

# Aging and human heat dissipation during exercise-heat stress: an update and future directions

Robert D Meade<sup>1</sup>, Sean R Notley<sup>1</sup> and Glen P Kenny<sup>1,2</sup>

Aging is known to influence the physiological control of the thermoeffector responses (cutaneous vasodilation and sweating) that facilitate heat dissipation during heat stress. However, it was only recently that these maladaptations were shown to translate to an attenuated capacity for whole-body (i.e. over the entire body surface) heat dissipation during exercise. Emerging evidence indicates that secondary factors (e.g. cardiorespiratory fitness, chronic disease, among others) may modify the impact of age on heat dissipation. Currently, however, a focused overview on this topic is unavailable. The purpose of this brief review was therefore to synthesize recent research on the independent and interactive effects of age on heat dissipation during exercise-heat stress and highlight areas for further exploration.

## Addresses

<sup>1</sup> Human and Environmental Physiology Research Unit, School of Human Kinetics, University of Ottawa, Ottawa, Ontario, Canada

<sup>2</sup> Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

Corresponding author: Kenny, Glen P ([gkenny@uottawa.ca](mailto:gkenny@uottawa.ca))

**Current Opinion in Physiology** 2019, **10**:219–225

This review comes from a themed issue on **Exercise physiology**

Edited by **Harry B Rossiter** and **Brian Glancy**

For a complete overview see the [Issue](#) and the [Editorial](#)

Available online 9th July 2019

<https://doi.org/10.1016/j.cophys.2019.07.003>

2468-8673/© 2019 Elsevier Ltd. All rights reserved.

## Introduction

Older adults are susceptible to heat-related illness and other adverse health effects during heat stress [1–3] and experience greater heat-induced reductions in exercise tolerance compared to young individuals [4]. This is likely due, in part, to impairments in the thermoeffector responses (cutaneous vasodilation and sweating) that facilitate heat dissipation [5<sup>\*\*</sup>]. While this risk is compounded by elevated global temperatures and escalating frequency and intensity of extreme heat events [6], exercise is increasingly recommended as a means of preventing the age-related decline in physiological function [7,8] and the number of older adults performing physical activity in hot environments on a daily basis (e.g. in occupational settings) is growing [9]. Classic

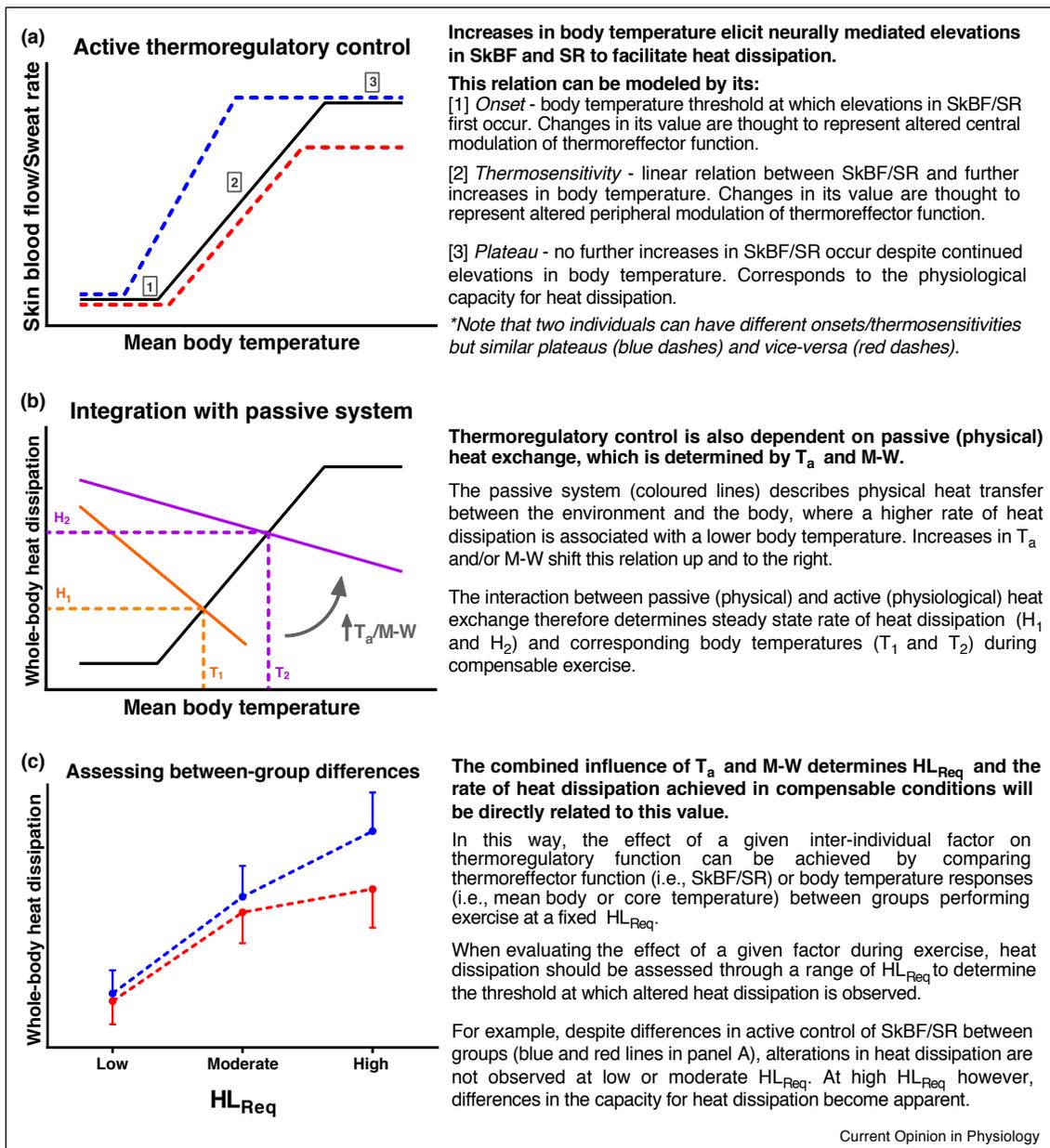
studies have demonstrated age-related maladaptations in the physiological control of cutaneous vasodilation and sweating. However, whether those impairments influence the capacity for heat dissipation and the subsequent change in body heat storage is what will ultimately define one's risk of developing potentially dangerous levels of hyperthermia during heat stress. Accordingly, evaluating the independent bearing of age on heat dissipation during exercise-heat stress is an on-going and highly active field of study.

