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Measurement and Evaluation of Body Temperature: Implications for Clinical Practice

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**Measurement and evaluation of body temperature:
Implications for clinical practice**

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Akademisk avhandling

som för avläggande av medicine doktorsexamen kommer att offentligens försvaras i
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Abstract

The general aim was to explore factors influencing the normal variation and measurement of body temperature. Additional aims were to study morbidity, mortality and the clinical presentation of pneumonia and predictors for survival in elderly nursing-home residents. Two hundred and thirty seven non-febrile nursing home residents (aged 66-99 years) and 87 healthy adults (aged 19-59 years) were included. In elderly individuals, the morning ear and rectal body temperature was measured at baseline and pneumonia and survival was observed at one- two and three-year. In healthy adults the rectal, ear, oral and axillary temperature were measured simultaneously on one morning and repeated measurements were performed in three subjects.

Overall, the range of normal body temperature was wider than traditionally stated. In elderly nursing-home residents, functional and cognitive impairment and BMI < 20 were related to a lower body temperature and medication with analgesics to a higher. Compared to adults < 60 years elderly persons had a higher average ear and a lower rectal temperature. Men and postmenopausal women < 60 years had lower body temperature than premenopausal women. The repeated measurements showed a wide individual variability irrespective of the site of measurement, and that replicated measurements do not improve accuracy. When comparing the rectal temperature with oral, ear and axillary readings the average difference was > 0.5°C with a wide individual variation.

The yearly incidence of nursing-home acquired pneumonia varied between 6.9% and 13.7%. Functional impairment, chronic obstructive pulmonary disease (COPD) and male sex were related to a higher risk of acquiring pneumonia and presenting non-specific symptoms were common. Age and functional impairment predicted mortality, irrespective of gender, while cerebral vascular insult, a lower body mass index and malnutrition in women and heart disease, COPD, medication with sedatives and mortality rate index in men were gender specific predictors. Surviving women had a higher baseline body temperature than non-surviving, while no such difference was found in men.

When assessing body temperature, it is important to consider the site of measurement, technical design, operator technique, age and gender and, in elderly nursing-home residents, physical and cognitive impairment, body constitution and medication with analgesics. The best approach is to use an unadjusted mode, without adjusting to another site. To prevent a delayed diagnosis of pneumonia, one should be aware of a low baseline body temperature and lack of specific clinical symptoms in elderly nursing-home residents. Preserving and/or improving functional, cognitive, nutritional status and preventing agitation and confusion would improve survival in nursing-home residents.

Keywords: Assessment, body temperature measurement, elderly, evaluation, infection, nursing home, pneumonia, survival.

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Would it not be wise to remove the little red arrows from the thermometer?

E F DuBois 1951

To my mother, Maj
In memory of my father, Sture
To Lars, Martin and Maria

ORIGINAL PAPERS

This doctoral thesis is based on the following papers, which will be referred to by their Roman numerals.

1. Sund-Levander, M. and L.K. Wahren, *The impact of ADL-status, dementia and body mass index on normal body temperature in elderly nursing home residents*. Archives of Gerontology and Geriatrics, 2002. **35**: p. 161-169.
2. Sund-Levander, M., E. Grodzinsky, D. Loyd, and L.K. Wahren, *Errors in body temperature assessment related to individual variation, measuring technique and equipment*. International Journal of Nursing Practice, 2004. **10**: p. 216-23.
3. Sund-Levander, M., Å. Örtqvist, E. Grodzinsky, Ö. Klefsgård, and L.K. Wahren, *Morbidity, mortality and clinical presentation of nursing home-acquired pneumonia in a Swedish population*. Scandinavian Journal of Infectious Diseases, 2003. **35**: p. 306-310.
4. Sund-Levander, M., E. Grodzinsky, and L.K. Wahren, *Gender differences in predictors for survival in elderly nursing-home residents. A long-term follow-up*. 2004. Manuscript. Submitted.

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Papers I – IV

DEFINITIONS

Baseline	A value or starting point on an imaginary scale with which other values be compared [1].
Core body temperature	The temperature in the thoracic and abdominal contents and some of the muscles and the brain [2].
Fever	A state of elevated core temperature, which is often, but not necessarily, part of the defensive responses of multicellular organisms (the host) to the invasion of live (microorganisms) or inanimate matter recognised as pathogenic or alien by the host [3].
Nursing-home acquired pneumonia	Pneumonia acquired in chronic care facilities [4].
Normal	Usual and ordinary, in accordance with what people expect [1].
Peripheral body temperature	The temperature in the skin and subcutaneous tissue [2].
Set point	The range of the regulated average body temperature, defended by means of behavioural and/or autonomic reflexes [5].

ABBREVIATIONS

ADL	Activities of daily living.
BMI	Body mass index.
IRED	Infrared radiation ear device
NHAP	Nursing-home acquired pneumonia

INTRODUCTION

Evaluation of body temperature is one of the oldest known diagnostic methods [6, 7] and is still an important sign of health and disease, both in everyday life and in medical care. Increased body temperature is associated in the first place with infectious disease and fever [8] and the accompanying feelings of illness. In general, the individual can describe feelings of illness and discomfort, but in conditions where individuals are unable to explain themselves, the nurse has to interpret the clinical signs and rely on objective measurements. This is especially important when assessing elderly individuals [9], as atypical presentation of infection are common in this age group [10].

Before the 17th century, the humoral theory, established by Galen in the second century A.D., dominated medical thinking [7], and the interpretation of symptoms and explanations of disease were closely related to philosophy and religion [11]. Evaluation of body temperature rested on objective and subjective feelings of warmth, i.e. physicians used touch as their principal criterion for evaluating body heat [12]. The discovery of the circulation of the blood emphasised the use of natural sciences in medicine and clinicians started to use the pulse rate to diagnose fever [13]. This remained to be the most important tool even when the first thermometers were available in the late 18th century. At that time, the improved scientific knowledge of human anatomy and physiology, attributed to the introduction of autopsy [14], and new technical knowledge [9] increased the interest in objectively observing the patient [12, 15] and thus the possibility to differentiate between health and disease using biological parameters in terms of what was considered normal and abnormal.

The first comprehensive report on body temperature related to normality was published in 1868 by the German physician Wunderlich [16], who established the use of thermometers in medical practice [17]. Wunderlich measured axillary temperature in patients and declared the normal body temperature to be 37.0°C with a range of 36.2°C to 37.5°C. He defined temperatures above 37.5°C as “the territory of fever” and $\geq 38.0^\circ\text{C}$ as fever [18].

Today there is a general acceptance of normal body temperature as a range rather than a fixed temperature, although there is still widespread confusion in the assessment and evaluation of body temperature in adults [19], especially in elderly individuals [20-22]. A recently performed systematic review of the literature [23] found that the range in normal body temperature was 33.2°C to 38.2°C and that few studies reported average values of body temperature equal to or above 37.0°C, i.e. the rectal temperature in six studies and the ear temperature in one study [20, 24-28]. In addition, calibration of the thermometers, how the measurement was performed (i.e. measuring technique and training of the operators, insertion of the devices), ovulatory

status, time of day and indoor temperatures were not clearly described. Hence, there is a lack of studies performing temperature measurements in a standardised way. Also, studies presenting strong evidence were mainly found in investigations of oral temperature, and in studies reporting body temperature in men [23].

In clinical practice, the nurse retains responsibility for care of the individual [29] including the evaluation of body temperature and notifying the physician of individual changes in the thermal status. The nurse also frequently determines when to start antipyretic therapy and initiate a physical cooling on or without the physician's order. Hence, nurses have a great impact on both the observation of body temperature as a sign of infection and on implementing nursing care during fever.

Nursing care should be based on sound scientific knowledge and evidence-based experience [30]. The nursing process, i.e. the assessment, diagnosis, planning and implement actions of interventions and evaluating the outcome [29], is a basic framework which ensures that nursing care is performed in a systematic and structured way. In relationship to body temperature, this means that adequate measurement and evaluation are the necessary prerequisites for the nursing process [29].

AIMS OF THE INVESTIGATION

The general aim was to explore factors influencing the normal variation and measurement of body temperature in adults in order to improve the assessment of body temperature measurement.

The specific objectives were to study

- Factors predicting low body temperature in non-febrile seniors (I).
- Errors introduced by individual variation, repeated measurements, measuring technique and equipment used for rectal, oral, ear and axillary body temperature measurement (II).
- Morbidity, mortality and clinical presentation of pneumonia in a Swedish group of elderly nursing-home residents (III, IV).
- Modifiable factors and the influence of baseline body temperature on survival with two- and three-year follow-ups in elderly nursing-home residents (IV).

