

Cold work and disease

A narrative review

*Albin Stjernbrandt*¹

*Eirik Reierth*²

*Tohr Nilsson*¹

Author affiliations:

ISSN: 3035-9821

¹ Department of Epidemiology and Global Health, Umeå University, Umeå, Sweden

² The Arctic University of Norway (UiT), Tromsø, Norway

Table of contents

Table of contents	i
Abbreviations and definitions	iii
Executive summary	v
1. Introduction	1
1.1 Cold work	1
1.2 Effects of cold exposure	4
1.3 The aging workforce	9
1.4 Overall objective and specific questions	11
2. Methods	11
2.1 Systematic literature search	11
2.2 Targeted literature search	13
2.3 Synthesis and evaluation	13
3. Results	13
3.1 Risk assessment of cold work	13
3.2 Cold work and aging	22
3.3 Cold work and specific diseases	23
3.3.1 Cardiovascular disease	24
3.3.2 Obstructive airway disease	29
3.3.3 Diabetes mellitus	34
3.3.4 Musculoskeletal disorders	36
4. Discussion	39
4.1 Overall objective	39
4.2 Specific questions	40
4.3 Recommendations	42
4.3.1 Cardiovascular disease	42
4.3.2 Obstructive airway disease	43
4.3.3 Diabetes mellitus	43
4.3.4 Musculoskeletal disorders	44
4.3.5 Periodic medical examinations	44
4.4 Methodological considerations	44
4.5 Knowledge gaps	46
5. Conclusions	48
6. References	49
Annex 1. Search string for the systematic literature search	65
Annex 2. Assessment of risk of bias	66

Abbreviations and definitions

ACGIH American Conference of Governmental Industrial Hygienists

ACT Asthma Control Test

CAT Chronic Obstructive Pulmonary Disease Assessment Test

FEV1 Forced expiratory volume during the first second

FVC Forced vital capacity

IREQ Required clothing insulation

ISO International Organization for Standardization

COPD Chronic obstructive pulmonary disease

MET Metabolic equivalents

mmHg Millimeter mercury

NYHA New York Heart Association (-class)

TRP Transient Receptor Potential (channel)

Cold work Work involving exposure to air temperatures at or below 10°C [1]

Clo One clo is the amount of insulation that allows a person at rest to maintain thermal equilibrium at 21°C and 0.1 m/s air movement ($\text{Kelvin} \times \text{meter}^2 \div \text{Watt}$) [2]

Cold exposure Cooling climate exposure, regardless of the type of physical environmental factors

Freezing cold injury Local cold injury (with the formation of ice crystals in the tissues) occurring at temperatures below 0°C.

Hypothermia Core temperature below 35°C [3]

Non-freezing cold injury Local cold injury (without the formation of ice crystals in the tissues) resulting from prolonged exposure to cold, moisture, and immobilization in temperatures above 0°C.

Climate exposure The ambient temperature, air speed, and humidity to which a person is exposed [3]

Cooling effect The net effect that exposure to cold has on the human body [4]

Cold allodynia Abnormal sensation where cold stimuli are perceived as painful

Cold-induced vasodilation	Hunting or Lewis reaction, meaning that blood vessels in the fingers recurrently dilate at a certain degree of local cooling [5]
Thermal climate	Physical factors affecting heat balance, such as ambient temperature, wind speed, and humidity [3]
Older workers	Working subjects between 55–70 years of age [6]

Executive summary

Stjernbrandt A, Reiherth E, Nilsson T. Cold work and disease. *Arbete och Hälsa* 2026;60(1):1-66.

This narrative review aimed to describe how health risks associated with cold work are affected by age and disease. A systematic literature search was conducted in MEDLINE, Embase, and Web of Science for the period 1980–2023, including three main concepts: cold environment, work, and risk assessment. The search resulted in 6965 articles, of which 277 were reviewed in full text, and 13 were included in the review regarding risk assessment and risk management of cold work. In addition to the systematic literature search, a targeted literature search was conducted, focusing on ageing and diseases.

The systematic literature search showed that established methods for structured risk assessment of work in cold environments exist, although working environments can vary widely. Most report that both age and disease can affect the vulnerability to cold.

The targeted literature search identified several small experimental studies showing that vulnerability to cold increases with age. This vulnerability may be due to changes in heat production, insulating capacity, peripheral vasoregulation, and temperature discrimination.

For cardiovascular disease, there was scientific evidence that exposure to cold leads to higher blood pressure, both in those with and without anti-hypertensive medication. Subjects with pre-existing cardiovascular disease have a lower physical work capacity and an increased likelihood of acute ischemic heart events and arrhythmias when exposed to cold. Cold exposure also appears to increase the likelihood of stroke.

In obstructive airway disease, the literature indicated that exposure to cold can increase symptom burden in subjects with asthma or chronic obstructive pulmonary disease. In particular, exposure of the face to cold can induce obstructive airway symptoms. There is also some evidence that previously healthy subjects exposed to cold may develop obstructive airway disease.

In the case of diabetes, exposure to cold can lead to impaired metabolic control, increased risk of hypoglycemia, increased susceptibility to hypothermia, and possibly increased risk of local cold injury and abnormal cold sensitivity.

Regarding the musculoskeletal system, there were studies showing that working in the cold increases the likelihood of reporting pain in various parts of the body. Working in the cold can also increase the likelihood of reporting nerve-related disorders such as sciatica and carpal tunnel syndrome.

In summary, there is scientific evidence that cold work may be associated with increased health risks for older subjects and with chronic diseases. The impact of cold work on work capacity and prognosis is unclear. There are methods for structured risk assessment and risk management of cold work, as well as practical suggestions for workers, employers, and occupational health services. Identified

knowledge gaps include the health effects of long-term, low-level occupational exposure to cold, sex differences, acclimatization, exposure-response relationships, and potential synergistic effects of cold and other exposures.

Keywords: Cold temperature; Cooling; Older Workers; Cardiovascular Diseases; Lung Diseases, Obstructive; Diabetes Mellitus; Musculoskeletal Diseases

1. Introduction

There are many occupational health and safety risks to consider, and they receive varying levels of attention across the workplace, health care, and research communities. Working in the cold can be an underestimated risk that often occurs alongside other physical work environment risks, such as exposure to hand-transmitted vibration, noise, and heavy lifting. This narrative review is intended to describe the risks of working in the cold from the perspective of particularly vulnerable groups, such as older workers and those with pre-existing conditions. The target group for the review is primarily medically trained personnel working in occupational health care, primary care, and occupational and environmental medicine clinics. The content may also benefit other stakeholders, such as employers and trade unions. The current publication is an abbreviated translation of a previous Swedish report: *Arbete & Hälsa* 2024;58(3).

1.1 Cold work

Cold work is defined as work performed at air temperatures at or below 10°C, according to the current ISO standard [1]. Older literature has used a temperature below 12°C instead [7]. Other definitions do not use temperature limits but are based on subjective experiences of cold [8], on the notion that heat loss occurs [5], or on the activation of the thermoregulatory system [9]. In both research and occupational health and safety work, there are no standard and uniform definitions of what cold means. Thermal climate refers to the physical factors that affect the heat balance, such as ambient temperature, wind speed, and humidity [3]. In outdoor work, climate exposure refers to the ambient temperature, air speed, and humidity to which a person is exposed. Regarding cooling climate exposure, one can use the terms cold or cooling exposure instead. The cooling effect describes the impact on the human body when exposed to cold. In this narrative review, we have used 'cold' as an overarching term and have not defined it in more detail with respect to the actual climate exposure.

Exposure to cold can lead to heat loss in several ways (Table 1) [4]. When working at low ambient temperatures, heat is mainly lost by convection, with the heated air around the body surface being transported away. This effect is enhanced by wind speed. When simultaneously exposed to both low ambient temperatures and strong wind, it is therefore valuable to consider the combined effect by calculating the wind chill equivalent temperature index [10]. Heat radiation from the body also contributes to heat loss, though this effect is much less significant than convection for a clothed person in a cold climate. However, if clothing is inadequate, thermal radiation can become the dominant type of heat loss, accounting for about two-thirds of total heat loss [11]. Radiant heat transfer can also result in a net gain, for example, through emission from dark surfaces, infrared heaters, and sunlight. Breathing can also contribute to cooling when cold air is inhaled, heated and humidified in the airways, and then exhaled. These losses increase with respiratory rate, which in turn correlates with physical exertion. As moisture from the skin surface evaporates, heat

is also lost, and this effect is enhanced by sweating. In the cold, this mechanism is generally inefficient because multiple layers of clothing prevent vapor from escaping from the body, which can instead be absorbed into the clothing, reducing its insulating capacity. Both respiratory and evaporative heat loss are mainly dependent on ambient temperature and humidity [11]. The body preserves core temperature by allowing cooling of more distal parts, for example, by peripheral vasoconstriction in the hands and feet. This means that local cold injury can occur long before any signs of hypothermia (whole-body cooling) are seen. Body parts in contact with cold objects, surfaces, liquids, or gases can be cooled very rapidly. Some materials, such as aluminum, have high thermal conductivity, meaning heat is effectively conducted away from the skin through contact surfaces. This heat conduction can be counteracted by wearing gloves or by covering such materials with an insulating layer of foam padding. Water conducts heat about 25 times more efficiently than air, and both direct contact with water and wet clothing can produce a very noticeable cooling effect [12]. Some fuels used in cold environments, such as gasoline, ethanol, and kerosene, have freezing points below 0°C and can therefore quickly cause severe local cold injury if they come into contact with unprotected skin [13]. In addition, many of these fuels evaporate rapidly, thereby physically increasing heat loss, since evaporation is an endothermic process (absorbing heat from its surroundings). Liquefied gases such as propane, butane, and liquid nitrogen can also cause extremely rapid local cooling for the same reasons. The proportions of heat loss from different types vary widely depending on environmental and individual factors. Still, a general scenario for a standing person dressed outdoors in a cold climate is presented below (Table 1).

Table 1. Schematic description of heat losses in a cold environment for a standing person dressed for outdoor activities.

Type of heat loss	Mechanism	Proportion
Convection	Heated air around body surfaces is dispersed	50–80 %
Respiration	Heated and humidified air is ventilated out of the respiratory tract	10–15 %
Radiant heat	Mainly infrared radiation emitted from body surfaces	10–20 %
Evaporation	Moisture on skin surfaces evaporates	5–20 %
Conduction	Heat is transferred through contact surfaces	2–3 %

In the Nordic countries, the climate is highly variable, mainly due to westerly and southerly air currents influenced by the Scandinavian mountain range, inducing shifts between distinctly cold and warm periods [12]. Temperature variations in the Nordic countries are among the largest in the world, as are cloudiness levels. In

Sweden, it is estimated that over 20% of men and 10% of women spend at least a quarter of their working time in a cold environment [14]. Work environments can vary widely depending on place of residence and occupation. Some involve working outdoors for whole days in temperatures as low as -30°C in the north of the country during winter. In contrast, other situations may involve much shorter and less intense exposures. Some jobs also involve rapid transitions between hot and cold environments, requiring dynamic physiological temperature regulation and advanced workwear. For example, when working with heavy lifting in a warehouse with typical indoor temperatures and only occasionally being outdoors in the cold, adequate clothing in the latter environment may pose a risk of sweating in the former. Conversely, there is a risk of hypothermia when outdoors if clothing is adapted for physically demanding work in normal indoor temperatures instead. In addition, time constraints may make it difficult for workers to adjust their clothing to the thermal climate. In outdoor settings, climatic factors other than ambient temperature can influence exposure to cold, such as wind, humidity, and precipitation. In addition, ambient exposure to cold is often seasonal, occurring only during a limited part of the year [5]. Thus, when assessing the risks of working in the cold, it is essential to account for actual climate exposure rather than relying on single measurements of ambient temperature [3]. Some jobs are conducted wholly or partly in artificially cooled indoor environments, such as chilled and freezing cold rooms. In such environments, exposure is more constant, and the climate is usually strictly regulated. However, it can still involve exposure to draught (and therefore convection) due to high air turnover and extremely low temperatures, sometimes colder than -50°C .

Industries where cold work is common in Sweden include construction, transportation, outdoor environmental management, and childcare. In some specialized sectors, such as forestry, agriculture, reindeer herding, fishing, and mining, exposure can also be very pronounced even if fewer workers are employed. Statistics Sweden conducts the biennial Work Environment Survey on behalf of the Swedish Work Environment Authority to map the physical and psychosocial work environment in Sweden [14]. According to these surveys, men generally report greater exposure to cold than women (Figure 1). There is also a tendency for occupational cold exposure to decrease with age, for both men and women [14]. This pattern has also been described in a study from northern Sweden, which found that occupational exposure to cold appears to become less pronounced with increasing age [15]. Conversely, in Finland, the duration of cold exposure at work was highest among men aged 55–64 years, whereas no age difference was observed among women [9]. Another interesting finding in the Work Environment Survey is that the proportion of older subjects (50–64 years) exposed to cold appears to have increased slightly over time, suggesting a larger proportion of the older workforce is continuing in cold-exposed jobs now than before. This aligns with a general trend of more people working at older ages, including in physically demanding outdoor jobs such as construction [16, 17].

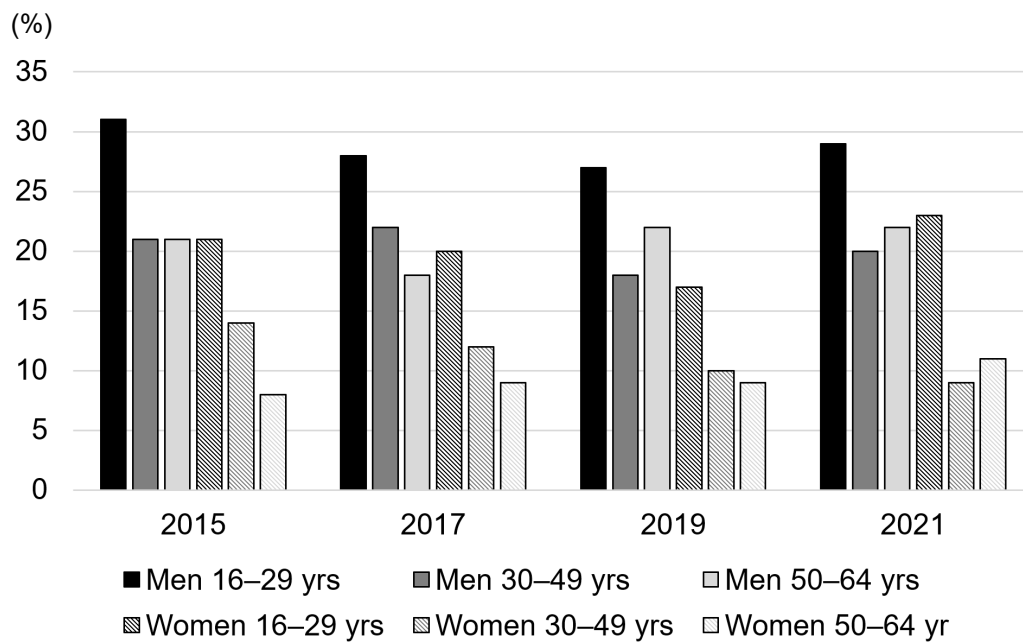


Figure 1: Percentage of respondents who reported working in the cold at least a quarter of the time, stratified by sex and age group. Data from The Work Environment 2015–2021 [18].

Work injury statistics from the United States show that cold-related injuries are most common in the oil and gas industry, transportation, electricity and gas distribution, sanitation, automotive service, food manufacturing, and construction sectors [11]. Corresponding statistics from Sweden are not available, but according to Afa Insurance, about 2% of serious occupational accidents are related to temperature (heat, fire, explosion, welding, electricity, or cold) [19].

Global climate change involves a gradual increase in average temperature, and the rate of warming is higher in the northern regions [20]. In the Arctic setting, warming is estimated to be about four times faster than the global average [21]. Climate change also results in more severe weather events such as heat waves, cold spells, storms, and floods [22]. Despite global warming, extreme cold periods will continue to occur and, based on predicted trajectories, there is reason to believe that adverse health impacts related to exposure to cold rather than heat will dominate in Arctic and subarctic regions in the coming decades [22, 23]. According to some estimates, direct temperature-related mortality in Europe will remain greater for cold than for heat for the foreseeable future [23, 24].

1.2 Effects of cold exposure

The impacts of cold exposure on the human body depend on several individual factors, such as age, sex, body composition (proportion of skeletal muscle and subcutaneous fat), fitness, anthropometric measures [typically height, weight, and body mass index (BMI)], diseases, medication, clothing, and physical activity level. [25]. People with physical disabilities and pregnant women can be considered

particularly vulnerable [26]. The body functions most effectively if the core temperature is kept very close to 37°C. Skeletal muscles are vital for heat generation, and the intensity of physical activity largely determines the effect, as reflected in energy expenditure. Physical activity levels are often described in terms of metabolic equivalents (METs), defined in terms of oxygen consumption. For example, complete rest is equivalent to 1 MET, and heavy physical effort, such as running, is equivalent to about 10 METs. This also reflects the range of our heat-generating effect (Table 2). This effect can also be expressed in watts (W), and ranges from around 100 W at rest to 1000 W during heavy physical activity. However, at work, the physical activity level rarely reaches above 5 MET (500 W) [4]

Table 2: Examples of physical activity levels and heat production for different tasks.

Task	Metabolic equivalent (MET)	Heat production (Watt)
Resting	1	100
Very light work (sitting manual work, standing observation)	1,5	150
Light work (sitting assembly or sorting, standing drilling, slow walking)	2	180
Moderately heavy work (standing nailing, grinding, raking)	3	280
Heavy work (standing lifting, shoveling, paving, moderate walking)	4	400
Very heavy work (climbing, fast walking)	5	500

Adapted from data from Holmér [4].

In addition, the efficiency of our muscles varies with the degree of physical exertion. In dynamic work with large muscle groups, efficiency is around 30%, meaning that the remaining 70% of energy expenditure is converted into heat rather than force development [3]. For less physically demanding work, such as arm movements, the efficiency is much lower, around 15%.

The insulating capacity of clothing can be expressed in units of clo, where one clo corresponds to the amount of insulation that allows a person at rest to maintain thermal equilibrium at 21°C and 0.1 m/s air movement [2]. Normal indoor clothing corresponds to approximately 0.3–1.2 clo [27]. A full polar suit can reach around four clo but is also the practical limit of how warmly one can dress while retaining any degree of mobility. For the hands, it is more challenging to provide sufficient

insulation, and gloves with fingers usually correspond to about one clo, while mittens can reach about two clo [28]. Insulation capacity in clo can be expressed for a single garment or calculated for the entire outfit [29].

Temperature regulation in the human body can be divided into afferent and efferent systems. The afferent system consists primarily of thermoreceptors, which are temperature-sensitive ion channels found in free nerve endings in the skin, but also in the abdominal cavity, the large blood vessels, and the central nervous system [30]. Thermoreceptors belong to the family of transient receptor potential (TRP) channels, and several types are activated over different temperature ranges [31]. In most parts of the body, information about temperature is conveyed through sensory spinal nerves that connect to the lateral spinothalamic tract, which in turn projects to the thalamus and the sensory cortex [32]. Temperature stimuli on the face are transmitted via the trigeminal nerve to the thalamus, which is essential for certain reflex responses to facial cooling [33]. The efferent system consists of the hypothalamus as the main temperature-regulating center of the central nervous system, which initiates various physiological responses to maintain thermal balance, including shivering and peripheral vasoconstriction. Shivering is defined as involuntary, asynchronous contractions of antagonistic skeletal muscle groups, such as the biceps and triceps of the upper arm. Shivering can increase heat production effectively (at least 4–5 times) but only for a limited time due to the high energy expenditure [34]. In addition, shivering is generally perceived as very uncomfortable and therefore serves as an important signal to seek shelter and warmth [4]. Shivering is initiated when core temperature decreases (below about 36°C), is most effective at 35°C, and then diminishes as body temperature decreases, disappearing completely at about 33°C. Shivering occurs preferentially at low levels of physical activity [3].

The cutaneous circulation also plays a vital role in temperature regulation. In thermoneutral conditions, the average cutaneous blood flow is about 0.3–0.5 liters per minute [35]. Under severe cold exposure, this can decrease to almost zero, and under maximum heat stress, it increases to around 7–8 liters per minute [36]. This large variation in perfusion results in great capacity to regulate thermal balance, and also affects the insulating capacity of peripheral tissues (since hypoperfusion results in lower conductance). Thus, at maximal peripheral vasoconstriction, heat losses are reduced in several ways. Firstly, the gradient between the skin surface and the surroundings is lower, and secondly, the thermal conductivity of the hypo-perfused tissues is reduced. In addition, blood flow is redirected to deeper vessels, acting as a heat exchanger. Although many vasoactive substances have local effects on vascular tone, the sympathetic nervous system appears to be the main controller of vasoregulation, via the release of noradrenaline. In the glabrous skin covering the hands, feet, and parts of the face, there is an extensive network of arteriovenous anastomoses where blood can be shunted directly from arterioles to venules without passing through the capillary bed, providing a particularly effective means of regulating thermal balance. These shunts are mainly regulated by adrenoceptors in the vessel walls with an affinity for noradrenaline [35]. Unlike glabrous skin, blood flow to the head is relatively constant. Therefore, more than half of the body's heat

loss can come from the unprotected head of an otherwise appropriately dressed person at -10°C [4].