Recent work in this domain indicates that aging attenuates heat dissipation in adults as young as 40-years of age compared to their younger counterparts during exercise-heat stress [10]. In more recent years, emphasis has been directed to understanding how secondary factors known to independently modulate thermoeffector function (e.g. cardiorespiratory fitness, chronic disease) may modify the effect of age on heat dissipation [11<sup>\*\*</sup>,12,13,14<sup>\*\*</sup>]. Since aging is accompanied by changes in those factors, such information is of critical importance for understanding age-related changes in thermoregulatory function. Currently, however, a focused overview of those advancements is unavailable. In this brief review, we therefore provide a summary of contemporary studies on the independent effects of age on heat dissipation during exercise-heat stress. We also include an update of recent work uncovering interactions between the effects of aging, cardiorespiratory fitness and chronic disease (among other factors) on heat dissipation, as well as highlight important areas for future exploration.

## Isolating the effect of age on heat dissipation

During exercise, heat dissipation is facilitated by elevations in skin blood flow and sweat secretion occurring in response to increased deep-body (core) and peripheral (skin, muscle) temperatures. Findings from many classic studies indicate an altered relation (i.e. onset and thermosensitivity; [Figure 1a](#)) between mean body temperature (weighted sum of body core and mean skin temperatures) and the activation of these heat loss responses with aging [5<sup>\*\*</sup>,15]. More recent studies in this domain have focused on the mechanisms underpinning altered modulation of thermoeffector responses in older adults. This work has identified roles for microvascular and autonomic dysfunction in attenuated vasomotor responsiveness, as recently reviewed in depth by Kenney [16] and Greaney *et al.* [17], respectively, as well as altered pre-synaptic and post-synaptic control of sweating as

Figure 1



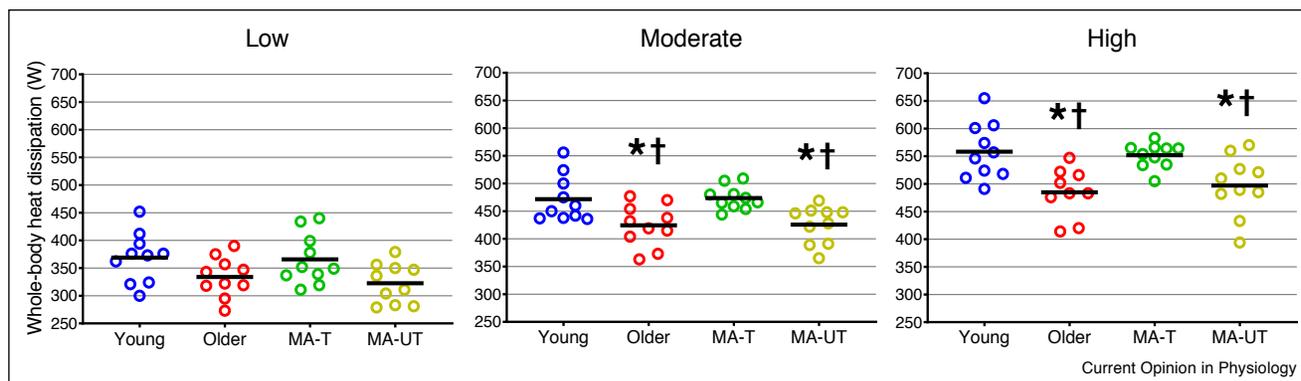
Schematic illustration of the integrated thermoregulatory control during exercise. Relation between active physiological control of skin blood flow and sweating (Panel (a)) and passive (physical) heat exchange with the environment (Panel (b)); redrawn in part from Gisolfi *et al.* [50]) determines required heat dissipation and prevailing body temperature. Exercise bouts of increasing requirements for heat dissipation to achieve heat balance ( $HL_{Req}$ ) can be used to assess the effect of a given factor on the capacity for heat dissipation (Panel (c)). SkBF, skin blood flow; SR, sweat rate;  $T_a$ , ambient temperature; M-W, metabolic heat production.

