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Urinary tract infection

- a serious health problem in old women

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To my wonderful daughters, Louise and Sofia

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ABSTRACT

Urinary tract infection (UTI) is a common bacterial infection in women of all ages but the incidence and prevalence increase with age. Despite the high incidence of UTI, little is known about its impact on morale or subjective wellbeing and daily life in old women. UTI in older people can be a complex problem in terms of approach to diagnosis, treatment and prevention because in these patients it frequently presents with a range of atypical symptoms such as delirium, gastrointestinal signs and falls. Even if UTI has been shown to be associated with delirium it has frequently been questioned whether UTI can cause delirium or if it is only accidentally detected when people with delirium are assessed.

The main purpose of this thesis was to describe the prevalence of UTI, to identify factors associated with UTI among very old women and to illuminate the impact of a UTI on old women's health and wellbeing.

This thesis is based on two main studies, the GERontological Regional DATabase (GERDA) a cross-sectional, population-based study carried out in the northern parts of Sweden and Finland during 2005-2007 and a qualitative interview study in western Sweden 2008-2009. Data were collected from structured interviews and assessments made during home visits, from medical records, care givers and relatives. UTI was diagnosed if the person had a documented symptomatic UTI, with either short- or long-term ongoing treatment with antibiotics, or symptoms and laboratory tests judged to indicate the presence of UTI by the responsible physician or the assessor.

One hundred and seventeen out of 395 women (29.6%) were diagnosed as having suffered from at least one UTI during the preceding year and 233 of these 395 (60%) had had at least one diagnosed UTI during the preceding 5 years. These old women with UTI were more dependent in their activities of daily living, and had poorer cognition and nutrition. In these women, UTI during the preceding year was associated with vertebral fractures, urinary incontinence, inflammatory rheumatic disease and multi-infarct dementia.

Eighty-seven of 504 women (17.3%), were diagnosed as having a UTI with or without ongoing treatment when they were assessed, and almost half (44.8%) were diagnosed as delirious or having had episodes of delirium during the past month. In all, 137 of the 504 women (27.2%) were delirious or had had episodes of delirium during the past month and 39 (28.5%) of them were diagnosed as having a UTI. Delirium was associated with Alzheimer's disease, multi-infarct dementia, depression, heart failure and UTI.

Forty-six out of 319 women (14.4%) were diagnosed as having had a UTI with or without ongoing treatment and these had a significantly lower score

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on the Philadelphia Geriatric Center Morale Scale (PGCMS), (10.4 vs 11.9, $p=0.003$) than those without UTI, indicating a significant impact on morale or subjective wellbeing among very old women. The medical diagnoses significantly and independently associated with low morale were depression, UTI and constipation.

The experience of suffering from repeated UTI was described in interviews conducted with 20 old women. The interviews were analysed using qualitative content analysis. The participants described living with repeated UTI as being in a state of manageable suffering and being dependent on alleviation. Being in a state of manageable suffering was described in terms of experiencing physical and psychological inconveniences, struggling to deal with the illness and being restricted regarding daily life. Being dependent on alleviation was illustrated in terms of having access to relief but also experiencing receiving inadequate care.

In conclusion, UTI is very common among old and very old women and is a serious health problem. UTI seems to be associated with delirium and to have a significant impact on the morale or subjective wellbeing of old women and those affected suffer both physically and psychologically and their social life is limited. UTI was also associated with vertebral fractures, urinary incontinence, inflammatory rheumatic disease and multi-infarct dementia which might raise the suspicion that UTI can have serious medical effects on health in old women.

Key words: urinary tract infection, old women, risk factors, delirium, experience, nursing

SVENSK SAMMANFATTNING (SUMMARY IN SWEDISH)

Urinvägsinfektion (UVI) är en vanlig bakteriell infektion bland kvinnor i alla åldrar men förekomsten ökar med stigande ålder. Trots den höga förekomsten av UVI är inte mycket känt om dess betydelse för subjektivt välbefinnande (*morale**) och hur en UVI kan påverka det dagliga livet hos gamla kvinnor. UVI hos gamla människor kan vara komplicerat att diagnostisera, behandla och förebygga då de ofta uppvisar mer atypiska symtom som t ex delirium, symtom från mag-tarmkanalen och fall. Även om tidigare forskning har visat att UVI är associerat med delirium så ifrågasätts det ofta om UVI kan orsaka delirium eller om det bara råkar upptäckas när personer med delirium undersöks.

Det övergripande syftet med avhandlingen var att beskriva förekomsten av UVI och identifiera faktorer associerade med UVI hos mycket gamla kvinnor samt att belysa betydelsen UVI har för hälsa och välbefinnande hos gamla kvinnor.

Avhandlingen utgår från två huvudstudier, Gerontologisk Regional Databas (GERDA), som är en populationsbaserad studie av mycket gamla människor i norra Sverige och Finland under 2005-2007 samt en kvalitativ intervjustudie utförd i västra Sverige under 2008-2009. UVI diagnostiserades om personen hade en dokumenterad, symtomatisk UVI, med eller utan pågående kort- eller långtidsbehandling med antibiotika, eller symtom och laboratorietest bedömt som UVI av ansvarig läkare eller undersökare.

Etthundrasjutton av 395 kvinnor (29.6%) hade haft minst en diagnostiserad UVI under det senaste året och 233 av dessa 395 kvinnor (60%) hade haft minst en diagnostiserad UVI under de senaste 5 åren. Dessa gamla kvinnor med UVI var mer beroende i aktiviteter i det dagliga livet, hade sämre kognition och nutritionstillstånd. UVI under det senaste året var bland dessa kvinnor associerat med kotkompression, urininkontinens, inflammatorisk reumatisk sjukdom och multi-infarkt demens.

Åttiosju av 504 kvinnor (17.3%) hade en diagnostiserad UVI med eller utan pågående behandling när de undersöktes och nästan hälften av dem (44.8%) var deliriösa eller hade haft episoder av delirium under den senaste månaden. Etthundratrettiosju av 504 kvinnor (27.2%) var deliriösa eller hade haft episoder av delirium under den senaste månaden och 39 (28.5%) hade en diagnostiserad UVI. Delirium var associerat med Alzheimer's demens, multi-infarkt demens, depression, hjärtsvikt och UVI.