Previous research has suggested that adaptations to a cold climate occur both over a lifetime and across generations. Adaptations have been proposed to occur in at least three different ways [5]:

1. Hypothermia adaptation, where the body temperature is allowed to fall slightly to reduce heat loss.
2. Insulating adaptation, where heat losses are reduced by increasing the amount of adipose tissue (which may be more or less metabolically active) and gradually adjusting anthropometric measures that affect surface area relative to volume (such as shorter and thicker fingers).
3. Metabolic adaptation, whereby resting heat production is increased, for example, through thyroid hormone activation and increased energy metabolism in adipose tissue, muscles, and liver (sometimes referred to as 'non-shivering thermogenesis').

These adaptations involve the overall heat balance. In addition, there are likely to be more short-term adaptations of temperature regulation in the hands and feet through altered cutaneous perfusion. These adaptations include attenuation of physiologic peripheral vasoconstriction or a more pronounced response in the form of cold-induced vasodilation (also referred to as the hunting or Lewis reaction) [5]. The latter is a physiological response to severe cold exposure that has been studied mainly in the hands. When the tissue temperature in the fingers falls below about 10 to 15°C , maximal vasoconstriction is replaced by cyclic vasodilation that occurs at intervals of about 5–10 minutes. This partially rewarms the fingers to protect against local cold injury and maintain some sensation and motor function. However, with continued exposure to cold, periods of vasodilation become shorter and more frequent until they finally disappear completely. The cold-induced vasodilation response may be particularly pronounced in subjects who are frequently exposed to contact cooling, but has been reported to be less pronounced in some ethnic groups, such as African Americans [37]. Finally, there are also psychological adaptations in which the experience of cold may change with regular exposure [3].

Cooling effects can be categorized by the body part affected: whole-body cooling, local cooling (peripheral body parts), and respiratory cooling [38]. Both whole-body and local cooling can occur at temperatures above freezing (0°C) [11]. Local cooling can lead to local cold injuries, which are usually divided into two main types, depending on whether they occur at sub-zero temperatures ("freezing cold injuries") or above freezing temperatures ("non-freezing cold injuries") [39]. In military contexts, non-freezing cold injuries affecting the feet have sometimes been referred to as trench foot or immersion foot, highlighting the importance of simultaneous exposure to cold and moisture in their development.

In addition to local cold injuries, which have an obvious association with cold climate, a large number of other symptoms, diseases, and injuries have been linked to cold exposure (Figure 2) [25]. Interpretations of the association between exposure

and outcomes often differ. In some cases, a causal relationship between exposure to cold and the onset of a particular condition has been established. In other cases, cold exposure is considered a contributing factor that cannot alone cause the condition, an aggravating factor for a condition that has been caused by other factors, or a trigger that produces symptoms of a particular disease. An example is Raynaud's phenomenon (white fingers), where some consider exposure to cold a causative factor, while others see it primarily as a trigger [40-42]. In many cases, drug treatments can also exacerbate the effects of cold. An example of this is ischemic heart disease, which can be treated with beta-receptor antagonists that alter peripheral and central vasoregulatory responses [43, 44]. Other examples of drugs that can affect susceptibility to cold are central stimulants (methylphenidate, lisdexamfetamine, atomoxetine), alkaloids (quinine, ergotamine, atropine), benzodiazepines (diazepam, oxazepam, lorazepam, alprazolam), opiates and opioids (morphine, codeine, tramadol, oxycodone, methadone), and neurotoxic cytostatics. Finally, exposure to severe cold generally induces subjective discomfort that is likely to occur earlier than most adverse somatic health effects and prompts a range of behavioral measures to reduce exposure [5]. Examples of such measures include increasing physical activity, increasing clothing, and seeking heat sources or shelter.

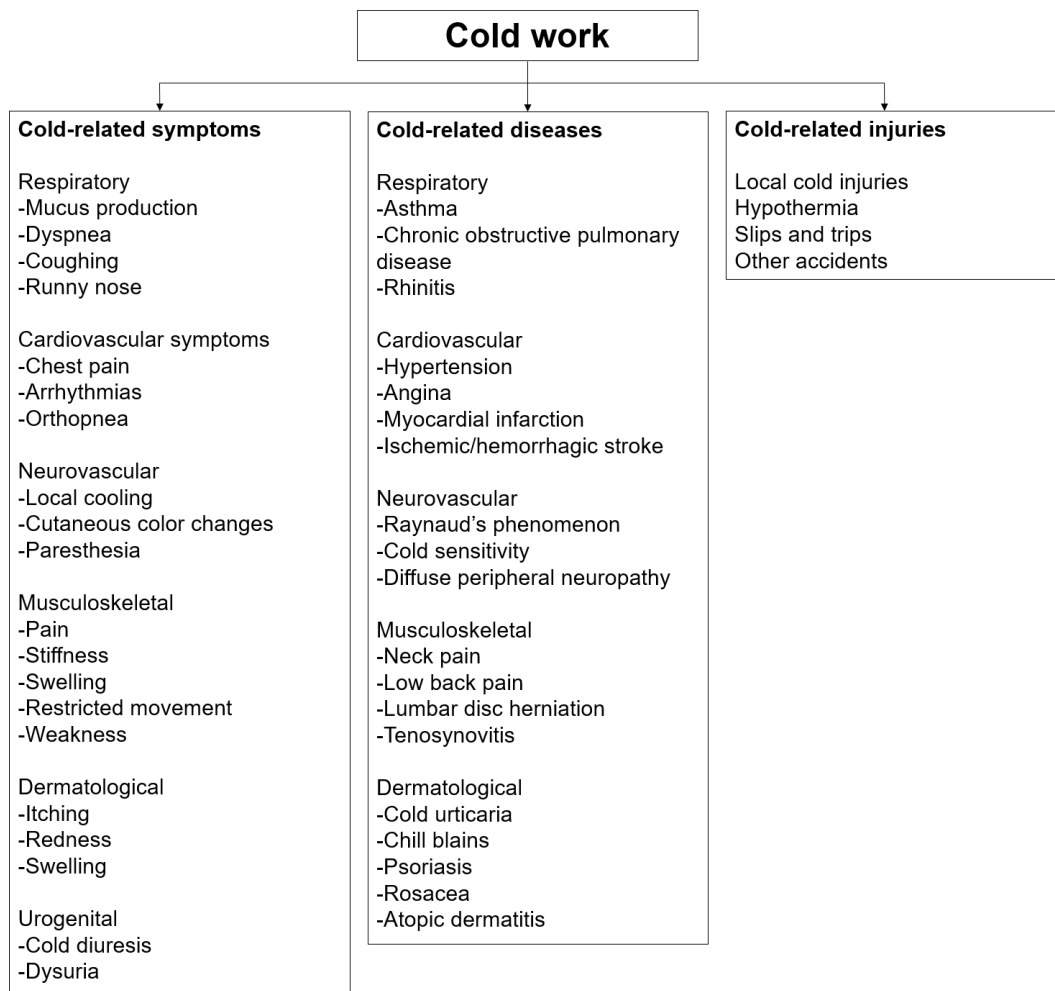


Figure 2. Symptoms, diseases, and injuries associated with working in the cold. Adapted from Mäkinen et al. [25].

1.3 The aging workforce

In most parts of the world, populations are characterized by an increasing proportion of older people, as birth rates decline, and people live longer. This changes the ratio of working-age to retired people and has implications for pension and other social security systems [6]. Current estimates suggest that the proportion of the European population aged over 60 will have doubled to around 40% by 2050 [6]. There is no single definition of older workers, but it has been suggested that it should include subjects aged 55–70, with the caveat that the range may need to be shifted to even higher ages in the future [6]. As health issues increase with age (Figure 3), more people will be working with chronic diseases, and exposure to cold can potentially increase symptom burden, reduce work ability, or worsen the prognosis of the underlying condition.

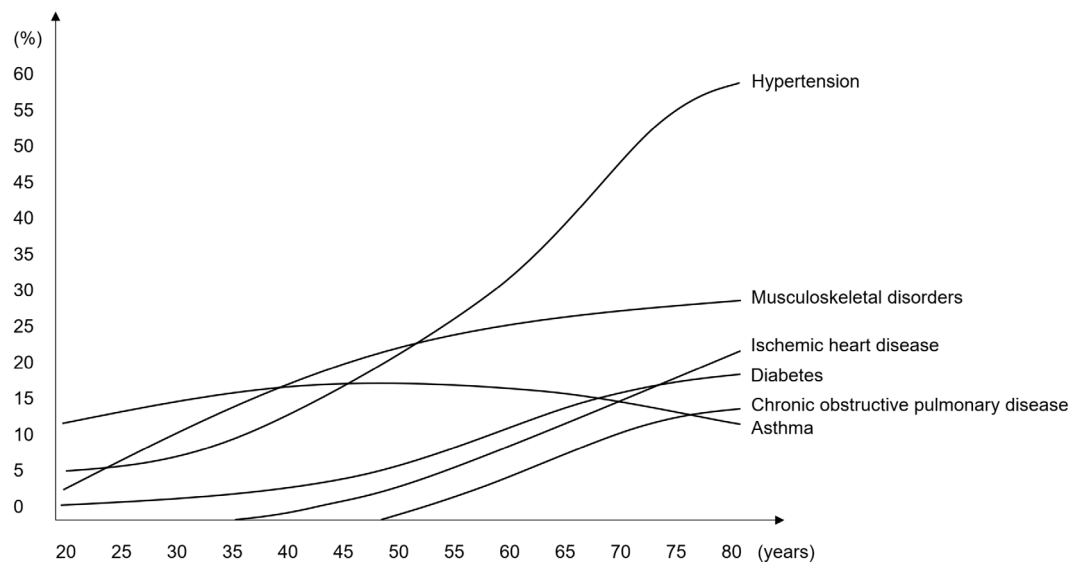


Figure 3. Schematic description of the prevalence of different diseases in Sweden according to age. Based on data from the National Board of Health and Welfare [45] and the Public Health Agency of Sweden [46].

Work ability is a complex concept that can encompass both the ability to perform a specific job that has been mastered at some stage, as well as a more generic ability in relation to normally occurring jobs [47]. In the latter, more general definition, work ability can be understood as the balance point between job demands and the individual's functional capacity (Figure 4). However, this balance can be shifted by external factors, such as exposure to cold, and by individual factors, including age and disease. Chronic diseases that develop in middle age, even if treatable, can often affect work capacity, both through limitations in specific tasks and in overall productivity. Therefore, there is a need to shift perspectives from focusing on limitations to emphasizing residual capacity [6]. In this context, it may also be necessary to consider how exposure to cold can limit work capacity.

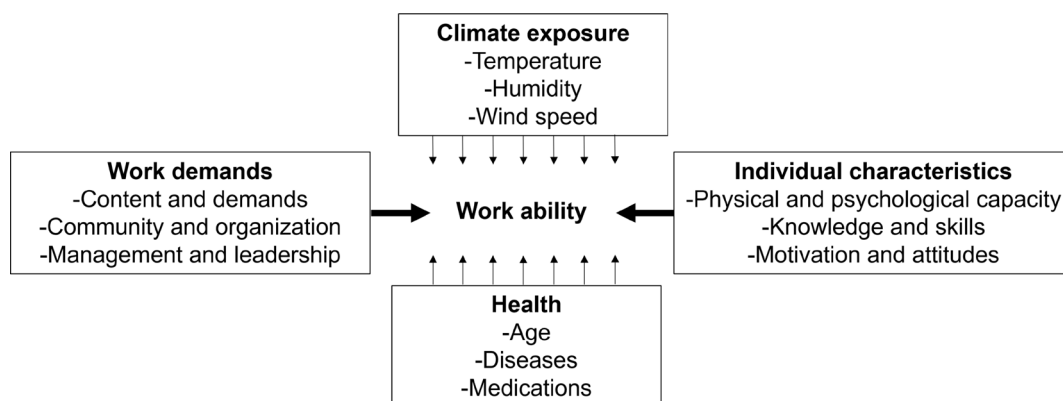


Figure 4: Schematic representation of how climate exposure and health could affect work ability, loosely based on the concept of Ilmarinen et al. [48].

1.4 Overall objective and specific questions

This narrative review aimed to describe how health risks associated with cold work are affected by age and disease. Specific questions included:

1. How can the risks of working in the cold be assessed in relation to age and disease?
2. How does ageing affect the susceptibility to cold?
3. What are the specific health risks of working in the cold if you have pre-existing cardiovascular disease, obstructive airway disease, diabetes, or musculoskeletal disorders?
4. What are the knowledge gaps in this area?

2. Methods

2.1 Systematic literature search

The literature review was based on a systematic search in MEDLINE, Embase, and Web of Science. The rationale for searching in several overlapping databases was that they index articles from different journals. Standardized search terms (MeSH/Emtree index) were combined with free-text searches of the title, abstract, and keywords. The search was limited to English-language medical literature and to human studies published between 1980 and 2023. The search string comprised three main concepts: cold environment, work, and risk assessment (Annex 1). The literature search yielded 6965 articles, and their abstracts were reviewed by two independent reviewers and assessed against pre-established inclusion criteria.

Disagreements were resolved by consensus discussion with a third reviewer. After selection based on the abstracts, 273 articles remained; upon review, four additional papers were identified from their reference lists. A total of 277 full-text articles were thus reviewed (Figure 5).

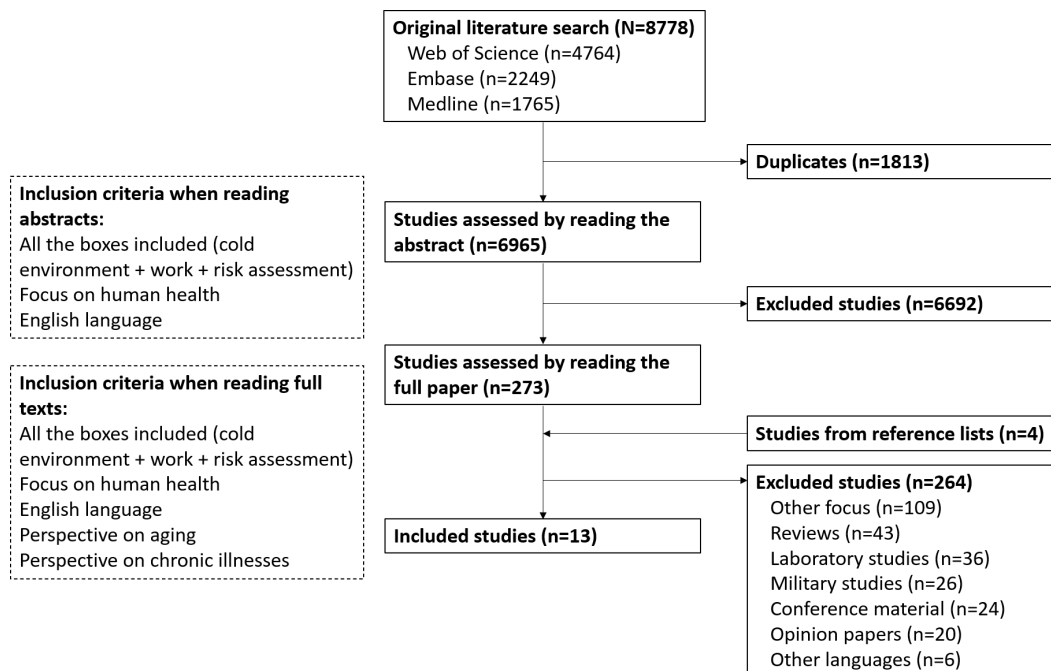


Figure 5. Flowchart showing the systematic literature search.

When reading the abstracts, most studies were excluded because they lacked one or more of the three main concepts defined in the inclusion criteria. Most were not studies in human medicine but rather entailed, for example, microbiological agents, meteorological conditions, or the tensile strength of materials in relation to temperature.

Studies excluded due to other focus (n=109) lacked any of the following perspectives: work, cold, risk assessment, human health, ageing, or chronic diseases. Review articles (n=43) were excluded from the systematic literature search but were included in the targeted literature search. Laboratory studies (n=36) that lacked a human perspective were excluded, such as technical testing of clothing, gloves, and shoes. Articles that strictly dealt with military conditions (n=26), such as the composition of food rations during field exercises, were also excluded. Conference material (N=24) referred to indexed conference abstracts and proceedings. Opinion pieces (n=20) included position papers and letters to the editors, where original data and analysis were missing. Finally, some articles had English summaries (n=6) but were written in another language.

2.2 Targeted literature search

In addition to the systematic literature search, a targeted literature search in MEDLINE was performed, where the third main concept (risk assessment) was replaced with MeSH terms for the concepts of interest to the narrative review: Aging; Cardiovascular Diseases; Hypertension; Myocardial Infarction; Stroke; Heart Failure; Peripheral Arterial Disease; Lung Diseases; Asthma; Pulmonary Disease, Chronic Obstructive; Diabetes Mellitus; Musculoskeletal Pain; and Musculoskeletal Diseases. This search included all article types, publication years, and languages.

2.3 Synthesis and evaluation

From the 13 articles included in the systematic literature search, information was extracted regarding authors, title, year of publication, overall purpose, country of study, study population (occupation, number of subjects, and age composition), exposure to cold, sex, perspective on ageing, and which individual factors were investigated or discussed. To make a basic assessment of risk of bias, information was also extracted on how exposure and health outcomes were defined, the study design, population size, response rate, and non-response during follow-up. These data were entered into a matrix (Annex 2) inspired by Farbu et al. [49]. The outcomes of these variables were considered when evaluating the studies, but the results were not stratified by risk of bias. For the articles identified in the targeted literature search, no systematic extraction was performed. We also drew on the authors' prior knowledge of the published literature in this field. Statistical measures (such as odds ratios, relative risks, and confidence intervals) were rounded to one decimal place. Age was rounded to whole numbers.

3. Results

3.1 Risk assessment of cold work

Thirteen studies met the selection criteria for the systematic literature search (Table 3). These were published between 1995 and 2022. Six articles were from a Nordic university, the others from Germany, France, Iran, the USA, Canada, Brazil, and China. Three reported results separately for men and women, and six reported on artificially cooled indoor environments.

Table 3. Studies analyzed in the systematic literature search, ordered by year of publication.

Author and year	Aim	Country	Study population	Exposure (° C)	Sex-stratified results	Ageing perspective	Individual perspective
Olesen 1995 [50]	To evaluate methods for assessing cold and hot work environments and individual physiological parameters of workers	Germany	Not specified	Indoor and outdoor thermal climate	No	No	Individual capability
Holmér 2001 [51]	To describe a method for assessing exposure to cold	Sweden	Workers in cold environments	Low ambient temperatures (below -5°C)	No	Yes	Special illnesses
Mäkinen et al. 2002 [52]	To develop methods for the assessment and management of specific risks associated with occupational exposure to cold, and improve the knowledge of cold environments of participating companies	Finland, Sweden, Norway	Construction workers in Finland and Sweden, forestry and road workers in Sweden, and fish workers in Norway	Outdoor work and artificially cooled indoor environments	No	No	Health-related limitations

Hassi et al. 2003 [53]	To produce a health survey for workers exposed to cold	Finland	Not specified	Low ambient temperatures (at or below 10 °C)	No	No	Abnormal cold sensitivity, cold urticaria, respiratory symptoms, angina pectoris, arrhythmia, disturbed peripheral circulation, migraine, Raynaud's phenomenon, local cold injury, musculoskeletal pain
Besnard et al. 2004 [54]	To develop a computer program to help physicians assess the thermal balance at different physical activity levels and environmental conditions, and to suggest exposure duration limits	France	Not specified	Not specified	No	Yes	No
Risikko et al. 2008 [55]	To evaluate the implementation of risk management strategies for working in the cold	Finland	Outdoor workers in the Finnish Maritime Administration (n=314); average age 48 years	Outdoor work	No	No	Cold-related adverse effects

Gao et al. 2008 [56]	To compile information on wintertime slipping accidents with a focus on footwear and workers' perspectives	Sweden	Newspaper deliverers (n=66), military conscripts (n=40), miners (n=52), and construction workers (n=25) in northern Sweden; age range <20 to 69 years	Outdoor work	Yes	No	Illness
Noroozi et al. 2014 [57]	To propose a new methodology to assess the impact of cold working environments on human performance	Canada, USA	Operators and engineers in offshore oil and gas processing	Working in Arctic and subarctic environments	No	Yes	Ill health
Ceballos et al. 2015 [58]	To describe working conditions in an airline catering facility and propose improvements regarding the working environment	USA	Food workers (N=130)	Artificially cooled indoor environments (5 to 6°C)	No	No	Certain infectious diseases, cardiovascular and metabolic disorders, musculoskeletal problems

Jussila et al. 2017 [59]	To investigate miners' protection strategies against cold and assess whether adequate protective clothing is used	Finland	Open-pit miners in northern Sweden, Norway, Finland, and Russia (N=1323); average age 40 years with a range of 18–78 years	Outdoor work	Yes	Yes	Poor general health
Tirtoni et al. 2018 [60]	To analyze finger temperature in butchers and how it can be linked to individual and organizational factors	Brazil, Brazil	Slaughterers and food technicians in poultry handling (N=143); average age for women 32 years with a range of 18–55 years, for men 29 years with a range of 18–54 years	Artificially cooled indoor environments (9 to 12°C), handling of food products (1 to 11°C)	Yes	Yes	No
Tsang et al. 2018 [61]	To propose a risk monitoring system for both occupational health and safety risks and product quality in food logistics based on an Internet of Things-based risk monitoring system	China	Manufacturers, distributors, and retailers of temperature-sensitive foods	Artificially cooled indoor environments (–25 to 8°C).	No	Yes	No

Golbabaei et al. 2022 [62]	To assess the health effects of cold exposure in petroleum industry workers	Iran	Technicians (n=18), mechanics (n=10), and control room operators (n=8) at fuel transfer stations; most in the 36–45 age range	Outdoor work (–24 to 5°C)	No	No	Hypertension, angina pectoris, and asthma
-----------------------------------	---	------	---	---------------------------	----	----	---

Olesen et al. [50] presented various ISO standards for assessing indoor and outdoor thermal climates, both hot and cold. The authors described that when working in the cold, clothing is the single most important factor in maintaining adequate thermal balance, and that calculating the required clothing insulation (IREQ) can aid risk management. It is based on an equation that considers physical activity level and various environmental factors, including air temperature. The article did not assess the effects of ageing. Still, it was emphasized that there may be a need to assess workers' individual capacity to perform given tasks under challenging conditions, and that this can be done either in the field or in a laboratory.