highlighted by Shibasaki *et al.* [15]. For example, elevated arginase activity and depletion of essential cofactors have been shown to contribute to attenuated nitric oxide-dependent cutaneous vasodilation in older adults during whole-body heating [18].

While that research has been instrumental to our understanding of the relation between age and declining

thermoeffector function, it does not allow for isolation of the full effect of age on heat dissipation. Studies imposing encapsulated heat stress (e.g. with a water perfused suit) provide valuable information regarding differences in open-loop control of skin blood flow and sweating between young and older adults but little insight into the effect of age on heat dissipation during exercise (Figure 1a). Even when exercise models are employed,

Figure 2



Whole-body heat dissipation measured at the end of three 30 min exercise bouts at low ( $\sim 410$  W), moderate ( $\sim 520$  W) and high ( $\sim 620$  W) requirements for heat loss ( $HL_{Req}$ ). Data reported for young (blue symbols;  $VO_{2peak}$ :  $50 \text{ ml kg}^{-1} \text{ min}^{-1}$ ) and older (red symbols;  $VO_{2peak}$ :  $38 \text{ ml kg}^{-1} \text{ min}^{-1}$ ) as well as endurance-exercise trained (MA-T, green symbols;  $VO_{2peak}$ :  $51 \text{ ml kg}^{-1} \text{ min}^{-1}$ ) and untrained (MA-UT, yellow symbols;  $VO_{2peak}$ :  $37 \text{ ml kg}^{-1} \text{ min}^{-1}$ ). \*, Difference in versus young; †, versus middle-aged trained;  $P \leq 0.05$ . Redrawn from Stapleton *et al.* with permission from the authors [11\*\*].

thermoeffector responses are often assessed between groups exercising at a fixed percentage of peak aerobic power ( $VO_{2peak}$ ), which can lead to differences in metabolic heat production (due to different absolute work rates) and thereby passive (physical) heat exchange (Figure 1b).

For those reasons, contemporary studies have evaluated the effect of aging (among other factors) by matching groups for the relative stimulus for heat dissipation, or requirement for heat loss ( $HL_{Req}$ ), which is determined by the heat load generated by exercise (metabolic) as well as the convective, radiative and conductive heat gained from the environment when exercise is performed in hot ambient conditions [19\*,20,21].  $HL_{Req}$  represents the balancing point between heat dissipation facilitated by increases in cutaneous vasodilation and sweating (Figure 1a) and heat exchange occurring passively (physical) with the surrounding environment (Figure 1b). This model therefore allows for assessment of negative feedback control of heat dissipation and mean body temperature. As illustrated in Figure 1a (blue dashes), the effect of a given factor, age or otherwise, on the relation between body temperature and the activation of effector responses does not necessarily reflect a reduction in heat loss capacity. Heat dissipation is therefore best assessed through a range of exercise- $HL_{Req}$  to determine the threshold at which between-group differences occur (Figure 1c); a model akin to using an incremental exercise protocol to evaluate  $VO_{2peak}$ .