BACKGROUND

The concept of normality

Normal is defined as something usual and ordinary, in accordance with what people expect [1]. However, a function *per se* has no meaning except in relation to something else [14, 31]. Hence, in order to define normality, it is necessary to delineate cut-off limits for what is normal and abnormal. In 1944 Iwy [31] expressed this as the duty of physiology to define in quantitative terms the criteria of normality as the basis for the study and diagnosis of human disease. He defined normality according to the *normative view*, i.e. only those who manifest the ideal healthy state are normal; the *clinical or pathological view*, i.e. anyone is normal who is well and not disabled by some disturbance manifested by symptoms; the *statistical viewpoint*, which varies depending on where it draws the line between the normal and abnormal and the *non-arbitrary statistical view*, which calculates the extent to which an individual deviates from the mean of the group, but does not sharply distinguish a group or an individual as normal or abnormal. Galen and Gambino [14] defined normality as a *probability function*; the value *most representative* of its class; the most *commonly encountered* in its class; the *most suited to survival*; *carrying no penalty* (i.e. does not cause disease); or the *most commonly aspired to* or *most perfect* of its class.

Iwy [31] underlined that it is important to understand variability and to be cautious in pronouncing persons normal or abnormal in order to avoid mistakes in the interpretation of the individual condition. Galen and Gambino [14] further stated that the concept of normality is itself inadequate for the proper interpretation of test results if it is not interpreted in relationship to a reference value. They further declared that to use the usual lower and upper limit of normal as a reference value is not enough, as this has varying utility when applied to individual patients. They claimed that to obtain meaningful reference values it is necessary to study and define reference populations. In addition, an individual reference value, i.e. a baseline estimation, defined as a value or starting point on an imaginary scale with which other values are compared [1], may be appropriate when assessing individual changes.

Thermoregulation

Thermosensitive neurons in the preoptic anterior area of the hypothalamus (POAH) integrate information from the surrounding blood and peripheral receptors in order to maintain the body temperature within an individual temperature range, the set point [5, 32]. In addition, there are thermosensitive neurons in the midbrain reticular formation and neurons in the spinal cord that respond to thermal stimulation of the skin [33]. Recently, it was proposed that the vagus nerve is also involved as a signal-transfer pathway from the periphery to the brain [34].

The peripheral receptors in the skin are concentrated in the hands, the feet

and the face and, in the deep tissue, mainly in the spinal cord, the abdominal viscera and the large veins. In a thermally neutral environment, heat loss responses are activated when the POAH is warmed above the set point, and heat production responses when the area is cooled below the set point. In a warm environment, the set point shifts to a lower level to increase heat loss responses and inhibit heat production, and in a cold environment the set point shifts to a higher level to evoke heat production and inhibit heat loss mechanisms [5, 32].

Heat gain and heat loss are effectuated by sympathetic constriction or dilation of cutaneous blood vessels, but also with local release of vasodilating nitric oxid [35, 36]. Cold-induced changes in vasomotor tone depend primarily on noradrenaline release and α -adrenoreceptor-mediated vasoconstriction, while the transmitter substance inducing vasodilation is not yet known [32, 37]. In the hands, feet and ears, the blood is also supplied to the venous plexus directly from small arteries by arteriovenous anastomoses, allowing high flow rates directly from arterioles to venules [32].

Piloerection and humoral thermogenesis, i.e. noradrenaline, adrenaline, growth hormone, glucagon, insulin, adrenocorticotropic hormone and thyroxine secretion contribute to the preservation and increase of body temperature, but shivering is the physiological response to a rapid rise in body temperature [33]. The primary motor centre for shivering in the posterior hypothalamus is normally inhibited by the POAH, but is activated when the gradient between the set point and skin or core temperature increases too much [38, 39].

Heat loss is improved by sweating, decreased heat production and the inhibition of mechanisms triggering shivering and chemical thermogenesis. Aside from the autonomous mechanisms, the skin and the subcutaneous tissues effectively insulate the body, and behavioural control re-establish comfort through conscious adjustments [40, 41].

Factors influencing “normal” body temperature

Exercise [42], ambient temperature [43], diurnal variation, cellular metabolism [33, 44], hormones [45] and age [33, 46] influence body temperature. The diurnal rhythm is consistent within the individual both in health and disease. Temperatures near the minimum (early morning) vary less compared with maximum temperatures (afternoon–early evening), underscoring the influence of exogenous factors during the daytime [44]. In addition, there is a close relationship between the circadian modulation of sleep, the diurnal rhythm of body temperature, the basal metabolic rate, baseline physical activity, and the amount of skin blood flow [33].

Body temperature has been reported to be higher in women than in men in subjects < 65 years of age [24, 47]. This was explained by a rise in core temperature after the postovulatory progesterone phase [48], and a higher

sweat onset and lower sweating capacity in women compared to men when exposed to heat [40]. In addition, women have a lower basal metabolism rate and it is therefore suggested that they maintain thermal equilibrium by convective and radiant exchange at higher ambient temperatures than men. Furthermore, women generally have a thicker layer of subcutaneous fat, which helps to insulate the core from heat gain during hot conditions [49]. A higher body mass index (BMI) in relation to a lower body temperature has been observed, but only in men [50]. No differences in the average normal body temperature in healthy elderly women and men (> 64 years) have been found [51, 52]. However, Moe et al. [53] reported that healthy elderly women showed a higher peak temperature and an advanced acrophase compared to men, while men showed a greater variability in acrophase than women.

Although data on normal body temperature in older age are sparse [28] and changes in temperature regulation with aging have been studied with conflicting results [51, 54-56], an increased frequency of hypothermia (core temperature $\leq 35^{\circ}\text{C}$) [57] and an altered shivering response have been reported [37, 46]. Thermoregulation is suggested to be impaired in older people due to age-related factors and secondary to impairment and disease. Age-related factors include a reduced proportion of heat-producing cells, a decrease in total body water, enhanced baseline vasoconstriction [33], a delayed and reduced vasoconstriction response to body cooling [37, 58], an increased threshold and delayed and reduced cutaneous vasodilatory response [36, 59] and a decreased sweating rate on body warming [58]. The decline in vascular responses is probably due to impaired thermoregulatory control of sympathetic nerve traffic and a decreased release of local nitric oxide [36, 60]. The intake of food and the basal metabolic rate decrease in elderly persons [61], which, in turn is associated with malnutrition and loss of fat-free heat-producing tissue and a decreased level of fitness [33]. Elderly persons also show fewer behavioural adjustments to thermal discomfort [37]. In addition, the sedentary lifestyle of many elderly people lowers heat production [33]. Hence, a subset of aged individuals might have lower normal body temperatures than younger subjects [21].

Body temperature measurements

The core temperature refers to the thoracic and abdominal contents and some of the muscles and the brain, while the peripheral temperature refers to the skin and a relatively small amount of subcutaneous tissue [2]. Generally, a thermal gradient exists between the body surface and the deeper tissues, such that for each 4 mm of depth, there is a rise in temperature of approximately 1°C [62]. The temperature in the pulmonary artery (PA) is generally considered the gold standard of core temperature, as it measures the temperature of mixed venous blood from the upper and the lower parts of the

body as well as the core and the periphery [63, 64]. In clinical practice non-invasive methods, such as rectal, oral, ear and axillary measurement are used to estimate the core temperature [65]. Traditionally, oral and axillary readings are adjusted to the rectal temperature by adding 0.3°C and 0.5°C, respectively.

Two different technical designs of thermometers to measure body temperature non-invasively are used. The digital electronic thermometers have a thermistor or thermocouple sensor that produces electronic signals that change with differences in tissue temperature. The temperature is displayed as an unadjusted or adjusted value either in the steady-state mode after the sensor has reached equilibrium, or the predictive mode. The infrared radiation ear device (IRED) estimates the infrared heat waves from the tympanic membrane [65]. As the probe is placed about 1.5 cm away from the tympanic membrane [66], the thermometer reading is therefore a mix of heat from the tympanic membrane and the aural canal [67]. To compensate for the deviation, there is an offset system included in the instrument [68]. The ear temperature can be measured in the unadjusted (equal) mode, in contrast to the adjusted mode, when the manufacturer has readjusted the value with an offset beforehand in order to equalise the oral, rectal or PA temperatures [69].