Holmér [51] described a method for assessing occupational exposure to cold, focusing on temperatures below -5°C . The article addressed the effects of cold on the whole body, the extremities, the skin, and the airways. It described how age, sex, health, fitness, acclimatization, experience, and knowledge modify cooling effects but did not specify how. It was suggested that subjects who are particularly sensitive to cold or have certain "special illnesses" might need to be assessed using methods beyond those included in current ISO standards. However, these methods were not specified.

Mäkinen et al. [52] reported on the process that later resulted in ISO 15743 – Ergonomics of the thermal environment – Cold workplaces – Risk assessment and management - and the study was based on construction workers in Sweden and Finland, forestry and road workers in Sweden, and fish workers in Norway. It focused on identifying health-related limitations to cold work using a survey tool that asked workers whether they had any problems related to cold exposure. However, health conditions that could be important for cold work were not reported. A process for disseminating information and training on the health risks associated with cold work was also briefly described.

Hassi et al. [53] described the content of the survey presented above in more detail, stating that health conditions of importance for the assessment may be abnormal cold sensitivity, cold urticaria, respiratory symptoms, angina pectoris, arrhythmia, compromised circulation in hands or feet, blurred vision, migraine, Raynaud's phenomenon, local cold injuries, and musculoskeletal pain. The survey also assessed performance in cold work, including concentration, motivation, grip strength, and other musculoskeletal functions. If there were signs of reduced comfort or specific vulnerability, a nurse suggested actions. If there were symptoms of disease, it was recommended that medical doctors be involved in the assessment. It was also suggested that periodic medical examinations could be useful for subjects with cold-related conditions or other health and performance limitations, but no further details were provided.

Besnard et al. [54] reported on the development of a computer program to help doctors prevent temperature-related disorders. This program, called PREDICTOL®, was used to calculate how long subjects could work in cold environments without risk of adverse health effects. These calculations were based on physical activity and technical clothing parameters. Still, individual factors such as age, height, weight,

and body fat percentage were also included in the list of variables. However, it was not clear how age was considered to modify cooling effects.

Risikko et al. [63] evaluated the implementation of a risk assessment tool for cold work in the Finnish Maritime Administration. It was based on systematic work environment management and four levels of implementation: management system changes (organizational level), risk management strategies across workplaces (action level), worker training (awareness level), and occupational health activities (support level). The project was evaluated after three years, including a survey of 314 subjects with an average age of 48. In summary, the authors reported increased awareness of working in the cold, but no real improvements in exposure to physical workplace risks in general, nor any difference in cold-related adverse effects. Cold conditions were described as affecting human health by exacerbating symptoms of many chronic diseases, but the details were not specified.

Gao et al. [56] investigated slipping accidents among 183 subjects working in cold outdoor environments. The study included newspaper deliverers, military conscripts, miners, and construction workers in northern Sweden. There were a few subjects aged 60 or over among the newspaper deliverers and miners, but not in the other occupational groups. Both sexes were represented. The emphasis was on environmental factors considered important for slipping accidents. Still, individual factors that could be assumed to increase the risk of slipping were also described (impaired vision, balance, proprioception, musculoskeletal function, or other illness). It did not specify which diseases could affect risk or how.

Noroozi et al. [57] presented a risk assessment tool for human error in the Arctic and Subarctic offshore industry. Human error referred to the risk of accidents but also incorrectly performed work tasks in a broader sense. The tool included individual parameters, such as excess physical capacity and operator ill health, and specifically addressed the importance of personnel age in performing perceptual tasks. The relative importance of different risks was also assessed, with old age receiving the lowest weighting among the 38 variables included in the model, indicating that old age per se was not considered a particularly important explanation for human error in this environment.

Ceballos et al. [58] described the physical work environment of factory workers preparing food for air travel, including 130 subjects whose age was not specified. These environments were cooled to around 5 to 6°C, and the tasks involved contact with cold objects and repetitive work. The study was technically oriented, with no actual human health outcome parameters. Still, it was reported that there were specific risks associated with cold work for subjects with pre-existing conditions such as infectious diseases, cardiovascular and metabolic disorders, or musculoskeletal problems.

Jussila et al. [59] investigated the insulating capacity of workwear among miners in the Arctic region, including 1323 subjects, most of whom worked in a Russian open-pit mine but some also worked in mines in northern Sweden, Norway, and Finland. The mean age was 40 years (standard deviation 11 years), and 46 subjects (3.5%) were 60 years or older. Both sexes were represented. The amount of clothing workers

chose to wear was analyzed in relation to age, sex, weight, or BMI. The study found no statistically significant differences based on these individual factors and the insulating capacity of the chosen clothing. However, there was a trend where subjects with a low or normal BMI ($<25 \text{ kg/m}^2$) appeared to choose clothing with a higher insulating capacity than those with a high BMI ($\geq 25 \text{ kg/m}^2$). Workers reporting bad general health also tended to choose clothing with a higher insulating capacity than those with good self-rated health.

Tirloni et al. [60] investigated 143 poultry slaughterhouse workers exposed to artificially cooled indoor environments. Both sexes were represented. The ambient temperature ranged from 9 to 12°C, and the workers handled foodstuffs at temperatures ranging from 1 to 11°C. Finger temperature was measured by infrared thermography, and 66% of the workers had at least one finger with a temperature $\leq 15^\circ\text{C}$. The workers were aged 18–55 years, and no statistically significant effect of age on finger temperature was found.

Tsang et al. [61] described a fuzzy-logic software system aimed, among other things, at assessing risks in the working environment of cold transport chains for foodstuffs. The project was based on a cyber-physical system ("Internet of Things") in which technical devices are connected to the Internet and communicate within a complex system. The working environments included both chilled cold rooms (0 to 8°C) and freezing cold rooms (–25 to –18°C). The assessment was partly based on ISO 11079 – Ergonomics of the thermal environment – Determination and interpretation of cold stress when using required clothing insulation (IREQ) and local cooling effects, and the program used age and BMI as variables in the risk assessment. Still, the article did not specify how these factors were considered to modify the risks.

Finally, Golbabaie et al. [62] described a risk assessment strategy for working in the cold at fuel transfer stations in Iran. The ambient temperature during the study ranged from –24 to 5°C among 18 technicians and ten mechanics, and there was also a control group of eight subjects working indoors at 22°C with supervisory tasks. The authors asked about the age range in a questionnaire, and most were aged 36–45 years. It was described that exposure to cold could exacerbate symptoms of certain diseases, such as high blood pressure, angina, and asthma. Based on this, screening and medical examinations may be warranted for workers operating in cold environments.

Conclusions:

- There are established methods for structured risk assessment of work in the cold.
- Cold work is a heterogeneous concept encompassing many different working environments and climate exposures.
- Most identified studies on risk assessment of cold work report that both age and the presence of disease can affect the vulnerability to cold, but do not specify how.

3.2 Cold work and aging

We wanted to identify how aging affects the cooling effects at work. Our systematic literature search identified no studies that specifically examined the risks of cold work at older ages. In the complementary targeted literature search, most studies on age and cold had a physiological focus without an occupational context.

One study found that the physical activity levels practiced in most occupations produce less metabolic heat than physical exercise, suggesting that, in many cases, workers cannot sufficiently compensate for severe cooling climate exposure through physical activity [64]. This is an important difference from, for example, elite-level endurance athletes, for whom several studies have investigated the effects of prolonged exposure to cold and shown that a high level of physical activity can largely compensate for it [65]. Moreover, it is difficult to separate the specific effects of ageing from the impact of chronic diseases and changes in body composition (body fat percentage and skeletal muscle mass), both of which are strongly associated with age [64]. Regarding the ratio of body fat to other constituents, the main beneficial effect of subcutaneous adipose tissue is maintaining body temperature through passive insulation, but this mechanism appears less effective in older compared to younger people. For example, a UK study compared core temperature in older men ($n=5$; 63–70 years) and younger men ($n=4$; 18–24 years) with comparable proportions of body fat and found that core temperature decreased by an average of 0.3°C in the older men and 0.1°C in the younger men after two hours of exposure to a low ambient temperature (6°C) [66]. The authors reasoned that age-related changes in aerobic capacity (fitness) likely explain some of this increased vulnerability to cold. A Canadian study compared younger men ($n=8$; 21–29 years) with two groups of older men ($n=8$ and 11 ; 55–70 years), one of which had physical capacity comparable to that of the younger group, while the other consisted of less physically active men [67]. The subjects were allowed to rest and perform moderate physical effort on a test cycle in thermoneutral and cold conditions (5°C for one hour). It was reported that both groups of older men had a greater decrease in core temperature in cold conditions than the younger subjects, regardless of whether they had a high aerobic capacity or not, and the authors thus concluded that age-related reduction in aerobic capacity could not be the only explanation for an increased vulnerability to cold in the elderly. Instead, as an alternative explanation, it has been argued that ageing limits the capacity for peripheral vasoconstriction in response to cold exposure, which may increase heat loss [64]. Such a change could be due to altered or reduced sensory afferent signaling conveying information about cold exposure, reduced efferent sympathetic nervous system output, or impaired responses of target organs (blood vessels) due to atherosclerosis or other age-related functional changes. An age-related reduction in the ability to induce peripheral vasoconstriction could therefore increase heat dissipation to the environment, leading to a loss of core temperature. However, such effects on core temperature during cold exposure in men have been reported to occur only after 45 years of age [68]. In a study of men in Antarctica ($N=12$; 26–52 years), a logistic regression model showed that age was inversely correlated with cold tolerance in a provocation test (whole-body cooling at 10°C for two hours) [69]. Regarding cold-induced vasodilation in the hands, some studies have shown

that older men may be less able to elicit this response. A Japanese study compared older men (n=6; 62–70 years) with younger men (n=7; 20–29 years) and described a delayed and reduced cold-induced vasodilation in the older men, and in two of them, the reaction could not be elicited at all [70]. In another Japanese study, younger (n=9; 20–25 years) and older men (n=10; 60–71 years) of comparable build (in terms of subcutaneous fat and body surface area-to-mass ratio) were recruited [71]. In this study, heat loss was similar in both groups, while heat-generating capacity was lower in the older men. There may also be differences in the subjective experience of cold, with older individuals having a reduced ability to perceive temperature compared to younger individuals. In a UK study comparing healthy older men and women (n=16; 68–87 years) with younger ones (n=16; 19–39 years), using standardized clothing and ambient temperatures, less precise temperature discrimination was observed in the older subjects, although comfort temperature was the same for both groups [72].

In studies on women only, somewhat different results have been described. In a US study of younger (21–28 years) and older (60–72 years) women, no difference in core temperature was observed after three hours of exposure to 17°C ambient temperature [73]. In another US study, older women (n=7; 51–72 years) had higher core temperatures than younger women (n=10; 20–29 years) after two hours of exposure to 10°C ambient temperature [74]. However, in both cases, the older women had a higher proportion of fat and a smaller body surface area-to-mass ratio, which may have attenuated an age-related difference.

Conclusions:

There is a lack of studies examining the effects of ageing from an occupational perspective.

Small experimental studies show that vulnerability to cold increases with age. This vulnerability may be due to changes in heat production, insulating capacity, peripheral vasoregulation, and temperature discrimination.

A modifying effect of age on heat balance will likely become apparent only after about 40–50 years of age.

There is insufficient scientific evidence to conclude on sex differences in vulnerability to cold in older age.

3.3 Cold work and specific diseases

We wanted to investigate the risks of working in the cold for subjects with common chronic diseases and how these conditions modify the cooling effects. Exposure to cold has different consequences depending on the condition being studied, but it is reasonable to assume that any additional thermal stress is undesirable in the case of permanent disease [26]. In our systematic literature search, we could not identify any studies reporting on how certain diseases affect work ability in cold conditions or on how disease prognosis is affected by continued work in cold conditions. Instead, below is a description of studies identified in the targeted literature search that have

investigated the link between exposure to cold and various diseases, without necessarily focusing on mechanisms and causation, highlighting effects on work ability, or examining long-term prognosis. Also, the studies did not necessarily include only working subjects.

3.3.1 Cardiovascular disease

Hypertension is defined as a sustained elevation of arterial blood pressure above a certain threshold [75]. In Swedish health care, 140/90 millimeters of mercury (mmHg) is often used as the threshold for hypertension in otherwise healthy subjects, while those with certain underlying diseases, such as ischemic heart disease or diabetes, may have a lower target value. It has been challenging to establish a level below which there is no increased risk of cardiovascular disease and, at least above 115/75 mmHg, an excess risk can be demonstrated [75]. Both short- and long-term exposure to cold can raise blood pressure [76]. Experimental studies have shown that blood pressure can increase by 20–30 mmHg (both systolic and diastolic) with short-term exposure to generalized [77] and local [78] cooling. Some have found that systolic blood pressure is more affected than diastolic [79]. In a longer perspective, higher average blood pressure has been observed during the cold winter period compared to the rest of the year [76], mainly reflected in systolic blood pressure [80], and blood pressure treatment does not fully counteract this effect [81]. It has also been suggested that the rise in blood pressure related to cold exposure may be amplified with age due to increasing arterial stiffness [82]. The mechanisms underlying hypertension associated with cold exposure are not fully understood [79, 81]. To some extent, short-term increases in blood pressure in cold environments can be considered an adaptive response to increase heat-generating capacity. Still, in the case of sustained increases in blood pressure, the risks likely outweigh any benefits. It has been suggested that exposure to cold mainly activates the sympathetic nervous system, but may also modify the response of the renin-angiotensin-aldosterone system and the local turnover of vasoactive substances such as nitric oxide and endothelins [79, 81]. Particular interest has also been directed towards reflexively increased blood pressure upon facial exposure to cold [33, 83], which is mediated via temperature-sensitive nerve fibers (of A δ type) in the trigeminal nerve [84]. This reaction has also been reported to be less pronounced in older subjects compared to younger [85]. Similar reflex mechanisms have been described in other parts of the body, where local cooling of the skin surface can produce a sympathetic-induced peripheral cutaneous or visceral vasoconstriction [35, 36, 86]. An increase in blood pressure due to peripheral cutaneous vasoconstriction results in central pooling of blood, which is gradually compensated for by a decreased heart rate, decreased cardiac output based on stroke volume, and increased filtration in the kidneys (cold diuresis). An experimental study comparing cardiac load in younger (n=11; 20–34 years) and older (n=11; 58–76 years) healthy subjects described that the older group had increased cardiac strain (expressed as both "preload" and "afterload") during cooling and thus greater oxygen demand in the heart muscle compared to the younger group [87].

In ischemic heart disease, atherosclerotic narrowing of the coronary arteries restricts blood flow to the heart muscle. Several literature reviews have surveyed the scientific evidence for a link between cold exposure and ischemic heart disease [79, 88-91]. Studies have generally not been designed to examine whether cold exposure increases acute manifestations of underlying ischemic heart disease or other etiologies or whether cold exposure itself increases the risk of developing ischemic heart disease [92]. Working in the cold increases myocardial oxygen demand, and cold exposure can also induce vasoconstriction of the coronary arteries [93]. Inhalation of cold air in an otherwise warm environment also induces vasoconstriction in the coronary arteries [94]. Other physiological effects include increased arterial pressure and interstitial fluid leakage, where up to 15% of the plasma volume can leave the circulation [3]. This, in turn, leads to a concentration of erythrocytes (red blood cells) and thrombocytes (platelets), higher viscosity, and affects hemostasis [95]. This is likely to increase the risk of angina pectoris and acute myocardial infarction. Congestive heart disease, or heart failure, means that the capacity of the heart to pump blood (often expressed in cardiac output) is less than the body needs [96]. It can occur as a result of ischemic heart disease or other structural heart diseases, such as valvular heart disease and cardiomyopathies. Functional capacity in heart failure can be graded using the New York Heart Association (NYHA) classification, where NYHA I indicates being symptom-free and NYHA IV indicates dyspnea (air hunger) and fatigue even at rest.

Similar mechanisms as for ischemic heart disease have been proposed for ischemic stroke, where underlying atherosclerosis may be a risk factor for developing, in particular, lacunar cerebral infarcts (small local infarcts in deep parts of the brain usually due to occlusion of smaller vessels) and thrombi (clots) from ruptured plaques in larger vessels [97]. The risk of ischemic stroke is also increased in atrial fibrillation, where emboli (blood clots that travel with the blood circulation) from the left atrium can be deposited into the cerebral circulation. In a recent review article on cold exposure and stroke, several established risk factors for stroke were suggested to vary with season and temperature, including hypertension, hyperglycemia, hyperlipidemia, and atrial fibrillation [98]. In addition, exposure to cold can activate the sympathetic nervous system, leading to increased blood pressure, platelet aggregation, and an inflammatory response. Upon exposure to cold, such platelet aggregation may be particularly pronounced in stroke in subjects aged 65 years or older [99]. Hemorrhagic stroke, in turn, has some risk factors in common with ischemic stroke, such as hypertension and smoking, but there are also subtypes with different risk factor patterns. For instance, in subarachnoid hemorrhage, hereditary factors and connective tissue diseases often contribute to the development and rupture of intracranial aneurysms [100]. It has been suggested that cold-related hemorrhagic stroke may be more common than ischemic stroke, based on results from large registry studies and a possible mechanistic explanation in the form of cold-triggered blood pressure rise [101]. The regions of the central nervous system damaged in a stroke may also influence subsequent vulnerability to cold work. If the stroke affects the hypothalamus, pituitary gland, or somatosensory cortex, the ability to regulate heat balance may be affected, as well as the ability to perceive both general and local cooling [102]. In brainstem infarcts, the physiological pulse and

blood pressure response may be absent when the face is exposed to cold [84]. There are also several other vascular outcomes that have a higher incidence in the cold, such as hypertensive crisis, deep vein thrombosis, pulmonary embolization, and dissection or rupture of the aorta [79, 103]. Below are brief descriptions of the studies identified as relevant to the review questions.

A Korean study examined male workers (n=68) employed in freezing cold rooms (–50 to –20°C) and unexposed controls (n=68). The mean age of the cold-exposed workers was 37 years (standard deviation 9 years), while the mean age of the controls was 39 years (standard deviation 9 years). Statistically significantly higher systolic and diastolic blood pressure was described in cold-storage workers compared to controls [104]. There was also an exposure-response trend in which both systolic and diastolic blood pressure increased with decreasing core temperature. A multiple regression model found that age ≥ 40 years increased the likelihood of hypertension in cold work environments (odds ratio 2.7; 95% confidence interval 1.1–6.6). The authors suggested that older workers who are cold-exposed should have their blood pressure and electrocardiogram checked periodically. A Polish study of workers (N=102) employed in cold storage units with a mean age of 39 years (standard deviation 10 years) described higher systolic and diastolic blood pressure in those working in colder environments (0 to 10°C) compared with slightly warmer ones (10 to 14°C) [105]. The blood pressure response in this study appeared more pronounced in female workers (n=41).

A Finnish study examined the prevalence of cold-related complaints in the general population (N=6951; 25–74 years) and stratified the results by chronic disease status [106]. An increased prevalence of cold-related angina and arrhythmia was described in those with known ischemic heart disease compared with healthy individuals, and the burden of symptoms also increased with age. In a regression model, previous cardiovascular disease (hypertension, angina, heart failure, myocardial infarction, percutaneous coronary intervention, coronary artery surgery, or stroke) was the most important explanatory variable for cold-related angina or arrhythmia. Conversely, age had no statistically significant effect, although there was a non-significant trend towards increased incidence after the general retirement age (65–74 years). An in-depth study on the same material found that men with treated hypertension and an additional manifestation of cardiovascular disease (physician-diagnosed angina, myocardial infarction, ischemic or hemorrhagic stroke, coronary artery bypass surgery, or percutaneous coronary intervention) were more likely to report cold-related angina (odds ratio 22.8; 95% confidence interval 10.0–52.3) and arrhythmia (odds ratio 42.2; 95% confidence interval 8.7–205.0) after adjusting for age, BMI, smoking, alcohol habits, cholesterol level, and presence of diabetes [76]. For women, there was a slightly lower point estimate for the likelihood of cold-related angina (odds ratio 18.9; 95% confidence interval 9.0–39.9) and a lower point estimate for arrhythmia (odds ratio 9.4; 95% confidence interval 4.2–21.0). It was concluded that hypertension combined with manifest cardiovascular disease is strongly associated with an increased prevalence of cardiac symptoms in cold conditions for both men and women, and that these individuals can be considered as a particularly vulnerable group that may benefit from preventive interventions.

