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Mind–heart links in ASCVD: Evidence for chronic risk, acute triggers, and clinical prevention

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ABSTRACT

The background for this review includes negative emotions—including anger, sadness, and chronic stress—that are biologically active contributors to atherothrombosis but remain under-integrated in prevention. The objective is to synthesize epidemiologic, mechanistic, and interventional evidence linking emotional dysregulation to the pathogenesis and acute expression of ASCVD, and to contextualize effect sizes alongside traditional risk factors. The methods include a narrative review of large cohorts and case-crossover studies, neural and immunologic mechanisms (amygdala–bone marrow–arterial axis), and trials of β-blockers, SSRIs, cognitive behavioral therapy (CBT), mindfulness, and endothelial function responses to provoked emotions. We found that depressive symptoms and trait anger confer ~30–50 % higher incident MI risk; intense anger outbursts transiently raise MI risk up to ~8–9 ×, and bereavement up to ~20 × within 24 h. Stress-evoked amygdalar activity predicts myelopoiesis, arterial inflammation, and events. Mechanisms include HPA axis activation, IL-6/NLRP3 signaling, eNOS uncoupling, and catecholamine-driven platelet activation. Interventions such as β-blockers, SSRIs, CBT, and mindfulness improve vascular/inflammatory markers and may reduce event susceptibility. We conclude that emotions are causal drivers of atherothrombosis and acute coronary events. Incorporating emotion metrics, inflammatory biomarkers, and targeted behavioral/pharmacologic strategies into preventive cardiology can close residual risk gaps.

Introduction

Negative emotions such as anger, anxiety, grief, and depression contribute both to the chronic development of ASCVD and act as acute triggers of myocardial infarction, yet they remain underemphasized relative to traditional risk factors [1–16]. Negative emotions elicit physiological changes that can harm the heart [1–16]. Acute stress responses – whether from rage or grief – trigger surges in catecholamines (e.g. adrenaline), causing spikes in heart rate and blood pressure, vasoconstriction, and heightened clotting tendency [1–16]. Chronically, conditions like depression or anxiety dysregulate the hypothalamic-pituitary-adrenal axis and autonomic nervous system, leading to sustained inflammation, endothelial dysfunction, and metabolic changes (e.g. elevated cortisol, blood sugar, abdominal fat) that accelerate atherosclerosis [1–16]. These theoretical pathways were substantiated by Shimbo et al. (2024) in a randomized, controlled laboratory trial involving 280 healthy adults [17]. The study demonstrated that an 8-minute anger recall task—but not sadness or anxiety recall—resulted in a statistically significant reduction in reactive hyperemia index (RHI), a validated marker of endothelial function. The anger group exhibited impaired endothelium-dependent vasodilation 40 min post-task (ΔRHI −0.30 compared to neutral, $P = .007$), while no significant endothelial impairment was observed following the anxiety or sadness conditions. This finding provides direct experimental confirmation that anger may acutely compromise vascular endothelial function, underscoring its physiologically distinct cardiovascular risk compared to other negative emotions [17]. Beyond these vascular observations, accumulating evidence points to a broader multi-organ stress network that connects emotional distress to ASCVD risk, as detailed in the sections that follow.

In the following sections, we integrate evidence across three complementary dimensions. First, we examine the *chronic biological pathways* through which sustained emotional dysregulation—such as depression, anxiety, and hostility—contributes to atherogenesis and plaque vulnerability via neuroendocrine, inflamma-

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tory, and endothelial mechanisms [18,19]. Second, we explore *acute emotional triggers* (anger, grief, fear) that transiently precipitate myocardial infarction by amplifying sympathetic, hemodynamic, and pro-thrombotic responses. Finally, we outline *clinical prevention strategies* that integrate emotional and psychosocial health into cardiovascular risk management, including pharmacologic, behavioral, and rehabilitative approaches aligned with recent AHA and ESC prevention guidelines [20,21]. This tripartite framework situates the "mind–heart" connection as both a chronic substrate and an acute catalyst of ASCVD, emphasizing the need for integrated, emotion-informed preventive cardiology. Beyond synthesizing epidemiologic and mechanistic data, this review seeks to contextualize emotional health as an actionable dimension of preventive cardiology. By framing psychosocial and emotional regulation alongside traditional risk management, we highlight an integrated model of cardiovascular prevention that bridges biological, behavioral, and therapeutic domains. This approach underscores that emotion-informed care is not ancillary but essential to closing residual ASCVD risk gaps.

Pathways linking negative emotions to ASCVD

Building on this conceptual framework, we next delineate the biological pathways through which emotional stress translates into vascular injury and atherosclerotic progression. Acute and chronic negative emotions engage a multi-organ stress network. In humans, higher resting amygdalar activity predicts future cardiovascular events in part via bone-marrow activation and arterial inflammation [18]. In animals, chronic adrenergic signaling within the marrow niche reduces CXCL12, expands hematopoietic stem-cell proliferation, and increases inflammatory monocyte output—accelerating atherogenesis [22]. Stress elevates IL-6 and TNF-α, induces oxidative stress with eNOS uncoupling, up-regulates VCAM-1 and ICAM-1, and primes platelets/coagulation, collectively lowering the threshold for plaque rupture or supply–demand ischemia [19,23]. Notably, in a randomized trial, anger—but not sadness or anxiety—acutely impaired endothelial function, substantiating an emotion-specific vascular vulnerability (see Mechanistic Box) [17].