Fyrtiosex av 319 kvinnor (14.4%) hade en diagnostiserad UVI med eller utan pågående behandling och dessa kvinnor hade signifikant lägre poäng på Philadelphia Geriatric Center Morale Scale (PGCMS), (10.4 vs 11.9,

p=0.003) jämfört med dem som inte hade UVI vilket tyder på en signifikant påverkan på morale eller subjektivt välbefinnande bland dessa mycket gamla kvinnor. De medicinska diagnoser som var signifikant oberoende associerat med lågt subjektivt välbefinnande var depression, UVI och förstoppning.

Upplevelsen av att lida av upprepade UVI:er beskrevs i intervjuer genomförda med 20 gamla kvinnor. Intervjuerna analyserades med hjälp av en kvalitativ innehållsanalys. Upplevelsen av att leva med upprepad UVI beskrevs som att vara i ett hanterbart lidande samt att vara beroende av lindring. Vara i ett hanterbart lidande beskrevs som att uppleva fysiska och psykiska besvär, kämpa för att hantera sjukdomen samt att vara begränsad i sitt dagliga liv. Vara beroende av lindring beskrevs i termer av att ha tillgång till lindring av besvären men också upplevelser av att de fått bristfällig vård.

Sammanfattningsvis visar avhandlingen att UVI är mycket vanligt hos gamla och mycket gamla kvinnor samt att UVI är ett allvarligt hälsoproblem. UVI verkar vara associerat med delirium samt signifikant påverka subjektivt välbefinnande hos gamla kvinnor och de som upplevde upprepade UVI:er påverkades både fysiskt och psykiskt och deras sociala liv var begränsat. UVI var också associerat med kotkompression, urininkontinens, inflammatorisk reumatisk sjukdom samt multi-infarkt demens vilket gör att man måste misstänka att UVI kan ha allvarliga medicinska hälsoeffekter bland gamla kvinnor.

**Morale*, som är ett engelskt begrepp utan svensk översättning, definieras på engelska som "a basic sense of satisfaction with oneself, a feeling that there is a place in the environment for oneself, and a certain acceptance of what cannot be changed". Ordet ersätts i denna svenska översättning med subjektivt välbefinnande.

ABBREVIATIONS

ADL	Activities of Daily Living
ASB	Asymptomatic Bacteriuria
BMI	Body Mass Index
CAM	Confusion Assessment Method
CFU	Colony-Forming Unit
CI	Confidence Interval
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4 th edition
GERDA	Gerontological Regional DAtabase
GDS-15	Geriatric Depression Scale (15-item version)
IUC	Indwelling Urinary Catheter
M	Mean value
MADRS	Montgomery-Åsberg Depression Rating Scale
MID	Multi-Infarct Dementia
MMSE	Mini-Mental State Examination
MNA	Mini Nutritional Assessment
OBS	Organic Brain Syndrome (scale)
OR	Odds Ratio
P-ADL	Personal Activities of Daily Living
PGCMS	Philadelphia Geriatric Center Morale Scale
RA	Rheumatoid Arthritis
SD	Standard Deviation
SLE	Systemic Lupus Erythematosus
STRAMA	Swedish Strategic Programme Against Antibiotic Resistance
UI	Urinary Incontinence
UTI	Urinary Tract Infection
WHOQOL	World Health Organization Quality of Life assessment

ORIGINAL PAPERS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

- I. Eriksson, I, Gustafson, Y, Fagerström, L, Olofsson, B. Prevalence and factors associated with urinary tract infections (UTIs) in very old women. *Archives of Gerontology and Geriatrics*. 2010; 50: 132-135.
- II. Eriksson, I, Gustafson, Y, Fagerström, L, Olofsson, B. Urinary tract infection in very old women is associated with delirium. *International Psychogeriatrics*. 2011; 23(3): 496-502.
- III. Eriksson, I, Gustafson, Y, Fagerström, L, Olofsson, B. Do urinary tract infections affect morale among very old women? *Health and Quality of Life Outcomes*. 2010; Jul 22; 8:73.
- IV. Eriksson, I, Olofsson, B, Gustafson, Y, Fagerström, L. Older women's experiences of suffering from urinary tract infections. Submitted.

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INTRODUCTION

With increasing age the prevalence of urinary tract infection (UTI) increases in both women and men ^{1, 2}. However, it seems that UTI is more common among women and when an old woman suffers from a UTI it might often be regarded as a harmless and banal condition while in men, in contrast, the suggestion is that it should be carefully assessed and followed up ^{3, 4}. Old women suffering from symptoms of UTI are common throughout the healthcare system; in primary healthcare, in nursing homes, in hospitals and among those living in their own homes. In primary healthcare and as a district nurse, I have often met these women. My clinical experience is that these old women's problems are often regarded as trivial, both by the general practitioners and the districts nurses. These old women can get an appointment at the healthcare centre, at least with a district nurse rather quickly. If they have a positive nitrite stick they are given their treatment but are then sent home. If they suffer from a new UTI the procedure will be repeated with no investigation of the underlying causes. This could be because these women's inconvenience is not taken so seriously by the caregivers, who may not understand how much the symptoms affect these old women. Seldom is a thorough investigation made of why UTI occurs and of the underlying causes that may exist. It might be possible to prevent UTI instead of just treating it with antibiotics if the caregivers increase their knowledge about why UTI occurs and the underlying causes. Despite UTI being very common, the knowledge about how it affects old women is poorly investigated and previous research in relation to UTI has focused mainly on younger women. Hopefully, this thesis will contribute to increasing knowledge about how common UTI is, the factors associated with UTI and an improved understanding of the impact UTI has on old women's health and wellbeing, in order to improve the care.

DEMOGRAPHICS

Old and very old people are a fast growing age group. In Sweden, older people are commonly defined as those aged 65 years and older and the very old as aged 80 years or older. Sweden has a population of approximately 9.4 million, 1.7 million of whom (18%) are aged 65 years or older. Of these people, 494 000 (29%) are 80 years or older ⁵. It is estimated that the proportion of 80-year-olds or older will increase even more over the next two decades and in twenty years they will number almost 800 000. Simultaneously, during this period, the average length of life is expected to increase, by about 5 years for men and 3.5 years for women. Today, the average length of life for men is 79.5 year and for women 83.4 year ⁵.