Regarding occupational exposure to cold, a Swedish registry study based on men in the Construction Workers Cohort (n=194501; 15–67 years) found an excess risk of myocardial infarction (relative risk 1.1; 95% confidence interval 1.01–1.2) but not stroke (relative risk 1.1; 95% confidence interval 0.9–1.3) among construction workers living and working in the coldest area, after adjusting for age, BMI, and smoking [107]. The authors restricted the analyses to workers with normal blood pressure at the first survey and used Norrland as the coldest area and Götaland as the reference area. An interaction effect with noise was also described, where subjects who were exposed to noise in addition to cold at work had an even higher risk of myocardial infarction.

There are also laboratory studies on subjects with ischemic heart disease who have been assessed on exercise bikes in different temperatures. In a Swedish study on men with angina pectoris (N=9; 44–63 years) who cycled up to 130 W at –8°C and room temperature, the same work capacity and heart rate development were seen in both environments, but a more pronounced increase in blood pressure during exercise in the cold [108]. In another Swedish study of men with cold-related angina pectoris (N=17; 45–60 years), exercise tests at –10°C were compared with those at 20°C, and it was found that work capacity was lower in the cold setting, while heart rate and blood pressure increased more [109]. A similar Norwegian study of men with angina pectoris (N=10; 30–61 years) compared exercise tests at –17°C and 18°C and reported reduced work capacity and an exaggerated blood pressure response in the cold [110]. Treatment with nitroglycerin improved work capacity in the cold to the same level as in the warm setting.

A meta-analysis examining the short-term associations between ambient temperature and stroke reported 20 studies in which the cumulative effect of a 1°C decrease in temperature resulted in a 1.2% increase in the relative risk of stroke (defined using a composite variable consisting of incidence, emergency room visits, hospitalization, and mortality) [111]. Proposed mechanisms included increases in blood lipids, blood glucose, fibrinogen, and platelets during cold periods, as well as hemoconcentration and vasoconstriction. Since this meta-analysis, new studies have been published, including some that have focused on working-age populations. A Lithuanian population-based crossover study (N=5396; 25–64 years) showed an increased likelihood of ischemic stroke in colder weather (odds ratio 1.1; 95% confidence interval 1.01–1.1) but not hemorrhagic stroke (odds ratio 1.0; 95% confidence interval 0.9–1.1) [112]. There was also no effect of age and sex on the association between cold exposure and stroke. A French prospective population study (N=160782; 18–69 years) investigated associations between working in temperatures <10°C and ischemic or hemorrhagic stroke [113]. For those who worked at least two hours per day in such cold environments, there was no increased likelihood of incident stroke (odds ratio 1.1; 95% confidence interval 0.5–2.8) after adjusting for age, sex, BMI, smoking, occupation, hypertension, diabetes, hyperlipidemia, and heredity. Some studies have suggested that stroke risk depends not only on absolute temperature but also on rapid fluctuations in temperature over a 24-hour period, with a rapid drop in ambient temperature potentially leading to increased platelet activation [114].

Peripheral arterial insufficiency, or intermittent claudication, involves the presence of atherosclerotic narrowing of the arteries of the legs, which can induce exertion-related ischemic pain mainly in the lower legs. We could not identify any studies that investigated associations with cold work. However, it has been described that subjects with this condition have an increased risk of sustaining local cold injuries to the extremities when working in cold climates [115].

There is very limited scientific evidence on the relationship between congestive heart disease and cold work. There are reports of increased incidence of decompensated heart failure and hospitalizations during winter, but the underlying mechanisms are incompletely understood [103]. In a Swiss study of older men with heart failure (n=12), coronary artery disease (n=13), and healthy controls (n=12), there was no difference in the hemodynamic response to cold water immersion during sauna bathing between those with heart failure and healthy controls [116]. The average age of the men with heart failure was 62 years (standard deviation of 9 years), while the corresponding figures for those with coronary artery disease were 61 years (standard deviation 11 years) and for healthy controls 61 years (standard deviation 9 years). A Canadian experimental study of subjects with heart failure (n=33) and healthy controls (n=12) performing exercise tests in a thermoneutral environment and in a cold environment (-8°C) found that those with heart failure had reduced physical capacity in the cold, whereas the healthy controls showed the opposite response [117]. The mean age of the men with heart failure was 60 years (standard deviation 11 years), while the controls were 52 years (standard deviation 14 years). A similar Canadian study of heart failure patients (N=11) with a mean age of 61 years (standard deviation 6 years) who performed exercise tests found a similar reduction in physical capacity in cold conditions [118].

Conclusions:

- Exposure to cold leads to higher blood pressure, both in those with and without anti-hypertensive medication. The blood pressure-raising effect of cold is particularly pronounced when the face is exposed.
- Individuals with pre-existing cardiovascular disease show a lower physical work capacity and an increased likelihood of acute ischemic cardiac events and arrhythmias when exposed to cold.
- Cold exposure also appears to increase the likelihood of stroke, but there are conflicting results regarding differences in the risk of ischemic and hemorrhagic stroke.
- Subjects with peripheral arterial insufficiency may be at increased risk of local cold injury.
- Subjects with heart failure may have a reduced physical capacity in the cold.

3.3.2 Obstructive airway disease

The term obstructive airway disease usually refers to asthma, chronic obstructive pulmonary disease (COPD), and mixed forms [119]. Asthma is an inflammatory disease of the lower airways with varying degrees of airway obstruction [120]. The disease shows heterogeneous expression, with several phenotypes (clinical variants). Common symptoms are dyspnea (air hunger), wheezing, and coughing. Inhalation of cold, dry air dehydrates the bronchial tree and induces bronchoconstriction [121]. It is well established that asthma, regardless of its underlying etiology, can be exacerbated by inhaling cold, dry air [121]. Older studies also reported that up to one-third of asthmatics avoid outdoor activities in cold weather to prevent exacerbations [122], but this proportion has likely decreased with modern, more effective treatments. There is also reason to suspect that new-onset asthma may be caused by exposure to cold, although this is much less studied [123]. As the name suggests, COPD involves more continuous bronchial obstruction, but there is still some variation in airway resistance [119]. A review article suggests that airway symptoms and obstruction triggered by cold exposure may impair work capacity in cold environments, especially in subjects with asthma or COPD [25]. However, the authors conclude that there are few studies on respiratory symptoms in relation to cold work environments. Bronchial hyperreactivity is a closely related condition to obstructive airway disease and involves excessive bronchial constriction in response to various inhaled chemical and physical stimuli [124]. The condition is defined as an abnormal decrease in expiratory capacity (often estimated using forced expiratory volume in the first second, FEV1) following direct or indirect provocation with, for example, methacholine, mannitol, exercise, or cold air. Asthma usually involves bronchial hyperresponsiveness, but this can also be found in asymptomatic individuals, in interstitial lung diseases (such as sarcoidosis and cystic fibrosis), in rheumatic conditions, and after respiratory infections. Various tools are available to assess the severity of obstructive airway disease. For example, in asthma, one can use the Asthma Control Test (ACT), which asks the person to rate their symptom burden using five questions that add up to a score of 0–25, with a lower score indicating poorer disease control [125]. For COPD, the Chronic Obstructive Pulmonary Disorders Assessment Test (CAT) consists of 8 questions that yield a score of 0–40, with lower scores indicating better disease control [126].

The physiologically oriented scientific literature describes how exposure to cold environments can affect the lower respiratory tract. Inhalation of large volumes of cold, dry air causes fluid loss from the bronchial tree, cooling the mucosa and triggering vasoconstriction, reactive hyperemia, vascular leakage, and edema. Dehydration of the mucosa increases the osmolarity of the periciliary fluid and stimulates the release of substances that induce bronchial smooth muscle contraction [120]. Signs of inflammation and epithelial damage can also be detected by aggregation of different types of leukocytes in bronchial lavage fluid and epithelial tissue biopsies [127, 128]. There are also descriptions that the function of the immune system, regardless of cell count, can be impaired by cold exposure, for example, in terms of antibody production and cytokine secretion [129].

In a review article on respiratory symptoms, the authors note that artificially cooled indoor environments can also exacerbate asthma and COPD, but the emphasis was on air-conditioned home environments rather than work environments [130]. Modern air conditioning systems can introduce large volumes of cold, dry air into close proximity to where subjects spend time indoors, which can induce various respiratory symptoms (dyspnea, wheezing, and mucus production) and possibly increase susceptibility to infections. In this context, it is worth noting that such air-conditioning systems may also serve as reservoirs for specific respiratory pathogens, such as *Legionella* [131]. Subjects with bronchial hyperreactivity are more sensitive to changes in ambient air temperature than those without a tendency to excessive bronchial constriction, and it has been shown that an indoor temperature drop of 2 to 3°C may be sufficient to trigger exacerbations in asthma and COPD [130]. Not only air temperature but also the respiratory rate influences the magnitude of the cooling effect. Under normal physiological conditions, the air in the alveoli is approximately 37°C and saturated with water vapor. According to a previous experimental study, a person breathing 15 liters per minute with an air temperature of 20°C will have a local tissue temperature in the trachea of around 34°C, while increasing the volume to 100 liters per minute with the same air temperature will reduce the temperature to 31°C [132]. This means that physically demanding work in cold environments can have a greater cooling effect on the airways than low-intensity work with lower respiratory rates. High volume turnover in the cold setting can also affect surfactant function and lead to dehydration and hypertonicity. Breathing through the nose provides some warming and moisture to the inhaled air, but with increased exertion, there is usually a shift to mouth breathing, which also increases exposure to cold, dry air. Breathing through the nose can also dilate the submucosal venous plexus in the nasal mucosa, leading to nasal congestion and a runny nose [121]. This reaction has been reported to be more pronounced in asthmatics than in healthy subjects [133]. In light physical work, bronchoconstriction is unlikely to be mediated by exposure to cold and dry air in the lower airways, but rather via reflexes triggered through the sensory innervation of the face and upper airways.

There are descriptions of a correlation between low temperatures and increased levels of particulate matter in ambient air [134]. Many combustion particles increase in concentration during cold periods, due to the use of different fuels for heat and electricity production. In addition, transportation patterns also change, as more people use vehicles powered by fossil fuels, which adds combustion particles. In addition, studded tires are used, tearing up particles from the road surface. Meteorological phenomena, such as inversion, can cause particulate matter to accumulate during cold periods. This means it can sometimes be difficult to distinguish the effects of low temperature from those of increased particle concentrations. There are also potential synergistic effects between cold exposure and tobacco smoking. One possible common mechanism is the activation of specific temperature-sensitive ion channels (TRP channels), leading to hypersecretion of mucus and impaired ciliary function [135]. Finally, apart from bronchoconstriction, cold-mediated vasoconstriction of the pulmonary circulation has been described but has mainly been studied in subjects with primary Raynaud's phenomenon [136].

For a fully clothed person, the face and airways are the only parts exposed to ambient cold air. An experimental study showed that cooling the face (-10°C and wind speed 5 m/s) can induce a statistically significant decrease in FEV1 during spirometry in healthy men ($N=8$; 21–25 years) [33]. Similar effects have also been shown in subjects with asthma and COPD, and have been attributed to a reflex pattern in which trigeminal nerve stimulation produces a bronchoconstrictive response, effected via the vagus nerve [137]. It is difficult to protect the airways from cold as effectively as the rest of the body. Increasing the insulating capacity of clothing has a very limited effect on airway temperature. Various types of heat exchangers covering the mouth and often the nose can be used, but these have mainly been evaluated for winter athletes. Heat exchangers appear impractical in the workplace, since they take up space, can be challenging to use with other protective equipment, hinder communication, impair gas exchange, and increase breathing resistance [25, 120]. Therefore, it has been suggested that workers with chronic respiratory diseases benefit more from optimized drug therapy [25].

Several large studies have shown increased morbidity and mortality in obstructive airway diseases in relation to periods of low ambient temperatures [106, 138–147]. In most cases, meteorological data have been used without examining individual exposure. Thus, it is not known whether subjects were exposed to cold at work.

However, there are also studies that have emphasized occupational exposure. A large Finnish population-based study ($N=6633$; 20–69 years) conducted in the central part of the country reported that asthma prevalence did not differ between indoor and outdoor workers [123]. In contrast, the prevalence of chronic bronchitis was higher among outdoor workers (4.2%) than among indoor workers (2.1%; $p<0.01$). When comparing outdoor workers across age groups, a higher prevalence of asthma, chronic bronchitis, dyspnea, and wheezing was observed in the older age group (49–69 years) than in the younger one (19–44 years). In a multiple logistic regression model, it was described that cold-related dyspnea was associated with outdoor work (odds ratio 1.2; 95% confidence interval 1.03–1.5), age between 60–69 years (odds ratio 1.6; 95% confidence interval 1.2–2.1), smoking (odds ratio 1.9; 95% confidence interval 1.7–2.2), heredity for obstructive airway disease (odds ratio 2.0; 95% confidence interval 1.7–2.3), and allergy (odds ratio 1.7; 95% confidence interval 1.4–1.9). When the independent variable was airway diseases, there was no relationship between outdoor work and asthma (odds ratio 0.9; 95% confidence interval 0.6–1.3), but there was with chronic bronchitis (odds ratio 1.8; 95% confidence interval 1.2–2.6). In another Finnish population study ($N=12695$; 20–69 years), partly based on the same material as above but also including a more urban population from southern Finland, the prevalence of long-term productive cough was highest in smoking outdoor workers and lowest in non-smoking indoor workers [148]. The difference between outdoor and indoor workers was statistically significant ($p<0.05$). A similar pattern was found for the wheezing outcome ($p<0.01$). Cold-related respiratory symptoms (dyspnea, wheezing, or severe cough) were more common in people living in the north of the country compared to the south ($p<0.001$) and in women ($p<0.001$). A Swedish cross-sectional study of the working population ($N=8740$; 18–70 years) described an association between occupational exposure to cold and wheezing

(odds ratio 1.3; 95% confidence interval 1.1–1.4), chronic cough (odds ratio 1.2; 95% confidence interval 1.1–1.4), and productive cough (odds ratio 1.3; 95% confidence interval 1.1–1.4) after adjusting for sex, age, BMI, smoking habits, asthma and COPD [149]. After six years of follow-up, in the same cohort (N=5017, 24–76 years), occupational exposure to cold at baseline was statistically significantly associated with incident respiratory symptoms in previously healthy individuals in the form of wheezing (odds ratio 1.4; 95% confidence interval 1.1–1.9) and productive cough (odds ratio 1.4; 95% confidence interval 1.1–1.8) but not chronic cough (odds ratio 1.0; 95% confidence interval 0.7–1.3) after excluding subjects with asthma and COPD and non-workers and adjusting for age, sex, BMI, smoking habits and physical exertion at work [150]. There was an association between exposure to cold at work and physical exertion, with those who were heavily exposed to cold at work also more likely to perform physically strenuous tasks ($p<0.001$).

There are also several studies based on pure occupational cohorts. One example is a Finnish study of male reindeer herders (N=211; 21–69 years) working outdoors in cold environments, in which no increased incidence of respiratory symptoms or deterioration in lung function was observed compared with healthy controls [151]. However, among reindeer herders, 14% reported experiencing dyspnea when breathing cold air. There was an age-dependent trend with this symptom being least common among the youngest (3% in the 21–29 years group) and then increasing with age. A French study compared food workers in artificially cooled indoor environments (n=12) with an average age of 47 years (standard deviation 2 years) with unexposed controls (n=6) with an average age of 44 years (standard deviation 2 years). An increased prevalence of respiratory symptoms, bronchial hyperreactivity, and impaired lung function was found in workers exposed to 3 to 10°C compared with unexposed controls (n=6), with effects discernible after approximately six months of exposure [152]. A more recent German prospective study followed workers (N=46) who spent 15–30 minutes at a time in a freezing cold room (–55°C), most of whom worked more than 16 hours per month in this environment [153]. The mean age was 35 years (standard deviation 9 years). Spirometry data were collected on average nine times per worker over a ten-year follow-up period. In this study, no abnormal decline in lung function over time was detected, as assessed by FEV1, forced vital capacity (FVC), FEV1 /FVC, and diffusion capacity.

Winter sports can be considered a special case of working in the cold, as elite athletes can be regarded as workers in a broader sense. A 2020 literature review described the emergence of knowledge of asthma in cross-country skiers in the 1990s [120]. Different temperature limits between –12 and –25°C have been proposed to reduce risk, depending on race distance, weather conditions, and competitors' age. In a Swedish survey of endurance athletes (N=402), the prevalence of physician-diagnosed asthma among skiers aged 20–34 years was 35%, compared with 16% among summer orienteers in the same age range [154]. In a Swedish survey of elite skiers of high-school age (N=244), the prevalence of physician-diagnosed asthma was 27%, with a clear overrepresentation of women [155]. The mean age was 17 years (standard deviation 1 year). A Finnish study of elite skiers (N=40; 16–20 years) showed that 75% had bronchial hyperreactivity on methacholine testing and

an accumulation of inflammatory cells in the bronchial mucosa [156] It has also been suggested that asthma in recreational athletes may represent a distinct phenotype that cannot be clearly linked to allergic sensitization or rhinitis but is instead characterized by distinct exercise-induced symptoms, especially in cold environments [157]. However, there are conflicting views on the role of conventional risk factors (such as allergies and heredity for asthma) in the development of asthma in recreational athletes [154].

Several experimental studies have investigated associations between exposure to cold and obstructive symptoms. A Swedish study used a climatic chamber with temperatures ranging from 0 to -10°C , in which subjects were asked to exert moderate effort on a treadmill and rate cold-related symptoms [158]. Healthy subjects ($n=13$; 26–65 years), subjects with allergic rhinoconjunctivitis ($n=7$; 25–47 years), physician-diagnosed asthma ($n=11$; 21–55 years), or COPD due to smoking ($n=3$; 70–73 years) were recruited. The study showed that cold-triggered lower respiratory symptoms (cough and dyspnea) occurred only in those with asthma and COPD. Subjects with obstructive airway disease also had lower physical work capacity in cold climates (as estimated by maximum oxygen uptake) than healthy subjects and subjects with allergic rhinoconjunctivitis. In a Finnish laboratory study, patients with stable asthma ($N=19$; 16–56 years) were exposed to cold by staying in climatic chambers (-20°C) with normal indoor clothing, which resulted in a statistically significant decrease in FEV1 (mean 5%) [159]. Moderate physical activity, as measured by a six-minute treadmill test in the same cold environment, resulted in a further decrease in FEV1 (mean 12%).

There are also studies that have investigated COPD as the primary outcome, but most have not focused on occupational cold exposure. Instead, meteorological data have been used [160], sometimes supplemented with measurements of ambient temperature [161]. In a Danish study of older men ($N=3387$; 53–75 years), a multiple regression model showed that more than five years of occupational exposure to cold and draught was associated with chronic bronchitis (odds ratio 1.4; 95% confidence interval 1.1–1.7) after adjusting for age, smoking, alcohol habits, height, MNS blood group, blood pressure, and exposure to dust and organic solvents [129].

A Finnish laboratory study in COPD patients ($n=20$) and healthy controls ($n=13$) demonstrated that whole-body exposure to cold air (-17°C) decreased FEV1 in both groups, with no statistically significant difference between groups [137]. The average age of the COPD patients was 64 years (standard deviation 10 years), and that of the controls was also 64 years (standard deviation 9 years). When subjects were instructed to hyperventilate with cold air (-13°C) for three minutes, FEV1 decreased in COPD patients but not in healthy controls. The authors concluded that cold air exposure to the face can cause some bronchial constriction in both COPD patients and healthy subjects, but that the response is more pronounced in COPD patients during activities that involve heavy breathing. In a Canadian laboratory study of COPD patients with severe pulmonary impairment ($N=26$; 49–74 years), increased obstruction (defined as a fall in FEV1 $>20\%$) was observed in 23% during cold-air hyperventilation [162]. Pre-provocation lung function parameters did not predict those who later had an obstructive spirometry during cold air exposure. In another

Canadian laboratory study in COPD patients (N=27; 26–79 years), cold-air hyperventilation (–18°C) reduced FEV1 by at least 10% in only three patients, while 19 had a positive methacholine test [163]. In a study of Canadian fur trappers (N=176), spirometry findings consistent with COPD were observed in older individuals (>40 years), and the authors reasoned that a high respiratory rate in extremely cold environments may have contributed to the lung function impairment [164]. In the cohort, most were aged 16–49 years, but there were some older individuals, of whom ten (5.7%) were >70 years. Another similar study in a Canadian indigenous population (N=211; 20–60 years) showed a similar trend of accelerated decline in FEV1 compared to the reference population, and this was attributed to cold-air inhalation [165], although smoking, tuberculosis, and systematic differences in body size may have contributed to the findings. Particular emphasis was placed on cold exposure during snowmobile driving, when the respiratory rate increased, and the insulating effect of clothing (especially the jacket hood) decreased.

Conclusions:

- Exposure to cold can increase the burden of symptoms in subjects with asthma or COPD. In particular, exposure of the face to cold can induce obstructive airway symptoms.
- There is some evidence that previously healthy subjects exposed to cold can develop obstructive airway disease.
- Protecting the airways from the cold is difficult, especially in situations involving heavy breathing. Heat exchanger masks can be difficult to use in many jobs.
- For elite athletes, heat exchange masks can be useful to reduce the cooling effect on the airways when training in low ambient temperatures.