1. Neuro-immune–arterial axis (human): Stress-evoked amygdalar activity predicts cardiovascular events via bone-marrow activation and arterial inflammation (PET-CT cohort) [18].
2. Sympathetic–hematopoietic coupling (preclinical): Chronic stress β3-adrenergic signaling in marrow niche $\downarrow$ CXCL12, expands HSC proliferation, $\uparrow$ inflammatory monocytes $\rightarrow$ accelerates atherogenesis [22].
3. Inflammation: Stress elevates IL-6/TNF-α; NLRP3 inflammasome and oxidative pathways destabilize plaque [19].
4. Endothelium: Acute anger impairs endothelium-dependent vasodilation ($\downarrow$RHI), corroborating an emotion-specific vascular effect [17].
5. Adhesion & coagulation: Stress up-regulates VCAM-1/ICAM-1, enhances platelet priming and coagulation, promoting thrombosis [23].
6. Metabolic/autonomic: HPA-axis dysregulation (cortisol) drives insulin resistance, visceral adiposity, dysglycemia; $\downarrow$ HRV and vagal tone signal autonomic imbalance [24].

Together, these converging pathways illustrate why different emotions exert non-identical cardiovascular effects, with anger showing particularly distinct endothelial consequences. This reinforces the concept that not all emotional stressors affect the heart through equivalent biological pathways. These insights are well illustrated in the schematic below, which depicts how emotional and other acute stressors trigger a cascade of physiological responses—including sympathetic nervous system activation, surges in blood pressure and heart rate, platelet hyperactivity, and vasoconstriction. These changes can destabilize vulnerable plaques, promote thrombosis, and in susceptible individuals, precipitate an acute coronary syndrome or lethal arrhythmia [25].

Search strategy and selection criteria

We searched MEDLINE/PubMed and Google Scholar from inception through May 2025 for English-language studies using combinations of the terms *anger, anxiety, sadness, grief, depression, psychosocial stress, myocardial infarction, acute coronary syndrome, endothelial function, case-crossover, INTERHEART*. Priority was given to large epidemiologic studies, meta-analyses, mechanistic investigations, and randomized trials. Reference lists of key articles were also hand-searched to identify additional relevant sources. Because this is a narrative (non-systematic) review, we did not conduct formal risk-of-bias grading, nor did we include a PRISMA flow diagram.

Negative emotions and chronic ASCVD pathophysiology

Several negative emotions have been linked to the long-term progression of ASCVD. Among these, depression, chronic anxiety, and persistent hostility stand out as consistent contributors, not only through behavioral pathways but also via direct physiological mechanisms [1–16]. Below, we summarize how each of these affect cardiovascular health:

- **Depression:** Numerous prospective studies show that clinical depression is an independent risk factor for developing coronary heart disease. A meta-analysis found depression associated with about a *30 % increased risk* of myocardial infarction (MI) or coronary events in initially healthy people [1–16,26]. Depression often coexists with unhealthy behaviors (smoking, poor diet, inactivity) and physiological changes (autonomic imbalance, systemic inflammation) that accelerate atherosclerosis. For instance, depressed individuals have higher levels of inflammatory cytokines and cortisol, which can injure vascular endothelium and worsen plaque buildup.
- **Chronic Anxiety and Stress:** Long-term anxiety disorders or high perceived stress (e.g. work stress or caregiving strain) similarly elevate risk. Chronic anxiety can lead to hyperactivation of the sympathetic "fight or flight" response, keeping heart rate and blood pressure persistently elevated. Over time this contributes to hypertension, left ventricular hypertrophy, and vascular wear-and-tear. Epidemiological data indicate that people reporting high general stress are significantly more likely to suffer heart attacks than those with low stress [1–16,27–30]. Psychosocial stress factors (including stress at work/home or major life events) carried an odds ratio $\sim$2.7 for acute MI and accounted for $\sim$32 % of population attributable risk in the INTERHEART study—on par with hypertension and abdominal obesity as contributors [31]. Importantly, this $\approx$32 % PAR reflects the composite psychosocial domain; depression alone contributes a smaller PAR, though consistent meta-analyses show it confers a modest but independent relative risk (RR $\sim$1.3–1.5) for incident CHD/MI [26]. Cross-national ecological comparisons are confounded by cultural and diagnostic variability, and therefore we avoid inferring country-level depression–MI correlations. This highlights that chronic stress is a *major* modifiable factor worldwide.
- **Hostility and Anger Proneness:** Beyond acute anger outbursts (discussed later), an angry or hostile disposition can chronically impact the heart. Studies have linked higher levels of trait anger or cynical hostility with increased incident coronary disease [1–16]. The likely mechanisms include repeated surges of

Table 1
Biomarker signatures in bereavement.