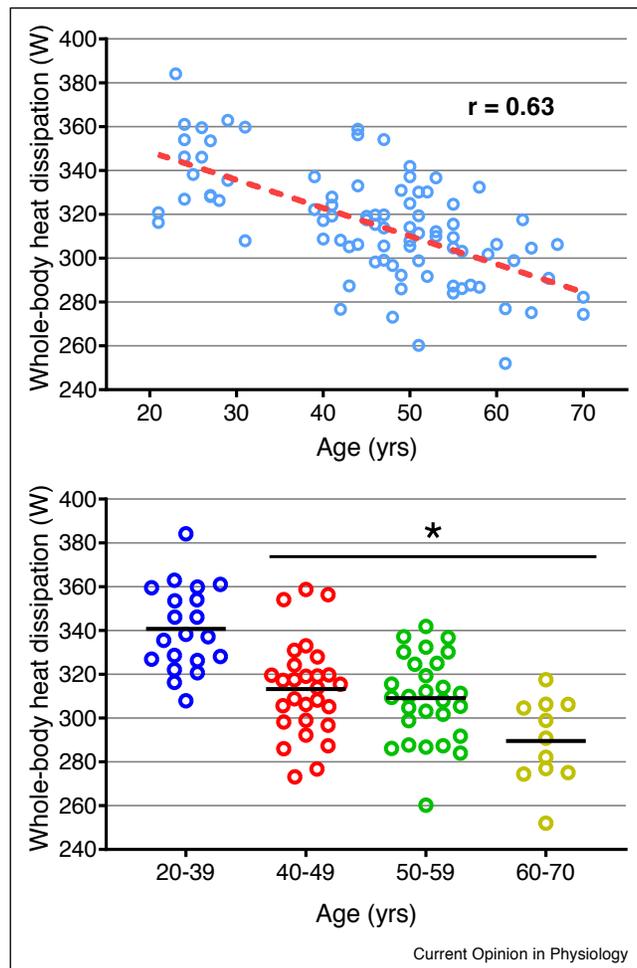
Original investigations matching  $HL_{Req}$  between age groups during exercise (by prescribing a fixed rate of metabolic heat production) reported attenuated whole-body heat dissipation in adults as young as 40 years of age relative to younger individuals [10,22–25]. However,

because those studies employed a single exercise- $HL_{Req}$ , the threshold at which age-related attenuations in thermo-effector function occurred could not be determined. This issue was addressed by Stapleton *et al.*, who, employing an incremental- $HL_{Req}$  protocol, demonstrated that heat dissipation was similar between older and younger men [11\*\*] and women [26] during light exercise but attenuated in older adults at moderate and high exercise- $HL_{Req}$  by  $\sim 25$  and  $\sim 30\text{--}40 \text{ W m}^{-2}$ , respectively (Figure 2). Moreover, in the largest study to date ( $n = 87$  healthy adults aged 20–70 years), McGinn *et al.* [27] showed that increasing age displays a significant negative association with heat dissipation during exercise at a moderate  $HL_{Req}$  ( $\sim 200 \text{ W m}^{-2}$ ), amounting to a  $\sim 4\%$  reduction in heat dissipation per decade (Figure 3). Importantly, in those studies heat dissipation was most often assessed in healthy young and older participants who were homogeneous for secondary factors known to influence thermoregulatory function (e.g. sex, body morphology, cardiorespiratory fitness), indicating that the attenuation in heat dissipation observed in older versus younger adults is independently related to both  $HL_{Req}$  and age. Finally, it should be noted that the effect of aging on heat dissipation is mediated primarily via attenuated sweat output, which reduces evaporative heat loss [10,11\*\*,22–26], the major pathway for heat dissipation during exercise [19\*,20,21]. That said, age-related alterations in dry heat exchange (i.e. conductive, convective and radiative heat exchange) have also been observed [22,28].

### Emerging interactions

When assessed in heterogeneous groups of participants, a large portion of the inter-individual variation (23–100%) in thermoregulatory responses (e.g. heat dissipation, body core temperature, local sweat rate) during exercise at a fixed  $HL_{req}$  remains unexplained by the independent effects of factors known to modulate thermo-effector

Figure 3



Progressive reductions in whole-body heat loss with increasing age. Whole-body heat dissipation during exercise at a fixed requirement for heat loss of  $\sim 200 \text{ W m}^{-2}$ , presented as a simple linear regression (top panel) and subgroup analysis (bottom panel). \*, Difference versus young;  $P \leq 0.05$ . Redrawn from McGinn *et al.* with permission from the authors [27].

function [29]. This raises the possibility that interactions between those factors may contribute greatly to individual differences in heat dissipation [29]. Aging is accompanied by a host of physiological and physical changes, including morphological changes (e.g. weight, lean mass, adiposity), reductions in cardiorespiratory fitness and the development of chronic disease. Appropriately, recent studies have been directed toward evaluating age-related alterations in heat dissipation in the context of those factors. The following sections will focus primarily on the physiological interactions.

### Cardiorespiratory fitness

Since  $\text{VO}_{2\text{peak}}$  declines naturally with age [7,8] and elevated cardiorespiratory fitness has been linked with augmented skin blood flow and sweating in older adults

during heat stress [15], Stapleton *et al.* [11\*\*] evaluated the interaction between age and cardiorespiratory fitness on heat dissipation (Figure 2). While heat dissipation was reduced in both non-endurance trained older ( $\sim 65$  years-old) and middle-aged ( $\sim 48$  years-old) men compared to their younger counterparts ( $\sim 21$  years-old) at exercise- $\text{HL}_{\text{Req}} > 260 \text{ W m}^{-2}$ , heat loss was maintained at a level similar to the young in endurance-trained middle-aged men ( $\sim 49$  years-old). This effect is likely associated with improved cardiorespiratory fitness *per se* [30], rather than the thermoregulatory adaptation associated with regular physical activity [31], although this has not been directly confirmed in older adults. Regardless, endurance-training appears to attenuate age-related reductions in the physiological capacity for heat dissipation; a notion consistent with current consensus regarding the importance of regular physical activity to the preservation of physiological function [7,8].