AGING AND HEALTH

Growing old implies effects on the human body, biologically, psychologically and socially but variations in the rapidity of the aging process are individual. Although there is variability in health status among old people, increased age is associated with a decline in physical ability and cognitive function and also with the prevalence of several acute and chronic diseases ⁶. The combination of aging and the increased probability of diseases results sooner or later in health problems for the majority of old people.

Common conditions among the very old are impaired vision and hearing, sleeping disturbance, malnutrition ⁶ and impaired cognition ⁷. Diagnoses such as stroke, hypertension, dementia, heart failure, depression ⁶ and infections ⁸ are also common in very old people. Falls and fractures, especially hip fractures, and osteoporosis are also major health problems in the very old and themselves cause increased morbidity and mortality ⁹⁻¹². Other common conditions among the very old are autoimmune diseases and systemic inflammatory diseases such as rheumatic diseases ¹³.

Although growing old is often associated with declining functions, losses and diseases, aging can still have positive aspects. A good aging is often described using synonymous concepts such as healthy aging, active aging and successful aging and includes physical, psychological, social and spiritual components of life ¹⁴. Previous research has shown that despite the presence of disease, old people still can rate their health as good and women rate their health as being as good as that of men even though old women have a higher prevalence of diseases and symptoms ⁶.

The aging woman

Old women often have a complex health situation with several diseases. They live longer than men and have more years with diseases. These women suffer more often than men from dementia, rheumatic disease, osteoporosis, vertebral fracture, malnutrition, depression, UTI, hip fracture and often take a large number of prescribed drugs ^{6, 15-17}. One way to describe this complex health situation is by using the concept of frailty. The above age-related diseases and conditions are regarded to linked to frailty which is a multi-dimensional geriatric syndrome ¹⁸. Age-changes are accompanied by a reduced reserve capacity and an increased sensitivity to stress, especially in relation to a disease ¹⁹. Many of these old women are frail ²⁰⁻²³ and generally vulnerable to diseases which means that an apparently banal condition in a frail person can have very serious consequences ¹⁹. Infections are an example of this as there is an age-related dysfunction of the immune system ²⁴.

The immune system and aging

Aging changes the immune system which means that cytokine release increases and the anti-inflammatory feed-back system declines ²⁵. The increase in chronic inflammation with age contributes to a host of physiological, psychological and behavioural changes and during the inflammatory response the body undergoes a cascade of metabolic and behavioural changes. These changes, called sickness behaviour, include such symptoms as fatigue, increased sleep, reduced appetite, anhedonia, malaise, weakness and depression. This syndrome can develop in sick individuals during the course of an infection ²⁶ with cytokines such as interleukin-6 (IL-6) and IL-1 β as possible primary agents in the development. With increased age, the balance between proinflammatory and anti-inflammatory cytokines shifts towards a proinflammatory state, which means that the proinflammatory cytokines (e.g. IL-6) increase and the levels of anti-inflammatory mediators such as IL-10 decrease. This state, therefore, makes the aged brain more vulnerable to diseases, infections or stress ²⁵. Changes in the aging immune system contribute an age-related increase in autoimmune diseases such as rheumatic diseases as well as systemic lupus erythematosus (SLE) which can affect the brain ²⁷.

URINARY TRACT INFECTION

UTI is one of the most common bacterial infections in women of all ages and the incidence and prevalence increase with age. More than half of all women have at least one UTI in their lifetime and the risk of contracting a UTI increases in postmenopausal women ²⁸⁻³⁰. Among healthy non-institutionalized old women UTI is the most common infection ³¹⁻³³ and in residents of long-term care facilities UTI is even more common ³⁴. UTI is more common among old women because of a variety of anatomic and functional changes which arise with aging, such as hormonal changes, reduced uromucoid secretions, decreased renal ability and increased bacterial adherence to uroepithelial cells ³⁵. Hormonal changes, such as decreased oestrogen may contribute to increased UTI prevalence in older women ³⁶. Reduced uromucoid secretions may contribute to a decreased antibacterial activity and reduced renal ability to excrete acid and urea, which in turn may increase the bacterial colonization of the bladder ³⁵. Several other factors contribute to the high occurrence of UTI among the old, such as incomplete bladder emptying, previous stroke, the presence of a indwelling urinary catheter (IUC) and a history of UTI at younger ages ^{36, 37}. Important contributory factors among those living in institutions are those which reduce functional status and cognition due to comorbidity as a result of e.g. dementia or stroke, and such diseases are often accompanied by a neurogenic bladder ³⁸. In combination with reduced functional status and cognition there could be changes in personal hygiene which may promote

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UTI³⁹. An impaired immune system can be regarded as a contributory factor to UTI and one of the most important causes of decreased function of the immune system is malnutrition which is common among old people and leads to a major risk of infections²⁴.

For symptomatic UTI, $\geq 10^5$ colony-forming units (CFU)/ml is one of the most common diagnostic standards⁴⁰ but this limit for significant bacteriuria has gradually been reduced and revised for different situations. It has been proposed that the finding of $\geq 10^3$ CFU/ml of urine defines significant bacteriuria in acute, uncomplicated UTI⁴¹ and in some cases even $\geq 10^2$ CFU/ml^{40, 42}. One of the most common pathogens is *Escherichia coli* followed by *Staphylococcus saprophyticus*⁴⁰. Other common pathogens which are seen frequently especially in older women are *Proteus mirabilis*, *Klebsiella pneumoniae* and *Enterobacter*^{35, 40, 43}.

In connection with UTI, the most common presenting urinary symptoms are frequency, urgency, pain or burning during urination, suprapubic discomfort and inability to empty the bladder completely^{38, 44}. Older patients with UTI often present a more atypical range of symptoms such as delirium, gastrointestinal signs and common urinary symptoms such as urinary incontinence (UI) are often present both before and during the UTI^{30, 45, 46}. Increased risk of falling has been shown to be associated with UTI among old people, especially among those with dementia^{10, 47, 48}. Some general symptoms, such as tiredness and irritability, have also been reported from previous studies both among younger and older women^{49, 50}.