Domain	Biomarker	Direction	Context/Population	Clinical Note
Inflammation	IL-6	↑	Bereaved adults vs. controls	Pro-inflammatory milieu
Endothelial activation	Soluble E-selectin	↑	Bereaved adults vs. controls	Marker of endothelial activation
HPA axis	Diurnal cortisol slope	Flattened	Spousal/complicated grief	HPA dysregulation linked to cardiometabolic risk
Autonomic	HRV (heart rate variability)	↓ (qualitative)	Early bereavement	Lower vagal tone; arrhythmic vulnerability
Hemostasis	Platelet reactivity	↑ (qualitative)	Mental stress / grief	Hypercoagulability during stress

Abbreviations: HPA = hypothalamic–pituitary–adrenal; HRV = heart rate variability. Data adapted from Cohen et al., *Behav Med* 2015; O'Connor et al., *Psychoneuroendocrinology* 2012; Buckley et al., *Int J Nurs Stud* 2010; Tofler & Muller, *Circulation* 2006.

blood pressure and stress hormones during frequent anger, as well as lower heart rate variability (a sign of stress on the cardiac autonomic system) [1–16]. Over time, this can injure arterial walls and promote plaque formation. Hostile individuals may also have poorer health habits, compounding their risk. For example, the INTERHEART study noted that *permanent stress at home or work* (analogous to being chronically angry/tense) was associated with a doubling of MI risk (OR ~2.1) compared to low stress [1–16,27,32–35].

- **Persistent Sadness/Grief:** Extended periods of profound sadness or bereavement can similarly degrade cardiovascular health. The prolonged grieving process after a major loss is often accompanied by sleep disturbances, depression, and anxiety, which together can raise blood pressure and sympathetic tone for weeks or months [1–16]. Some evidence suggests that bereaved individuals have higher levels of inflammatory markers and hypercoagulability [1–16]. For example, in the MIDUS II cohort, Cohen and colleagues demonstrated that bereaved adults had significantly elevated IL-6 and soluble E-selectin compared to non-bereaved peers [36]. In addition, in the setting of complicated grief, O'Connor and colleagues showed that women exhibit flattened diurnal cortisol slopes relative to non-bereaved controls [37], reflecting HPA-axis dysregulation. In one study, people who had lost a partner or child showed elevated markers of cardiovascular risk for several weeks, indicating that severe grief can act like a sustained stressor on the body [1–16]. These findings are summarized in Table 1, which highlights representative biomarker signatures in bereavement, spanning inflammation (IL-6) [36], endothelial activation (sE-selectin) [36], HPA-axis disruption (flattened diurnal cortisol slope), autonomic changes (reduced HRV) [38], and hemostatic alterations (platelet reactivity) [39]. Thus, while grief is an acute event, the stress response it induces may persist and contribute to chronic cardiac strain if not managed.
- **Psychosocial Factors and Risk Profiles:** It's important to note that depression and chronic stress often cluster with traditional risk factors. For example, depressed patients are more likely to smoke or neglect medications, and stress can lead to overeating or alcohol use. This clustering means emotional factors can exacerbate classical risk factors (like causing weight gain or uncontrolled blood pressure), creating a vicious cycle. Conversely, good psychosocial well-being may encourage healthier lifestyles. This interplay partly explains why managing mental health is associated with better cardiac outcomes. For instance, cardiac patients with strong social support and stress-coping skills tend to have fewer recurrent events.

Clinically, the chronic impact of negative emotions manifests as higher incidence of hypertension, atherosclerosis, and arrhythmias over time [1–16]. Depression has even been termed a "non-traditional risk factor" for CVD by the American Heart Association. Compared to someone without depression, a person suffering from depression not only is more likely to develop coronary disease, but if they do have a heart attack, their prognosis is worse [1–16]. In fact, depression after an MI is associated with a markedly higher risk of mortality – one analysis noted a 5-fold increase in cardiac death in post-MI patients with major depression [1–16,40–42]. This startling statistic underscores that emotional health profoundly influences outcomes.

Bottom line: Chronic negative emotions create a pro-inflammatory, high-stress internal environment conducive to vascular damage and arrhythmogenesis. They amplify other risk factors and directly contribute to ASCVD pathophysiology, even though they act less visibly than, say, high LDL cholesterol. Preventatively, this means that addressing mental health, stress, and emotional well-being should be a component of long-term cardiovascular risk reduction, alongside managing blood pressure, lipids, and lifestyle. However, as we will discuss, medical practice has been slow to prioritize these psychosocial interventions, partly due to historical emphasis on the "traditional" risk factors.

Negative emotions as acute triggers of myocardial infarction

While chronic stress lays the groundwork for heart disease, acute intense emotions can be the spark that lights the fire – triggering an acute coronary syndrome or MI in a susceptible individual [1–16]. It has long been observed that severe emotional events (both negative and even extreme positive excitement) sometimes immediately precede heart attacks. Here we explore how specific negative emotions – anger, anxiety/fear, sadness/grief – act as *acute triggers* and the magnitude of risk they confer in the hours after an outburst. Importantly, these triggers often operate on a backdrop of existing coronary plaque; they trigger an MI by causing plaque rupture or arterial spasm/arrhythmia at a moment of extreme stress [1–16]. Each emotion can provoke a slightly different physiological cascade, but all share the ability to acutely destabilize the cardiovascular system [1–16].

Anger: the "Perfect storm" trigger

Case-crossover studies show that in the two hours after an outburst of anger, MI risk more than doubles; with very intense anger, risk rises up to ~8.5-fold [2,43]. This 8-fold spike is enormous—on par with the risk one might have during extremely strenuous exercise or even cocaine use—emphasizing how harmful extreme anger can be to the heart [25,44]. Acutely, anger provokes sympathetic surges—adrenaline, hypertension, vasoconstriction, platelet priming—creating a 'perfect storm' for plaque rupture or arrhythmia [23]. This heightened risk persists for at least 2 h, as the body remains in a pro-thrombotic state [45]. Real-world data show that about two-thirds of anger-triggered MIs follow arguments (often with family), while one-third occur after work or driving-related anger [2,43]. While the absolute risk per episode is low, recurrent anger can significantly increase annual MI risk, particularly in CAD patients [45]. Beta-blockers may blunt these effects [25]. Beyond hemodynamics, Shimbo et al. (2024) showed anger—but not sadness or anxiety—directly impaired endothelial function, underscoring its unique vascular toxicity [17]. Thus, anger is a potent transient trigger: relative risk 2–8 × within hours, small per episode but clinically important in high-risk patients [43].