### Chronic disease

Aging is also accompanied by the development of chronic health conditions that can increase the risk of heat-related morbidity/mortality [1,32]. Recent studies have therefore sought to assess the effect of those conditions on thermoregulatory function in older adults and their outcomes suggest that specific conditions may exacerbate age-related impairments in heat dissipation during exercise.

The effect of heart failure on thermoregulatory function during heat stress has received much attention in recent years [33]. While heart failure has been associated with attenuated skin blood flow during passive heating [34–36], alterations in sweating have been less consistently observed [34,35]. In line with those findings, Balmain *et al.* [12] demonstrated reduced cutaneous vasodilation in heart failure patients ( $\sim 60$  years-old) compared to age-matched controls during relative intensity-matched exercise ( $60\% \text{VO}_{2\text{peak}}$ ) in a warm environment ( $30^\circ\text{C}$ ). However, the sweating response did not appear altered and core temperature was not different between groups. Similarly, Benda *et al.* [14\*\*] reported comparable elevations in core temperature between patients with heart failure ( $\sim 65$  years-old) and healthy controls during exercise at  $65\% \text{VO}_{2\text{peak}}$  in temperate conditions ( $22^\circ\text{C}$ ). Since exercise was prescribed as a relative intensity,  $\text{HL}_{\text{Req}}$  was lower in the heart failure group in both studies [12,14\*\*]. The similar core temperature responses may therefore indicate a heart failure-related impairment in heat dissipation, though this remains to be confirmed (see future directions section below). Furthermore, thermoregulatory responses have solely been evaluated in individuals with reduced ejection fraction (systolic heart failure) [12,14\*\*], which potentially explains the consistent observations of reduced skin blood flow [12,34–36]. However,  $\sim 50\%$  of heart failure diagnoses are characterized by preserved ejection fraction (diastolic heart failure) [37]. Whether

those individuals also exhibit altered thermoregulatory function remains to be determined.

Typically affecting adults >54 years of age [38], type 2 diabetes mellitus is associated with reduced microvascular responsiveness to local skin heating [39] and pharmacological stimulation [40] as well as attenuated sweating during passive exposure to a hot (39°C) environment [41]. In the context of exercise, those functional reductions translate to attenuated heat dissipation, as reported by Kenny *et al.* [13] who observed impaired whole-body heat loss in individuals with type 2 diabetes (~55 years-old) exercising at an  $HL_{Req}$  of  $\sim 160 \text{ W m}^{-2}$ , when compared to age-matched controls without the disease. It is important to consider, however, that heat dissipation was studied in individuals with well controlled diabetes (Hemoglobin A<sub>1c</sub> of  $\sim 7.3\%$ ) and no diagnosed peripheral neuropathy. It is therefore likely that diabetes-related impairments in heat dissipation are exacerbated in individuals with less well controlled type 2 diabetes and/or advanced peripheral neuropathy, especially considering reduced sweat rate to pharmacological stimulation is used to screen for diabetic peripheral neuropathy [42].

### Future directions

While we have begun to uncover interactions between age and other inter-individual (i.e. factors that differ primarily between individuals) physiological modulators of heat dissipation, more thorough investigation into their interplay is needed, especially in light of the potentially interactive effects of these factors on heat dissipation among individuals with heterogeneous characteristics [29]. For example, the capacity for heat dissipation is reduced in young women versus men during exercise at high  $HL_{Req}$  ( $\sim 300 \text{ W m}^{-2}$ ) [43]; however, while age-related impairments in heat loss have been demonstrated in both men [11<sup>••</sup>] and women [26], it is currently unknown if the magnitude of that impairment differs between sexes. Likewise, the interaction between age and intra-individual modulators (i.e. factors modifiable within individuals over relatively short periods) of heat loss such as heat acclimation/acclimatization and hydration state should be explored. In fact, the latter has been recently shown to exert differential influence on thermoregulatory function between young and middle-aged men [28].