The detection, diagnosis and treatment of UTI among older women is more complex due to the more atypical symptoms, possibly multiple underlying causes and frailty and there is a lack of knowledge about treatment specifically addressed to UTI among the old^{30, 43}. The treatment of UTI can lead to the development of bacteria resistance against antibiotics and in Sweden STRAMA⁴² has written guidelines for the treatment of UTI aimed at improving the quality of treatment and reducing resistance. In Sweden, the indication for antibiotic treatment of women according to STRAMA⁴², is symptoms of UTI and a positive nitrite stick or urinary culture. Alternation of the first choice antibiotics, which are nitrofurantoin or pivmecillinam, is recommended. The second choice antibiotics are cephalosporins or trimethoprim while fluoroquinolones such as ciprofloxacin are only recommended in cases of complicated UTI, recurrent UTIs and failure of therapy⁴². Treatment guidelines in other countries may differ slightly since it is more common to use fluoroquinolones such as ciprofloxacin and norfloxacin abroad^{30, 51}.

In addition to adequate treatment of UTI, any underlying causes might need to be identified. According to STRAMA⁴², a follow-up is not recommended for an uncomplicated, sporadic UTI. Women with recurrent UTI, i.e. at least two documented UTIs in the preceding half year or more

than three in the preceding year, should be given a gynaecological examination. An atrophic mucosa or cystocele could cause relapse and lead to impaired bladder emptying. Surgery is possible in women with cystocele thus preventing UTI. Women with abnormal or unclear gynaecological status should be referred to a gynaecologist. The prevention of UTI focuses mainly on local oestrogen therapy and sometimes on long-term treatment with nitrofurantoin or trimethoprim. As an alternative, metenaminhippurat is occasionally used, but its effect has not been scientifically documented⁴². Prevention also means that IUC should be avoided as far as possible as they are an accessible pathway for bacteria^{39, 52}. Dehydration can be a risk factor for UTI and should be prevented by providing adequate fluid intake which increases urine output and acts as a washing mechanism for the bladder^{39, 53, 54}. Patients with recurrent UTIs should also be taught to empty the bladder regularly and completely and it is important to detect and treat urinary retention to reduce the risk of developing a UTI^{39, 42, 54}. Hygiene advice is also important for these patients covering personal hygiene after urination or defecation and avoiding products that are irritating to the genital area^{39, 53, 54}. The use of tannic beverages such as cranberry juice for the prevention of UTI has been proposed but the scientific evidence of its effect is contradictory. Some studies suggest that a daily ingestion of cranberry juice is effective in reducing the number of UTIs in women^{55, 56} while another study found it had no preventive effect⁵⁷. The hypothesis concerning the mechanism behind tannins is that they may act by inhibiting the adhesion of some uropathogenic strains of *Escherichia Coli* to uroepithelial cells⁵⁸.

Urinary tract infection and malnutrition

Malnutrition contributes to adverse metabolic events that compromise the immune system and increase susceptibility to infections⁵⁹ and it is associated with poor health-related quality of life⁶⁰. One previous study has shown that malnutrition was not associated with UTI among patients living in nursing homes⁶¹ while another study found an association between malnutrition and UTI among patients in hospital care⁶². Whether or not malnutrition is a risk factor for UTI, it is important to detect, prevent and treat malnutrition among old people in order to reduce the risk of illnesses in old age such as UTI.

Asymptomatic bacteriuria

Asymptomatic bacteriuria can be abbreviated both as ASB and ABU but ASB was chosen for use in this thesis. ASB is a common finding, both in community-dwelling and in institutionalized old women⁶³. Factors which might precipitate ASB are multiple comorbid chronic diseases, age-related changes in urologic function and interventions to manage urinary incontinence³⁴. A recommended standard for diagnosis of ASB in women is

two consecutive voided specimens with the isolation of $\geq 10^5$ colony-forming units (CFU)/mL of the same organism^{41, 64}. Generally, treatment of ASB is not recommended among the old since previous research has found that treatment does not reduce the number of symptomatic episodes or the prevalence of bacteriuria⁶⁵. Distinguishing between ASB and UTI can be difficult among the old because of impaired cognition and functional impairment which means that they may have minimal or atypical symptoms of UTI⁶⁶. One important unanswered question is why ASB does not produce local symptoms and one explanation could be that the immune system does not react to the bacteria. This could indicate that the ASB is not less harmful despite the lack of symptoms since it occurs in a person with an impaired immune system. A large proportion of old people are treated with analgesics and anti-inflammatory drugs which could mask the local symptoms. The distinction between these two conditions may also be difficult because the old women frequently present with certain acute comorbidities simultaneously such as acute pulmonary disease⁶⁷.

RISK FACTORS AND ASSOCIATED FACTORS FOR UTI

A number of risk factors for and factors associated with UTI have been described in previous research. The distinction between these two is still not clear. Likewise, various factors may promote UTI and will vary in importance for different individuals³⁷ and also vary over the course of a person's life²⁹. Risk factors may differ among old women and younger women but they may also differ depending on whether or not the old women live in an institution.

It has been suggested that risk factors for UTI can be categorized as anatomic and physiologic, genetic and behavioural. Anatomical and physiological anomalies, which restrain the flow of urine, delay bladder emptying or cause an increased post-void residual volume, seem to be risk factors for UTI²⁹. Such anomalies can be cystoceles, rectoceles and bladder diverticula^{29, 37}. UI is also a suggested risk factor for UTI^{68, 69} but how UI predisposes women to UTI is not entirely clear⁷⁰. Since UTI and UI are both frequent postmenopausal conditions they might be partly explained by reduced levels of oestrogen⁷¹. Another contributory physiological factor has been reported to be the effect of loss of the oestrogen on the genitourinary mucosa which can lead to fragile mucous membranes³⁷. Genetic risk factor means that some women seem to have a genetic predisposition to UTI with a history of recurrent UTI and a maternal history of UTI. Interleukin-8, an inflammatory cytokine, is another factor with genetic variability, that may influence the development of UTI²⁹ and both urinary immunoreactive interleukin-1 and interleukin-6 have been measured more frequently in the urine in bacteriuric than in non-bacteriuric institutionalized old persons⁷².

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Behavioural factors, such as sexual activity, are suggested as an important risk factor for UTI in women of all ages ^{29, 68}.

