826. doi: 10.1093/eurheartj/ehad191
145. Thygesen K, Alpert JS, Jaffe AS*, et al.* Fourth universal definition of myocardial infarction (2018). *European Heart Journal* 2018;**40**:237-269. doi: 10.1093/eurheartj/ehy462
146. Gaba P, Gersh BJ, Muller J, Narula J, Stone GW. Evolving concepts of the vulnerable atherosclerotic plaque and the vulnerable patient: implications for patient care and future research. *Nature Reviews Cardiology* 2023;**20**:181-196. doi: 10.1038/s41569-022-00769-8
147. Libby P, Pasterkamp G, Crea F, Jang I-K. Reassessing the Mechanisms of Acute Coronary Syndromes. *Circulation Research* 2019;**124**:150-160. doi: doi:10.1161/CIRCRESAHA.118.311098
148. Fahed AC, Jang I-K. Plaque erosion and acute coronary syndromes: phenotype, molecular characteristics and future directions. *Nature Reviews Cardiology* 2021;**18**:724-734. doi: 10.1038/s41569-021-00542-3
149. Libby P. The changing landscape of atherosclerosis. *Nature* 2021;**592**:524-533. doi: 10.1038/s41586-021-03392-8
150. He L, Qin Y, Xu Y*, et al.* Predictors of non-stenting strategy for acute coronary syndrome caused by plaque erosion: four-year outcomes of the EROSION study. *EuroIntervention* 2021;**17**:497-505. doi: 10.4244/eij-d-20-00299
151. Pasterkamp G, den Ruijter HM, Libby P. Temporal shifts in clinical presentation and underlying mechanisms of atherosclerotic disease. *Nature Reviews Cardiology* 2017;**14**:21-29. doi: 10.1038/nrcardio.2016.166
152. Stone GW, Maehara A, Lansky AJ*, et al.* A Prospective Natural-History Study of Coronary Atherosclerosis. *New England Journal of Medicine* 2011;**364**:226-235. doi: doi:10.1056/NEJMoa1002358
153. Karlsson S, Anesäter E, Fransson K*, et al.* Intracoronary near-infrared spectroscopy and the risk of future cardiovascular events. *Open Heart* 2019;**6**:e000917. doi: 10.1136/openhrt-2018-000917
154. Stone PH, Maehara A, Coskun AU*, et al.* Role of Low Endothelial Shear Stress and Plaque Characteristics in the Prediction of Nonculprit Major Adverse Cardiac Events: The PROSPECT Study. *JACC Cardiovasc Imaging* 2018;**11**:462-471. doi: 10.1016/j.jcmg.2017.01.031
155. Tomaniak M, Katagiri Y, Modolo R*, et al.* Vulnerable plaques and patients: state-of-the-art. *Eur Heart J* 2020;**41**:2997-3004. doi: 10.1093/eurheartj/ehaa227
156. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *The Lancet* 2003;**361**:13-20. doi: 10.1016/S0140-6736(03)12113-7

157. Fibrinolytic Therapy Trialists' Collaborative G. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *The Lancet* 1994;**343**:311-322. doi: 10.1016/S0140-6736(94)91161-4

158. Pinto DS, Kirtane AJ, Nallamothu BK*, et al.* Hospital Delays in Reperfusion for ST-Elevation Myocardial Infarction. *Circulation* 2006;**114**:2019-2025. doi: doi:10.1161/CIRCULATIONAHA.106.638353

159. Kite TA, Kurmani SA, Bountziouka V*, et al.* Timing of invasive strategy in non-ST-elevation acute coronary syndrome: a meta-analysis of randomized controlled trials *European Heart Journal* 2022;**43**:3148-3161. doi: 10.1093/eurheartj/ehac213

160. Head SJ, Milojevic M, Daemen J*, et al.* Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. *The Lancet* 2018;**391**:939-948. doi: 10.1016/S0140-6736(18)30423-9

161. Sabatine MS, Bergmark BA, Murphy SA*, et al.* Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis. *The Lancet* 2021;**398**:2247-2257. doi: 10.1016/S0140-6736(21)02334-5

162. Hofmann R, James SK, Jernberg T*, et al.* Oxygen Therapy in Suspected Acute Myocardial Infarction. *New England Journal of Medicine* 2017;**377**:1240-1249. doi: doi:10.1056/NEJMoa1706222