Rectal measurement

The rectal site is thought to be an indication of the deep visceral temperature, modified by the temperature of the skin of the buttocks, the iliac artery and the iliac vein [2]. The rectal temperature is higher than at other places in steady state [66, 70-75], which is probably due to the low blood flow and high isolation of the area, giving a low heat loss [76]. As it significantly lags behind changes at other core sites, especially during rapid temperature changes such as warming and cooling during surgery, exercise and fever [66, 77-80], the rectal temperature may be both higher or lower than the core temperature [65]. In cold conditions the difference can be as high as 2.3°C [66] and in head-injured patients, the rectal temperature may underestimate brain temperature by as much as 2.1°C [81]. The reading can also be influenced by hard stool, as this might obstruct adequate placement of the thermometer, by inflammation around the rectum [82] and heat-producing activity of microorganisms in faeces [65, 78]. The insertion by depth may introduce serious variations in rectal temperature [76] due to variation in blood flow from the skin of the buttocks, the upper leg and external genitalia, especially during cooling of the skin [83]. In addition, there is a risk of rupturing the walls of the rectum [65]. As the temperature increase by 0.8°C with each 2.54 cm the device is inserted [66, 80] a standardised depth of 4 cm in adults is recommended [65].

Oral measurement

As a branch of the external carotid artery perfuses the area of the posterior sublingual pockets the oral temperature has been suggested to follow changes in core temperature closely [65], but the sublingual temperature may differ between the posterior pocket and the front area [84], as well as between the posterior pockets [85]. Also, vasomotor activity in the sublingual area affects the temperature [86], e.g. a fall in oral temperature during the onset of fever may occur due to a reduced blood flow [77, 87]. Other factors influencing the oral temperature readings are salivation, open versus closed mouth [65], previous intake of hot or cold food and fluids [27, 65, 88], gum chewing, smoking [88] and rapid breathing [87]. However, smoking [27], the respiratory rate, the presence or absence of teeth, open versus closed mouth [89] and administration of oxygen have been reported not to influence oral measurements [90]. The method is contraindicated in unconsciousness, confused patients and when there is a risk of seizures, and it might be inappropriate in individuals with uncooperative or disturbed behaviour [91].

Ear measurement

The tympanic membrane and hypothalamus share their blood supply from the internal and external carotid arteries [92, 93] and the area is relatively devoid of metabolic activity [80]. The accuracy of IRED for the tympanic membrane temperature [94-97], the repeatability and accuracy for changes in the core temperature during physical exercise and warming [98] and for estimating cranial temperature [99] is reported to be good. The ambient temperature has been suggested to alter IRED readings [69, 73, 96], although the auditory temperature was not affected by a decrease in skin temperature resulting from facial cooling or fanning [95, 96]. The influence of cerumen is inconsistent, with some studies reporting no influence [85, 100, 101], while others observed a higher variability [88] and an underestimation by an average of 0.3°C [102]. The occurrence of otitis media has been associated with 0.1°C higher values [100], while others reported no effect [103]. The value of IRED measurements in clinical practice is not consistent, with some authors in favour of them [47, 73, 78, 80, 94-98, 104-112] and others not [76, 79, 113-117].

Axillary measurement

Historically axillary measurement have been used to estimate core temperature, although the ambient temperature, local blood flow, underarm sweat, inappropriate placing of the probe, inappropriate closure of the axillary cavity, and insufficient duration of the reading strongly affect the accuracy [65]. In addition, temperature differences between the right and left axilla of up to 1.4°C in steady state have been reported [118]. As axillary measurements, even with careful positioning, are slow to register changes in

core temperature, the readings exhibit a wide deviation from other sites [78]. In consequence, during fever, the skin temperature varies dynamically due to vasomotor activity. Since 12 minutes are required to equalise the core temperature [119], monitoring the skin temperature is an insensitive technique for estimating the core temperature [64, 120].

The febrile response

Fever is defined as a state of elevated core temperature, which is often, but not necessarily, part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter recognised as pathogenic or alien by the host [3]. During fever the set point is shifted to a higher level due to the influence of pyrogenic cytokines [121]. Cytokines are produced from, and act on, both leucocytic and non-leucocytic cells [122] and possess additional biological proprieties apart from their ability to induce fever, e. g. acting as mediators in the acute phase response by increasing the synthesis of hepatic acute-phase proteins. The most prominent pyrogenic cytokines are interleukin-1 (IL-1 α and IL-1 β), interleukin-6 (IL-6) and tumour necrotic factor (TNF α and TNF β).

Detailed mechanisms of the induction of fever are still incomplete, though the current view is that the chain of reactions starts with the secretion of pyrogenic cytokines, mainly IL-1 in the phagocytic ingestion by macrophages and monocytes. Pyrogenic cytokines convey the message to the POAH neurons, inducing production of prostaglandin E₂ (PGE₂) in the brain, causing a rise in the set point temperature, which is defended as seriously as the old one [121]. The PGE₂ release in the brain is thought to be induced by enzymatic action of microsomal prostaglandin E synthase-1 [123] and the release of cyclic AMP [124].

Data from experimental studies confirm that endogenous substances, such as arginine-vasopressin, α -melanocyte-stimulating hormone, catecholamines, glucocorticoids and adrenocorticotrophic hormone, and IL-1, TNF and IL-6 themselves act as antipyretic agents [122, 125-127]. Recently, Van Someren [33] suggested that the observed increased skin blood flow during nocturnal sleep is aimed at enhancing immunological host defence by transporting lymphocytes into the extravascular tissue during sleep. The adaptive value of fever is supported by experimental and clinical studies reporting beneficial effects of fever and the adverse effect of antipyretics on the outcome of infection [128-130].

Infection and fever in elderly individuals

There is an increased risk of infection in elderly persons [131], with the highest incidence in the institutionalised elderly [10, 132]. National data on the incidence of specific infectious diseases in nursing homes are not

available in Sweden, but the overall rate of infection increase from 0.9% in the age group 45-64 years to 2.1% at 75-84 years [133]. Factors contributing to a higher morbidity and mortality in infectious diseases are physiological changes affecting host defence mechanisms, i.e. the skin, mucosa and changes in T cell immunity and altered function of antigen-presenting cells, chronic disease and functional impairment [131, 132, 134] and malnutrition, which impair immune and respiratory function responses in elderly people [135, 136].

Apart from the fact that chronic disease and disability may mimic infectious processes [22], an atypical presentation of infection, including an absence of fever, is common [10, 137], especially in the frail elderly [138]. Infection was estimated to be present in 77% of episodes with a decline in function, defined as new or increasing confusion, incontinence, falling and deteriorating mobility [139]. The mechanisms underlying a blunted fever response are still unclear, but abnormalities in pyrogenic cytokines, decreased sensitivity of the hypothalamus and failure to produce and conserve body heat are suggested explanations [138]. The absence of fever may also be due to a decreased intake of proteins, which may influence the production of cytokines [135, 140], although no relationship between malnutrition and blunted fever has been reported [28, 141]. In addition, it has been suggested that the febrile response may actually be similar in elderly and younger populations, but the degree of fever being lower in the older age groups [142, 143] due to a low normal body temperature [10, 22].

Nursing-home acquired pneumonia (NHAP) is the second most common infection [10, 134, 144], accounting for 15% to 50% [134, 145] and the highest case-fatality rate among all infections occurring in geriatric settings [134, 145, 146]. A change in cognitive or functional physical capacity from baseline and worsening of underlying illness may appear as a single manifestation [145, 147, 148]. The absence of a classic presentation of pneumonia correlates with advanced age and baseline functional and cognitive impairment [147, 149]. Approximately 30% to 57% of nursing-home residents with pneumonia are assessed as being afebrile [137, 150]. The atypical symptoms are associated with a delay in establishing the diagnosis and antibiotic therapy [120] and contribute to a high fatality rate [151].

Predictors of survival in elderly nursing-home residents

Previous research has addressed age, male gender, functional/cognitive decline and chronic disease, such as heart failure and respiratory, neurological, endocrine or metabolic disease and cancer and a poor nutritional status as predictors of mortality in elderly nursing-home residents [152-160]. In a gender perspective, the number of medical diagnoses, sleep disturbance [152], and functional impairment [161] have been observed to be predictors of decreased survival in women and incontinence [152], Chronic

obstructive pulmonary disease (COPD) [155] and dementia and delirium [161] specifically in men. However, previous research was mainly conducted in male populations [160]. In addition, studies of survival in relationship to factors that can be modified are sparse [158]. As chronic diseases and physical and cognitive impairment are common in this population [160], the ability to manage daily living by themselves frequently affects the quality of daily life.