It seems that the most important associated factors for UTI vary between women living in the community and those living in institutions. Studies have shown that the most common characteristics predisposing older institutionalized women to UTI are advancing age, diabetes, urologic abnormalities, debilitating comorbid conditions, functional impairment and IUC ^{29, 30, 37}. Comorbid conditions seem to have a greater impact on contracting a UTI among old women living in institutions than those living in the community. One explanation could be that in these institutions diseases such as Alzheimer's, Parkinson's and cerebrovascular disease are common and that these diseases may be associated with impaired bladder control. This leads to impaired voiding, increased residual urine volumes and sometimes ureteric reflux ³⁷. However, studies regarding the association between residual urine and UTI have produced conflicting results, although it is generally assumed that residual urine is a risk factor for UTI because it creates a favourable environment for bacteria ^{29, 73}. A previous study has found that the use of diapers is a risk factor for UTI in old hospitalized persons ⁷⁴. There is also a relationship between urinary stones and UTIs and these types of infections stones are often caused by urease-producing gram-negative organisms ⁷⁵.

Among old women living in the community, UTI is associated with diabetes ⁶⁸, hip fracture surgery ⁷⁶ and delirium ⁴⁵. Pharmacologically treated diabetes has been found to be associated with a higher risk of UTI in a study by Hu et al ⁶⁸ but there was no increased risk of UTI among those women with diabetes who did not receive pharmacological treatment. The production of glycosuria seems to provide a better culture medium for bacterial colonization and diabetic persons may be more susceptible to infection because of immunologic impairments ⁷⁷. Little seems to be known about pharmacological treatment with cortisone and the risk of getting a UTI but in an animal study it was found that cortisone increased the risk of intracellular colonization by common bacterial strains ⁷⁸.

UTI is associated with hip fracture surgery among old women ⁷⁶ and with fractures in general ⁷⁹. However, it is not clear if this association is a result of reduced oestrogen levels or of the general ageing process ⁷⁹. The importance of oestrogen supplementation in the prevention of recurrent UTIs still seems to be unclear and studies have reported conflicting results ^{68, 80, 81}. The relationship between UTI and hip fractures may also depend on or be associated with malnutrition, dementia and polypharmacy. Those who suffer from a hip fracture often have dementia, are malnourished and suffer from a UTI preoperatively ^{82, 83} but also postoperatively because they have been catheterized ⁸⁴. UTI might also increase the risk of falls and fractures ^{10, 47}.

INTRODUCTION

Previous studies have shown that UTI is associated with delirium but the explanatory mechanisms behind this association are still rather unclear^{45, 46}. A previous study has shown that in 64% of the participants in a psychogeriatric unit delirium has reversed with appropriate treatment of UTI⁴⁶. Another study found that delirium were more common in patients with UTI than in those with ASB. The authors also suggest that in older patients exhibiting delirium or change in mental status UTI should be excluded⁶⁷.

Risk factors for UTI among young healthy women and among older, debilitated women living in institution are rather well described in the literature^{29, 30}. But, there has not been so much focus on risk factors for UTI among generally healthy community-dwelling postmenopausal women or very old people. A study by Hu et al which included women aged between 55-75 years, found the same risk factors for UTI among younger, postmenopausal women as among older, debilitated women⁶⁸. Contradictory results have shown that factors predisposing to UTI in postmenopausal women differ from those in premenopausal women, but that study focused on recurrent UTIs⁷⁰.

To summarize, predisposing factors for UTI can differ depending on age, living in the community or living in an institution. Few studies have included both institutionalized and home-dwelling old women, especially among the very old. The lack of clarity between what constitute risk factors and what are associated factors, regarding age and living in an institution or not, means that additional research is needed.

Urinary incontinence

UI, which is one of the most common associated factors with UTI, is a symptom frequently presented among old women^{31, 85, 86}. The prevalence of UI is estimated to be 15-43% among community-dwelling old women and at least 50% among those living in residential care⁸⁶⁻⁸⁸. Women also seem to be more likely to be incontinent if they have had a hysterectomy, suffer from diabetes or are limited in activities of daily living⁶⁹. UI is regarded as a geriatric condition that can involve several interacting factors but it is not caused by aging alone and should rather be considered as a symptom. It is suggested that age-related changes, such as reduced oestrogen levels, contribute to UI⁶⁶. The view that UI is a natural part of aging may mean that these women are not receiving adequate treatment⁸⁷. UI is defined as an involuntarily loss of urine sufficient in amount or frequency to be a social or hygienic problem that effects both physical health and psychosocial wellbeing⁶⁶. UI is usually classified into two basic types, acute and persistent UI. Acute UI is often associated with an acute or subacute medical condition and with potentially reversible factors such as delirium, urinary retention, UTI and heart failure. Persistent UI is classified into four basic

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types, stress UI, urge UI, overflow UI and functional UI. However, the potentially reversible factors associated with acute UI may contribute to persistent forms of UI ⁶⁶. Other factors associated with UI are dementia, physical impairments, falls, BMI, constipation, stroke and diabetes ^{69, 85}. Some studies describe UI as a risk factor for UTI ^{68, 69} while other studies express the view that UI is associated with UTI ^{31, 70}. The symptoms of UI and UTI are similar and often occur simultaneously which may make it difficult to separate them ³⁰. Thus, the relationship between UI and UTI remains quite unclear.

DELIRIUM

It has been suggested that UTI is associated with delirium but the scientific evidences for this is limited. It has been reported that one of the most common infections associated with delirium are UTIs, 40% in a frail in-hospital geriatric population with diagnosed delirium were shown to have UTI ⁴⁵.

Delirium is a common syndrome among older patients and a frequent presenting symptom in relation to acute illness ⁸⁹. The prevalence of delirium among the old varies depending on the clinical setting, e.g. in hospital care, in nursing homes or in old people's homes ⁹⁰⁻⁹². The prevalence of delirium has been reported to be 45.9% in emergency hospital care, 57.9% in nursing homes, 35.2% in old people's homes and 34.5% in home medical care ⁹². Delirium is very common among the old in relation to surgery. Delirium occurred in 62% of patients treated for femoral neck fractures ⁸² and in 20-40 % of patients undergoing cardiac surgery ^{93, 94}.

Delirium, according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM -IV)* ⁹⁵ is defined as an acute disorder concerning cognition, perception and attention. A delirium develops over a short period of time, fluctuates during the course of the day and always has an underlying cause.