Recent work indicates that common chronic diseases (i.e. heart failure, type 2 diabetes) may exacerbate age-related impairments in thermoeffector function and/or body temperature regulation during exercise-heat stress [12,13,14<sup>••</sup>]. In those studies, however, responses were evaluated during exercise at a single  $HL_{Req}$  or matched for relative exercise intensity thereby prohibiting evaluation of the full extent to which these conditions impact thermoregulatory function (Figure 1c). While the similar core temperatures observed between heart failure

patients and healthy controls by Balmain *et al.* [12] and Benda *et al.* [14<sup>••</sup>] may be related to a reduced physiological capacity for heat dissipation (e.g. red dashes in Figure 1a), they may just as easily stem from an altered relation between thermoeffector function and mean body temperature (e.g. blue dashes in Figure 1a). As discussed, those studies also only evaluated specific subpopulations of individuals with the disease in question (e.g. individuals with reduced ejection fraction or individuals without diabetic peripheral neuropathy). Additionally, there are multiple other prevalent health conditions including obesity [44,45] and hypertension [46] that can effect thermoregulatory function. However, their influence on heat dissipation during exercise and potential interactions with age remain uncertain. Delineation of the interactive effects of age and common chronic diseases on whole-body heat dissipation (and the associated mechanisms) represents an important avenue for further exploration, especially given that not only do these conditions elevate the risk of adverse health effects during heat stress [1,32] but in many cases exercise is an important adjunct to their management [1,8,47].

Finally, given the small number of studies on this topic, it remains uncertain whether the effects observed in specific exercise and environmental conditions translate into other conditions. This is important, as it is known that one's physiological response to a fixed  $HL_{req}$  can differ depending on the relative contribution of metabolic and environmental heat load [21]. As discussed, the majority of studies have shown that aging reduces the capacity for evaporative heat dissipation [10,11<sup>••</sup>,22–26], which is the primary mechanism of heat loss during exercise, especially in the heat [19<sup>•</sup>,20,21]. However, it is currently unclear whether the magnitude of those age-related impairments is similar during exercise in temperate conditions, wherein the skin-environment temperature gradient allows convective and radiative heat loss [19<sup>•</sup>,20,21]. This may also complicate the evaluation of secondary factors, such as heart failure, which primarily influence skin blood flow [34–36] and may therefore have greater thermoregulatory implications in temperate environments. Indeed, a recent example of the differential effect of the ambient environment on heat dissipation between young and older adults can be found in a study by Gagnon *et al.* [48<sup>•</sup>,49], who observed electric fan use (increased air velocity) exacerbated hyperthermia in older (~68 years-old) but not younger (~26 years-old) men in response to progressive elevations in ambient humidity while resting in a hot environment (42°C). Presumably, these findings stem from an elevated convective heat gain that was offset by improved sweat evaporation in the young but not older adults.

### Conclusions

Recent years have brought considerable advances in our understanding of the isolated influence of age on whole-body

heat dissipation during exercise-heat stress, while uncovering exciting new interactions between aging and other individual factors (e.g. cardiorespiratory fitness, chronic disease). Nonetheless, our understanding of these interrelations remains incomplete. Future work is therefore required to delineate the independent and interactive effects of factors influencing heat dissipation and the development of hyperthermia during exercise in the heat in the context of aging.

### Author contributions

R.D.M. drafted the manuscript. All authors edited and approved the final version.

### Conflict of interest statement

Nothing declared.

### Funding

Work supported by the Natural Sciences and Engineering Research Council of Canada (Discovery grant, RGPIN-06313-2014; funds held by Dr. Glen P. Kenny). G. P. Kenny was supported by a University of Ottawa Research Chair. R.D. Meade was supported by a Natural Sciences and Engineering Research Council of Canada Alexander Graham Bell Scholarship (CGS-D). S.R. Notley is supported by a Postdoctoral Fellowship from the Human and Environmental Physiology Research Unit.

### Acknowledgement

None.