Recently, a lower baseline body temperature was associated with longevity in men [162], which was probably related to caloric restriction and reduced cellular metabolism and oxyradical production [33]. Also, a decline in body temperature preceding death has been observed in aged mice [163].

MATERIAL AND METHODS

Subjects

Papers I, III, IV

Three hundred and nine residents, ≥ 65 years of age, were invited and the informed consent of 262 (85%) was obtained. As 25 of the included residents dropped out for medical reasons, the final sample consisted of 237 individuals (aged 66-99, 75% ≥ 80 years) in study I, 159 of whom was women and 78 men. Forty-five per cent were living in service flats, 29% in nursing homes and 26% in group housing for the elderly. The sample during the one-year observation of pneumonia and the three-year follow-ups (III, IV) consisted of 234 residents, as three residents died before the observation period started.

At baseline, women were older, more dependent in ADL, suffered more often from thyroid disease and malnutrition and were treated with antidepressants more often than men, while smoking and COPD were more frequent among men. In those surviving after three years, the ADL status was higher in women and smoking was more usual in men (Table I).

Paper II

In part 1, the sample consisted of three volunteers (45 to 58 years) and, in part 2, of a convenience sample of students and hospital staff, 62 women and 22 men (19 to 59 years old). In the convenience sample, 45 women were premenopausal and 17 postmenopausal. Twenty of the premenopausal women were in the follicular phase and 20 in the luteal phase and 11 were on contraceptives. Six premenopausal and 8 postmenopausal women were on daily oestrogen medication. No subject had an ongoing febrile illness, was on daily medication or had received analgesics prior to the measurements.

Table I. Background data, presented as frequency (%) or $m \pm SD$, for elderly nursing-home residents (66 to 99 years old), at baseline and for survivors three year after baseline. The number of individuals is given in brackets.

Variable	Baseline Papers I, III		Three-year follow-up Paper IV	
	Women (159)	Men (78)	Women (70)	Men (32)
Age	85.5 \pm 6.1	82.6 \pm 7.4**	83.3 \pm 5.9	82.0 \pm 7.6
ADL ^a	7.0 \pm 5.1	5.0 \pm 3.6**	5.5 \pm 3.6	3.9 \pm 3.8*
BMI ^b	25.1 \pm 4.9	26.1 \pm 4.8	-	-
S-albumin g/l	37.4 \pm 3.7	37.7 \pm 4.1	-	-
Ear temperature °C	37.0 \pm 0.6	36.8 \pm 0.5	-	-
Rectal temperature °C	36.9 \pm 0.4 ¶	36.8 \pm 0.3 ¶¶	-	-
Dementia	39.6	30.8	38.6	28.1
Cardiovascular disease	60.4	64.1	75.7	78.1
COPD ^c	1.3	9.0**	4.3	9.4
Smoking	0.6	11.5***	1.4	12.5*
CVI ^d	23.3	26.9	32.9	31.3
Diabetes	16.4	12.8	22.9	21.9
Autoimmune disease	3.8	7.7	4.3	6.3
Cancer	7.5	12.8	15.7	31.3
Thyroid disease	11.9	2.6*	14.3	6.3
Cortisone	2.5	6.4	1.4	6.3
Sedatives/tranquillisers	30.2	25.6	32.9	28.1
Antidepressants	37.7	24.4*	32.9	21.9
Paracetamol \geq 3 g daily	49.7	44.9	65.7	51.6
Malnutrition	22.2	9.1*	-	-
Influenza vaccination	28.3	14.1*	-	-
Pneumococcal vaccination	8.2	5.1	-	-

^a Activities of daily living

^b Body mass index.

^c Chronic obstructive pulmonary disease.

^d Cerebral vascular insult.

¶ n = 115. ¶¶ n = 46.

*p < 0.05. **p < 0.01. ***p < 0.001.

Procedure

The interindividual variability was investigated in two descriptive correlational studies (I, II). The intraindividual variability and the influence of the measuring technique and the equipment used in body temperature measurement were studied in paper II. Factors related to a lower baseline body temperature in elderly individuals were studied in paper I. To study the morbidity, mortality and clinical presentation of nursing home-acquired pneumonia, a prospective design was used in paper III and a three-year follow-up was conducted in paper IV. Predictors of survival in elderly individuals were also studied in paper IV.

In studies I, III and IV the research was conducted in special housing for the elderly, including separate apartments and special units for elderly persons with physical impairment and/or dementia. The facilities were located in three communities in southern Sweden, comprising 35 houses, 6 of which were randomly assigned to participate in the study. Primarily, nurse's aides, under the direction of geriatric nurses, provided the daily care. General practitioners paid weekly visits to the settings for examinations and to prescribe drugs. Between visits, the geriatric nurses handled acute consultations with the general practitioners at the primary health care centres. Study II was conducted in the subject's home (part 1) and in a research laboratory at the Linköping University (part 2).

Paper I

Data on chronic diseases, including dementia, and medication, were collected from the medical records. ADL status and malnutrition were assessed, and the ear and rectal temperatures were measured on one day: once at 7–9 a.m. and then at 6–8 p.m. One person (M S-L) performed all the ear measurements. The rectal temperatures were measured by the residents themselves or by nurse's aides. Measurements in individuals with ongoing infectious disease were delayed until two weeks had passed after recovery or the end of antibiotic treatment.

Paper II

In part 1, three volunteers performed five repeated measurements of the oral, the right and the left ear and the right and the left axillary temperatures for five consecutive mornings immediately after wakening. At least 60 seconds passed between the repeated measurements in the same ear [164, 165]. The rectal temperature was measured twice the first morning, with cooling of the body between the measurements, and then once the following four mornings. In part 2, the morning rectal, oral, ear and axillary temperatures were measured once in 62 women and 22 men. No subject had performed any vigorous activity and had sat resting for 20 minutes while answering a questionnaire about diseases and medication prior to the

measurements. Two registered nurses measured the ear temperature in both ears and positioned the oral thermometer, while the subjects themselves performed the rectal and axillary readings. Room temperature was noted in both the repeated and single measurements.

Paper III

The physician in charge observed the occurrence of pneumonia for 12 months. Specific symptoms (cough, sputum production, chest pain, respiratory rate > 20/min), non-specific symptoms (fever, change in cognitive or functional status, worsening of chronic disease and anorexia) and findings on chest examination and chest X-rays were noted. The nurses and physicians assessed whether the resident was febrile or not. Finally the cases were classified into three categories: (1) Pneumonia verified by a chest radiograph; (2) Clinical pneumonia; and (3) No pneumonia. Only one episode per patient was included in the statistical analysis.

Paper IV

A follow-up of individuals included in paper III was performed three-years after baseline. For residents surviving the three-year follow-ups, updated data on chronic disease, medication, smoking habits and ADL status were obtained from medical journals and nurse's aides. In addition, the cause of death and the occurrence of suspected NHAP during years 2 and 3 was confirmed retrospectively from death certificates and medical records. Baseline data from paper I and a mortality risk index score (MRIS) was used to predict one,- two- and three-year survival. MRIS was computed as follows: A point value equal to the hazard ratio in the regression model was assigned to each factor related to mortality and then summarised for all mortality-related factors present in each subject [158]. When survival and the incidence of NHAP were analysed, each year was regarded as a separate follow-up period.

Measurements

Body temperature

The ear temperature was measured with IRED thermometers in the unadjusted mode (First Temp Genius, model 3000 A, TYCO Health Care Kendall, Stockholm, Sweden (I, III) and Thermo Scan type 6014, BRAUN Gillette, Kronberg, Germany (II)), and the rectal, oral and axillary temperatures with electronic thermometers in the unadjusted mode (MC-638, MC-63, MC-63B, Omron Health Care Europe BV, Täby, Sweden). The devices were calibrated according to the manufacturer's standard before the study. After the study, the devices were also calibrated in an accredited laboratory (Pentronic, Gunnebo, Sweden). Room and bed temperatures were measured with a portable device (Viking AB, Eskilstuna, Sweden).