Delirium is associated with longer hospital stays, increased mortality and has a negative impact on health outcomes ⁹⁶⁻⁹⁸. Risk factors for delirium can be divided in to predisposing and precipitating factors. Predisposing factors in delirium, apart from age, are male sex, earlier stroke, dementia, depression, impaired vision, functional dependence and fractures ^{45, 99, 100}. Precipitating factors in delirium are infections, adverse metabolic events, cardiovascular events, pain, anaemia, orthopaedic surgery and adverse drug effects ^{45, 101, 102}.

The pathogenesis of delirium remains unclear but cholinergic deficiency emerges as having an important role ¹⁰³. Other hypotheses include dopamine excess, inflammation and chronic stress. Deficiency or disturbed acetylcholine metabolism is considered a central mechanism ¹⁰⁴ and impairments in global metabolism, cytokine interactions and

neurotransmitters are also regarded as mechanisms that contribute to delirium^{103, 105}. Different environmental and medical stressors activate the immune system and stimulate cytokine release¹⁰⁶. The hypothesis concerning cytokines is that they mediate inflammatory and immune responses to stress, which may increase the risk of delirium¹⁰⁷. Cytokines may also lead to cholinergic deficits and the inflammatory processes may also play an important role in the pathogenesis of Alzheimer's disease¹⁰⁸.

One of the most common disorders to consider in the differential diagnostics of delirium is dementia for, although dementia and delirium are distinct clinical syndromes they share pathogenic mechanisms¹⁰⁹. Another common differential diagnosis of delirium is depression. Depression is characterized by reduced neuro-transmitter levels in the brain, which might increase the risk of developing delirium⁸⁹. To distinguish delirium from dementia can be difficult and delirium is, therefore, often under-diagnosed and undetected¹¹⁰. Thus, when old people undergo acute changes in behaviour or cognition it is important to consider delirium⁹⁹. Patients who have been delirious often describe the situation as very awful and frightening¹¹¹⁻¹¹³. They describe situations they had experienced during the delirious episode as very real and often depict them in detail¹¹¹. The patients also describe their experiences as if they were dreaming but were at the same time awake^{111, 113}. It is also common for them to see different things, frightening as well as pleasurable. After the delirium the patients often experiences feelings of fear, discomfort, remorse and relief¹¹¹.

To avoid unnecessary suffering, it is important to detect, prevent and treat delirium among old people. Nurses play a central role in this work. The implementation of interdisciplinary nurse-led programs has shown that delirium can be detected and treated more quickly among patients with hip fractures¹¹⁴. Good geriatric competence in combination with intervention programs reduced the severity and duration of delirium¹¹⁵. Previous intervention studies have shown that postoperative delirium can be successfully prevented and treated, resulting in a shorter hospitalization and fewer complications^{116, 117}. Because of the patients' experiences of fear, caregivers must consider the importance of a trusting and caring relationship and give the patients an opportunity to talk about their experiences when delirious. This gives the caregivers a chance to explain what may have caused the delirium¹¹³. A multifactorial, multi-professional, postoperative intervention program for patients with hip fractures resulted in a reduced incidence and duration of delirium. The patients in the intervention group suffered from fever UTI which might have contributed to the effect of the intervention program¹¹⁷.

DEPRESSION

There is also an association between the immune system and depression, where a dysfunction of the immune system or immunological activation has been found in depressed patients ¹¹⁸. It has been suggested that depression can be regarded as an inflammatory disease with an increased production of interleukin-1 β (IL-1 β), IL-6 and tumor necrosis factor- α (TNF α) but the key factor in depression is suggested to be the cell-mediated immune activation with T cells and T helper (Th)-1-like cells ¹¹⁹. Depression is also associated with hypercortisolism which might impair the immune system ^{118, 120} and this might increase the risk of contracting infections. The immune activation has been interpreted as a reflection of the unspecific stress perceived by patients due to an acute illness ¹¹⁸. Cortisol is considered to affect the brain and it has been found that approximately half of all patients with major depression have increased levels of cortisol in plasma, urine and cerebrospinal fluid ¹²¹. It has been suggested that an activation of immune responses and the release of inflammatory cytokines might play a role in the pathophysiology of major depression. An underlying mechanism is considered to be that cytokines affect the glucocorticoid receptor in the brain ¹²⁰.

MORALE

Various concepts, such as quality of life, life satisfaction, subjective or psychological wellbeing and morale are often used synonymously in the literature ¹²². Morale, or subjective wellbeing, which was chosen for use in this thesis, is defined by Lawton as a basic sense of satisfaction with oneself, a feeling that there is a place in the environment for oneself, and a certain acceptance of what cannot be changed ¹²³. Those with high morale are often active, sociable and optimistic in their attitudes but these attributes are not essential components of high morale. People can still have high morale even if their philosophy of life is pessimistic and if they are inactive and solitary. Morale has been reported to be influenced by various medical conditions such as diabetes, stroke, depression, Parkinson's disease and heart failure ¹²⁴⁻¹²⁶. Morale can be influenced by depression but it is not known whether low morale is a predictor of depression or depression is a predictor of low morale ^{125, 126}.

Lawton ¹²³ developed the Philadelphia Geriatric Center Morale Scale (PGCMS) to assess morale or subjective wellbeing among old people. It includes components such as agitation, attitude toward one's own aging and lonely dissatisfaction. The component agitation contains symptoms of anxiety and dysphoric mood elements. The component attitudes towards one's own aging is associated with a change you experience yourself during aging but can be influenced to some extent by stereotypic attitudes toward aging present in the society. The component lonely dissatisfaction suggests

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acceptance or dissatisfaction with things as they are now ¹²³. The PGCMS has been analyzed by Ranzijn and Luszcz ¹²² in order to identify the core components of wellbeing contained in the scale and they believe that it contains factors with both positive and negative affect. The present study considers that the components agitation and lonely dissatisfaction seem to reflect ill-being whereas the component attitude towards own aging rather reflects wellbeing. Ranzijn and Luszcz ¹²² suggest that psychological wellbeing has as its core positive and negative affect, which most wellbeing scales can be regarded as containing today.

Sullivan ¹²⁷ considers that debates about what is normal aging and what is abnormal are relevant because morale in aging may be tied to what one thinks is normal versus abnormal aging. This means that morale may be more directly related to subjective age and health rather than objective health and age. Aging is often presented as a negative concept that implies loss and decline and that an aging population will carry an increased burden of chronic diseases that cannot be cured. This has to be dealt with and morale has to be seen as important in this context. The type of health problems an individual experiences may influence how their morale is affected. Health problems that affect morale most adversely are those that cannot be coherently incorporated into a life story. Diseases such as arthritis and diabetes appear to be coped with better than e.g. bladder trouble and difficulty walking, due to obscurity regarding treatment and causes ¹²⁷.