3.3.3 Diabetes mellitus

Diabetes mellitus is a group of metabolic conditions characterized by elevated blood glucose, either due to a lack of insulin or its action on target organs [166, 167]. Diabetes can affect both peripheral blood vessels and nerves, and thereby thermoregulation [25]. There are studies that indicate that peripheral vasoregulation is impaired in subjects with diabetes [168, 169] and that blood flow to peripheral tissues may become insufficient during exposure to cold [170, 171]. This impaired vasoregulation may also lead to a failure to maintain core temperature and a greater risk of developing hypothermia in cold environments [172]. Shivering can help maintain core temperature, but this response can be attenuated by insulin treatment [5]. A common complication of diabetes, particularly with poor metabolic control, is various forms of nerve involvement that can be divided into clinical syndromes. The most described is a distal symmetric and mainly sensory polyneuropathy, but there are also autonomic and focal neuropathies [173]. Diabetes-induced peripheral neuropathy has been suggested to increase sensitivity to cold in the hands and feet [174, 175], but other studies have not found such associations [176, 177]. In a

Swedish study of subjects undergoing surgery for carpal tunnel syndrome (N=66; 31–77 years), a persistent abnormal cold sensitivity in the hands was noted among subjects with diabetes [174]. However, a five-year follow-up of the same group showed that this cold sensitivity decreased over time, interpreted as a slow regrowth of small sensory nerve fibers [178]. Similar findings have been described in the feet, where a study of men (N=33; 42–76 years) undergoing nerve biopsy in the lower extremity noted a higher postoperative prevalence of abnormal cold sensitivity in subjects with diabetes [179]. There are also descriptions of abnormal pulse responses in subjects with diabetes when the face is exposed to cold, which could indicate an involvement of the central nervous system [84].

A meta-analysis described five major studies linking meteorological data to mortality statistics for subjects with diabetes [169]. The authors analyzed populations in Canada, China, and the Philippines, and found a slight excess risk of cold-weather mortality among subjects with diabetes (meta-relative risk 1.2; 95% confidence interval 1.1–1.5). In addition to this meta-analysis, other studies have reported similar results [180]. The underlying mechanisms are not known, but it has been speculated that increased mortality may be related to reduced physical activity, changes in dietary intake (less fruit and vegetables and more saturated fats), and lower vitamin D levels [181]. There may also be an unadjusted covariance with cardiovascular disease. However, another recent review article highlighted studies showing no increased mortality among subjects with diabetes in relation to cold exposure and called for larger studies [182]. One publication recommended that diabetes be considered a risk factor for cold work but did not specify the reasons [183]. A Finnish population study (N=6951; 25–74 years) described that subjects with diabetes more often reported cold-related angina pectoris or arrhythmia (7.6% of men and 7.3% of women) compared to healthy subjects (1.0% and 2.0%, respectively) [106]. An in-depth study in the same population, which also included a follow-up survey five years later, found that subjects with type 2 diabetes had an increased likelihood of reporting cold-related angina (odds ratio 2.1; 95% confidence interval 1.3–3.3), arrhythmia (odds ratio 1.7; 95% confidence interval 1.02–3.0), and dyspnea (odds ratio 1.7; 95% confidence interval 1.3–2.3) after adjusting for age, sex, BMI, education, smoking, alcohol habits, geographical area, hypertension, and cardiovascular disease [184]. The authors also described a consistent increase in various cold-related symptoms with worsening metabolic control. For subjects with insulin-treated diabetes, an increased risk of hypothermia due to hypoglycemia and ketoacidosis has been described [166]. It has also been argued that metabolic control may be impaired because hypothermia could lead to impaired endogenous insulin release, increased peripheral insulin resistance, and impaired metabolism of common energy substrates such as glucose [166]. It may also be more difficult to reliably measure blood glucose by capillary blood sampling in cold work environments due to peripheral vasoconstriction in the fingers [185]. It has been suggested that subjects with insulin-treated diabetes should be assessed by occupational physicians for fitness to work at extremely low temperatures with particular regard to hypothermia risk, and that glycemic control and the presence of diabetes-related complications should guide the assessment [166]. A review article stated that subjects with diabetes working in cold environments need counseling on

the adverse health effects of cold exposure, particularly cardiovascular disease [25]. In a study based on the same Finnish population as mentioned above (N=6951; 25–74), diabetes was associated with an increased likelihood of sustaining a severe local cold injury (odds ratio 2.6; 95% confidence interval 1.1–5.7) after adjusting for age and sex [186]. The mechanism was suggested to be that diabetes increases the incidence of peripheral neuropathy and abnormal thermoregulation, which, in turn, may increase the risk of local cold injury. However, in a similar Swedish population study (N=5017; 24–76 years), no association between diabetes at baseline and incident local cold injury to the face, hands, or feet was observed after six years of follow-up [187].

Conclusions:

- Exposure to cold can pose problems for subjects with diabetes, including impaired metabolic control, increased risk of hypoglycemia, increased susceptibility to hypothermia, and possibly also increased risk of local cold injury and abnormal cold sensitivity.
- The risks of working in the cold for subjects with diabetes appear to be greater in the case of insulin treatment and possibly also for those with diabetic neuropathy.

3.3.4 Musculoskeletal disorders

Musculoskeletal disorders have been defined as all complaints related to muscles, joints, tendons, ligaments, and bones [188]. Some definitions also include nerves, cartilage, and disks [189]. Nerve involvement may manifest as neuropathic pain components in a generalized pain syndrome or in conditions involving some degree of peripheral neuropathy. Examples of the latter include cervical radiculopathy, sciatica, and carpal tunnel syndrome. Long-term musculoskeletal disorders can affect both quality of life and work ability, especially in those with physically demanding jobs [190]. In statistics on sick leave and disability, neck and low back pain account for a substantial proportion [191]. There is extensive knowledge of how the musculoskeletal system is affected by cold, mainly from physiological studies in laboratory environments, where reduced muscular endurance, force, speed, and coordination have been demonstrated [101]. The ability to perform muscle work is initially reduced by up to 10% for each degree decrease in tissue temperature, and at muscle temperatures below 27°C, force development is even more affected. Joint mobility also deteriorates in the cold, and at tissue temperatures below 22°C, finger dexterity begins to deteriorate [101]. Supportive tissues, such as tendons and ligaments, can also lose tensile strength in the cold [192]. Nerve conduction velocity is reduced by approximately 1–2 meters per second for each degree decrease in tissue temperature, affecting tendon reflexes and proprioception. Several proposed mechanisms link cold work to an increased incidence of musculoskeletal disorders. For example, it has been shown that subjects with long-term low back pain have a greater propensity for vasospasm, which also correlates with estimated pain intensity [193]. One possible mechanism is that heavy physical work in a cold environment results in oxygen demands of the skeletal muscles exceeding supply,

leading to ischemic muscle pain. Higher basal skeletal muscle tone at rest and impaired force development during exertion in cold environments have also been hypothesized, resulting in a greater relative muscle load [194-197]. Central sensitization due to cold exposure has also been suggested as a contributing mechanism [198]. For spine disorders, it has been reasoned that hypothermia may affect fluid distribution and load-bearing capacity of the intervertebral discs and possibly increase the risk of herniation of disc material [199]. Finally, the clothing used when working in the cold may also contribute to an increased incidence of musculoskeletal discomfort by being heavy and bulky and restricting mobility [196, 200].

There are a large number of studies investigating the extent to which cold work is associated with musculoskeletal pain, many of which are summarized in previous literature reviews [49, 188, 199]. Some Scandinavian studies have examined associations between cold work and musculoskeletal disorders. A Swedish population study (N=12627; 18–70 years) described a logistic regression model showing associations between cold work and neck pain (odds ratio 1.4; 95% confidence interval 1.2–1.6), low back pain (odds ratio 1.4; 95% confidence interval 1.2–1.6), and sciatica (odds ratio 1.4; 95% confidence interval 1.1–1.7) after adjusting for age, sex, BMI, physical workload, smoking, and stress [201]. A six-year follow-up of the same population showed that those who were pain-free but worked in the cold at baseline had an increased likelihood of developing neck pain (odds ratio 1.5; 95% confidence interval 1.03–2.2), low back pain (odds ratio 1.6; 95% confidence interval 1.1–2.3), and sciatica (odds ratio 1.9; 95% confidence interval 1.1–3.2) after adjusting for the same factors as above [202]. In a Norwegian population study (N=6533; 30–67 years), associations were seen in logistic regression models between working in the cold at least a quarter of the time and long-term musculoskeletal pain [203]. The strongest associations were for neck pain (odds ratio 1.5; 95% confidence interval 1.1–1.9), shoulder pain (odds ratio 1.4; 95% confidence interval 1.1–1.8), and leg pain (odds ratio 1.5; 95% confidence interval 1.1–2.0) after adjusting for age, sex, education level, BMI, sleep quality, occupational and leisure-time physical activity, and smoking. A long-term follow-up after 7–8 years showed that working in the cold at least a quarter of the time was associated with incident long-term musculoskeletal pain [204]. A German case-control study (N=587) in which the majority (52%) of cases were older than 55 years found that working in a cold environment was associated with lumbar degenerative disc disease in men (odds ratio 2.2; 95% confidence interval 1.3–3.7) but not women (odds ratio 1.6; 95% confidence interval 0.8–3.3) [205].

There are also studies that have examined the prevalence of musculoskeletal disorders in pure occupational cohorts. A Finnish study in meat factories and dairies examined workers (N=1117; 18–64 years) who mainly worked in ambient temperatures between 0 and 10°C but in some cases as low as –25°C [190]. In a logistic regression model, local cooling at work was associated with an increased likelihood of neck pain (odds ratio 6.5; 95% confidence interval 2.8–15.0), shoulder pain (odds ratio 6.3; 95% confidence interval 2.5–15.7), wrist pain (odds ratio 21.7; 95% confidence interval 11.6–40.5), and low back pain (odds ratio 5.8; 95%

confidence interval 2.9–11.3), after adjusting for sex, BMI, years of work, work ability, and leisure-time physical activity. Work ability was also used as a dependent variable, rated on a scale of zero to ten, with a score below seven defined as reduced work ability. In a logistic regression model, there was a borderline significant association between exposure to draughts and reduced work ability (odds ratio 1.6; 95% confidence interval 1.00–2.4) but not exposure to a cold work environment (odds ratio 1.4; 95% confidence interval 0.9–2.2) after adjusting for sex, employment duration, work absenteeism, and leisure-time physical activity. A Norwegian study investigated the prevalence of musculoskeletal disorders among workers in seafood factories (N=744) where the age distribution was not clearly reported, but the proportion over 50 years varied between 19–28% depending on sex [191]. It was found that those who often felt cold at work had an increased likelihood of reporting musculoskeletal disorders in the neck/shoulder (odds ratio 10.5; 95% confidence interval 3.1–35.3), wrist/hand (odds ratio 7.6; 95% confidence interval 2.9–20.3), elbow (odds ratio 5.4; 95% confidence interval 1.6–17.9), back (odds ratio 11.0; 95% confidence interval 4.5–26.8), and lower extremity (odds ratio 8.9; 95% confidence interval 3.0–26.1) compared with those who never felt cold, after adjusting for age, sex, smoking, education level, and work experience. The likelihood of reporting musculoskeletal problems in the neck/shoulder, wrist/hand, and elbow was higher in women than in men. The prevalence of all musculoskeletal disorders except back pain also increased with age.

Regarding peripheral nerve involvement, studies have shown an increased incidence of symptoms consistent with carpal tunnel syndrome. A Taiwanese study on workers (N=207) employed in chilled and freezing cold rooms described an increased risk of carpal tunnel syndrome ascertained by nerve conduction studies in those working in cold with repetitive tasks (odds ratio 9.4; 95% confidence interval 2.4–37.2) compared to unexposed controls, which was significantly higher than in those working only repetitively (odds ratio 2.2; 95% confidence interval 0.2–21.2), after adjusting for age, sex and duration of employment [206]. The average age was 42 years (standard deviation 14 years) for those exposed to cold and repetitive tasks, 38 years (standard deviation 13 years) for those working only repetitively, and 40 years (standard deviation 12 years) for unexposed controls. An Israeli study of patients operated on for carpal tunnel syndrome (n=127) and sex- and age-matched controls (n=102) found an increased incidence of carpal tunnel syndrome diagnosed using nerve conduction studies in those working in cold environments (odds ratio 3.5; 95% confidence interval 1.1–11.5), after adjusting for BMI, education level, and repetitive wrist movements [207]. The mean age was 52 years (standard deviation 8 years) for cases and 50 years (standard deviation 10 years) for controls. In a Swedish population study (N=5017; 24–76 years), both contact with cold objects and exposure to ambient cold were associated with an increased likelihood of reporting subjective symptoms of carpal tunnel syndrome [208]. The association was strongest in those who almost always worked in conditions involving cold, wet, or wind that induced cooling despite proper clothing (odds ratio 4.0; 95% confidence interval 2.1–7.7), after adjusting for age, sex, BMI, smoking, diabetes, joint disease, and hand-transmitted vibration exposure. The authors also described exposure-response relationships between working in the cold and symptoms of carpal tunnel syndrome.

Conclusions:

- Working in the cold increases the likelihood of reporting musculoskeletal disorders.
- Cold work can also increase the likelihood of reporting nerve-related disorders such as sciatica and carpal tunnel syndrome.
- There is limited knowledge about how existing musculoskeletal disorders affect work ability in the cold.
- High-insulation clothing can reduce the cooling effect but increase musculoskeletal strain by increasing the load and restricting movement.

4. Discussion

4.1 Overall objective

This narrative review aimed to describe how health risks associated with cold work are affected by age and disease. As a first step, we wanted to explore how these modifying factors can be incorporated into the risk assessment of cold work. Our systematic literature search identified 13 studies that included age or disease in the assessment. Several of the included studies indicated that cold work at older ages may pose greater health risks, but not in what way [51, 54, 57, 61]. It was not possible to determine the magnitude of the risk or whether there is an age threshold at which cold-related problems become a relevant concern. There were also studies that investigated but found no effect of ageing [59, 60]. Regarding diseases, several conditions were suggested as potentially posing difficulties or risks in cold work, including cardiovascular disease [53, 58, 62], obstructive airway disease [53, 62], and musculoskeletal disorders [53, 56, 58]. This selection of diseases then guided our targeted literature search. Body composition was included as a parameter in the risk assessment in several studies identified in the systematic literature search [54, 59, 61], in which a low proportion of body fat or low BMI was considered to be associated with an increased risk of adverse health effects in cold work. Additional medical conditions suggested as potential problems in cold settings were cold urticaria, previous local cold injuries, peripheral circulatory disorders, migraines, arrhythmias, metabolic conditions, and infections [53, 58, 62]. However, it was difficult to understand on what basis these conditions had been identified as particularly important for risk assessment of cold work.

Only three of the identified studies reported whether subjects of both sexes were included in the study population [56, 59, 60], but one additional study considered the effects of sex [51]. Based on this rather limited evidence, it was not clear how sex affects risk assessment in cold work.

Almost half of the identified studies focused on artificially cooled indoor environments, such as chilled and freezing cold rooms. This made them less applicable to Swedish conditions, where most exposure to cold occurs during outdoor work. For example, a previous population survey in northern Sweden has shown that only about 3% of women and 4% of men report working in cold indoor environments at least a quarter of the time [209]. Artificially cooled environments differ from cold outdoor environments in several ways. First, environmental factors are strictly regulated, such as temperature, humidity, and draught. This differs from outdoor environments, where weather conditions are seasonal and subject to rapid change, and precipitation also occurs. Furthermore, temperatures in artificially cooled indoor environments can be extremely low, for example -55°C [153] which hardly occurs outdoors in Sweden. In addition, cold objects are often handled in such environments, such as foodstuffs and packages, which means that workers can be exposed to both ambient and local cooling [190].

One of the included studies investigated the insulation properties of the chosen clothing among open-pit miners [59]. The study showed that subjects with lower self-rated health seemed to compensate by choosing warmer clothing, which is an example of how subjects with chronic diseases could adapt to their conditions. Several studies suggested that periodic medical examinations could be organized for subjects working in cold environments, especially those with health conditions that may imply a particular susceptibility [50, 51, 53, 62].

4.2 Specific questions

We wanted to investigate how ageing affects work ability in the cold. Our systematic literature search was inconclusive in this respect, but the targeted literature search included studies indicating that older age per se, even in the absence of disease, may increase vulnerability to cold work [64]. This notion was largely based on older experimental studies with few participants and limited female representation. Heat-generating capacity is generally reduced due to changes in body composition, mainly in the form of reduced skeletal muscle mass [66]. Increased insulation from subcutaneous adipose tissue does not appear to compensate for reduced heat production by skeletal muscles. There was also evidence that peripheral regulation of vascular tone is less effective in older age [64], suggesting that dynamic peripheral vasoregulation to maintain core temperature is less effective. In addition, the sensory ability to discriminate temperature decreases with age [72]. However, for all these potential effects of ageing, there is substantial inter-individual variation. Some studies suggest that the effects of ageing become relevant only after 40–50 years of age [68] while others indicate that susceptibility to cold may develop earlier [69]. There is a lack of occupational studies on ageing, as well as insufficient evidence to draw any firm conclusions about vulnerability at older ages in relation to sex. In addition to these arguments, it is worth noting that the prevalence of chronic diseases increases with age, making it difficult to distinguish the pure effects of ageing from the modifying effects of disease.

Therefore, we also wanted to identify the specific risks associated with certain medical conditions. We found that exposure to cold generally leads to a rise in blood pressure, but that there was a lack of knowledge about how cold work could be an etiologic factor in the development of cardiovascular disease [92]. However, it was found that subjects with pre-existing cardiovascular disease may be at increased risk of acute effects when exposed to cold [76] and that the risks appear to be greatest for those with ischemic heart disease. These individuals are also likely to have lower physical work capacity in cold conditions than healthy workers. Stroke appears to be linked to cold exposure, but it is not entirely clear how the risk profile differs for ischemic and hemorrhagic stroke. For peripheral arterial insufficiency, the scientific evidence was insufficient to conclude on the potential risks associated with cold exposure. Heart failure often implies reduced physical capacity, but it is a relatively rare condition among working-age subjects. In subjects with heart failure, the limited scientific evidence indicates that physical capacity may be further impaired by exposure to cold.

For obstructive airway disease, there was scientific evidence indicating that exposure to cold, in itself, could contribute to the etiological development of the condition, and this was mainly studied in asthma [123]. The studies investigating the relationship between cold exposure and COPD-related symptoms [137, 160-163] were mainly conducted on subjects older than those typically found in the working population. Only a few studies indicated a higher prevalence of chronic bronchitis in cold-exposed workers [123, 129] and an accelerated pulmonary impairment in cold-exposed indigenous people in Canada [164]. Subjects with pre-existing obstructive airway disease were widely reported to experience worsening symptoms with cold exposure. It was also noted that it is very difficult to protect the airways from cold exposure. From an occupational perspective, it is worth noting that although cold work can exacerbate obstructive airway symptoms, there is likely considerable inter-individual variation, making it difficult to provide universal recommendations. In general, subjects with more severe obstructive airway disease are more vulnerable to various provoking factors, but sensitivity to a respiratory irritant such as dust does not predict the response to cold, and vice versa [210].

For diabetes, no studies indicated that cold exposure contributed to its development, but the disease itself could increase mortality in cold environments from a population perspective [169] and pose a risk when working in the cold [166]. The risk of impaired metabolic control and hypoglycemia was particularly emphasized. Evidence of impaired temperature regulation in diabetes was also described, both in terms of core temperature [172] and peripheral temperature [170, 171]. In general, the risks appeared to be more pronounced in subjects with insulin-treated diabetes. Impaired regulation of peripheral tissue temperature could possibly increase the risk of local cold injury in subjects with diabetes, but the results were conflicting [186, 187].

Several studies indicated an increased risk of developing musculoskeletal disorders when working in the cold, with emphasis on neck and lumbar pain [49, 188, 199]. There were also several postulated mechanisms that could explain the associations [201]. However, few studies examined how existing musculoskeletal disorders

affected work ability in the cold. A number of studies described an increased risk of nerve-related disorders, such as sciatica [201, 202, 205] and carpal tunnel syndrome [206-208]. In summary, based on the literature, there are clear incentives to consider the risk of long-term musculoskeletal pain among those who work in cold environments, especially when other ergonomic risk factors are present, such as a bent and twisted trunk, heavy lifting, or exposure to whole-body vibration [197]. Several apparently paradoxical relationships are still incompletely understood. For example, increased physical exertion may generate more heat, which reduces the risk of hypothermia, while musculoskeletal strain may increase the risk of discomfort. Another example is the effect of heavy winter clothing, which increases insulation against cold but at the same time limits mobility, impairs manual fine-motor skills, and increases physical strain [196, 200].

In summary, many studies have investigated how exposure to cold is statistically associated with various diseases and symptoms, but there is limited evidence on how aging and disease affect work ability in cold environments or their effects on prognosis. Most studies on occupational cohorts were small and not generalizable. The included experimental studies largely lacked an occupational perspective. Attempts to extrapolate results from studies on the general population to the occupational setting entail risks of both over- and underestimating issues related to cold exposure. More knowledge in the form of specific occupational studies is therefore needed to answer our questions.

4.3 Recommendations

Based on the literature and our clinical experience, general recommendations can be made regarding appropriate measures for cold work for subjects with pre-existing disease. Since the recommendations are general, an individual medical assessment by an occupational physician will often be warranted.