ADL status

The ADL Staircase was used to assess dependency in personal and instrumental activities of daily living (P-ADL and I-ADL) [166, 167]. The cumulative structure was based on the Katz ADL index [168]. The P-ADL consists of 6 categories, bathing, dressing, toileting, transfer, continence and feeding, and the I-ADL of cooking, transportation, shopping and cleaning. The residents were graded from 0 to 10 or “other” (O), i.e. 0 = independent in all 10 activities, 10 = dependent in all 10 activities, and O = dependent in two or more activities but was not possible to classify in grade 0 to 10. Grade 5 means dependency in all I-ADL activities and in one P-ADL activity [166]. The Katz ADL index is a widely used validated and reliable instrument [169-171], and the cumulative construction of the ADL Staircase has been tested in elderly populations in Sweden [172].

Nutritional status

Nutritional status was measured in terms of anthropometrical, i. e. height, weight index, mid-arm circumference (MAC), triceps skinfold thickness (TSF), arm muscle circumference (AMC) and biochemical measurements, i. e. S-albumin and S-transferrin. Height was measured in the supine position or on a flat bed and body weight with a digital electronic wheelchair scale (VETEK W 1500) or a mechanical balance chair (LIBRA). MAC was measured with non-stretch tape and TSF (average of three measurements) with Harpenden skinfold callipers (British Indicators Ltd, Sussex, UK) on the unparalysed arm midway between the tip of the acromion and the olecranon process. Local reference values were used for S-albumin (BCG, Axam, Beyer, Germany) and transferrin (Turbidimetry, Axam, Dacho Pack, Denmark). Malnutrition was declared if two or more nutritional variables were subnormal, including one anthropometrical and one biochemical variable [173, 174]. Table II.

Table II. Criteria for definition of malnutrition.

	Age	Men	Women
Weight index ^a		< 80 %	< 80 %
TSF ^b		≤ 6 mm	≤ 12 mm
AMC ^c	≤ 79	≤ 23 cm	≤ 19 cm
	> 79	≤ 21 cm	≤ 18 cm
S-Transferrin		< 0.23 g/l	< 0.23 g/l
S-Albumin		< 36 g/l	< 36 g/l

^a The actual weight/reference weight x 100, calculated as 0.65 x height (cm) – 40.4 (kg) in women and as 0.80 x height (cm) – 62 (kg) in men [175].

^b Triceps skinfold thickness.

^c Arm muscle circumference, calculated as MAC – 0.1 (π x TSF) [173].

Body mass index

BMI was calculated as kg/m^2 [176]. Suggested cut-off points for low BMI are 18.5 kg/m^2 [177], 20 kg/m^2 [178] or 24 kg/m^2 [179]. In this study a cut-off value of $< 20 \text{ kg/m}^2$ is defined as underweight as this is the recommendation in Sweden [180].

Dementia

A geriatric physician at the Geriatric Rehabilitation Clinic of the Högländ Hospital, County of Jönköping, established the diagnosis. The diagnosis was based on interviews with the patient and next of kin, physical examination including neurological status, biochemical and neuropsychological testing, electroencephalography, photon emission computed tomography, magnetic X-ray and neuropsychological testing. The intellectual deficits had to be severe enough to cause impairment in social and occupational ability. Memory impairment and changed personality had to be included, and one or more of inability to think abstractly, reduced judgement, aphasia, apraxia, agnosia or spatial disorientation [181].

Statistics

The statistical software SPSS for Windows (10.1 and 11.1) was used for the statistical calculations. The level of significance was set at $p < 0.05$. Parametric data were tested with Student's two-tailed t- test or ANOVA with Sheffe's post hoc test and non-parametric data using the Mann-Whitney U-test, the Wilcoxon signed ranks test, the Chi^2 test or Fisher's exact test. Pearson's correlation coefficient or Spearman's rho was used to analyse associations. A stepwise regression analysis was performed in order to analyse factors affecting baseline body temperature and a multivariate logistic regression to explore risk factors of NHAP. A Cox hazard regression analysis was performed to explore predictive factors of survival, and Wilcoxon's statistic for probability to explore the actual survival time [182]. The frequency of NHAP was estimated as the incidence proportion [183]. Clinical reproducibility [47], was used to analyse the repeated measurements. The estimated coefficient of repeatability includes 95% of the differences between the repeated measurements [76]. The method of Bland and Altman [184] was used to compare limits of agreement (mean difference ± 2 SD) between different sites of measurement. Rectal temperature was delineated as the reference temperature [76]. When comparing the temperature between groups in the convenience sample (paper II), a body temperature index, (rectal + oral + ear + axillary temperature)/4, was calculated for each individual (Table III).

Table III. Statistical analyses used in the thesis.

Statistical methods	Paper			
	I	II	III	IV
Student's t-test, two-tailed	X	X	X	X
Mann-Whitney U-test		X		
ANOVA with Sheffe's post hoc test		X		
Chi ² test or Fisher's exact test	X		X	X
Wilcoxon signed ranks test		X		
Pearson's correlation or Spearman's rho	X			X
Stepwise regression analysis	X			
Multivariate logistic regression			X	
Coefficient of repeatability		X		
Limits of agreement		X		
Life table with Wilcoxon's statistic for probability				X
Cox hazard regression analysis				X
Incidence proportion			X	X

Ethical considerations

The studies in the thesis were conducted in accordance with the Declaration of Helsinki and were approved by the local Ethics Committee of the Faculty of Health Sciences, Linköping University (990302, 010508) and the health service directors of community care and geriatric staff nurses. Written and oral information was given to eligible residents or, if the resident was unable to respond, to their next of kin and it was made clear that participation was voluntary and could be interrupted at any time. In the case of cognitively impaired residents, additional information was given before every phase in the examination. The staff nurse decided when to direct the invitation to the resident or the next of kin.

Individuals with a functional and cognitive deficit might experience discomfort and anxiety when an unknown person performs personal care. To avoid threats to their integrity, all rectal measurements were performed by the residents themselves, if possible, or by nurse's aides. Before data collection, the researcher was present at the unit to familiarise herself with the residents, and the next of kin or a nurse's aides was invited to be present when the examinations were conducted. If the resident showed in verbal or nonverbal communication that he or she did not want to participate the measurements were stopped. It can be assumed that actions have been taken to minimise threats to personal integrity.

It may be questionable to perform research in aged, frail people, but the advantages is that the results can contribute to a better knowledge in nursing care and improve the quality of life at the end of life.

RESULTS

Interindividual variability

In both elderly and younger individuals the range of the rectal temperature was 35.6°C to 38.0°C (I, II). In elderly individuals the range of the ear temperature was 33.8°C to 38.4°C (I) and in younger adults 35.0°C to 37.8°C (II). In younger adults the range of the oral and axillary temperatures was 34.5°C to 37.4°C (II). The average rectal temperature was lower and the ear temperature was higher in elderly compared to younger persons (Figure 1).

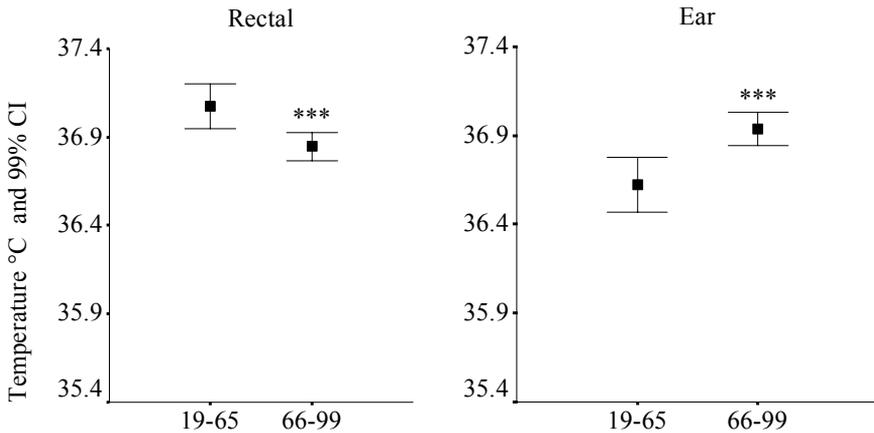


Figure 1. Baseline morning rectal and ear temperatures in 84 adults (aged 19-59 years) and 237 elderly nursing-home residents (aged 66-99 years). Average values are indicated as filled squares and the 99% confidence interval (CI) as horizontal lines. *** $p < 0.001$.

The ear temperature was higher in elderly individuals irrespective of gender, and the rectal temperature lower in elderly women than in younger females, while no difference was found in men (Table IV).