Anxiety, fear, and acute stress

Acute anxiety and fright trigger sympathetic surges, transient vasospasm, and arrhythmias, increasing MI risk about 2–3-fold in the immediate hours [45,46]. Episodes of intense pressure or sudden shocks (panic attacks, traumatic news, disasters) can precipitate events, particularly in those with underlying CAD. Case-crossover studies, including SHEEP, show up to 6-fold excess risk in the day after severe stress [47]. Among firefighters, alarm response combined with exertion raised cardiac death risk more than ten-fold [48]. These data confirm that while absolute risk per episode remains low, patients with coronary plaque face clinically important danger during acute fear or panic.

Profound sadness, grief, and "Broken heart" syndrome

Bereavement is among the strongest acute emotional triggers: MI risk rises ∼21-fold in the first 24 h after losing a loved one and ∼8-fold in the first week, tapering thereafter. Grief provokes sympathetic surges in blood pressure, heart rate, and clotting, overlapping with anger and anxiety pathways [5,23]. Severe emotional shocks can also precipitate Takotsubo ('broken heart syndrome'). This condition underscores how *massive adrenaline rush* from grief/fear can "stun" the heart muscle directly. At supraphysiological epinephrine, β2-adrenergic receptors switch from Gs to Gi coupling [49], producing regional negative inotropy (apical stunning). This effect interacts with microvascular spasm and heterogeneous sympathetic innervation [50], so both central and peripheral nervous system mechanisms contribute to the characteristic wall-motion patterns of Takotsubo cardiomyopathy [51]. Although the absolute risk per individual remains low, patients with CAD are particularly vulnerable, highlighting the need for vigilance and continuation of therapies during bereavement.

Depression and despair as triggers

Acute plunges into despair or severe sadness can transiently destabilize the cardiovascular system. In a case-crossover study, episodes of depressed mood were linked to ∼2.5 × higher ACS risk, and up to ∼5 × if severe [52]. Ambulatory monitoring also showed sadness associated with transient myocardial ischemia [53]. Mechanisms include surges in cortisol, autonomic imbalance, and pro-inflammatory activity [5,23]. Though less dramatic than anger, acute depressive episodes may still precipitate events in vulnerable patients with CAD.

How emotional triggers compare to physical triggers and traditional risk factors

Are these emotional triggers *really* significant compared to well-known triggers or risk factors? This section compares the magnitude of risk from emotional episodes against other acute triggers (like heavy exercise or overeating) and contrasts the overall impact of psychosocial factors versus classical risk factors (like high cholesterol, blood pressure, etc.). We will look at relative risks, absolute risk increases, and population-attributable risks to put things in perspective. The comparison reveals a fascinating paradox: Emotional triggers can be as powerful as – or stronger than – many physical triggers in the short term, yet because they are fleeting and hard to quantify, they contribute less to the total public health burden than chronic risk factors do. This partly explains why they've been under-emphasized historically.

First, let's consider acute triggers of MI side by side: an episode of anger or grief versus, say, shoveling heavy snow or eating a high-fat holiday meal. All of these exposures can strain the cardiovascular system and precipitate an infarction, particularly in individuals with underlying coronary artery disease.

As demonstrated in case-crossover and epidemiologic studies, the acute risk window for these triggers is typically 1–2 h post-exposure, and up to 24 h for bereavement. While relative risks (RRs) in this period can be substantial—ranging from 2 × to over 20 × for certain emotions—the absolute risk per episode remains low, often requiring thousands of exposures to cause a single MI in the general population. However, the aggregate impact becomes significant in individuals with frequent emotional episodes or elevated baseline risk, such as those with existing plaque, diabetes, or prior events [1–16].

Looking at Table 1, Table 2 we see that emotional triggers like anger or grief can match or even exceed the potency of physical triggers like exercise or heavy meals in terms of relative risk. An anger outburst (∼2.5 × risk on average) is roughly equivalent to shoveling snow or vigorous exercise for a sedentary person in triggering potency [1–16]. An extremely heavy meal (think holiday feast) quadruples risk, much like extreme anger does [1–16,54]. In fact, authors have explicitly noted: "Eating a heavy meal may act as a trigger for heart attack in much the same way as extreme physical exertion and outbursts of anger might" [1–16,54]. Grief in the early hours is in a league of its own (20 × increase) – few physical triggers approach that (perhaps except acute medical triggers like cocaine use, which has ∼24 × risk) [1–16]. So in the short term, the heart doesn't distinguish whether stress comes from emotion or exertion – both can precipitate an infarction if the conditions are right [1–16].

Table 3 summarizes key emotional triggers and their physiological impact, highlighting differences in relative risk and vascular effects. This comparison underscores that while several emotions can acutely stress the cardiovascular system, anger appears uniquely capable of directly compromising endothelial function, whereas grief and anxiety act primarily through hemodynamic and behavioral pathways.