4.3.1 Cardiovascular disease

Well-controlled hypertension alone does not require any specific measures, but a person who frequently works in the cold may need to have their blood pressure checked more often (preferably also during the working day) to ensure the individual treatment goal is met. Individuals with manifest ischemic heart disease may require task modifications when working in the cold, and these may include less physically demanding tasks (due to reduced physical work ability in the cold), shorter periods of work in the cold (to reduce the risk of hypothermia), access to hot drinks (due to hypothermia risk and enhanced cold diuresis), and access to protective clothing with increased insulation (due to increased risk of peripheral cooling and circulatory stress). [211]. The extent of preventive measures should be related to both the nature and extent of the exposure, but also the worker's individual susceptibility. Drug treatment may also need to be adapted, for example, by selecting a beta-receptor

antagonist with strong β_1 affinity, such as bisoprolol, to reduce the risk of hand and foot cooling associated with other beta-receptor antagonists. After a stroke, there may be an increased vulnerability to cold exposure, particularly in lesions of the hypothalamus, pituitary, or somatosensory cortex. This may mean that it is more difficult to regulate body temperature or to perceive if parts of the body are being cooled, so there may be reasons to avoid work in the cold [102]. In the case of peripheral arterial insufficiency, there is a lack of robust scientific evidence, but if there is a major restriction in lower limb perfusion (defined as a ratio of systolic blood pressure at the ankle divided by that in the upper arm of less than 0.7), there are reasons to advise against cold work [115]. Similarly, in heart failure with more severe functional impairment (NYHA class III–IV), we recommended that work in the cold should be avoided.

4.3.2 Obstructive airway disease

For subjects with asthma or COPD, an individual assessment is required. The severity of symptoms should be assessed, for example, using the ACT for asthma and the CAT for COPD. In addition, patient history should focus on whether exposure to cold at work actually aggravates respiratory symptoms. If the subject has pronounced respiratory symptoms (ACT < 20 for asthma or CAT $\geq$ 20 for COPD), especially paired with an incomplete effect of drug treatment despite optimization, task modification is warranted [210]. Such modifications could include less physically demanding tasks, shorter work periods in the cold, or access to heat-exchanger masks. If the work requires respiratory protection, devices that do not produce high breathing resistance or significant cooling of inhaled air should be chosen, preferably a heated, powered air respirator system designed for cold settings. For elite athletes, stricter, age-appropriate temperature limits should be established for competition, and the use of heat-exchanger masks for training in the cold should also be encouraged.

4.3.3 Diabetes mellitus

Most subjects with well-controlled type 2 diabetes with oral treatment should be able to work in the cold without task modification. Subjects with diabetes, regardless of type, are at risk of poorer metabolic control when working in the cold because generalized cooling can reduce residual endogenous insulin release, increase peripheral insulin resistance, and reduce glucose metabolism [166]. Therefore, more frequent monitoring of metabolic control (using HbA1c) may be required. For subjects with insulin-treated diabetes, there may be an increased risk of hypoglycemia and ketoacidosis, both of which may in turn increase the risk of hypothermia. It has also been reported that insulin treatment can inhibit shivering, further increasing the risk of hypothermia [5]. Therefore, subjects with insulin-treated diabetes who work in the cold should not work alone but be observed by a supervisor or colleague.

4.3.4 Musculoskeletal disorders

Long-term musculoskeletal disorders can make working in the cold more difficult, as pain and stiffness can be exacerbated in cold conditions. Warm protective clothing can also be challenging to wear, since it is often heavy, bulky, and restricts mobility. Some people with long-term pain also develop abnormal cold sensitivity or cold allodynia, which can make working in the cold almost impossible [212]. For most people with long-standing musculoskeletal disorders, an ergonomic assessment is likely to be more important than measures targeting cold exposure. For subjects with carpal tunnel syndrome, it may be appropriate to avoid handling cold objects or working in cold environments, particularly if there are motor symptoms or insufficient relief after conservative non-surgical treatment such as wrist orthoses.

4.3.5 Periodic medical examinations

In certain situations, periodic medical examinations could be justified. The indication could be based on the exposure, including those who regularly work in extreme cold settings, below -18°C with wind or -25°C without wind [11]. Alternatively, workers could be included based on a technical risk assessment showing specific risks as defined in Annex A of *ISO 15743 – Ergonomics of the thermal environment – Cold workplaces – Risk assessment and management*. Examples of such specific risks include working with cold objects, liquids, or gases, or in ambient cooling conditions for long continuous periods without the possibility of resting in a heated environment.

Another approach would be to focus on the medical perspective and use a screening questionnaire, with subjects with cold-related health issues offered a complementary medical examination, as per Annex D of the same ISO standard. The examination should ideally include a doctor's visit with patient history and physical examination (general condition, heart, blood pressure, lungs, skin, peripheral circulation, and neurosensory function of the hands and feet), spirometry, and blood tests in specific cases (such as assessment of metabolic control in diabetes). The periodicity would be preferably every three years. [213]. The monitoring could otherwise follow the recommendations of *ISO 12894 – Ergonomics of the thermal environment — Medical supervision of individuals exposed to extreme hot or cold environments*. However, we do not support the view that medical surveillance should result in an assessment of fitness for duty.

4.4 Methodological considerations

A fundamental challenge in this research field is defining cold exposure. The current nomenclature is neither fully accepted nor uniform in the scientific literature. Some authors define cold based on subjective comfort, while others base it on physical

parameters such as ambient temperature. This fact makes it difficult to compare exposure between studies.

Our systematic literature search was designed around one main concept of risk assessment, along with concepts of cold and work. This strategy was used to limit the selection of literature to be assessed by reading abstracts. Despite this choice, the search yielded nearly seven thousand unique studies. An alternative strategy would have been to conduct several parallel literature searches using age or different diseases as a main concept together with cold and work, but this would likely have resulted in a much larger number of irrelevant results. For example, in MEDLINE, the MeSH terms Cardiovascular Diseases and Lung Diseases yielded approximately 2.7 million and 1.3 million results, respectively. We believe it is unlikely that our literature search missed any larger proportion of studies that had investigated how age or disease affects cold work. We also wanted to find literature that described how to systematically assess and manage risks associated with cold work in relation to ageing and disease, and our literature search met this objective well. We supplemented our systematic literature search with a targeted literature search to provide a broader basis for assessing the effects of ageing and various diseases, and we believe that the overall evidence presented in this narrative review should provide a sound overview of this scientific field.

A thorough risk-of-bias assessment was not conducted because the purpose was to write a narrative review, and the included studies were highly heterogeneous. However, we made a simple assessment using a matrix inspired by Farbu et al. [49] (Annex 2). The general impression was that the systematic literature search yielded studies with a wide range of methods, contexts, and sample sizes. The number of participants included in the studies ranged from 36 to 1323, and seven of the studies lacked information on the study population. Only three studies reported including workers of both sexes. There is a risk of selection bias in which subjects working in the cold are particularly healthy (the so-called 'healthy worker effect'), but this risk could not be determined from the descriptions of the study populations. Four studies included measurements of ambient temperature, which ranged from -25 to 12°C, thus representing very different conditions. In other studies, the exposure measures were non-specific or dichotomous (cold-exposed/not cold-exposed). Outcome variables were also poorly defined and often self-reported.

In terms of methods, our narrative review included a large number of register-based cross-sectional studies that associated exposure with outcomes without further consideration of mechanistic explanations. There were also population-based cross-sectional studies, some of which attempted to restrict the sample to working-age populations or those who had indicated in questionnaires that they worked in cold environments. However, these studies still lacked information on whether exposure preceded the onset of the disorder, making it impossible to conclude temporal relationships. Some studies examined specific occupational groups, such as reindeer herders or miners, but still used cross-sectional methodology. Our review identified only a very limited number of prospective studies investigating the health risks of working in the cold [150, 153, 202, 204]. Finally, there were experimental

studies that focused mainly on physiological parameters but did not generally consider the occupational perspective.

A central question in our narrative review was how ageing affects the ability to cope with cooling effects. In epidemiological studies, increasing age is associated with period and cohort effects, and cumulative exposure to cold will, in many cases, be strongly associated with age. In addition, the prevalence of diseases increases with age, regardless of occupational exposures. Taken together, these factors make it difficult to disentangle the effects of ageing per se on vulnerability to cold.

We limited our review to cardiovascular disease, obstructive airway disease, diabetes, and musculoskeletal disorders. However, there are other medical conditions that can be affected by working in the cold, as outlined in Figure 2. For example, there is solid evidence that symptoms of Raynaud's phenomenon can be exacerbated by cold environments [214, 215] and that cold exposure may also be an etiologic factor in the development of the condition [41, 216]. Neurosensory symptoms in the hands and feet are also strongly associated with working in the cold [15]. There are studies showing that sensory thresholds in the hands are negatively affected by exposure to cold [217], especially when a local cold injury is sustained [218]. At the interface between Raynaud's phenomenon and peripheral neuropathy of the hands is a condition often termed abnormal cold sensitivity or cold intolerance, which is defined as a collection of acquired symptoms resulting in avoidance of cold, in the form of pain, numbness, stiffness, or color changes, which may occur after an injury [219]. This condition can occur after a local cold injury [176] but also as a sequela to hand-transmitted vibration injuries and various forms of traumatic hand injuries [220]. In addition to obstructive airway disease, both upper airway symptoms and restrictive lung diseases are likely to be associated with cold work [121, 164]. Several skin diseases worsen in the cold, including atopic eczema, psoriasis, rosacea, and some forms of urticaria [25]. Some rheumatic diseases can also be aggravated in the cold, such as rheumatoid arthritis [221]. Furthermore, there are studies describing a link between exposure to cold and mental health problems such as anxiety, depression, and sleep disorders [222, 223]. There are also reports that subjects with mental health problems may be more likely to report cold-related symptoms [106]. Susceptibility to some infectious diseases is likely to be affected to some extent by exposure to cold, although seasonality of infectious agents and behavioral patterns are probably of greater importance [224]. Regardless of the presence or absence of disease, working in the cold can impair both physical and cognitive abilities [38, 192, 225] and increase the risk of workplace accidents [226]. Thus, there are more aspects of cold work to consider than those covered by this review.

4.5 Knowledge gaps

In 2010, Knardahl et al. identified several knowledge gaps regarding working in cold environments [227]. Among other things, the authors noted that most studies on cold-related health effects have examined the short-term effects of intense

exposure, while long-term, lower-level exposure has rarely been studied. Most experimental studies have recruited young men, and the results may not be generalizable to older people or women. The studies that have investigated sex differences are mainly experimental, and there is a lack of evaluation of the relevance in an occupational context. Working in the cold during uncomfortable working hours is also insufficiently investigated. Shift work (especially night work) disrupts circadian rhythms and temperature regulation. Therefore, shift work in cold environments may be particularly unhealthy. There is also a need for systematic evaluation of short- and long-term acclimatization to cold, with respect to ethnicity and labor migration. Finally, there is a lack of studies assessing the impact of pre-existing medical conditions on work ability in the cold. Since the review by Knardahl et al., there have been several epidemiological and experimental studies that have mainly investigated the relationship between exposure to cold and various adverse health effects. Unfortunately, few of these still relate to a specific occupational context. Exposure to cold is often defined using less precise measures, such as dichotomous survey questions. In some cases, ambient temperature has been measured, but a thorough evaluation of the net cooling effect (which considers ambient temperature, wind speed, humidity, the insulating capacity of clothing, physical activity level, and relevant individual factors) is extremely rare. There is also a lack of studies detailing effect sizes, exposure-response relationships, and possible threshold effects. Such knowledge would help to answer questions about appropriate temperature limits for different types of health risks, which are sometimes requested by employers and trade unions. Furthermore, there is a lack of studies on cold work that focus on the physiological and cognitive effects of normal ageing. Previous studies on aging have often been conducted in laboratory settings without an occupational context, and the study populations have often been even older than what is currently common in working life. Therefore, there is a need for studies that identify the challenges faced by older workers aged 55–70 who spend time in cold environments. Such studies should preferably be designed with a participatory approach to consider both employers' and workers' perspectives. Measures of work capacity and preferred retirement age in relation to cold work should also be included. Regarding chronic diseases and cold work, previous studies have largely examined whether working in cold environments can trigger existing disease or cause incident disease in previously healthy subjects, but not how existing chronic conditions affect the work ability or prognosis. In this regard, prospective studies are needed to detail the development of disease over time among workers in cold environments. Finally, there is also a lack of knowledge about how several simultaneous exposures could interact. Examples of such exposure clusters that would be interesting to study are cold, noise, and hand-transmitted vibration in relation to vascular and neurosensory injuries in the hands, cold and inorganic dust in relation to obstructive or restrictive lung diseases, cold and shift work in relation to cardiovascular disease, and cold and ergonomic risk factors in relation to musculoskeletal disorders.

5. Conclusions

There is scientific evidence that cold work may be associated with increased health risks for subjects of older age and with chronic diseases. The impact of cold work on work capacity and prognosis is unclear. There are methods for structured risk assessment and risk management for cold work, as well as practical suggestions for risk mitigation targeted at workers, employers, and occupational health services. Identified knowledge gaps include the health effects of long-term, low-level occupational exposure to cold, sex differences, acclimatization, exposure-response relationships, and the potential synergistic effects of cold and other exposures.

6. References

1. International Organization for Standardization. ISO 15743:2008 – Ergonomics of the thermal environment – Cold workplaces – Risk assessment and management. Brussels: International Organization for Standardization; 2008.
2. International Organization for Standardization. ISO 11079:2007 – Ergonomics of the thermal environment – Determination and interpretation of cold stress when using required clothing insulation (IREQ) and local cooling effects. Geneva: International Organization for Standardization; 2007.
3. Gavhed D. Arbete i kyla och värme [Work in cold and heat]. In: Toomingas A, Mathiassen SE, Tornqvist EW, editors. Arbetslivsfysiologi [Work physiology], 1st edition. Lund: Studentlitteratur; 2008. p. 307-45.
4. Holmér I. Effekter på människan av kallt klimat [Human effects of cold climate]. Hassi J, Mäkinen T, Holmér I, Påsche A, Risikko T, Toivonen L, et al., editors. Handbok för kallt arbete [Handbook for cold work]. Stockholm: Arbetslivsinstitutet; 2002. p. 19-27.
5. Parsons K. Cold Stress. Human Thermal Environments, 3rd edition. Boca Raton: CRC Press; 2014. p. 355-85.
6. Goodall HN, Grimley Evans J. The older worker. Palmer KT, Brown I, Hobson J, editors. Fitness for work: The medical aspects. Oxford: Oxford University Press; 2013. p. 525-51.
7. BSI Group. BS 7915:1998 – Ergonomics of the thermal environment. Guide to design and evaluation of working practices for cold indoor environments. London: BSI Group; 1998.
8. Ikäheimo TH, J. Frostbite in circumpolar areas. Glob Health Action. 2011;4.
9. Mäkinen TM, Raatikka VP, Rytönen M, Jokelainen J, Rintamäki H, Ruuhela R, et al. Factors affecting outdoor exposure in winter: population-based study. Int J Biometeorol. 2006;51:27-36.
10. Lankford HV, Fox LR. The Wind-Chill Index. Wilderness Environ Med. 2021;32:392-9.
11. Krake AM. Extremes of Temperature. Levy BS, Wegman DS, Baron SL, Sokas RK, editors. Occupational and Environmental Health: Recognizing and Preventing Disease and Injury. Oxford: Oxford University Press; 2017. p. 271-88.
12. Hassi J, Rintamäki H, Raatikka V-P. Exposition för kyla [Exposure to cold]. Hassi J, Mäkinen T, Holmér I, Påsche A, Risikko T, Toivonen L, et al., editors. Handbok för kallt arbete [Handbook for cold work]. Stockholm: Arbetslivsinstitutet; 2002. p. 9-17.
13. Risikko T, Abeysekera J, Holmér I, Kuklane K, Mäkinen T, Påsche A. Riskbedömning och riskhantering [Risk assessment and risk management]. Hassi J, Mäkinen T, Holmér I, Påsche A, Risikko T, Toivonen L, et al., editors. Handbok för kallt arbete [Handbook for cold work]. Stockholm: Arbetslivsinstitutet; 2002. p. 51-79.

14. Swedish Work Environment Authority. The Work Environment 2021. Stockholm, Sweden: Swedish Work Environment Authority; 2022.
15. Stjernbrandt A, Björ B, Andersson M, Burström L, Liljelind I, Nilsson T, et al. Neurovascular hand symptoms in relation to cold exposure in northern Sweden: a population-based study. *Int Arch Occup Environ Health*. 2017;90:587-95.
16. Schwatka NV, Butler LM, Rosecrance JR. An aging workforce and injury in the construction industry. *Epidemiol Rev*. 2012;34:156-67.
17. Ilmarinen JE. Aging workers. *Occupational and Environmental Medicine*. 2001;58:546-52.
18. Statistics Sweden. Arbetsmiljöundersökningen [The Work Environment Survey] [Internet]. Solna: Statistics Sweden; 2024 [cited 2024-02-08]. Available from: <https://www.scb.se/hitta-statistik/statistik-efter-amne/arbetsmarknad/arbetsmiljo/arbetsmiljouundersokningen/>.
19. Afa Insurance. Allvarliga arbetsskador och långvarig arbetsfrånvaro [Serious occupational injuries and long-term absence from work]. Stockholm: Afa Insurance; 2023.
20. Previdi M, Smith K, Polvani L. Arctic amplification of climate change: a review of underlying mechanisms. *Environ Res Lett*. 2021;16:093003.
21. Rantanen M, Karpechko AY, Lipponen A, Nordling K, Hyvärinen O, Ruosteenoja K, et al. The Arctic has warmed nearly four times faster than the globe since 1979. *Commun Earth Environ*. 2022;3:168.
22. Hassi J, Rytönen M, Kotaniemi J, Rintamäki H. Impacts of cold climate on human heat balance, performance and health in circumpolar areas. *Int J Circumpolar Health*. 2005;64:459-67.
23. García-León D, Masselot P, Mistry MN, Gasparrini A, Motta C, Feyen L, et al. Temperature-related mortality burden and projected change in 1368 European regions: a modelling study. *Lancet Public Health*. 2024;9:e644-e53.
24. Friedman LS, Abasilim C, Fitts R, Wueste M. Clinical outcomes of temperature related injuries treated in the hospital setting, 2011–2018. *Environ Res*. 2020;189:109882.
25. Mäkinen TM, Hassi J. Health problems in cold work. *Ind Health*. 2009;47:207-20.
26. Parsons K. Human Thermal Environments, 3rd edition. Chapter 13, Thermal Comfort for Special Populations, 307-21. Boca Raton: CRC Press; 2014. p. 307-21.
27. Rijal HB, Humphreys MA, Nicol JF. Adaptive model and the adaptive mechanisms for thermal comfort in Japanese dwellings. *Energy Build*. 2019;202:109371.
28. Shitzer A, Stroschein LA, Santee WR, Gonzalez RR, Pandolf KB. Quantification of conservative endurance times in thermally insulated cold-stressed digits. *J Appl Physiol* (1985). 1991;71:2528-35.
29. International Organization for Standardization. ISO 9920:2007 – Ergonomics of the thermal environment – Estimation of thermal insulation and water vapour

resistance of a clothing ensemble. Geneva: International Organization for Standardization; 2007.

30. Hensel H. Thermoreception and temperature regulation. *Monogr Physiol Soc.* 1981;38:1-321.

31. Wang H, Siemens J. TRP ion channels in thermosensation, thermoregulation and metabolism. *Temperature (Austin).* 2015;2:178-87.

32. Yin K, Zimmermann K, Vetter I, Lewis RJ. Therapeutic opportunities for targeting cold pain pathways. *Biochem Pharmacol.* 2015;93:125-40.

33. Gavhed D, Mäkinen T, Holmér I, Rintamäki H. Face temperature and cardiorespiratory responses to wind in thermoneutral and cool subjects exposed to -10 degrees C. *Eur J Appl Physiol.* 2000;83:449-56.

34. Haman F, Blondin DP. Shivering thermogenesis in humans: Origin, contribution and metabolic requirement. *Temperature (Austin).* 2017;4:217-26.

35. Johnson JM, Minson CT, Kellogg DL, Jr. Cutaneous vasodilator and vasoconstrictor mechanisms in temperature regulation. *Compr Physiol.* 2014;4:33-89.

36. Charkoudian N. Mechanisms and modifiers of reflex induced cutaneous vasodilation and vasoconstriction in humans. *J Appl Physiol (1985).* 2010;109:1221-8.

37. Daanen HA. Finger cold-induced vasodilation: a review. *Eur J Appl Physiol.* 2003;89:411-26.

38. Holmér I. Work in the cold. Review of methods for assessment of cold exposure. *Int Arch Occup Environ Health.* 1993;65:147-55.

39. Imray C, Grieve A, Dhillon S, Caudwell Xtreme Everest Research Group. Cold damage to the extremities: frostbite and non-freezing cold injuries. *Postgrad Med J.* 2009;85:481-8.

40. Maricq HR, Carpentier PH, Weinrich MC, Keil JE, Palesch Y, Biro C, et al. Geographic variation in the prevalence of Raynaud's phenomenon: a 5 region comparison. *J Rheumatol.* 1997;24:879-89.

41. Stjernbrandt A, Pettersson H, Lundström R, Liljelind I, Nilsson T, Wahlström J. Incidence, remission, and persistence of Raynaud's phenomenon in the general population of northern Sweden: a prospective study. *BMC Rheumatology.* 2022;6.

42. Kriemler S, Mateikaitė-Pipirienė K, Rosier A, Keyes LE, Paal P, Andjelkovic M, et al. Frostbite and Mortality in Mountaineering Women: A Scoping Review-UIAA Medical Commission Recommendations. *High Alt Med Biol.* 2023;24:247-58.