Table IV. Baseline morning ear and rectal temperatures (°C) in adult men and women aged 19 to 59 years and elderly nursing-home residents aged 66 to 99 years. The number of subjects is given in brackets. *** $p < 0.001$. # $p < 0.08$.

	Ear temperature °C		Rectal temperature °C	
	19 to 59 years	66 to 99 years	19 to 59 years	66 to 99 years
Men	36.6 ± 0.6 (22)	36.8 ± 0.5 # (78)	36.7 ± 0.4 (21)	36.8 ± 0.3 (46)
Women	36.6 ± 0.5 (62)	37.0 ± 0.6*** (158)	37.2 ± 0.4 (62)	36.9 ± 0.4*** (115)

No difference was found between elderly men and elderly women, while the average body temperature in younger subjects was higher in women but the range was wider in men, irrespective of the site of measurement (Figure 2).

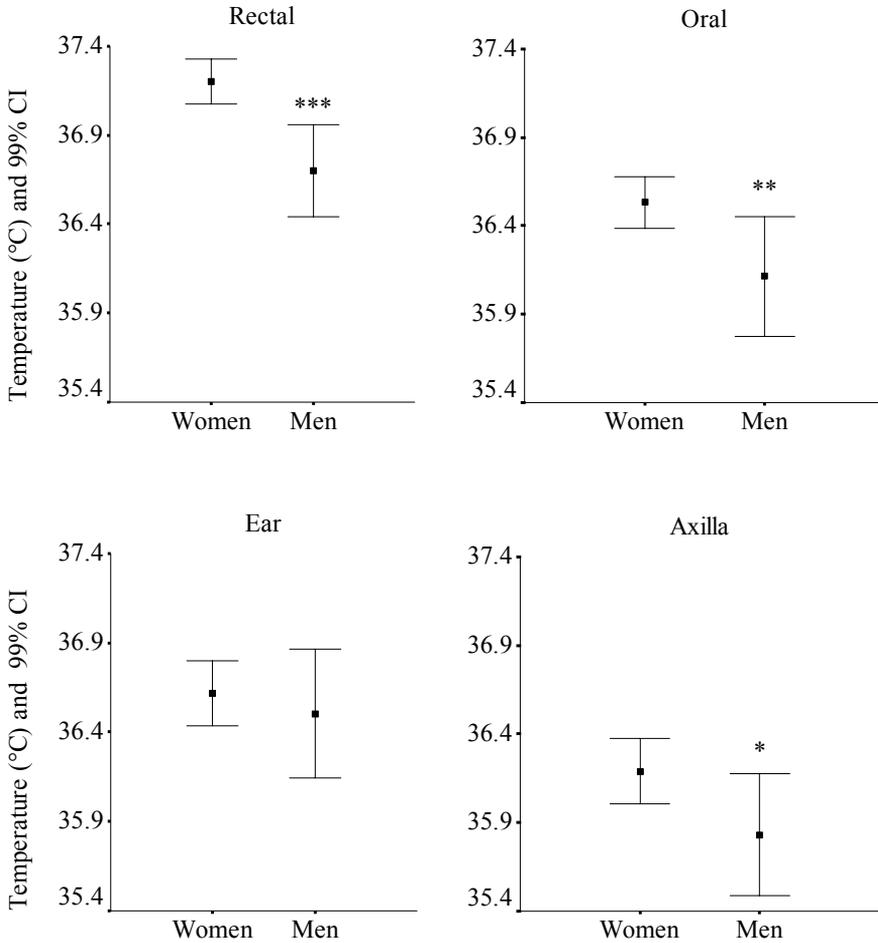


Figure 2. Baseline morning rectal, oral, ear and axillary body temperature in 62 women and 22 men aged 19-59 years. Average values are indicated as filled squares and the 99% confidence interval (CI) as horizontal lines.

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

In adults aged 19 to 59 years, the body temperature index was $36.6 \pm 0.3^{\circ}\text{C}$ in women and $36.3 \pm 0.6^{\circ}\text{C}$ in men ($p < 0.001$) and in premenopausal women in

the follicular phase $36.6 \pm 0.6^{\circ}\text{C}$ and in the luteal phase, $36.7 \pm 0.6^{\circ}\text{C}$, which values were significantly higher than in men ($p < 0.05$ and $p < 0.001$, respectively). Postmenopausal women ($36.4 \pm 0.6^{\circ}\text{C}$) differed from premenopausal women only in the luteal phase ($p < 0.05$). No difference between postmenopausal women and men was found, nor did the ovulatory phase or contraceptives affect body temperature (II).

Intraindividual variability

The deviation between the lowest and the highest readings when the repeated measurement were performed ranged from 0.1°C to 0.4°C in rectal and oral readings, from 0.2°C to 1.7°C in the ear and from 0.1°C to 0.9°C in the axillary temperatures. The mean difference, including the 95% CI, of the repeated measurements was 0.3°C for oral temperatures, 0.5°C for the right ear, 0.8°C for the left ear, 0.5°C for the right axilla and 0.6°C for the left axilla. The coefficient of repeatability was similar, irrespective of the number of replicated measurements.

In the convenience sample, there was no significant individual difference between simultaneously measured temperatures in the right and left ear, or between the two operators, irrespective of the site of measurement. Room temperature did not affect body temperature, regardless of whether single or repeated measurements were performed, nor did bed temperature influence body temperature (II).

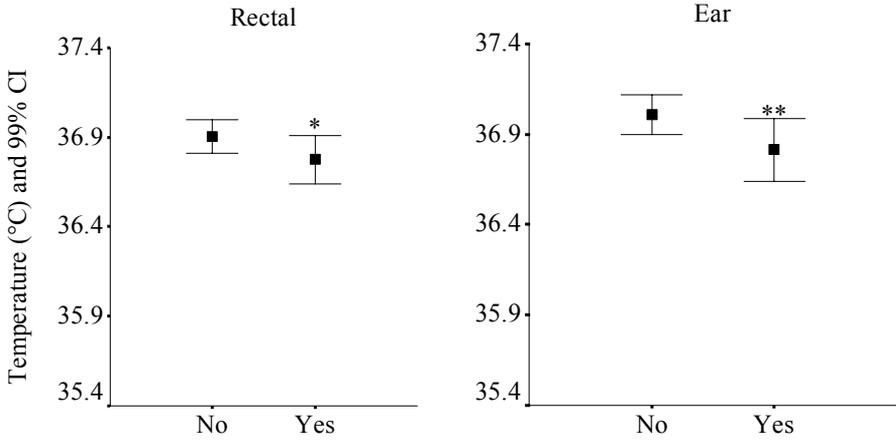
Adjustment to rectal temperature

On comparing the rectal temperature with oral, ear and axillary readings the average difference was $> 0.5^{\circ}\text{C}$, except for rectal-ear temperatures in men. The limits of agreement were larger for rectal-ear and rectal-axillary temperatures than for rectal-oral temperatures. There was also a trend towards an increase in the deviation at higher rectal temperatures (II) (cf. Figure 2 in paper II).

Factors related to a lower baseline body temperature in elderly nursing-home residents

The presence of dementia, dependency in ADL and a lower BMI were related to a lower ear temperature and dementia to a lower rectal temperature, while analgesics were associated with a higher ear temperature (I) (Figures 3 A and B).