163. Yndigegn T, Gilje P, Dankiewicz J*, et al.* Safety of early hospital discharge following admission with ST-elevation myocardial infarction treated with percutaneous coronary intervention: a nationwide cohort study. *EuroIntervention* 2022;**17**:1091-1099. doi: 10.4244/eij-d-21-00501

164. Junehag L, Asplund K, Svedlund M. A qualitative study: Perceptions of the psychosocial consequences and access to support after an acute myocardial infarction. *Intensive and Critical Care Nursing* 2014;**30**:22-30. doi: https://doi.org/10.1016/j.iccn.2013.07.002

165. Pragodpol P, Ryan C. Critical review of factors predicting health-related quality of life in newly diagnosed coronary artery disease patients. *J Cardiovasc Nurs* 2013;**28**:277-284. doi: 10.1097/JCN.0b013e31824af56e

166. Gander ML, von Känel R. Myocardial infarction and post-traumatic stress disorder: frequency, outcome, and atherosclerotic mechanisms. *Eur J Cardiovasc Prev Rehabil* 2006;**13**:165-172. doi: 10.1097/01.hjr.0000214606.60995.46

167. Fors A, Ekman I, Taft C*, et al.* Person-centred care after acute coronary syndrome, from hospital to primary care - A randomised controlled trial. *Int J Cardiol* 2015;**187**:693-699. doi: 10.1016/j.ijcard.2015.03.336

168. Holman H, Lorig K. Patients as partners in managing chronic disease. Partnership is a prerequisite for effective and efficient health care. *Bmj* 2000;**320**:526-527. doi: 10.1136/bmj.320.7234.526

169. Agård A, Herlitz J, Hermerén G. Obtaining informed consent from patients in the early phase of acute myocardial infarction: physicians' experiences and attitudes. *Heart* 2004;**90**:208-210. doi: 10.1136/hrt.2003.021501

170. International Ethical Guidelines for Health-related Research Involving Humans. In. Fourth ed. Geneva.: Council for International Organizations of Medical Sciences (CIOMS); 2016.
171. Kerrison S, Laws S, Cane M, Thompson A. The patient's experience of being a human subject. *J R Soc Med* 2008;**101**:416-422. doi: 10.1258/jrsm.2007.070288
172. Martin SS, Ou F-S, Newby LK*, et al.* Patient- and Trial-Specific Barriers to Participation in Cardiovascular Randomized Clinical Trials. *Journal of the American College of Cardiology* 2013;**61**:762-769. doi: doi:10.1016/j.jacc.2012.10.046
173. Planner C, Bower P, Donnelly A*, et al.* Trials need participants but not their feedback? A scoping review of published papers on the measurement of participant experience of taking part in clinical trials. *Trials* 2019;**20**. doi: 10.1186/s13063-019-3444-y
174. Chaudhari N, Ravi R, Gogtay NJ, Thatte UM. Recruitment and retention of the participants in clinical trials: Challenges and solutions. *Perspect Clin Res* 2020;**11**:64-69. doi: 10.4103/picr.PICR_206_19
175. Association WM. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Participants. *JAMA* 2024. doi: 10.1001/jama.2024.21972
176. Research NCftPoHSoBaB. The Belmont report: Ethical principles and guidelines for the protection of human subjects of research. In: Services USDoHaH, (ed); 1979.
177. Dal-Ré R, Avendaño-Solà C, de Boer A*, et al.* A limited number of medicines pragmatic trials had potential for waived informed consent following the 2016 CIOMS ethical guidelines. *J Clin Epidemiol* 2019;**114**:60-71. doi: 10.1016/j.jclinepi.2019.06.007
178. Gammelgaard A, Mortensen OS, Rossel P, Investigators D-. Patients' perceptions of informed consent in acute myocardial infarction research: a questionnaire based survey of the consent process in the DANAMI-2 trial. *Heart (British Cardiac Society)* 2004;**90**:1124-1128. doi: 10.1136/hrt.2003.021931
179. Williams BF, French JK, White HD. Informed consent during the clinical emergency of acute myocardial infarction (HERO-2 consent substudy): a prospective observational study. *Lancet* 2003;**361**:918-922. doi: 10.1016/s0140-6736(03)12773-0
180. Yuval R, Halon DA, Merdler A*, et al.* Patient comprehension and reaction to participating in a double-blind randomized clinical trial (ISIS-4) in acute myocardial infarction. *Arch Intern Med* 2000;**160**:1142-1146. doi: 10.1001/archinte.160.8.1142
181. Dickert NW, Fehr AE, Llanos A, Scicluna VM, Samady H. Patients' views of consent for research enrollment during acute myocardial infarction. *Acute Card Care* 2015;**17**:1-4. doi: 10.3109/17482941.2014.994642
182. Gammelgaard A, Mortensen OS, Rossel P. Patients' perceptions of informed consent in acute myocardial infarction research: a questionnaire based survey of the consent process in the DANAMI-2 trial. *Heart* 2004;**90**:1124-1128. doi: 10.1136/hrt.2003.021931