43. Heintzen MP, Strauer BE. Peripheral vascular effects of beta-blockers. *Eur Heart J.* 1994;15 Suppl C:2-7.

44. Simecková M, Janský L, Lesná II, Vybíral S, Srámek P. Role of beta adrenoceptors in metabolic and cardiovascular responses of cold exposed humans. *J Therm Biol.* 2000;25:437-42.

45. The National Board of Health and Welfare. Patientregistret [The Patient Registry] [Internet]. Stockholm: The National Board of Social Affairs and Health; 2024 [cited 2024-02-02]. Available from: <https://www.socialstyrelsen.se/statistik-och-data/register/patientregistret/>.
46. The Public Health Agency of Sweden. Nationella folkhälsoenkäten [The Public Health Survey] [Internet]. Solna: The Public Health Agency of Sweden; 2023 [cited 2023-12-22]. Available from: <https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/om-vara-datainsamlingar/nationella-folkhalsoenkaten/>.
47. Tengland PA. The concept of work ability. *J Occup Rehabil*. 2011;21:275-85.
48. Ilmarinen J, Tuomi K, Seitsamo J. New dimensions of work ability. *International Congress Series*. 2005;1280:3-7.
49. Farbu EH, Höper AC, Reiherth E, Nilsson T, Skandfer M. Cold exposure and musculoskeletal conditions: A scoping review. *Front Physiol*. 2022;13:934163.
50. Olesen BW. International Standards and the Ergonomics of the Thermal Environment. *Applied Ergonomics*. 1995;26:293-302.
51. Holmér I. Assessment of cold exposure. *Int J Circumpolar Health*. 2001;60:413-21.
52. Mäkinen TM, Hassi J, Pasche A, Abeysekera J, Holmér I. Project for developing a cold risk assessment and management strategy for workplaces in the Barents region. *Int J Circumpolar Health*. 2002;61:136-41.
53. Hassi J, Raatikka VP, Huurre M. Health-check questionnaire for subjects exposed to cold. *Int J Circumpolar Health*. 2003;62:436-43.
54. Besnard Y, Launay JC, Guinet-Lebreton A, Savourey G. PREDICTOL (R): a computer program to determine the thermophysiological duration limited exposures in various climatic conditions. *Comput Methods Programs Biomed*. 2004;76:221-8.
55. Risikko T, Remes J, Hassi J. Implementation of cold risk management in occupational safety, occupational health and quality practices. Evaluation of a development process and its effects at the finnish maritime administration. *Int J Occup Saf Ergon*. 2008;14:433-46.
56. Gao C, Holmér I, Abeysekera J. Slips and falls in a cold climate: Underfoot surface, footwear design and worker preferences for preventive measures. *Applied Ergonomics*. 2008;39(3):385-91.
57. Noroozi A, Abbassi R, MacKinnon S, Khan F, Khakzad N. Effects of Cold Environments on Human Reliability Assessment in Offshore Oil and Gas Facilities. *Human Factors*. 2014;56:825-39.
58. Ceballos D, Mead K, Ramsey J. Recommendations to Improve Employee Thermal Comfort When Working in 40 degrees F Refrigerated Cold Rooms. *J Occup Environ Hyg*. 2015;12:D216-21.

59. Jussila K, Rissanen S, Aminoff A, Wahlstrom J, Vaktskjold A, Talykova L, et al. Thermal comfort sustained by cold protective clothing in Arctic open-pit mining-a thermal manikin and questionnaire study. *Ind Health*. 2017;55:537-48.
60. Tirloni AS, Reis DC, Dias NF, Moro ARP. The use of personal protective equipment: Finger temperatures and thermal sensation of workers' exposure to cold environment. *Int J Environ Res Public Health*. 2018;15(11) (no pagination).
61. Tsang YP, Choy KL, Wu CH, Ho GTS, Lam CHY, Koo PS. An Internet of Things (IoT)-based risk monitoring system for managing cold supply chain risks. *Ind Manag Data Syst*. 2018;118:1432-62.
62. Golbabaie F, Azrah K, Goodarzi Z, Ahmadi O, Karami E. Risk assessment of cold stress in petroleum transfer station in the northwestern regions of Iran: Subjective and field measurements. *J Therm Biol*. 2022;110.
63. Risikko T, Remes J, Hassi J. Implementation of Cold Risk Management in Occupational Safety, Occupational Health and Quality Practices. Evaluation of a Development Process and Its Effects at the Finnish Maritime Administration. *Int J Occup Saf Ergon*. 2008;14:433-46.
64. Young AJ, Lee DT. Aging and human cold tolerance. *Exp Aging Res*. 1997;23:45-67.
65. Thein LA. Environmental conditions affecting the athlete. *J Orthop Sports Phys Ther*. 1995;21:158-71.
66. Collins KJ, Easton JC, Belfield-Smith H, Exton-Smith AN, Pluck RA. Effects of age on body temperature and blood pressure in cold environments. *Clin Sci (Lond)*. 1985;69:465-70.
67. Falk B, Bar-Or O, Smolander J, Frost G. Response to rest and exercise in the cold: effects of age and aerobic fitness. *J Appl Physiol* (1985). 1994;76:72-8.
68. Mathew L, Purkayastha SS, Singh R, Sen Gupta J. Influence of aging in the thermoregulatory efficiency of man. *Int J Biometeorol*. 1986;30:137-45.
69. Budd GM, Brotherhood JR, Hendrie AL, Jeffery SE. Effects of fitness, fatness, and age on men's responses to whole body cooling in air. *J Appl Physiol* (1985). 1991;71:2387-93.
70. Sawada S. Cold-induced vasodilatation response of finger skin blood vessels in older men observed by using a modified local cold tolerance test. *Ind Health*. 1996;34:51-6.
71. Inoue Y, Nakao M, Araki T, Ueda H. Thermoregulatory responses of young and older men to cold exposure. *Eur J Appl Physiol Occup Physiol*. 1992;65:492-8.
72. Collins KJ, Hoinville E. Temperature requirements in old age. *Build Serv Eng Res Technol*. 1980;1:165-72.
73. Bernstein LM, Hick FK, Inouye T, Johnston LC, Ryan R. Body composition as related to heat regulation in women. *J Appl Physiol*. 1956;9:241-56.

74. Wagner JA, Horvath SM. Influences of age and gender on human thermoregulatory responses to cold exposures. *J Appl Physiol* (1985). 1985;58:180-6.
75. Giles TD, Materson BJ, Cohn JN, Kostis JB. Definition and classification of hypertension: an update. *J Clin Hypertens* (Greenwich). 2009;11:611-4.
76. Ikäheimo TM, Lehtinen T, Antikainen R, Jokelainen J, Näyhä S, Hassi J, et al. Cold-related cardiorespiratory symptoms among subjects with and without hypertension: the National FINRISK Study 2002. *Eur J Public Health*. 2014;24:237-43.
77. Komulainen S, Oja T, Rintamäki H, Virokannas H, Keinänen-Kiukaanniemi S. Blood pressure and thermal responses to whole body cold exposure in mildly hypertensive subjects. *J Therm Biol*. 2004;29:851-6.
78. Korhonen I. Blood pressure and heart rate responses in men exposed to arm and leg cold pressor tests and whole-body cold exposure. *Int J Circumpolar Health*. 2006;65:178-84.
79. Ikäheimo TM. Cardiovascular diseases, cold exposure and exercise. *Temperature* (Austin). 2018;5:123-46.
80. Barnett AG, Sans S, Salomaa V, Kuulasmaa K, Dobson AJ. The effect of temperature on systolic blood pressure. *Blood Press Monit*. 2007;12:195-203.
81. Sun Z. Cardiovascular responses to cold exposure. *Front Biosci*. 2010;2:495-503.
82. Hess KL, Wilson TE, Sauder CL, Gao Z, Ray CA, Monahan KD. Aging affects the cardiovascular responses to cold stress in humans. *J Appl Physiol* (1985). 2009;107:1076-82.
83. Schlader ZJ, Coleman GL, Sackett JR, Sarker S, Johnson BD. Sustained increases in blood pressure elicited by prolonged face cooling in humans. *Am J Physiol Regul Integr Comp Physiol*. 2016;311:R643-R8.
84. Khurana RK, Watabiki S, Hebel JR, Toro R, Nelson E. Cold face test in the assessment of trigeminal-brainstem- vagal function in humans. *Ann Neurol*. 1980;7:144-9.
85. Collins KJ, Abdel-Rahman TA, Easton JC, Sacco P, Ison J, Doré CJ. Effects of Facial Cooling on Elderly and Young Subjects: Interactions with Breath-Holding and Lower Body Negative Pressure. *Clin Sci*. 1996;90:485-92.
86. Wilson TE, Sauder CL, Kearney ML, Kuipers NT, Leuenberger UA, Monahan KD, et al. Skin-surface cooling elicits peripheral and visceral vasoconstriction in humans. *J Appl Physiol* (1985). 2007;103:1257-62.
87. Wilson TE, Gao Z, Hess KL, Monahan KD. Effect of aging on cardiac function during cold stress in humans. *Am J Physiol Regul Integr Comp Physiol*. 2010;298:R1627-33.
88. Näyhä S. Cold and the risk of cardiovascular diseases. A review. *Int J Circumpolar Health*. 2002;61:373-80.
89. Fan JF, Xiao YC, Feng YF, Niu LY, Tan X, Sun JC, et al. A systematic review and meta-analysis of cold exposure and cardiovascular disease outcomes. *Front Cardiovasc Med*. 2023;10:1084611.

90. Manou-Stathopoulou V, Goodwin CD, Patterson T, Redwood SR, Marber MS, Williams RP. The effects of cold and exercise on the cardiovascular system. *Heart*. 2015;101:808-20.
91. Emmett JD. A review of heart rate and blood pressure responses in the cold in healthy subjects and coronary artery disease patients. *J Cardiopulm Rehabil*. 1995;15:19-24.
92. Kristensen TS. Cardiovascular diseases and the work environment. A critical review of the epidemiologic literature on nonchemical factors. *Scand J Work Environ Health*. 1989;15:165-79.
93. Price AE. Heart disease and work. *Heart*. 2004;90:1077-84.
94. Muller MD, Gao Z, Drew RC, Herr MD, Leuenberger UA, Sinoway LI. Effect of cold air inhalation and isometric exercise on coronary blood flow and myocardial function in humans. *J Appl Physiol* (1985). 2011;111:1694-702.
95. Donaldson GC, Keatinge WR. Early increases in ischaemic heart disease mortality dissociated from and later changes associated with respiratory mortality after cold weather in south east England. *J Epidemiol Community Health*. 1997;51:643-8.
96. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2012;33:1787-847.
97. Grysiewicz RA, Thomas K, Pandey DK. Epidemiology of ischemic and hemorrhagic stroke: incidence, prevalence, mortality, and risk factors. *Neurol Clin*. 2008;26:871-95, vii.
98. Chen Z, Liu P, Xia X, Wang L, Li X. The underlying mechanisms of cold exposure-induced ischemic stroke. *Sci Total Environ*. 2022;834:155514.
99. Chen Z, Liu P, Xia X, Cao C, Ding Z, Li X. Low ambient temperature exposure increases the risk of ischemic stroke by promoting platelet activation. *Sci Total Environ*. 2024;912:169235.
100. Lawton MT, Vates GE. Subarachnoid Hemorrhage. *N Engl J Med*. 2017;377:257-66.
101. Hassi J, Rintamäki H. Effekter av kyla på hälsa och arbetsförmåga [Effects of cold on health and work ability]. Hassi J, Mäkinen T, Holmér I, Påsche A, Risikko T, Toivonen L, et al., editors. *Handbok för kallt arbete [Handbook for cold work]*. Stockholm: Arbetslivsinstitutet; 2002. p. 29-49.
102. Hardie RJ, Pool J. Neurological disorders. Palmer KT, Brown I, Hobson J, editors. *Fitness for work: The medical aspects*. Oxford: Oxford University Press; 2013. p. 102-31.
103. Fares A. Winter cardiovascular diseases phenomenon. *N Am J Med Sci*. 2013;5:266-79.

104. Kim J-Y, Jung K-Y, Hong Y-S, Kim J-I, Jang T-W, Kim J-M. The Relationship between Cold Exposure and Hypertension. *J Occup Health*. 2003;45:300-6.
105. Bortkiewicz A, Gadzicka E, Szymczak W, Szykowska A, Koszada-Włodarczyk W, Makowiec-Dabrowska T. Physiological reaction to work in cold microclimate. *Int J Occup Med Environ Health*. 2006;19:123-31.
106. Näyhä S, Hassi J, Jousilahti P, Laatikainen T, Ikäheimo TM. Cold-related symptoms among the healthy and sick of the general population: National FINRISK Study data, 2002. *Public Health*. 2011;125:380-8.
107. Pettersson H, Olsson D, Järholm B. Occupational exposure to noise and cold environment and the risk of death due to myocardial infarction and stroke. *Int Arch Occup Environ Health*. 2020;93:571-5.
108. Rosengren A, Wennerblom B, Bjurö T, Wilhelmsen L, Bake B. Effects of cold on ST amplitudes and blood pressure during exercise in angina pectoris. *Eur Heart J*. 1988;9:1074-80.
109. Lassvik C. Angina pectoris in the cold. Effects of cold environment and cold air inhalation at exercise test. *Acta Med Scand Suppl*. 1981;644:21-2.
110. Stanghelle JK, Nilsson S. Angina pectoris and cold. *Int Rehabil Med*. 1983;5:189-91.
111. Lian H, Ruan Y, Liang R, Liu X, Fan Z. Short-Term Effect of Ambient Temperature and the Risk of Stroke: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2015;12:9068-88.
112. Vaičiulis V, Jaakkola JJK, Radišauskas R, Tamošiūnas A, Lukšienė D, Ryti NRI. Risk of ischemic and hemorrhagic stroke in relation to cold spells in four seasons. *BMC Public Health*. 2023;23:554.
113. Fadel M, Sembajwe G, Tripodi D, Bonnetterre V, Leclerc A, Roquelaure Y, et al. Association between reported work in cold environments and stroke occurrence in the CONSTANCES cohort: a prospective study. *BMJ Open*. 2022;12:e054198.
114. Zhai G, Zhang J, Zhang K, Chai G. Impact of diurnal temperature range on hospital admissions for cerebrovascular disease among farmers in Northwest China. *Sci Rep*. 2022;12:15368.
115. Golant A, Nord RM, Paksima N, Posner MA. Cold exposure injuries to the extremities. *J Am Acad Orthop Surg*. 2008;16:704-15.
116. Radtke T, Poerschke D, Wilhelm M, Trachsel LD, Tschanz H, Matter F, et al. Acute effects of Finnish sauna and cold-water immersion on haemodynamic variables and autonomic nervous system activity in patients with heart failure. *Eur J Prev Cardiol*. 2016;23:593-601.
117. Blanchet M, Ducharme A, Racine N, Rouleau JL, Tardif JC, Juneau M, et al. Effects of cold exposure on submaximal exercise performance and adrenergic activation in patients with congestive heart failure and the effects of beta-adrenergic blockade (carvedilol or metoprolol). *Am J Cardiol*. 2003;92:548-53.

118. Juneau M, Larivée L, White M. Cold temperature impairs maximal exercise performance in patients with heart failure: attenuation by acute ACE inhibitor therapy. *Can J Cardiol*. 2002;18:981-6.
119. Balmes J, Becklake M, Blanc P, Henneberger P. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. *Am J Resp Crit Care*. 2003;167:787.
120. Hanstock H, Ainegren M, Stenfors LE. Exercise in Sub-zero Temperatures and Airway Health: Implications for Athletes With Special Focus on Heat-and-Moisture-Exchanging Breathing Devices. *Front Sports Act Living*. 2020;2.
121. Koskela HO. Cold air-provoked respiratory symptoms: the mechanisms and management. *Int J Circumpolar Health*. 2007;66:91-100.
122. Millqvist E, Bengtsson U, Bake B. Occurrence of breathing problems induced by cold climate in asthmatics--a questionnaire survey. *Eur J Respir Dis*. 1987;71:444-9.
123. Kotaniemi J-T, Latvala J, Lundbäck B, Sovijärvi A, Hassi J, Larsson K. Does living in a cold climate or recreational skiing increase the risk for obstructive respiratory diseases or symptoms? *Int J Circumpolar Health*. 2003;62:142-57.
124. Borak J, Lefkowitz RY. Bronchial hyperresponsiveness. *Occup Med (Lond)*. 2016;66:95-105.
125. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol*. 2004;113:59-65.
126. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J*. 2009;34:648-54.
127. Sue-Chu M, Karjalainen EM, Altraja A, Laitinen A, Laitinen LA, Naess AB, et al. Lymphoid aggregates in endobronchial biopsies from young elite cross-country skiers. *Am J Respir Crit Care Med*. 1998;158:597-601.
128. Sue-Chu M, Larsson L, Moen T, Rennard SI, Bjermer L. Bronchoscopy and bronchoalveolar lavage findings in cross-country skiers with and without "ski asthma". *Eur Respir J*. 1999;13:626-32.
129. Suadcani P, Hein HO, Meyer HW, Gyntelberg F. Exposure to cold and draught, alcohol consumption, and the NS-phenotype are associated with chronic bronchitis: an epidemiological investigation of 3387 men aged 53-75 years: the Copenhagen Male Study. *Occup Environ Med*. 2001;58:160-4.
130. D'Amato M, Molino A, Calabrese G, Cecchi L, Annesi-Maesano I, D'Amato G. The impact of cold on the respiratory tract and its consequences to respiratory health. *Clin Transl Allergy*. 2018;8:20.
131. Ijaz MK, Zargar B, Wright KE, Rubino JR, Sattar SA. Generic aspects of the airborne spread of human pathogens indoors and emerging air decontamination technologies. *Am J Infect Control*. 2016;44:S109-20.

132. McFadden ER, Jr., Pichurko BM, Bowman HF, Ingenito E, Burns S, Dowling N, et al. Thermal mapping of the airways in humans. *J Appl Physiol* (1985). 1985;58:564-70.
133. Hanes LS, Issa E, Proud D, Togias A. Stronger nasal responsiveness to cold air in individuals with rhinitis and asthma, compared with rhinitis alone. *Clin Exp Allergy*. 2006;36:26-31.
134. Fuzzi S, Baltensperger U, Carslaw K, Decesari S, Denier van der Gon H, Facchini MC, et al. Particulate matter, air quality and climate: lessons learned and future needs. *Atmos Chem Phys*. 2015;15:8217-99.
135. Grace MS, Baxter M, Dubuis E, Birrell MA, Belvisi MG. Transient receptor potential (TRP) channels in the airway: role in airway disease. *Br J Pharmacol*. 2014;171:2593-607.
136. Fahey PJ, Utell MJ, Condemi JJ, Green R, Hyde RW. Raynaud's phenomenon of the lung. *Am J Med*. 1984;76:263-9.
137. Koskela HO, Koskela AK, Tukiaineu HO. Bronchoconstriction due to cold weather in COPD. The roles of direct airway effects and cutaneous reflex mechanisms. *Chest*. 1996;110:632-6.
138. Analitis A, Katsouyanni K, Biggeri A, Baccini M, Forsberg B, Bisanti L, et al. Effects of cold weather on mortality: results from 15 European cities within the PHEWE project. *Am J Epidemiol*. 2008;168:1397-408.
139. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. The Eurowinter Group. *Lancet*. 1997;349:1341-6.
140. Rocklöv J, Forsberg B. The effect of temperature on mortality in Stockholm 1998-2003: a study of lag structures and heatwave effects. *Scand J Public Health*. 2008;36:516-23.
141. Gasparrini A, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet*. 2015;386:369-75.
142. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? *Occup Environ Med*. 2007;64:93-100.
143. Näyhä S. Environmental temperature and mortality. *Int J Circumpolar Health*. 2005;64:451-8.
144. Harju T, Mäkinen T, Näyhä S, Laatikainen T, Jousilahti P, Hassi J. Cold-related respiratory symptoms in the general population. *Clin Respir J*. 2010;4:176-85.
145. Ikäheimo TM, Jokelainen J, Näyhä S, Laatikainen T, Jousilahti P, Laukkanen J, et al. Cold weather-related cardiorespiratory symptoms predict higher morbidity and mortality. *Environ Res*. 2020;191:110108.
146. Hyrkäs H, Jaakkola MS, Ikäheimo TM, Hugg TT, Jaakkola JJ. Asthma and allergic rhinitis increase respiratory symptoms in cold weather among young adults. *Respir Med*. 2014;108:63-70.