Dementia



ADL

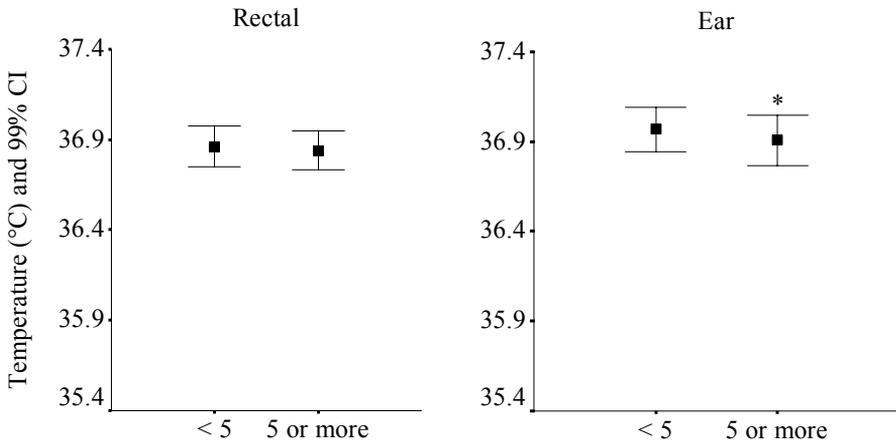
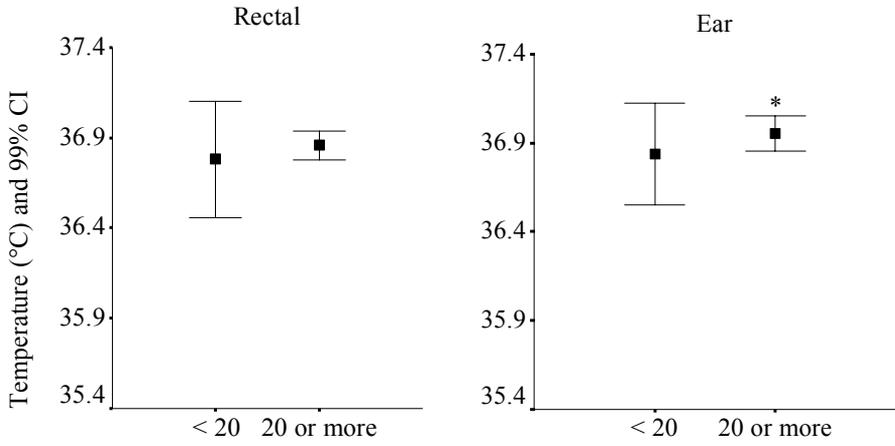


Figure 3 A. Baseline morning rectal and ear temperatures (°C) related to dementia and activities of daily living (ADL) in 237 elderly nursing home residents (aged 66-99 years). Average values are indicated as filled squares and the 99% confidence interval (CI) as horizontal lines.

* $p < 0.05$. ** $p < 0.01$.

BMI



Analgesics

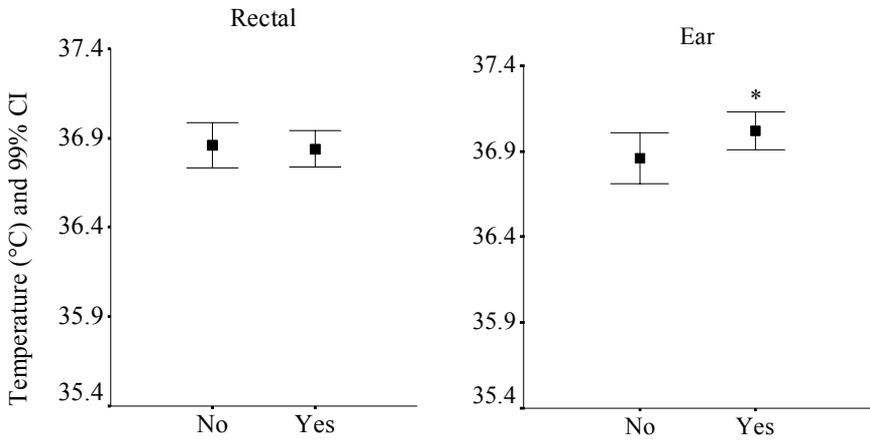


Figure 3 B. Baseline morning rectal and ear temperatures (°C) related to body mass index (BMI) and daily medication with analgesics in 237 elderly nursing-home residents (aged 66-99 years). Average values are indicated as filled squares and the 99% confidence interval (CI) as horizontal lines.

* $p < 0.05$. ** $p < 0.01$.

Pneumonia in elderly nursing-home residents

At one year of follow-up, 15 of the residents with suspected NHAP had X-ray-verified pneumonia and 17 clinical pneumonia, corresponding to a yearly incidence of 13.7%. The 30-day case-fatality rate was 28.2%. COPD ($p < 0.01$), ADL status > 5 ($p < 0.01$) and male sex ($p < 0.05$) were related to a higher risk of acquiring pneumonia, and heart disease to a lower one ($p < 0.05$). Cough and sputum production were the most frequent specific symptoms and, although fever was lacking in 22%, this sign and cognitive decline were the most common non-specific presenting symptoms (III).

At the three-year follow-ups, 80 episodes of antibiotic-treated NHAP (range 1 to 5) were found in 68 subjects. The yearly incidence the second year was 9.5 % and the third year 6.9 %, with no difference between genders, and an overall larger incidence in individuals with functional impairment. In women, the yearly mortality rate due to NHAP decreased, while it increased in men. In individuals with suspected NHAP in year 2 or 3, no differences in baseline background factors were found compared to subjects without NHAP (IV).

Predictors for survival in elderly nursing-home residents

The cumulative hazard ratio of survival for the total group was 76.1% for year 1, 57.3% for year 2 and 43.6% at the end of year 3. CVI (25.8%), NHAP (24.2%) and heart failure (23.5%) were the most common causes of death. Death due to dementia and old age was more frequent among women and to CVI and COPD among men. Age and dependency in the ADL status predicted one-year mortality irrespective of gender, while CVI, a lower BMI and malnutrition in women and heart disease, COPD, sedatives and MRIS in men were gender specific predictors. Age predicted two- and three-years mortality and dementia three-year mortality in women, while no factors predicted two- and three-year survival in men.

A lower baseline body temperature at one- and three-year follow-ups was more usual among non-surviving women ($p < 0.08$ and $p < 0.05$), while no difference was observed in men.

A lower S-albumin ($p < 0.01$), malnutrition ($p < 0.08$) and medication with sedatives ($p < 0.08$) were more usual in non-surviving men the first year, and a lower BMI ($p < 0.08$) was more frequent among non-surviving women at three-year follow-ups. No differences between non-surviving and surviving men at two or three-year follow-ups were found (IV).

GENERAL DISCUSSION

The paradigm of normal body temperature as 37°C and fever as > 38°C [18] was formulated at a time when the physiological mechanisms of body temperature regulation, the influence of hormones, cellular metabolism, physical activity and methods for calibration of the thermometers were not known. In addition, the measurements were performed on patients, indicating that a large number might have been febrile. Moreover, the axillary site was used, which gives only an estimate of peripheral temperature [64, 120], and the measurement were performed in a non-standardised way. Mackowiak et al. [185] also showed that the thermometer used at that time measured 1.4°C to 2.2°C higher compared to modern digital devices. Even so, this paradigm from the middle of the 19th century is still the basis for evaluation of body temperature, explaining the confusion in clinical practice [19], and that the measurement and evaluation of body temperature is still based more on imitation, hunches and tradition than a theoretical framework and scientific knowledge [186, 187].

The present results underline the lack of evidence for normal body temperature of 37°C and demonstrates that the variation, even with standardised measurements, is wider than traditionally stated [18] due to inter- and intraindividual variability. As normal body temperature shows individual variations, it is reasonable that the same should hold true for the febrile range [125]. However, the use of cut-off values depending on the normal range at different sites [28, 138], is confusing and not significant. This thesis explores in accordance with others [14, 31] that body temperature should be evaluated in relation to the normal range characteristic of a specific reference group and individual variability, i.e. a baseline value.

The results confirm that fertile women have a higher average body temperature than men [24, 47], but also that this difference disappears on comparing men and postmenopausal women. Contradicting Cagnacci et. al., [48] the postovulatory temperature rise in fertile women was not significant, but there was a difference between postmenopausal and fertile women in the luteal phase. Other factors which can explain dissimilarities between genders are that women have a thicker layer of subcutaneous fat, a lower baseline metabolic rate and a delayed sweat onset and a lower sweating capacity than men [40, 49].

Age-related alterations in thermoregulation, metabolic rate and vascular response [33, 36, 37, 58, 59, 61, 188, 189] may explain a higher ear temperature in elderly nursing-home residents compared to younger adults, i.e. the set point is at a higher level in order to improve the thermoregulatory responses. The difference in rectal temperature between younger and elderly persons can be understood in terms of the higher temperature in fertile females (cf Table I in paper II).

In line with the findings of others [51, 52], no difference between elderly

men and women was observed. More importantly, the results confirm that subgroups of elderly individuals have a lower baseline body temperature [28, 190] due to functional and cognitive impairment and loss of isolating tissue. However, earlier suggestions [189, 191] of a relationship between body temperature and malnutrition were not confirmed. Daily medication with paracetamol was related to an increased baseline body temperature, reflecting the possibility that pain, which is common in aged individuals [154], is related to chronic low-grade inflammation with increased circulating levels of IL-6 and consequent fever [192]. Together, the results indicate that body temperature is stable in adult men < 60 years of age, while pre- or postmenopausal status influences body temperature in females < 60 years of age and that body temperature in aged persons is affected by age-related changes and fragility.