Another concept, quality of life, is multidimensional and might be difficult to define faced with the lack of a consensual definition. Subjective indicators, however, such as sense of wellbeing and satisfaction with life can describe the concept. The World Health Organization Quality of Life Group (WHOQOL) ¹²⁸ defined quality of life as the "individual's perception of their position in life in the context of the culture and value systems in which they live and with regard to their goals, expectations, standards and concerns" (p. 1403). Quality of life includes at a minimum physical, psychological and social dimensions. The physical dimension describes the individual's perception of their physical state, the psychological dimension as the individual's perception of their cognitive and affective states and the social dimension describes the individual's perception of the interpersonal relationships and social roles in their life ¹²⁸. Most researchers appear to agree that quality of life should be broadly defined and include both objective and subjective components ¹²². Consensus on concept has been particularly difficult to obtain because of the definition of psychological wellbeing. Lawton ¹²⁹ considers that quality of life has two domain-specific indicators, objective and subjective indicators and that these two have a joint influence on psychological wellbeing. Furthermore he believes that both psychological wellbeing and perceived quality of life are evaluations that

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refer to the quality of inner experience and that together they may be denoted as subjective wellbeing ¹³⁰.

It is important to measure morale or wellbeing but it could be difficult among very old people because of cognitive impairment. For younger individuals, however, there are well-developed and validated scales. When the scales for old people were screened it was considered that the Philadelphia Geriatric Center Morale Scale (PGCMS), developed by Lawton, was appropriate for measuring morale or subjective wellbeing in old people ^{123, 131}, in both those in the community and those in institutions and also among those with mild to moderate cognitive impairment. The PGCMS is designed for old people and includes other dimensions than scales used for younger people making it easier to use in this old population. The questions are easy to understand and are in a yes/no format ¹³¹.

RATIONALE FOR THIS THESIS

UTI is a common bacterial infection in women of all ages but the prevalence increases with increased age. Well-known associated factors and risk factors for UTI, such as urinary incontinence, diabetes, sexual activity, a prior history of UTI, urinary retention and oestrogen deficiency have been described in previous research. Nevertheless, there could be other risk factors among the very old that are important but the research has not been focused on this age group. Thus, it remain to some extent unknown whether other states, conditions and factors, predisposing as well as precipitating factors, are associated with UTI among very old women. Delirium is a common condition in old age and it has been suggested UTI causes delirium but the scientific evidence is limited and has been questioned. Traditionally, an uncomplicated UTI in women is regarded as a somewhat banal, benign and self-limiting condition but there is little research into how old women experience their health and wellbeing in relation to UTI. It is important to be aware that old women might present more atypical symptoms of UTI which may complicate the detection of UTI and delay treatment. Despite the fact that UTI is considered a relatively banal condition, at least among younger women, the consequences might be more serious among the very old and may affect their health physically, psychologically and socially to a greater extent. It is important to generate increased knowledge and a deeper understanding of UTI and its associated factors and how old women's health and wellbeing is affected in relation to UTI for the purpose of promoting a good old age.

AIMS OF THIS THESIS

The overall aim of this thesis was to describe the prevalence of UTI, to identify factors associated with UTI among very old women and to illuminate UTIs impact on old women's health and wellbeing.

Specific aims

- Paper I** To describe the prevalence of UTI among very old women and to investigate those factors associated with it.
- Paper II** To investigate whether UTI in very old women is associated with delirium.
- Paper III** To explore whether a diagnosed symptomatic UTI, with or without ongoing treatment, had any impact on morale or subjective wellbeing among very old women.
- Paper IV** To illuminate old women's experiences of having suffered from repeated UTIs.

METHODS

This thesis is based on two main studies, the GERontological Regional DAtabase (GERDA) study and a qualitative interview study. The GERDA study, which is a continuation of the Umeå 85+ study, is a cross-sectional, longitudinal, population-based study performed in northern Sweden, in the county of Västerbotten and in northern Finland, in the county of Österbotten, during the years 2005-2007 (Papers I-III). The second, a qualitative interview study, was carried out during 2008-2009 in western Sweden, in the region of Västra Götaland (Paper IV).

The Umeå 85+/GERDA study

The purpose of the Umeå 85+/GERDA study was to investigate health and living conditions among individuals aged 85 years and older focusing on gaining a deeper knowledge about what constitutes good aging and a good life for old people. The first data collection was carried out in the urban municipality of Umeå during 2000-2001 and in five rural municipalities (Dorotea, Malå, Storuman, Sorsele and Vilhelmina) in Västerbotten in northern Sweden during 2002. A 5-year follow-up took place from 2005-2007, including both the same individuals and new participants in the corresponding age groups. In 2005, data collection also started in the municipalities of Vaasa and Mustasaari in northern Finland as a part of the Umeå 85+/GERDA study. The sample in this thesis (Papers I-III) is from the second data collection from 2005-2007.

Participants (Papers I-III)

The participants were selected from population records, acquired from the Swedish National Tax Board and the Finnish Population Register Centre, respectively. The individuals were selected from three age groups: 85, 90 and 95+, based on year of birth. As a rather large number of individuals aged 85 years were available, every second person was included and it was decided by lot whether odd or even numbers should be selected. Consequently, half of all 85-year-olds, all 90-year-olds and all those aged 95 years or older (based on year of birth) and living in the relevant geographical area on the 1st of January in the year of investigation were eligible for participation. An overview of the participants in this thesis is presented in Table 1.