However, when viewed through the lens of population health, a broader perspective emerges. Traditional cardiovascular risk factors—such as high LDL cholesterol, hypertension, smoking, and diabetes—exert persistent and cumulative effects on vascular biology and are more widely distributed in the general population. Consequently, their population-attributable risk (PAR) is significantly higher than that of acute emotional triggers [1–16]. Table 4, adapted from the INTERHEART study, illustrates how psychosocial stress compares with classical risk factors across both odds ratios and PAR. Despite its acute potency, anger as a trigger contributes a smaller share of total MI burden, largely because not everyone experiences such emotional spikes prior to their cardiac event. By contrast, chronic emotional distress—such as depression or persistent work-related stress—remains a major contributor to cardiovascular risk at the population level.

These comparisons offer important insights. On a global scale, psychosocial stressors account for approximately one-third of myocardial infarctions, with a population-attributable risk (PAR) comparable to, or even exceeding, that of several classical risk factors. For example, the INTERHEART study found that psychosocial factors had nearly double the PAR of physical inactivity [1–16]. However, it's important to note that the definition of psychosocial stress in such analyses is broad—encompassing work-related strain, major life events, and depressive symptoms. When isolated, a single emotional factor, such as an anger outburst, contributes a much smaller PAR, since not all individuals experience such acute triggers immediately before an event.

This comparison yields important insights:

- **Psychosocial factors collectively are very impactful** (32 % PAR) [1–16]. In fact, in that INTERHEART analysis, psychoso-

Table 2
Acute triggers of myocardial infarction – emotional vs physical exposures.

Trigger	Type	Short-term MI Risk (Relative Risk)
Outburst of anger	Emotional trigger (within 1–2 h)	RR ≈ 2.3 average; up to 8.5 for extreme rage
Severe anxiety/fear (panic, shock)	Emotional trigger (within hours)	RR ~2–3; >10 in extreme events (e.g. firefighters)
Profound grief (loss of loved one)	Emotional trigger (hours to days)	RR ~21 on day of loss; ~8 in first week
Heavy physical exertion (unaccustomed exercise)	Physical trigger (within 1–2 h)	RR ≈ 3–6 (2–3 in fit individuals)
Unusually heavy meal (high-fat overeating)	Chemical trigger (within 1–2 h)	RR ≈ 4 within 2 h of very heavy meal
Surge in blood pressure (hypertensive crisis/startle)	Physiological trigger (minutes to hours)	Difficult to assign single RR; often high with other triggers

Adapted from Mostofsky E et al., Buckley T et al., Mittleman MA et al., Lipovetzky N et al., Circulation and related sources. RR = relative risk.

Table 3
Differential Risk and Endothelial Impact of Emotional Triggers of Myocardial Infarction.

Trigger	Relative Risk	Reactive Hyperemia Index Impairment (JAHA 2024)
Anger	2–8.5 ×	Yes (ΔRHI = −0.30; $P = .007$)
Anxiety	2–3 ×	No significant change
Sadness	2.5–5 ×	No significant change

Note: Relative risk (RR) estimates reflect short-term increase in myocardial infarction risk. Data on endothelial function derived from JAHA 2024 randomized controlled trial.

cial stress had an OR (~2.7) similar to smoking's risk, and a PAR comparable to smoking and abdominal obesity. This tells us that, at a population level, *chronic emotional stress and depression are contributing to as many MIs as traditional factors like hypertension or obesity*. It dispels the notion that these are "soft" factors – they are quantitatively significant.

- However, when broken down into specific components, the impact of any single emotional trigger is smaller. For example, *depression alone* might account for a portion of that 32 % (say, depression had OR ~1.5 and PAR perhaps ~9 % on its own in some analyses), and *acute anger episodes alone* might only account for a few percent of Mis [1–16]. Many people have high cholesterol 24/7, but not everyone has an anger outburst today. So classical factors like LDL, which are continuously elevated in millions of people, cause a far larger absolute number of heart attacks than, say, today's incidents of rage do. Absolute risk perspective: As noted earlier, even a large relative risk from a brief trigger corresponds to a very small absolute risk increase because the exposure is so transient [1–16]. Researchers estimated, for instance, that vigorous exercise (RR ~6) caused only ~1.5 extra MIs per one million hours of exercise – a tiny absolute rate [25]. Similarly, an anger episode (RR ~2–3) in a person with moderate baseline risk might raise their *1-in-a-million chance* of an MI in the next hour to *2-in-a-million*, which is still exceedingly low. This is why, despite dramatic stories of "He got so mad it gave him a heart attack," the vast majority of angry episodes do not end in MI. In contrast, having high LDL every hour of every day confers a continual risk that accumulates, so its population impact is huge (hence ~50 % PAR) [55].
- **Population-Attributable Fraction of Triggers:** We can flip the question and ask: what fraction of heart attacks might be immediately precipitated by an emotional trigger? Some studies have tried to estimate this. One case-crossover study suggested that only about 2–3 % of MIs could be attributed to anger outbursts as the trigger (because not many patients had an anger episode in the hazard period before their MI). Even combining all acute triggers (physical exertion, anger, heavy meals, etc.), one analysis found they explained <10 % of MIs at a population level [25]. By far, the bulk of MIs are due to the chronic underlying risk factors "loading the gun," even if a trigger "pulls the trigger" in some cases [1–16].
- **Emotional vs Physical Triggers:** Emotional triggers can rival physical triggers in relative risk, but a key distinction lies in their long-term biological impact. Some physical triggers, such as acute bouts of exercise, are offset by protective adaptation. Regular physical activity lowers overall cardiovascular risk, even if it transiently increases MI risk during exertion. Fig. 1, Fig. 2 illustrates this distinction: a sedentary individual (dashed line) exhibits a high baseline risk and a dramatic spike during sudden exertion, while an active individual (solid line) maintains lower baseline risk and experiences only a modest increase during exercise [25]. By contrast, emotional stress offers no protective adaptation. Chronic anger, anxiety, or grief only accumulate harm over time—raising baseline stress hormone levels, impairing endothelial function, and fostering inflammation. In short, emotional triggers add risk without offsetting benefit, reinforcing the need to prioritize emotional health in cardiovascular prevention strategies. This again supports addressing chronic emotional health as a preventative measure.
- **Sudden Cholesterol Spikes & Rapid Weight Gain:** A *sudden cholesterol spike* typically refers to the post-prandial (after-meal) surge in fats in the blood when one eats a very high-fat meal. As shown, such a heavy meal can acutely trigger an MI (about 4 × risk) [54]. But outside of those rare giant meals, cholesterol is more a chronic issue – day-in, day-out elevated LDL causes plaque buildup. There isn't really an "acute" cholesterol trigger equivalent to an anger attack, except the meal effect (which is more about blood viscosity/endothelial dysfunction transiently) [25]. *Rapid weight gain* is not an instantaneous trigger per se;