Other studies have focused on the degree of closeness between different sites of measurement in order to define the best choice for estimating the core temperature non-invasively [23], but our results show that no factor does exist which allows accurate conversion of temperatures recorded at one site to estimate the temperature at another site [89]. The lack of agreement between measurements reflects the fact that it is not possible to interchange different temperatures [193] or to claim that there is one range of core body temperature [194]. To define an acceptable accuracy as $\pm 0.5^{\circ}\text{C}$ [73] or $\pm 0.6^{\circ}\text{C}$ [79] between sites or to use the term equivalence only contributes to misunderstandings and confusion [69]. The probably reason for adjustments is to make the readings more familiar to clinicians. However, temperatures at the rectal and oral sites are themselves estimates of the core temperature with their own variability [119]. In the case of IREDs, there are considerable variations in how manufactures have calculated the mathematical algorithm for adjusting to the rectal, oral or pulmonary artery site [74, 94, 107, 195, 196]. Therefore, the best approach is to use an unadjusted mode and become accustomed to typical values [119], irrespective of the site of measurement.

Our results confirmed the stability of rectal temperature, probably explaining why this site has long been regarded as the most accurate method for routine estimates of body temperature [64]. Since the number of repeated measurements did not improve the reproducibility, thereby contradicting earlier suggestions for duplicate or triplicate ear temperature measurements [47, 111, 114] the results indicate that one measurement is sufficient also when the ear, oral or axillary site is used.

The repeated ear readings showed the highest variability, which may be attributed in part to the technical design of the IREDs [95]. All methods require careful handling and experienced users [194, 195], but the results indicate that training in operator technique ensures consistency in ear temperature measurement in particular [108]. Childs et al. [111] recommended measurements at the same ear, but we suggest the right ear,

and also the right axilla, due to less variability. However, the temperatures measured in either the left [197] or the right ear [198] have been observed to be lower and more variable, indicating the possible impact of operator hand dominance on the temperature readings [197]. While Terndrup [195] recommended an ear tug technique, Erickson [119] pointed out that when not using this technique, the free hand of the operator can support the opposite side of the patient's head and thereby reduce the patient's tendency to move away from the probe. In this study, the use of an ear tug technique was not controlled for, implying that this does not affect the reading, as no deviation was found between the two operators in study II.

As the calibration of the ear devices showed different deviations from the target temperature, the results also indicate that it is preferable to use the same thermometer in one individual (data presented in paper II).

Use of the rectal temperature as the reference may result in the ear reading as an inaccurate and insensitive method for detecting fever when the reading instead reflects the fact that defervescence has already occurred, thus resulting in the recording of a lower ear temperature and a still high rectal temperature [47]. In addition, as medication with analgesics is common in elderly individuals and antipyretics are frequently used in febrile patients [130], the low reading may be due to antipyretics affecting the ear temperature while the rectal temperature is still increased. It is striking that medication with analgesics and anti-inflammatory agents with an antipyretic effect [199] is rarely discussed in research involving assessment of body temperature [73].

We found that NHAP was as frequent as CVI and heart failure as a cause of death in elderly nursing-home residents. Consistent with previous research [138, 139, 200], atypical symptoms were common in infected individuals. Non-specific symptoms are also present in a lot of other physical conditions [138], indicating that "something is going on". On the other hand, fever is a cardinal sign of infection, underscoring the importance of observation and evaluation of body temperature in the nursing home setting. In contrast to earlier observations [148, 201, 202], the presence of fever was associated with increased fatality. One explanation may be that a low baseline temperature, atypical symptoms and the fact that fever was not reported until the temperature was $\geq 38^{\circ}\text{C}$ contributed to a delayed diagnosis and antibiotic therapy [120] and, thereby, mortality [151]. In addition, high dependency in ADL was strongly associated with dementia, a low S-albumin and malnutrition, factors that correlate with morbidity and mortality in NHAP [203, 204]. Hence, as a lower baseline body temperature may be related to a lower febrile response [142, 143], there is an increased risk of both acquiring infection and not being assessed as febrile if stipulated thresholds are used. It would be wise to establish the individual baseline body temperature in the morning on admission to the nursing home facility as a basis for assessing fever. In order to manage infections early on in elderly persons [120], further

research is needed to clarify special characteristics of early signs of infection in the geriatric population.

Overall, fragility is related to mortality [152, 155, 160], but the present results explore important differences in predictors of survival in men and women. The decreased survival due to COPD, heart disease and MRIS in men reflects smoking habits [156, 158, 159], and the fact that men in this generation have done harder physical work than women. The negative effect of medication with sedatives on survival in men may indicate confusion in individuals suffering from dementia [161], but also disturbed behaviour associated with frustration, unmet needs and feelings of helplessness [152]. Non-pharmacological interventions, such as bright light during the daytime, physical activity and tactile stimulation have been found to prevent disruptive behaviour and improve the sleep-wake rhythm as effectively as pharmacological treatment in physically impaired and demented persons [205]. Also, psychosocial activities have positive effects on cognitive behaviour by satisfying psychosocial needs for communication, self-esteem, safety and security, personal identity and cognitive understanding [206]. Nocturnal sleep may also enhance the immunological host defence [33].

In women, nutritional status was an important predictor of survival, but, contradicting Lapani et al. [161], malnutrition was related to death irrespective of the cognitive status. Along with the fact that medication with antidepressants was common in women, this may reflect depression and loss of appetite when the ability to perform daily activities decrease. The tendency for malnutrition to influence survival in men can be attributed to loss of appetite due to serious disability, while no correlation between ADL and nutritional status was observed (data shown in paper IV).

Together, the present results indicate that preserving or improving capabilities in daily functioning and preventing malnutrition, agitation and confusion are modifiable factors that would improve survival in nursing-home residents.

Although body temperature was not a predictor of survival, surviving women had a higher baseline body temperature than non-surviving women. No such difference was found in men, thereby contradicting the findings of Roth et al. [162], who observed a relationship between a lower normal body temperature and longevity in men. As a lower baseline body temperature was related to impaired functional and cognitive status, a decline of body temperature might precede death also in humans, as has been reported in animal studies [163]. This interpretation should be considered with caution as body temperature was measured only once, and the deviation was small. Nevertheless, the finding indicates that it would be of interest to further study body temperature as an indicator of survival in aged individuals.

Methodological considerations

A larger, random sample and an interreliability test and documentation of the operator as right or left-handed [47, 111, 197] would have improved the validity and reliability of the measurements in paper II.

Although the sample was not randomly selected, the nursing homes were randomly chosen and the sample studied correspond to nursing home populations in Sweden [207] as well as in other countries [22].

Other infections are of interest, but NHAP was chosen as this is the most serious infection in long-term care facilities [134, 145, 146] and national data on morbidity and mortality from NHAP are lacking. Since a chest radiograph and a blood culture or sputum examination is difficult to perform in the nursing-home setting, a diagnosis based on clinical symptoms is a reasonable approach [149].

One limitation is that the occurrence of pneumonia was partly noted retrospectively and the cause of death was abstracted from death certificates completed by different physicians, with no available data on their validity.

Use of a proxy to assess ADL status is a reliable method for persons showing cognitive decline [208, 209]. Less than 5% (9/237) were assessed as O (other), which shows good reliability [210].

The influence of analgesics on lowering temperature in fever was avoided, as the residents had not received their morning medication when the baseline temperatures were measured. As the presence of infection or trauma was controlled for, the bias with decreased S-albumin because of synthesis of acute-phase proteins was avoided [211].

CONCLUSIONS

The range of body temperatures in healthy adults and non-febrile institutionalised elderly individuals is wider than traditionally asserted. The inter- and intraindividual baseline body temperature varies with age, gender, site of measurement and operator technique.

In elderly nursing-home residents, the baseline temperature is altered due to functional and cognitive impairment, loss of isolating tissue and chronic pain condition.

Body temperature should be evaluated in relation to the normal range characteristic of a specific reference group.

When measuring body temperature, the best approach is to use the unadjusted mode irrespective of the site of measurement, without adjusting to another site. Repeated measurements do not improve the accuracy of ear, oral or axillary temperature readings.

To prevent a delayed diagnosis of pneumonia, one should be aware of a low baseline body temperature and lack of typical symptoms in elderly nursing-home residents.

Preserving and/or improving the functional, cognitive and nutritional status and actions preventing agitation and confusion would improve survival in elderly nursing-home residents.

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