183. Shahzad A, Kemp I, Mars C*, et al.* Unfractionated heparin versus bivalirudin in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. *The Lancet* 2014;**384**:1849-1858. doi: 10.1016/S0140-6736(14)60924-7

184. Jernberg T, Attebring MF, Hambraeus K*, et al.* The Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART). *Heart* 2010;**96**:1617-1621. doi: 10.1136/hrt.2010.198804

185. Erlinge D, Koul S, Eriksson P*, et al.* Bivalirudin versus heparin in non-ST and ST-segment elevation myocardial infarction-a registry-based randomized clinical trial in the SWEDEHEART registry (the VALIDATE-SWEDEHEART trial). *Am Heart J* 2016;**175**:36-46. doi: 10.1016/j.ahj.2016.02.007

186. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Education Today* 2004;**24**:105-112. doi: https://doi.org/10.1016/j.nedt.2003.10.001

187. Wang L. Fundamentals of intrathoracic impedance monitoring in heart failure. *Am J Cardiol* 2007;**99**:3g-10g. doi: 10.1016/j.amjcard.2007.02.009

188. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama* 2013;**310**:2191-2194. doi: 10.1001/jama.2013.281053

189. Olsson A, Ring C, Josefsson J*, et al.* Patient experience of the informed consent process during acute myocardial infarction: a sub-study of the VALIDATE-SWEDEHEART trial. *Trials* 2020;**21**:246. doi: 10.1186/s13063-020-4147-0

190. Cohn E, Larson E. Improving Participant Comprehension in the Informed Consent Process. *Journal of Nursing Scholarship* 2007;**39**:273-280. doi: https://doi.org/10.1111/j.1547-5069.2007.00180.x

191. Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review. *Jama* 2004;**292**:1593-1601. doi: 10.1001/jama.292.13.1593

192. Nishimura A, Carey J, Erwin PJ*, et al.* Improving understanding in the research informed consent process: a systematic review of 54 interventions tested in randomized control trials. *BMC Med Ethics* 2013;**14**:28. doi: 10.1186/1472-6939-14-28

193. Kaye DK. Why 'understanding' of research may not be necessary for ethical emergency research. *Philos Ethics Humanit Med* 2020;**15**:6. doi: 10.1186/s13010-020-00090-7

194. Scicluna VM, Goldkind SF, Mitchell AR*, et al.* Determinants of Patient and Surrogate Experiences With Acute Care Research Consent: A Key Informant Interview Study. *J Am Heart Assoc* 2019;**8**:e012599. doi: 10.1161/jaha.119.012599

195. Faden RR, Beauchamp TL, Kass NE. Informed Consent, Comparative Effectiveness, and Learning Health Care. *New England Journal of Medicine* 2014;**370**:766-768. doi: doi:10.1056/NEJMhle1313674