Table 4
Chronic Cardiovascular Risk Factors: Odds Ratios and Population-Attributable Risk (INTERHEART Study).

Risk Factor (Chronic Exposure)	Odds Ratio for MI	Population-Attributable Risk
Abnormal lipids (high ApoB/ApoA1 ratio)	3.25 (top quintile vs lowest)	49.2 % (≈ half of MIs)
Smoking (current vs never)	2.87	35.7 %
Psychosocial stress (any significant stress/depression)	2.67	32.5 %
Hypertension (history of high BP)	1.91	17.9 %
Abdominal obesity (waist/hip ratio)	~1.6 (top tertiles vs lowest)	20.1 %
Diabetes mellitus	2.37	9.9 %
Lack of daily fruits/vegetables	1.43 (inverse OR 0.70 for adequate intake)	13.7 %
Physical inactivity (lack of regular exercise)	~1.2 (inverse OR 0.86 for active)	12.2 %
Regular alcohol consumption (moderate)	0.91 (slight protective effect)	6.7 %

Data adapted from Yusuf S et al., Lancet 2004. OR = odds ratio; PAR = population-attributable risk.

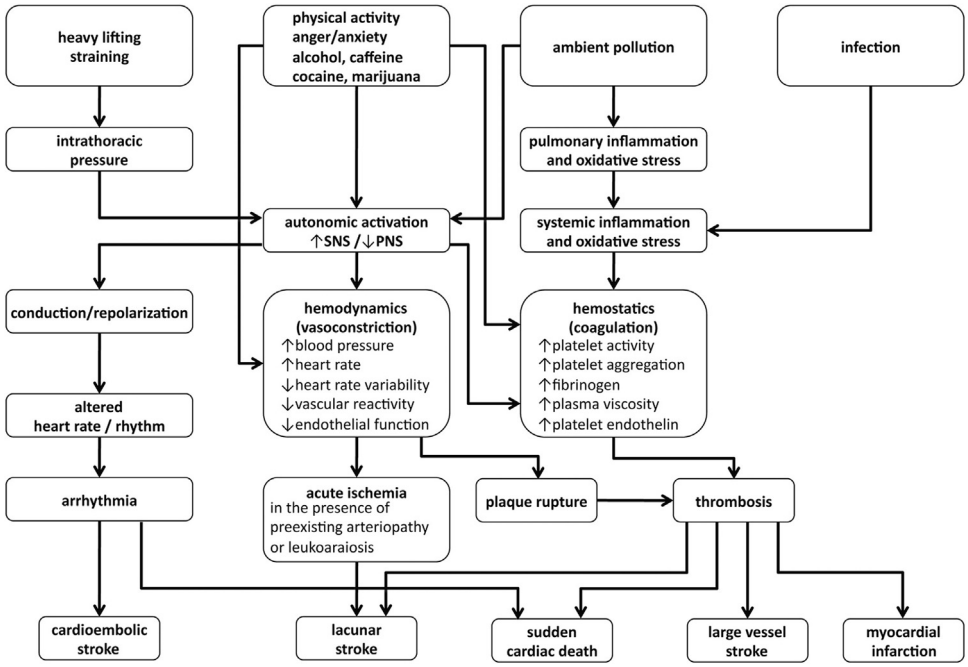

Fig. 1. (Central Illustration). Pathways from negative emotions to acute cardiovascular events. Negative emotions (anger, anxiety, grief) activate autonomic and neuroendocrine responses, induce hemodynamic load, platelet activation, and—in the case of anger—acute endothelial dysfunction, lowering the threshold for plaque rupture, thrombosis, arrhythmia, and MI.