### References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Kenny GP *et al.*: **Heat stress in older individuals and patients with common chronic diseases.** *CMAJ* 2010, **182**:1053-1060.
  2. Kenney WL, Craighead DH, Alexander LM: **Heat waves, aging, and human cardiovascular health.** *Med Sci Sports Exerc* 2014, **46**:1891-1899.
  3. Petitti DB *et al.*: **Occupation and environmental heat-associated deaths in Maricopa county, Arizona: a case-control study.** *PLoS One* 2013, **8**:e62596.
  4. Chodzko-Zajko WJ *et al.*: **Exercise and physical activity for older adults.** *Med Sci Sports Exerc* 2009, **41**:1510-1530.
  5. Balmain BN *et al.*: **Aging and thermoregulatory control: the clinical implications of exercising under heat stress in older individuals.** *Biomed Res Int* 2018, **2018**:8306154.
- An excellent summary of the role of age-related changes in heat dissipation in the elevated risk of heat-related illness and injury experienced by older adults during exercise, especially in those with chronic disease.
6. Mitchell D *et al.*: **Realizing the impacts of a 1.5 C warmer world.** *Nat Clim Change* 2016, **6**:735.
  7. Lazarus NR, Lord JM, Harridge SDR: **The relationships and interactions between age, exercise and physiological function.** *J Physiol* 2018, **597**:1299-1309.
  8. Lazarus NR, Harridge SDR: **The inherent human aging process and the facilitating role of exercise.** *Front Physiol* 2018, **9**:1135.
  9. Kenny GP *et al.*: **Age, human performance, and physical employment standards.** *Appl Physiol Nutr Metab* 2016, **41** (Suppl. 2):S92-S107.
  10. Larose J *et al.*: **Age-related decrements in heat dissipation during physical activity occur as early as the age of 40.** *PLoS One* 2013, **8**:e83148.
  11. Stapleton JM *et al.*: **Aging impairs heat loss, but when does it matter?** *J Appl Physiol* 2015, **118**:299-309.
- In their report, Stapleton *et al.* assessed the requirement ( $HL_{Req}$ ) for dissipation at which age-related impairments in whole-body heat dissipation occurred during exercise. They found that while there were no differences in heat loss between young and older adults at the lowest requirement  $HL_{Req}$  ( $205 \text{ W m}^{-2}$ ), age-related differences were observed at  $HL_{Req}$  of  $\sim 260$  and  $\sim 310 \text{ W m}^{-2}$ . Additionally, this study provided information regarding the modulatory effect of cardiorespiratory fitness on age-related reductions in thermoregulatory function by showing that untrained middle aged adults displayed similar heat dissipation to the older group, whereas heat loss in endurance trained middle aged participants was consistent with the young.
12. Balmain BN *et al.*: **Altered thermoregulatory responses in heart failure patients exercising in the heat.** *Physiol Rep* 2016, **4**.
  13. Kenny GP *et al.*: **Older adults with type 2 diabetes store more heat during exercise.** *Med Sci Sports Exerc* 2013, **45**:1906-1914.
  14. Benda NM *et al.*: **Altered core and skin temperature responses to endurance exercise in heart failure patients and healthy controls.** *Eur J Prev Cardiol* 2016, **23**:137-144.
- In this study by Benda *et al.*, thermoregulatory responses were compared between individuals with heart failure and healthy, age-matched controls during exercise at  $65\% \text{ VO}_{2peak}$ . Despite exercising at a lower absolute workload (due to reduced cardiorespiratory fitness), core body temperature in the heart failure group was similar to the controls (albeit skin temperature was higher in the latter group). These findings are consistent with impaired thermoregulation secondary to reduced skin blood flow in the heart failure patients and highlight the need for further work assessing the effect of this disease on heat dissipation during exercise.
15. Shibasaki M, Okazaki K, Inoue Y: **Aging and thermoregulation.** *J Phys Fitness Sports Med* 2013, **2**:37-47.
  16. Kenney WL: **Adolph distinguished lecture: skin-deep insights into vascular aging.** *J Appl Physiol* 2017, **123**:1024-1038.
  17. Greaney JL, Kenney WL, Alexander LM: **Sympathetic regulation during thermal stress in human aging and disease.** *Auton Neurosci* 2016, **196**:81-90.
  18. Stanhewicz AE *et al.*: **Local tetrahydrobiopterin administration augments reflex cutaneous vasodilation through nitric oxide-dependent mechanisms in aged human skin.** *J Appl Physiol* 2012, **112**:791-797.
  19. Cramer MN, Jay O: **Biophysical aspects of human thermoregulation during heat stress.** *Auton Neurosci* 2016, **196**:3-13.
- An excellent review describing biophysical considerations important to the design of studies aimed at assessing thermoregulatory responses between different populations.
20. Cramer MN, Jay O: **Partitional calorimetry.** *J Appl Physiol* 2019, **126**:267-277.
  21. Meade RD, Kenny GP: **Are all heat loads created equal?** *Med Sci Sports Exerc* 2017, **49**:1796-1804.
  22. Larose J *et al.*: **Age-related differences in heat loss capacity occur under both dry and humid heat stress conditions.** *J Appl Physiol* 2014, **117**:69-79.
  23. Larose J *et al.*: **Do older females store more heat than younger females during exercise in the heat?** *Med Sci Sports Exerc* 2013, **45**:2265-2276.
  24. Larose J *et al.*: **Whole body heat loss is reduced in older males during short bouts of intermittent exercise.** *Am J Physiol Regul Integr Comp Physiol* 2013, **305**:R619-R629.
  25. Notley SR *et al.*: **Aging impairs whole-body heat loss in women under both dry and humid heat stress.** *Med Sci Sports Exerc* 2017, **49**:2324-2332.