196. Berger BJ. Minimum risk and HEAT-PPCI: innovative ideas for informed consent in emergency medical research. *Ann Emerg Med* 2014;**64**:17a-19a. doi: 10.1016/j.annemergmed.2014.10.007
197. MacKay CR, Torguson R, Waksman R. Delayed consent: will there be a shift in approach for US primary percutaneous coronary intervention trials? *Lancet* 2015;**386**:714-716. doi: 10.1016/s0140-6736(15)60077-0
198. Fitzpatrick A, Wood F, Shepherd V. Trials using deferred consent in the emergency setting: a systematic review and narrative synthesis of stakeholders' attitudes. *Trials* 2022;**23**:411. doi: 10.1186/s13063-022-06304-x
199. Shamy MCF, Dewar B, Chevrier S*, et al.* Deferral of Consent in Acute Stroke Trials. *Stroke* 2019;**50**:1017-1020. doi: doi:10.1161/STROKEAHA.118.024096
200. Dickert NW, Hendershot KA, Speight CD, Fehr AE. Patients' views of consent in clinical trials for acute myocardial infarction: impact of trial design. *Journal of Medical Ethics* 2017;**43**:524. doi: 10.1136/medethics-2016-103866
201. Gammelgaard A, Rossel P, Mortensen OS. Patients' perceptions of informed consent in acute myocardial infarction research: a Danish study. *Soc Sci Med* 2004;**58**:2313-2324. doi: 10.1016/j.socscimed.2003.08.023
202. Polcwiartek C, Behrndtz P, Andersen AH*, et al.* Attitudes and considerations of patients with ST-elevation myocardial infarction toward participation in randomized clinical trials. *American Heart Journal* 2019;**208**:21-27. doi: https://doi.org/10.1016/j.ahj.2018.10.011
203. Agård A, Hermerén G, Herlitz J. Patients' experiences of intervention trials on the treatment of myocardial infarction: is it time to adjust the informed consent procedure to the patient's capacity? *Heart* 2001;**86**:632-637. doi: 10.1136/heart.86.6.632
204. Dickert NW, Metz K, Deeds SI*, et al.* Getting the Most out of Consent: Patient-Centered Consent for an Acute Stroke Trial. *Ethics Hum Res* 2022;**44**:33-40. doi: 10.1002/eahr.500122
205. Gillies K, Duthie A, Cotton S, Campbell MK. Patient reported measures of informed consent for clinical trials: A systematic review. *PLoS ONE* 2018;**13**. doi:
206. Henriksson C, Olsson A, Andersen K*, et al.* Patients' experiences of clinical trial participation involving a product remotely assessing study drug adherence. *Contemporary Clinical Trials Communications* 2024:101307. doi: https://doi.org/10.1016/j.conctc.2024.101307
207. Albrecht TL, Eggly SS, Gleason ME*, et al.* Influence of clinical communication on patients' decision making on participation in clinical trials. *J Clin Oncol* 2008;**26**:2666-2673. doi: 10.1200/jco.2007.14.8114
208. Wade J, Donovan JL, Lane JA, Neal DE, Hamdy FC. It's not just what you say, it's also how you say it: opening the 'black box' of informed consent appointments in randomised controlled trials. *Soc Sci Med* 2009;**68**:2018-2028. doi: 10.1016/j.socscimed.2009.02.023
209. Lincoln YS. Naturalistic inquiry: sage; 1985.
210. Olsson A, Thorén I, Mohammad MA*, et al.* Christmas holiday triggers of myocardial infarction. *Scand Cardiovasc J* 2021:1-5. doi: 10.1080/14017431.2021.1983638

211. Olsson A, Mohammad MA, Rylance R*, et al.* Sex differences in potential triggers of myocardial infarction. *Eur Heart J Open* 2023;**3**:oead011. doi: 10.1093/ehjopen/oead011

212. Nawrot TS, Perez L, Künzli N, Munters E, Nemery B. Public health importance of triggers of myocardial infarction: a comparative risk assessment. *The Lancet* 2011;**377**:732-740. doi: 10.1016/S0140-6736(10)62296-9

213. Moller J, Theorell T, de Faire U, Ahlbom A, Hallqvist J. Work related stressful life events and the risk of myocardial infarction. Case-control and case-crossover analyses within the Stockholm heart epidemiology programme (SHEEP). *J Epidemiol Community Health* 2005;**59**:23-30. doi: 10.1136/jech.2003.019349

214. Rosengren A, Hawken S, Ounpuu S*, et al.* Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;**364**:953-962. doi: 10.1016/s0140-6736(04)17019-0

215. Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies. *Bmj* 2011;**342**:d636. doi: 10.1136/bmj.d636