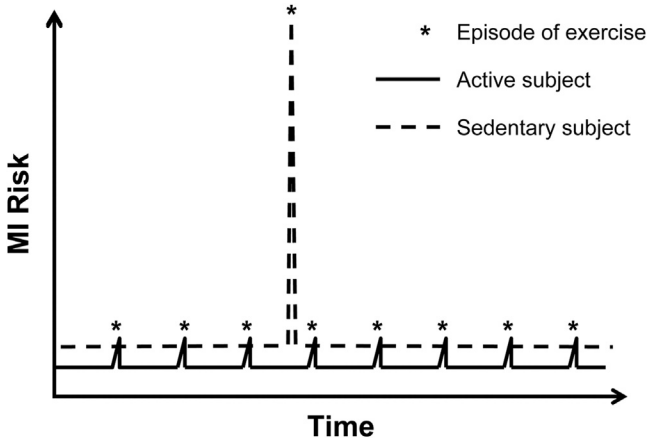

Fig. 2. Transient MI risk during exertion is attenuated by habitual activity. Sedentary individuals experience higher baseline risk and larger exertional spikes; physically active individuals show lower baseline risk and smaller spikes, illustrating physiologic adaptation to regular exercise.

rather, gaining weight over weeks can worsen blood pressure and insulin resistance, possibly leading to something like a hypertensive crisis or atrial fibrillation, but it's not like "I gained 5 pounds today and had a heart attack tonight" in most cases. Rapid fluid weight gain (e.g. in heart failure) can precipitate events, but generally weight gain is a chronic risk factor similar to obesity. It contributes to that 20 % PAR via abdominal obesity but doesn't usually act acutely [55]. So, these are more on the chronic side.

In conclusion on comparisons: Emotion-driven risk vs traditional risk is not an either/or – they interact. An analogy often used is that traditional risk factors load the gun (create the conditions for disease) and acute triggers pull the trigger. Most heart attacks will occur at some point even without a dramatic trigger, but triggers might decide *when* it happens. From a public health viewpoint, reducing LDL, blood pressure, and smoking has prevented countless MIs, which is why they get top priority. Psychosocial stress reduction is harder to quantify and hasn't been as easy to "prescribe," so it lagged behind. Yet, given psychosocial factors' substantial contribution (≈ one-third of risk) and their role in acute events, they merit far more attention than they currently receive.

Why are emotions under-emphasized in cardiovascular risk management?

If emotional factors are so clearly linked to heart attacks – both as chronic risks and acute triggers – why do they play second fiddle to cholesterol, blood pressure, and the like in guidelines and practice? Several reasons emerge from critical analysis of the evidence and historical trends:

- **Difficulty in Measurement & Quantification:** Blood pressure can be measured in mmHg, cholesterol in mg/dL – but how do you measure anger or grief? The lack of a simple quantitative metric made it harder to incorporate emotions into risk models. Risk calculators (Framingham, ASCVD, etc.) rely on numbers; psychosocial stress is not easily reducible to a single number. It wasn't until large studies like INTERHEART that we got a handle on quantifying psychosocial risk (e.g. OR ~2.5, PAR ~30 %) [55], but even then, implementing that clinically (e.g. "this patient has 2 points for stress") is not straightforward.
- **Intermittent and Unpredictable Nature:** Traditional risk factors are usually chronic exposures – if someone has high LDL or smokes, it's a persistent state increasing risk *all the time*. Emotional triggers tend to be episodic and unpredictable (you can't always know when a patient will have an outburst or a tragedy). This makes them harder to study and harder to address. Doctors and patients naturally focus on the constant risk factors that can be modified continuously (diet, meds, etc.), whereas telling a patient "don't get angry" is not as actionable. Moreover, because the *absolute* risk from any single episode is

low [2,25,38,45], patients and clinicians may become complacent ("I get mad often and nothing has happened so far") [1–16], The episodic nature also means that in clinical trials, showing a benefit of interventions (like stress management) on hard outcomes is challenging, requiring huge sample sizes.

- **Historically Mixed Trial Results:** There has been some skepticism in the cardiology community because trials targeting psychosocial factors yielded mixed results. For example, the ENRICHD trial (Enhancing Recovery in Coronary Heart Disease) treated post-MI depression with therapy – it improved depression but initially did not show a significant mortality reduction. Some later analyses showed a benefit in certain subgroups or with SSRIs, but the message many took was "treating depression didn't save lives" [56–58]. This dampened enthusiasm for integrating mental health into cardiac care. In contrast, trials of statins or antihypertensives robustly cut hard events, so focus stayed there. However, it's worth noting newer evidence is more encouraging – a 2022 RCT found that treating depression after acute coronary syndrome *did* reduce subsequent cardiac events over long-term follow-up [59], Still, guidelines move cautiously, and until recently there wasn't a strong consensus to aggressively treat psychosocial stress for the sake of heart outcomes.
- **Pathophysiological Perception – Root Cause vs Trigger:** Cardiologists have traditionally viewed atherosclerosis (plaque buildup from lipids, BP, etc.) as the root cause of heart attacks, relegating emotional triggers to a secondary role. In part, this remains true—without vulnerable plaque, most myocardial infarctions will not occur. Hence, prevention efforts have rightly emphasized lipid control, hypertension management, and smoking cessation. However, emerging evidence—including a 2024 randomized trial—now shows that acute anger alone can transiently impair endothelial function, even in apparently healthy individuals [17]. This suggests that emotional triggers do more than provoke—they may participate in pathophysiology by destabilizing vascular tone and potentiating plaque rupture. The longstanding mindset that "if we fix the cholesterol and blood pressure, the patient won't have an MI even if they get angry" is increasingly incomplete. While traditional risk factor control remains foundational, emotional regulation must be viewed not only as behavioral guidance but also as a vascular protective strategy.