147. Belachew AB, Rantala AK, Jaakkola MS, Hugg TT, Ruuhela R, Kukkonen J, et al. Effect of cold winters on the risk of new asthma: a case-crossover study in Finland. *Occup Environ Med.* 2023;80:702-5.
148. Kotaniemi JT, Pallasaho P, Sovijärvi AR, Laitinen LA, Lundbäck B. Respiratory symptoms and asthma in relation to cold climate, inhaled allergens, and irritants: a comparison between northern and southern Finland. *J Asthma.* 2002;39:649-58.
149. Stjernbrandt A, Stenfors N, Liljelind I. Occupational cold exposure is associated with increased reporting of airway symptoms. *Int Arch Occup Environ Health.* 2021;94:1945-52.
150. Stjernbrandt A, Hedman L, Liljelind I, Wahlström J. Occupational cold exposure in relation to incident airway symptoms in northern Sweden: a prospective population-based study. *Int Arch Occup Environ Health.* 2022;95:1871-9.
151. Reijula K, Larmi E, Hassi J, Hannuksela M. Respiratory symptoms and ventilatory function among Finnish reindeer herders. *Arctic Med Res.* 1990;49:74-80.
152. Jammes Y, Delvolgo-Gori MJ, Badier M, Guillot C, Gazazian G, Parlenti L. One-year occupational exposure to a cold environment alters lung function. *Arch Environ Health.* 2002;57:360-5.
153. Velasco Garrido M, Rentel N, Herold R, Harth V, Preisser AM. Does working in an extremely cold environment affects lung function?: 10 years follow-up. *Int Arch Occup Environ Health.* 2023;96:1039-48.
154. Norqvist J, Eriksson L, Söderström L, Lindberg A, Stenfors N. Self-reported physician-diagnosed asthma among Swedish adolescent, adult and former elite endurance athletes. *J Asthma.* 2015;52:1046-53.
155. Eklund LM, Irewall T, Lindberg A, Stenfors N. Prevalence, age at onset, and risk factors of self-reported asthma among Swedish adolescent elite cross-country skiers. *Scand J Med Sci Sports.* 2018;28:180-6.
156. Karjalainen EM, Laitinen A, Sue-Chu M, Altraja A, Bjermer L, Laitinen LA. Evidence of airway inflammation and remodeling in ski athletes with and without bronchial hyperresponsiveness to methacholine. *Am J Respir Crit Care Med.* 2000;161:2086-91.
157. Couto M, Stang J, Horta L, Stensrud T, Severo M, Mowinckel P, et al. Two distinct phenotypes of asthma in elite athletes identified by latent class analysis. *J Asthma.* 2015;52:897-904.
158. Sjöström R, Söderström L, Klockmo C, Patrician A, Sandström T, Björklund G, et al. Qualitative identification and characterisation of self-reported symptoms arising in humans during experimental exposure to cold air. *Int J Circumpolar Health.* 2019;78:1583528.
159. Koskela H, Tukiainen H, Kononoff A, Pekkarinen H. Effect of whole-body exposure to cold and wind on lung function in asthmatic patients. *Chest.* 1994;105:1728-31.

160. Schwartz J. Who is sensitive to extremes of temperature?: A case-only analysis. *Epidemiology*. 2005;16:67-72.
161. McCormack MC, Paulin LM, Gummerson CE, Peng RD, Diette GB, Hansel NN. Colder temperature is associated with increased COPD morbidity. *Eur Respir J*. 2017;49.
162. Arnup ME, Mendella LA, Anthonisen NR. Effects of cold air hyperpnea in patients with chronic obstructive lung disease. *Am Rev Respir Dis*. 1983;128:236-9.
163. Ramsdale EH, Morris MM, Roberts RS, Hargreave FE. Bronchial responsiveness to methacholine in chronic bronchitis: relationship to airflow obstruction and cold air responsiveness. *Thorax*. 1984;39:912-8.
164. Schaefer O, Eaton RD, Timmermans FJ, Hildes JA. Respiratory function impairment and cardiopulmonary consequences in long-time residents of the Canadian Arctic. *Can Med Assoc J*. 1980;123:997-1004.
165. Rode A, Shephard RJ. The ageing of lung function: cross-sectional and longitudinal studies of an Inuit community. *Eur Respir J*. 1994;7:1653-9.
166. Iavicoli I, Gambelunghe A, Magrini A, Mosconi G, Soleo L, Vigna L, et al. Diabetes and work: The need of a close collaboration between diabetologist and occupational physician. *Nutr Metab Cardiovasc Dis*. 2019;29:220-7.
167. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33 Suppl 1:S62-9.
168. Stansberry KB, Hill MA, Shapiro SA, McNitt PM, Bhatt BA, Vinik AI. Impairment of peripheral blood flow responses in diabetes resembles an enhanced aging effect. *Diabetes Care*. 1997;20:1711-6.
169. Song X, Jiang L, Zhang D, Wang X, Ma Y, Hu Y, et al. Impact of short-term exposure to extreme temperatures on diabetes mellitus morbidity and mortality? A systematic review and meta-analysis. *Environ Sci Pollut Res Int*. 2021;28:58035-49.
170. Winocour PH, Mitchell WS, Gush RJ, Taylor LJ, Baker RD. Altered hand skin blood flow in type 1 (insulin-dependent) diabetes mellitus. *Diabet Med*. 1988;5:861-6.
171. Mitchell WS, Winocour PH, Gush RJ, Taylor LJ, Baker RD, Anderson DC, et al. Skin blood flow and limited joint mobility in insulin-dependent diabetes mellitus. *Br J Rheumatol*. 1989;28:195-200.
172. Kenny GP, Sigal RJ, McGinn R. Body temperature regulation in diabetes. *Temperature (Austin)*. 2016;3:119-45.
173. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. *Nat Rev Dis Primers*. 2019;5:41.
174. Thomsen NO, Cederlund R, Rosen I, Bjork J, Dahlin LB. Clinical outcomes of surgical release among diabetic patients with carpal tunnel syndrome: prospective follow-up with matched controls. *J Hand Surg Am*. 2009;34:1177-87.
175. Konen JC, Curtis LG, Summerson JH. Symptoms and complications of adult diabetic patients in a family practice. *Arch Fam Med*. 1996;5:135-45.

176. Stjernbrandt A, Carlsson D, Pettersson H, Liljelind I, Nilsson T, Wahlström J. Cold sensitivity and associated factors: a nested case-control study performed in Northern Sweden. *Int Arch Occup Environ Health*. 2018;91:785-97.
177. Khabbazi A, Farzaneh R, Mahmoudi M, Shahi M, Jabbaripour Sarmadian A, Babapour E, et al. Cold intolerance and associated factors: a population study. *Sci Rep*. 2022;12:18029.
178. Thomsen NO, Cederlund RI, Andersson GS, Rosen I, Bjork J, Dahlin LB. Carpal tunnel release in patients with diabetes: a 5-year follow-up with matched controls. *J Hand Surg Am*. 2014;39:713-20.
179. Dahlin LB, Eriksson KF, Sundkvist G. Persistent postoperative complaints after whole sural nerve biopsies in diabetic and non-diabetic subjects. *Diabet Med*. 1997;14:353-6.
180. Li Y, Lan L, Wang Y, Yang C, Tang W, Cui G, et al. Extremely cold and hot temperatures increase the risk of diabetes mortality in metropolitan areas of two Chinese cities. *Environ Res*. 2014;134:91-7.
181. Yang J, Yin P, Zhou M, Ou CQ, Li M, Liu Y, et al. The effect of ambient temperature on diabetes mortality in China: A multi-city time series study. *Sci Total Environ*. 2016;543:75-82.
182. Vallianou NG, Geladari EV, Kounatidis D, Geladari CV, Stratigou T, Dourakis SP, et al. Diabetes mellitus in the era of climate change. *Diabetes Metab*. 2021;47:101205.
183. Weadock V. Winter woes. *Occup Health Saf*. 2003;72:46-8, 50-1.
184. Ikäheimo TM, Jokelainen J, Hassi J, Hiltunen L, Keinänen-Kiukaanniemi S, Laatikainen T, et al. Diabetes and impaired glucose metabolism is associated with more cold-related cardiorespiratory symptoms. *Diabetes Res Clin Pract*. 2017;129:116-25.
185. Haupt A, Berg B, Paschen P, Dreyer M, Häring HU, Smedegaard J, et al. The effects of skin temperature and testing site on blood glucose measurements taken by a modern blood glucose monitoring device. *Diabetes Technol Ther*. 2005;7:597-601.
186. Mäkinen TM, Jokelainen J, Näyhä S, Laatikainen T, Jousilahti P, Hassi J. Occurrence of frostbite in the general population--work-related and individual factors. *Scand J Work Environ Health*. 2009;35:384-93.
187. Moen K, Stjernbrandt A. A prospective study on local cold injuries in northern Sweden. *Int J Circumpolar Health*. 2022;81:2149381.
188. Pienimäki T. Cold exposure and musculoskeletal disorders and diseases. A review. *Int J Circumpolar Health*. 2002;61:173-82.
189. da Costa BR, Vieira ER. Risk factors for work-related musculoskeletal disorders: A systematic review of recent longitudinal studies. *Am J Ind Med*. 2010;53:285-323.

190. Sormunen E, Remes J, Hassi J, Pienimäki T, Rintamäki H. Factors associated with self-estimated work ability and musculoskeletal symptoms among male and female workers in cooled food-processing facilities. *Ind Health*. 2009;47:271-82.
191. Aasmoe L, Bang BE, Egeness C, Lochen ML. Musculoskeletal symptoms among seafood production workers in North Norway. *Occup Med (Lond)*. 2008;58:64-70.
192. Racinais S, Oksa J. Temperature and neuromuscular function. *Scand J Med Sci Sports*. 2010;20 Suppl 3:1-18.
193. Lapossy E, Gasser P, Hrycaj P, Dubler B, Samborski W, Muller W. Cold-induced vasospasm in patients with fibromyalgia and chronic low back pain in comparison to healthy subjects. *Clin Rheumatol*. 1994;13:442-5.
194. Oksa J, Rintamäki H, Rissanen S. Muscle performance and electromyogram activity of the lower leg muscles with different levels of cold exposure. *Eur J Appl Physiol Occup Physiol*. 1997;75:484-90.
195. Burström L, Järvholm B, Nilsson T, Wahlström J. Back and neck pain due to working in a cold environment: a cross-sectional study of male construction workers. *Int Arch Occup Environ Health*. 2013;86:809-13.
196. Dovrat E, Katz-Leurer M. Cold exposure and low back pain in store workers in Israel. *Am J Ind Med*. 2007;50:626-31.
197. Skandfer M, Talykova L, Brenn T, Nilsson T, Vaktiskjold A. Low back pain among mineworkers in relation to driving, cold environment and ergonomics. *Ergonomics*. 2014;57:1541-8.
198. Sundstrup E, Jakobsen MD, Brandt M, Jay K, Persson R, Andersen LL. Central Sensitization and Perceived Indoor Climate among Workers with Chronic Upper-Limb Pain: Cross-Sectional Study. *Pain Res Treat*. 2015;2015:793750.
199. Hildebrandt VH, Bongers PM, Dijk FJHv, Kemper HCG, Dul J. The influence of climatic factors on non-specific back and neck-shoulder disease. *Ergonomics*. 2002;45:32-48.
200. Piedrahita H, Punnett L, Shahnavaz H. Musculoskeletal symptoms in cold exposed and non-cold exposed workers. *Int J Ind Econ*. 2004;34:271-8.
201. Stjernbrandt A, Hoftun Farbu E. Occupational cold exposure is associated with neck pain, low back pain, and lumbar radiculopathy. *Ergonomics*. 2022:1-10.
202. Lewis C, Stjernbrandt A, Wahlström J. The association between cold exposure and musculoskeletal disorders: a prospective population-based study. *Int Arch Occup Environ Health*. 2023;96:565-75.
203. Farbu EH, Skandfer M, Nielsen C, Brenn T, Stubhaug A, Höper AC. Working in a cold environment, feeling cold at work and chronic pain: a cross-sectional analysis of the Tromso Study. *BMJ Open*. 2019;9:e031248.
204. Farbu EH, Höper AC, Brenn T, Skandfer M. Is working in a cold environment associated with musculoskeletal complaints 7-8 years later? A longitudinal analysis from the Tromso Study. *Int Arch Occup Environ Health*. 2021;94:611-9.

205. Elsner G, Nienhaus A, Beck W. Berufsbedingte degenerative Diskopathien im Lendenwirbelsäulenbereich [Occupational degenerative discopathies in the lumbar spine]. *Soz Präventivmed*. 1997;42:144-54.
206. Chiang HC, Chen SS, Yu HS, Ko YC. The occurrence of carpal tunnel syndrome in frozen food factory employees. *Gaoxiong Yi Xue Ke Xue Za Zhi*. 1990;6:73-80.
207. Yagev Y, Gringolds M, Karakis I, Carel RS. Carpal tunnel syndrome: under-recognition of occupational risk factors by clinicians. *Ind Health*. 2007;45:820-2.
208. Stjernbrandt A, Vihlborg P, Wahlström V, Wahlström J, Lewis C. Occupational cold exposure and symptoms of carpal tunnel syndrome - a population-based study. *BMC Musculoskeletal Disorders*. 2022;23.
209. Stjernbrandt A. Cold exposure and health: A study on neurological and vascular hand symptoms in northern Sweden [Thesis] 2021.
210. Palmer KT, Cullinan P. Respiratory disorders. Palmer KT, Brown I, Hobson J, editors. *Fitness for work: The medical aspects*. Oxford: Oxford University Press; 2013. p. 372-97.
211. Price AE, Petch MC. Cardiovascular disorders. Palmer KT, Brown I, Hobson J, editors. *Fitness for work: The medical aspects*. Oxford: Oxford University Press; 2013. p. 351-71.
212. O'Donnell A-M, Little C. Orthopaedics and trauma of the limbs. Palmer KT, Brown I, Hobson J, editors. *Fitness for work: The medical aspects*. Oxford: Oxford University Press; 2013. p. 233-67.
213. Hassi J, Huurre M. Företagshälsovård vid arbete i kallt klimat [Occupational health care during work in cold climate]. Hassi J, Mäkinen T, Holmér I, Påsche A, Risikko T, Toivonen L, et al., editors. *Handbok för kallt arbete [Handbook for cold work]*. Stockholm: Arbetslivsinstitutet; 2002. p. 81-9.
214. Wigley FM, Flavahan NA. Raynaud's Phenomenon. *N Engl J Med*. 2016;375:556-65.
215. Garner R, Kumari R, Lanyon P, Doherty M, Zhang W. Prevalence, risk factors and associations of primary Raynaud's phenomenon: systematic review and meta-analysis of observational studies. *BMJ Open*. 2015;5:e006389.
216. Maricq HR, Carpentier PH, Weinrich MC, Keil JE, Franco A, Drouet P, et al. Geographic variation in the prevalence of Raynaud's phenomenon: Charleston, SC, USA, vs Tarentaise, Savoie, France. *J Rheumatol*. 1993;20:70-6.
217. Carlsson D, Burström L, Lilliesköld VH, Nilsson T, Nordh E, Wahlström J. Neurosensory sequelae assessed by thermal and vibrotactile perception thresholds after local cold injury. *Int J Circumpolar Health*. 2014;73.
218. Burström L, Björ B, Nilsson T, Pettersson H, Rödin I, Wahlström J. Thermal perception thresholds among workers in a cold climate. *Int Arch Occup Environ Health*. 2017;90:645-52.
219. Campbell DA, Kay SP. What is cold intolerance? *J Hand Surg Br*. 1998;23:3-5.

220. Carlsson IK, Dahlin LB. Self-reported cold sensitivity in patients with traumatic hand injuries or hand-arm vibration syndrome - an eight year follow up. *BMC Musculoskelet Disord*. 2014;15:83.
221. Zeng P, Bengtsson C, Klareskog L, Alfredsson L. Working in cold environment and risk of developing rheumatoid arthritis: results from the Swedish EIRA case-control study. *RMD Open*. 2017;3:e000488.
222. Reed HL, Reedy KR, Palinkas LA, Van Do N, Finney NS, Case HS, et al. Impairment in cognitive and exercise performance during prolonged antarctic residence: effect of thyroxine supplementation in the polar triiodothyronine syndrome. *J Clin Endocrinol Metab*. 2001;86:110-6.
223. Palinkas LA. Mental and cognitive performance in the cold. *Int J Circumpolar Health*. 2001;60:430-9.
224. Eccles R. An explanation for the seasonality of acute upper respiratory tract viral infections. *Acta Otolaryngol*. 2002;122:183-91.
225. Falla M, Micarelli A, Hübner K, Strapazzon G. The Effect of Cold Exposure on Cognitive Performance in Healthy Adults: A Systematic Review. *Int J Environ Res Public Health*. 2021;18.
226. Ramsey JD, Burford CL, Beshir MY, Jensen RC. Effects of workplace thermal conditions on safe work behavior. *J Saf Res*. 1983;14:105-14.
227. Knardahl S, Medbø JI, Strøm V, Jebens E. Utredning om virkninger av arbeid i kalde omgivelser [Investigation of effects of work in cold environments]. Oslo: STAMI; 2010.

Annex 1. Search string for the systematic literature search

Main concept 1: Cold environment

Exp cold/ OR Cold temperature*.ti,ab,kw. OR Low temperature*.ti,ab,kw. OR Freezing.ti,ab,kw. OR Cold environment*.ti,ab,kw. OR Cold condition*.ti,ab,kw. OR exp extreme cold weather/ OR Extreme cold.ti,ab,kw. OR (Cold* adj3 Wet*).ti,ab,kw. OR (Cold* adj3 damp*).ti,ab,kw. OR (Cold* adj3 Rain*).ti,ab,kw. OR (Cold* adj3 Snow*).ti,ab,kw. OR exp cold climate/ OR Cold climate*.ti,ab,kw. OR Polar region*.ti,ab,kw. OR Antarctic*.ti,ab,kw. OR (Cold adj3 stress).ti,ab,kw. OR Sub-zero.ti,ab,kw. OR Below zero.ti,ab,kw. OR Cold work*.ti,ab,kw. OR Cold related.ti,ab,kw. OR Winter weather.ti,ab,kw. OR Cold weather.ti,ab,kw. OR (Work* adj3 Cold).ti,ab,kw. OR Cold exposure.ti,ab,kw. OR exp Arctic/ OR Arctic.ti,ab,kw. OR (low adj3 temperature*).ti,ab,kw. OR Wind chill.ti,ab,kw. OR Circumpolar.ti,ab,kw. OR Contact cooling.ti,ab,kw. OR Cold object*.ti,ab,kw.

Main concept 2: Work

Exp occupation/ OR Industr*.ti,ab,kw. OR exp employment/ OR employment*.ti,ab,kw. OR exp occupational exposure/ OR (Work* adj3 environment*).ti,ab,kw. OR Occupational exposure*.ti,ab,kw. OR Work related.ti,ab,kw. OR Job related.ti,ab,kw. OR Employe*.ti,ab,kw. OR exp workplace/ OR Workplace*.ti,ab,kw. OR Work place*.ti,ab,kw. OR Occupational.ti,ab,kw. OR exp work/ OR job.ti,ab,kw. OR exp army/ OR military.ti,ab,kw. OR exp personnel/ OR labo?r.ti,ab,kw. OR Defense force.ti,ab,kw. OR air force.ti,ab,kw. OR conscript*.ti,ab,kw. OR navy.ti,ab,kw.

Main concept 3: Risk assessment

Exp risk assessment/ OR Risk Assessment*.ti,ab,kw. OR Safety analysis*.ti,ab,kw. OR risk adjustment*.ti,ab,kw. OR Risk Analys*.ti,ab,kw. OR Risk-Benefit Assessment*.ti,ab,kw. OR exp risk management/ OR Risk* Management*.ti,ab,kw. OR Risk Reporting*.ti,ab,kw. OR Risk Report*.ti,ab,kw. OR Incident* Report*.ti,ab,kw. OR Preventive measure*.ti,ab,kw. OR exp occupational safety/ OR occupational safety.ti,ab,kw. OR exp protective clothing/ OR Insulation clothing*.ti,ab,kw. OR exp health care planning/ OR Health Planning Guideline*.ti,ab,kw. OR (Guideline* adj3 Health Plan*).ti,ab,kw. OR Health Planning Recommendation*.ti,ab,kw. OR exp practice guideline/ OR guideline*.ti,ab,kw. OR ISO.ti,ab,kw. OR Occupational safety plan*.ti,ab,kw. OR Occupational health care plan*.ti,ab,kw. OR Primary prevent*.ti,ab,kw. OR Secondary prevent*.ti,ab,kw. OR exp accident prevention/ OR Injur* prevent*.ti,ab,kw. OR exp safety/ OR Code of practic*.ti,ab,kw. OR Threshold limit*.ti,ab,kw. OR Legislation*.ti,ab,kw. OR Intervention*.ti,ab,kw. OR Standard*.ti,ab,kw. OR guide*.ti,ab,kw. OR prevent*.ti,ab,kw.

Annex 2. Assessment of risk of bias

Study	Health outcomes ^a	Exposure ^b	Study design ^c	Study size ^d	Response rate ^e	Total score
Olesen 1995 [50]	0	0	0	0	0	0
Holmér 2001 [51]	0	2	0	0	0	2
Mäkinen et al. 2002 [52]	0	1	1	0	0	2
Hassi et al. 2003 [53]	0	2	1	0	0	3
Besnard et al. 2004 [54]	0	0	0	0	0	0
Risikko et al. 2008 [55]	1	1	2	2	1	7
Gao et al. 2008 [56]	1	1	1	2	2	7
Noroozi et al. 2014 [57]	0	1	0	0	0	1
Ceballos et al. 2015 [58]	0	2	1	2	0	5
Jussila et al. 2017 [59]	1	2	1	2	0	6
Tirloni et al. 2018 [60]	1	2	1	2	0	6
Tsang et al. 2018 [61]	0	2	0	0	0	2
Golbabaie et al. 2022 [62]	1	2	1	1	0	5

^a Not clearly defined (0); subjectively reported (1); diagnosed through health care (2). ^b Not clearly defined (0); subjectively defined (1); objectively defined (2). ^c Not described/other (0); cross-sectional (1); longitudinal (2). ^d Not described (0); less than 50 subjects (1); more than 50 subjects (2). ^e Not described (0); lower than 70% at baseline and non-response at follow-up higher than 30% (1); higher than 70% at baseline and non-response at follow-up lower than 30% (2).