216. Carr S, Bryazka D, McLaughlin SA*, et al.* A burden of proof study on alcohol consumption and ischemic heart disease. *Nature Communications* 2024;**15**:4082. doi: 10.1038/s41467-024-47632-7

217. Gudmundsson K, Lyng P, Karlsson H, Rosenqvist M, Braunschweig F. Midsummer Eve in Sweden: A natural fluid challenge in patients with heart failure. *European Journal of Heart Failure* 2011;**13**:1172-1177. doi: 10.1093/eurjhf/hfr124

218. Ottenstein C, Lischetzke T. Recall bias in emotional intensity ratings: investigating person-level and event-level predictors. *Motivation and Emotion* 2020;**44**:464-473. doi: 10.1007/s11031-019-09796-4

Supplementary

Table 1. Responses of **Activity** the 24 hours -pre-MI or 24–26 Dec for control group. Values in percent unless otherwise stated.

MI Christmas (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total =189)
Physical activities	13.3	7.8	17.2	50.6	9.4	1.7	180
Longer trip	67.8	5.5	5.5	10.4	7.7	3.3	183
Snow shovelling	81.9	5.5	2.7	7.7	0.5	1.6	182
Cleaning	44.3	5.9	9.2	31.9	7.0	1.6	185
Cooking	29.2	3.2	5.9	42.2	14.1	5.4	185
Outdoor activities	27.9	8.2	16.4	42.1	3.8	1.6	183
Insomnia	33.1	5.5	4.4	35.9	17.1	3.9	181
Sexual activity	68.1	10.6	3.3	17.2	0.6	0.0	180
Compliance to prescribed medication	20.3	0.5	1.1	70.9	2.2	4.9	182
Chronic CAD (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total = 157)
Physical activities	3.2	7.0	23.6	58.6	4.5	3.2	157
Longer trip	55.8	10.4	8.4	16.9	7.1	1.3	154
Snow shovelling	71.4	15.6	3.9	7.8	1.3	0.0	154
Cleaning	17.3	7.1	8.3	46.2	18.6	2.6	156
Cooking	15.0	9.2	7.2	43.8	15.0	9.8	153
Outdoor activities	12.3	4.5	22.7	48.7	6.5	5.2	154
Insomnia	21.4	1.9	5.8	55.2	11.0	4.5	154
Sexual activity	56.2	9.8	7.8	24.8	1.3	0.0	153
Compliance to prescribed medication	0.6	0.0	0.6	91.6	1.9	5.2	155

Table 2. Responses of **Emotions** the 24 hours -pre-MI or 24–26 Dec for control group. Values in percent unless otherwise stated.

MI Christmas (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total =189)
Joy	2.2	3.8	12.5	54.3	23.4	3.8	184
Happiness	3.8	3.3	12.6	61.2	16.9	2.2	183
Stress	19.5	4.3	9.2	30.3	27.0	9.7	185
Exhilaration	19.2	6.0	8.2	47.3	18.7	0.5	182
Anxiety	49.2	4.9	4.3	23.2	11.4	7.0	185
Depression	44.6	2.7	6.5	26.3	13.4	6.5	186
Loneliness	60.2	3.9	2.8	22.7	7.7	2.8	181
Sadness	59.7	2.8	3.3	21.5	9.4	3.3	181
Worry	42.5	3.3	3.3	14.9	18.2	7.7	181
Anger	64.8	4.9	2.2	22.0	4.4	1.6	182
Upset	57.9	4.9	2.7	24.6	7.1	2.7	183
Troubles	44.8	4.4	3.3	28.4	15.3	3.8	183
Quarrel/conflicts	71.4	4.4	2.2	20.9	1.1	0.0	182
Economic worries	68.7	2.7	1.6	20.3	4.4	2.2	182
Chronic CAD (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total = 157)
Joy	0.0	4.5	10.9	55.1	23.1	6.4	156
Happiness	1.9	5.8	7.1	62.6	18.7	3.9	155
Stress	21.6	5.9	15.0	36.6	18.3	2.6	153
Exhilaration	13.9	3.3	10.6	56.3	13.9	2.0	151
Anxiety	48.3	4.6	6.0	30.5	9.3	1.3	151
Depression	42.1	4.6	9.2	33.6	7.2	3.3	152
Loneliness	41.7	4.0	10.6	31.8	7.3	4.6	151
Sadness	50.7	2.0	7.2	25.7	9.2	5.3	152
Worry	39.6	2.7	6.7	40.9	5.4	4.7	149
Anger	57.3	2.0	5.3	29.3	4.0	2.2	150
Upset	54.7	1.3	5.3	31.3	4.7	2.7	150
Troubles	39.7	1.3	4.0	41.7	9.3	4.0	151
Quarrel/conflicts	65.6	1.3	8.6	22.5	0.7	1.3	151
Economic worries	59.2	3.9	5.3	25.7	5.3	0.7	152