Other authors' work even suggests that improving baseline health (e.g. treating hypertension, keeping cholesterol low) *lowers the risk of an anger episode triggering an MI* [1–16]. So, traditional risk factor control remains foundational. But this viewpoint can lead to underestimating triggers – in reality, many patients on optimal meds still suffer ACS when under extreme stress. Triggers are the proximate cause in many events and acknowledging that does not undermine the importance of root causes. We need a dual approach: prevent plaque *and* manage triggers.

- **Lack of Training and Resources:** Cardiologists and primary doctors historically aren't trained to manage emotional health – that falls to mental health professionals. So, even if they recognize a patient is very stressed or depressed, they may not feel equipped to intervene beyond general advice. And healthcare systems often don't have integrated care models to address this (though this is improving with cardiac rehabilitation programs including stress management). With limited time and reimbursement issues, a doctor might prioritize adjusting medications over delving into the patient's emotional stressors. In contrast, prescribing a statin is straightforward and supported by guidelines. Essentially, system incentives and medical culture have not strongly supported treating psychosocial factors as part of cardiovascular care until recently.
- **Evidence of Benefit when Modified:** A key reason classical factors get emphasis is that interventions on them clearly save lives (e.g. statins lower LDL and reduce MI by ~25–30 %; antihypertensives reducing stroke/MI). For psychosocial factors, it's inherently harder to prove intervention efficacy. How do you "treat" anger or grief? Trials of stress reduction, meditation, or antidepressants in heart patients have shown mixed magnitudes of benefit, partly due to adherence and measurement issues. That makes guideline committees hesitate. However, it should be noted that comprehensive cardiac rehab (which includes exercise, nutrition, *and* stress management components) does improve survival [60]. Also, psychological therapy improves quality of life and, at least in depression's case, likely improves outcomes over the long haul (as suggested by newer data) [59]. The under-emphasis is slowly being corrected as evidence accumulates that treating the whole patient – mind (soul) and body – yields the best results.
- **Attribution and Mindset:** There may also be a human tendency to blame events on tangible factors. If a middle-aged man has an MI after yelling at someone, that dramatic moment stands out, but a clinician might still point to his 20-year history of high cholesterol as "the real cause." In truth, both are causes in different senses. Medicine has traditionally favored the "risk factor" model (quantifiable, long-term causes) over viewing emotions as direct causes. Only in recent decades has the field of psychocardiology gained traction to change this mindset, backed by studies we've discussed.

In light of all this, it's no surprise that emotions have been under-recognized in cardiovascular prevention. But this is changing. Major heart associations now acknowledge psychosocial stress as a risk factor. For example, the European Society of Cardiology's prevention guidelines include management of psychosocial risk (assessing stress, depression, etc.), and the American Heart Association has science advisories on screening for depression in heart patients [21]. These are important steps, though implementation is still variable.

Crucially, recognizing emotional triggers doesn't mean we tell patients to "just avoid stress" (often impossible advice). Instead, it means identifying those at risk and offering support: stress management programs, therapy or medications for depression/anxiety, anger management strategies, social support enhancement, relaxation techniques, etc. It also means acute care awareness – for instance, being vigilant for cardiac symptoms in a grieving patient, or ensuring someone with anger issues has their blood pressure controlled and perhaps a beta-blocker on board. Some authors have even proposed *"trigger prevention strategies"* such as instructing high-risk patients to take an aspirin or beta-blocker before a known potential trigger (like a fiery family meeting or shoveling snow). While somewhat speculative, it underlines an important concept: if we can't completely avoid triggers, we can at least mitigate their impact on vulnerable individuals.

Conclusion

Negative emotions are not merely contextual—they engage defined neuro-immune, endothelial, and hemostatic pathways that raise chronic ASCVD risk and acutely trigger events [18,22] Composite psychosocial stress contributes materially to global MI burden, while discrete emotions—especially anger—can transiently impair endothelial function and precipitate ACS in vulnerable patients [17,19]. Prevention should therefore pair aggressive control of traditional risks with routine screening and targeted management of depression, stress, and anger, leveraging behavioral therapy, pharmacotherapy when indicated, and cardiac rehabilitation components that include stress skills [17,26,60]. This integrated approach

addresses both the "loaded gun" and the "trigger," reducing residual risk in routine care.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author used OpenAI's ChatGPT only to support language refinement. After using this tool, the author reviewed and edited the content to ensure accuracy, clarity, and scientific integrity and takes full responsibility for the content of the published article. No generative AI or AI-assisted tools were used to create or alter figures, images, or artwork.

Ethical approval

This narrative review synthesizes previously published literature and did not involve human participants, identifiable patient data, or animal subjects. Accordingly, institutional review board/ethics committee approval and informed consent were not required. The work adheres to Elsevier's Publishing Ethics Policy and COPE guidelines for ethical publishing. Any third-party material is either original, appropriately licensed, or used with permission and fully credited. A separate Declaration of Generative AI and AI-assisted technologies in the writing process is provided immediately before the References. This article does not contain any studies with human participants or animals performed by the author.

Declaration of competing interest

The author declares no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Emmanuel Eroume A Egom: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Data curation, Conceptualization.

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Glossary

Acute trigger: Short-lived exposure transiently increasing MI risk (e.g., anger outburst).
Population-attributable risk (PAR): Proportion of events in a population attributable to a factor.
Reactive hyperemia index (RHI): Peripheral arterial tonometry measure of endothelial function.
Trait anger: Stable disposition toward anger, distinct from momentary state anger.