26. Stapleton JM *et al.*: **At what level of heat load are age-related impairments in the ability to dissipate heat evident in females?** *PLoS One* 2015, **10**:e0119079.
  27. McGinn R *et al.*: **Increasing age is a major risk factor for susceptibility to heat stress during physical activity.** *Appl Physiol Nutr Metab* 2017, **42**:1232-1235.
  28. Meade RD *et al.*: **Interactive effects of age and hydration state on human thermoregulatory function during exercise in hot-dry conditions.** *Acta Physiol (Oxf)* 2019, **226**:e13226.
  29. Notley SR *et al.*: **Revisiting the influence of individual factors on heat exchange during exercise in dry heat using direct calorimetry.** *Exp Physiol* 2019, **104**:1038-1050.
  30. Lamarche DT *et al.*: **Fitness-related differences in the rate of whole-body evaporative heat loss in exercising men are heat-load dependent.** *Exp Physiol* 2018, **103**:101-110.
  31. Lamarche DT *et al.*: **Self-reported physical activity level does not alter whole-body total heat loss independently of aerobic fitness in young adults during exercise in the heat.** *Appl Physiol Nutr Metab* 2019, **44**:99-102.
  32. Vaidyanathan A *et al.*: **Assessment of extreme heat and hospitalizations to inform early warning systems.** *Proc Natl Acad Sci U S A* 2019, **116**:5420-5427.
  33. Balmain BN *et al.*: **Heart failure and thermoregulatory control: can patients with heart failure handle the heat?** *J Card Fail* 2017, **23**:621-627.
  34. Cui J *et al.*: **Effects of heat stress on thermoregulatory responses in congestive heart failure patients.** *Circulation* 2005, **112**:2286-2292.
  35. Cui J *et al.*: **Chronic heart failure does not attenuate the total activity of sympathetic outflow to skin during whole-body heating.** *Circ Heart Fail* 2013, **6**:271-278.
  36. Green DJ *et al.*: **Impaired skin blood flow response to environmental heating in chronic heart failure.** *Eur Heart J* 2006, **27**:338-343.
  37. Dunlay SM, Roger VL, Redfield MM: **Epidemiology of heart failure with preserved ejection fraction.** *Nat Rev Cardiol* 2017, **14**:591-602.
  38. Centers for Disease Control and Prevention: *National Surveillance. Diabetes Health Resource.* 2014. Atlanta, GA.
  39. Fuchs D *et al.*: **The association between diabetes and dermal microvascular dysfunction non-invasively assessed by laser Doppler with local thermal hyperemia: a systematic review with meta-analysis.** *Cardiovasc Diabetol* 2017, **16**:11.
  40. Beer S *et al.*: **Comparison of skin microvascular reactivity with hemostatic markers of endothelial dysfunction and damage in type 2 diabetes.** *Vasc Health Risk Manage* 2008, **4**:1449-1458.
  41. Petrofsky JS *et al.*: **Sweat production during global heating and during isometric exercise in people with diabetes.** *Med Sci Monit* 2005, **11**:CR515-21.
  42. Krieger SM *et al.*: **Sudomotor testing of diabetes polyneuropathy.** *Front Neurol* 2018, **9**:803.
  43. Gagnon D, Kenny GP: **Sex differences in thermoeffector responses during exercise at fixed requirements for heat loss.** *J Appl Physiol* 2012, **113**:746-757.
  44. Dervis S *et al.*: **A comparison of thermoregulatory responses to exercise between mass-matched groups with large differences in body fat.** *J Appl Physiol* 2016, **120**:615-623.
  45. Tucker MA *et al.*: **Effect of hypohydration on thermoregulatory responses in men with low and high body fat exercising in the heat.** *J Appl Physiol* 2017, **122**:142-152.
  46. Kenney WL, Kamon E, Buskirk ER: **Effect of mild essential hypertension on control of forearm blood flow during exercise in the heat.** *J Appl Physiol Respir Environ Exerc Physiol* 1984, **56**:930-935.
  47. Sigal RJ *et al.*: **Physical activity and diabetes.** *Can J Diabetes* 2018, **42**:S54-S63.
  48. Gagnon D *et al.*: **Age modulates physiological responses during fan use under extreme heat and humidity.** *Med Sci Sports Exerc* 2017, **49**:2333-2342.
- In their report, Gagnon *et al.* demonstrate that fan use exacerbates physiological strain in older but not young during progressive increases in ambient humidity while resting in the heat (42°C). These findings demonstrate that environmental factors need to be taken into account when interpreting an effect of age on thermoregulatory function, even if  $HL_{Req}$  is similar between groups.
49. Gagnon D *et al.*: **Cardiac and thermal strain of elderly adults exposed to extreme heat and humidity with and without electric fan use.** *JAMA* 2016, **316**:989-991.
  50. Gisolfi CV, Lamb DR, Nadel ER: *Exercise, Heat, and Thermoregulation.* Cooper Publishing Group; 1993.