Table 3. Responses of **Food and drink** the 24 hours -pre-MI or 24–26 Dec for control group. Values in percent unless otherwise stated.

MI Christmas (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total =189)
Food consumption	0.5	2.2	4.9	59.5	29.2	3.8	185
Fatty-food	7.2	5.5	8.8	47.5	29.3	1.7	181
Sweets	24.7	4.9	7.7	30.2	30.8	1.6	182
Alcohol	49.5	8.7	4.9	20.7	14.7	1.6	184
Chronic CAD (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total = 157)
Food consumption	0.0	1.3	2.6	46.5	45.8	3.9	155
Fatty-food	7.9	3.9	11.8	37.5	35.5	3.3	152
Sweets	9.0	3.9	9.7	34.2	39.4	3.9	155
Alcohol	35.9	5.2	5.2	30.7	21.6	1.3	153

Table 4. Responses of **Symptoms** the 24 hours -pre-MI or 24–26 Dec for control group. Values in percent unless otherwise stated.

MI Christmas (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total =189)
Tiredness	13.7	1.1	1.1	40.4	29.5	14.2	183
Dyspnéa	28.8	1.1	2.2	30.4	25.0	12.5	184
Chestpain	30.8	0.0	1.6	14.6	28.1	25.9	185
Chestpain/dyspnea on slight exertion	23.4	1.1	1.1	25.0	31.0	18.5	184
Chronic CAD (% of responders)	Not at all/not applicable	Much less than usual	Little less than usual	As usual	Little more than usual	Much more than usual	Number of responders (total = 157)
Tiredness	16.1	0.6	3.2	63.9	11.6	4.5	155
Dyspnéa	40.1	2.0	3.3	40.1	11.2	3.3	152
Chestpain	55.6	3.3	2.6	29.8	6.6	2.0	151
Chestpain/dyspnea on slight exertion	46.4	3.3	2.6	36.4	8.6	2.6	151

Table 5. Sex differences in reported trigger and female:male odds ratios. Activities.
* Adjusted for age, previous MI, hypertension, diabetes, smoking, and NSTEMI-STEMI

				Crude female: male OR			Adjusted* female: male OR		
Reported trigger	**Valid *n***	**Male, *n* (%)**	**Female, *n* (%)**	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Activities		140 (44.2)	64 (47.8)	1.16	0.77–1.73	0.483	1.27	0.83–1.96	0.273
Cooking	442	24 (7.8)	23 (17.3)	2.48	1.35–4.58	0.004	2.77	1.45–5.27	0.002
Cleaning	442	14 (4.5)	11 (8.3)	1.90	0.84–4.30	0.124	2.39	1.01–5.67	0.047
Insomnia	440	49 (15.9)	41 (31,3)	2.42	1.50–3.90	<0.001	2.31	1.39–3.81	0.001
Snow shovelling	434	8 (2.6)	3 (2.4)	0.90	0.24–3.46	0.883	1.16	0.29–4.66	0.837
Compliance to medication	438	14 (4.5)	7 (5.4)	1.19	0.47–0.03	0.708	0.91	0.32–2.56	0.850
Longer trip	440	32 (10.4)	10 (7.6)	0.71	0.34–1.50	0.376	0.67	0.30–1.50	0.335
Physical activity	438	50 (16.2)	12 (9.2)	0.53	0.27–1.02	0.058	0.56	0.28–1.12	0.103
Outdoor activity	436	38 (12.4)	7 (5.4)	0.40	0.17–0.92	0.032	0.35	0.14–0.87	0.023
Sexual activity	436	2 (0.6)	0 (0.0)			0.996			0.996

Table 6. Sex differences in reported trigger and female:male odds ratios. Emotions.
* Adjusted for age, previous MI, hypertension, diabetes, smoking, and NSTEMI-STEMI

				Crude female: male OR			Adjusted* female: male OR		
Reported trigger	**Valid *n***	**Male, *n* (%)**	**Female, *n* (%)**	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Emotions		168 (53.0)	86 (64.2)	1,59	1,05-2,41	0,029	1,71	1,1-2,69	0,017
Sadness	434	25 (8.2)	30 (23.3)	3,39	1,90-6,05	<0,001	3,52	1,92-6,45	<0.001
Upset	435	30 (9.8)	26 (20.2)	2,32	1,31-4,11	0,004	2,69	1,47-4,95	0,001
Anger	437	20 (6.5)	16 (12.3)	2,01	1,01-4,02	0,047	2,49	1,2-5,16	0,014
Stress	443	94 (30.0)	65 (50.0)	2,33	1,53-3,55	<0,001	2,38	1,52-3,71	<0,001
Loneliness	432	27 (8.9)	24 (18.8)	2,37	1,31-4,29	0,004	2,33	1,24-4,40	0,009
Anxiety	441	47 (15.2)	39 (29.5)	2,34	1,44-3,80	<0,001	2,21	1,33-3,67	0,002
Worry	436	68 (22.1)	50 (38.8)	2,22	1,43-3,47	<0,001	2,17	1,36-3,46	0,001
Depression	443	53 (17.1)	42 (31.6)	2,24	1,40-3,58	<0,001	2,06	1,26-3,36	0,004
Troubles	437	55 (17.9)	28 (21.5)	1,26	0,76-2,09	0,378	1,39	0,81-2,37	0,230
Joy	440	50 (16.2)	22 (16.8)	1,05	0,60-1,81	0,874	1,08	0,60-1,94	0,793
Exhilaration	435	36 (11.8)	17 (13.2)	1,14	0,61-2,11	0,681	0,95	0,48-1,85	0,872
Happiness	439	38 (12.3)	14 (10.7)	0,85	0,44-1,63	0,625	0,85	0,43-1,71	0,655
Economic worries	438	23 (7.5)	8 (6.1)	0,79	0,35-1,82	0,586	0,83	0,33-2,08	0,693
Quarrel/conflicts	435	15 (4.9)	5 (3.8)	0,77	0,27-2,17	0,626	0,79	0,27-2,36	0,679

Table 7. Sex differences in reported trigger and female:male odds ratios. Food and alcohol.

* Adjusted for age, previous MI, hypertension, diabetes, smoking, and NSTEMI-STEMI

				Crude female: male OR			Adjusted* female: male OR		
Reported trigger	**Valid *n***	**Male, *n* (%)**	**Female, *n* (%)**	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Food and alcohol		168 (53.0)	86 (64.2)	1,59	1,05-2,41	0,029	1,71	1,1-2,69	0,017
Food	447	56 (17.9)	17 (12.7)	0,67	0,37-1,20	0,175	0,70	0,38-1,28	0,249
Fatty food	439	49 (15.8)	17 (13.2)	0,81	0,45-1,46	0,483	0,90	0,48-1,68	0,747
Sweets	442	52 (16.8)	23 (17.4)	1,05	0,61-1,80	0,868	1,19	0,68-2,10	0,537
Alcohol	441	38 (12.3)	13 (9.8)	0,78	0,40-1,52	0,462	1,02	0,51-2,06	0,949

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ANNELI OLSSON was born in Kungälv in 1973. She graduated as a Registered Nurse in 1995 and worked at Kungälv Hospital from 1995 to 2005. She then moved to Skåne, where she worked in the Cardiac Intensive Care Unit at Skåne University Hospital in Lund until 2014. Since then, she has been working as a Study Nurse and Study Coordinator in the Department of Cardiology at the same hospital. In 2021, she became a specialist in Nursing–Cardiac Care and earned a Master's degree in Nursing Science. Her thesis focuses on myocardial infarction, specifically patients' experiences of informed consent and study participation in the acute setting, as well as potential triggering factors for myocardial infarction during national holidays.

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