Table 1. Overview of the participants in this thesis

	Paper I n=395	Paper II n=504	Paper III n=319	Paper IV n=20
Age				
Median (range)	90(85-104)	90(84-104)	90(84-104)	79(67-96)
85 years old	132	172	119	
90 years old	135	169	110	
≥95 years old	128	163	90	
Sweden				
Umeå	X	X	X	
Rural municipalities		X	X	
Västergötland				X
Finland				
Vaasa and Mustasaari	X	X	X	

Procedure (Papers I-III)

Initially, the participants were sent a letter containing information about the study and about two weeks later they were informed, by means of a phone call, about the home visit procedure and their informed consent was obtained. For those living in institutions, the staff were contacted first regarding information about the person's cognitive status and if it was possible to contact them personally. Among cognitively impaired persons informed consent was obtained from the next of kin. The oldest participants were contacted first. The data were collected during one or more home visits, by an investigator who was a nurse, a physician, a physiotherapist or a medical student. Structured interviews and assessment scales were used in the collection. Each home visit took approximately two hours to complete. If a person refused a home visit, they were asked whether the investigators could retrieve information from medical records and/or from relatives and caregivers. All questions, assessments and scales were interviewer-administered by trained interviewers and performed in the same order. Data were also collected from medical records, from hospitals, from the patient's general practitioner and from caring institutions and from care givers and

next of kin. An overview of all means of assessments used in Papers I-III is shown in Table 2.

Table 2. Assessment instruments used in Papers I-IV

	Paper I	Paper II	Paper III	Paper IV
MMSE	X	X	X	X
GDS-15	X	X	X	X
MADRS		X		
OBS		X		
MNA	X	X		X
BMI	X		X	X
PGCMS		X	X	X
Barthel's ADL Index	X		X	X
P-ADL (KATZ ADL Index)	X	X	X	

Paper I

In Paper I, 580 women were eligible for participation. Three-hundred and nine women were from Umeå, Sweden, from the data collection during 2005, and 271 women were from Vaasa and Mustasaari in Finland, from the data collection during 2005-2006. Forty-eight women died before they could be asked, thus 532 were asked to participate. One hundred and seventeen out of 532 women (22%) declined to participate and for another 20 it was impossible to obtain reliable data regarding diagnosed UTI during the preceding year. The study sample thus comprised 395 women, 74% of those asked to participate (Figure 1).

Paper II

In Paper II, 698 women were selected for participation. Four-hundred and twenty-seven women were from Umeå and five rural municipalities in the county of Västerbotten in Sweden and from the data collection during 2005-2007. Two-hundred and seventy-one women were from Vaasa and Mustasaari in Finland, from the data collection that took place during 2005-2006. Fifty-five of the 698 died before they could be asked and 124 out of 643 women (19%) declined to participate. Their age distribution was the same as those who participated. It was not possible to obtain reliable data regarding delirium for another 15 women. The study sample thus comprised 504 women, 78% of those asked to participate (Figure 2).

FIGURE 1. Flow chart for Paper I

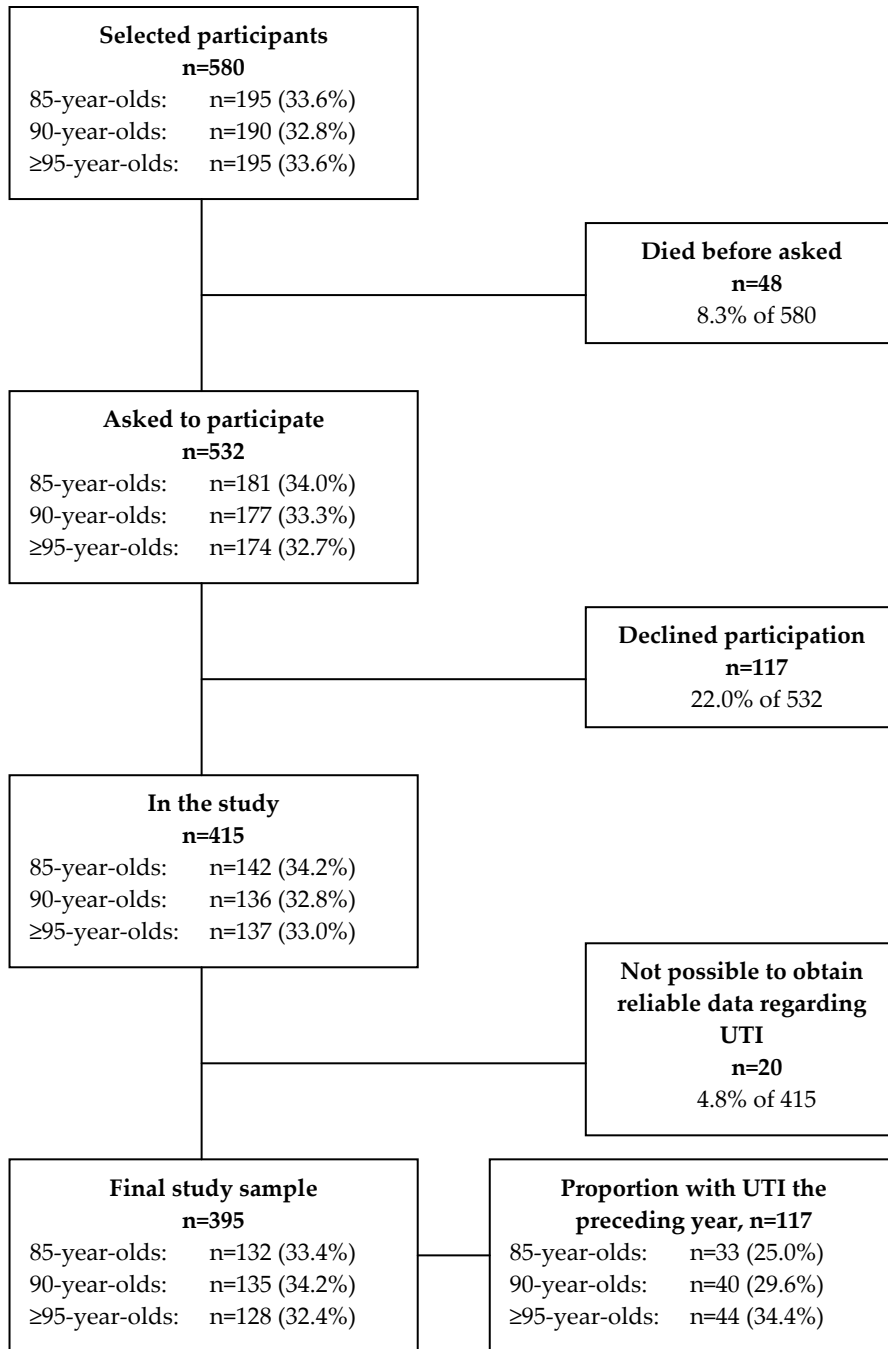
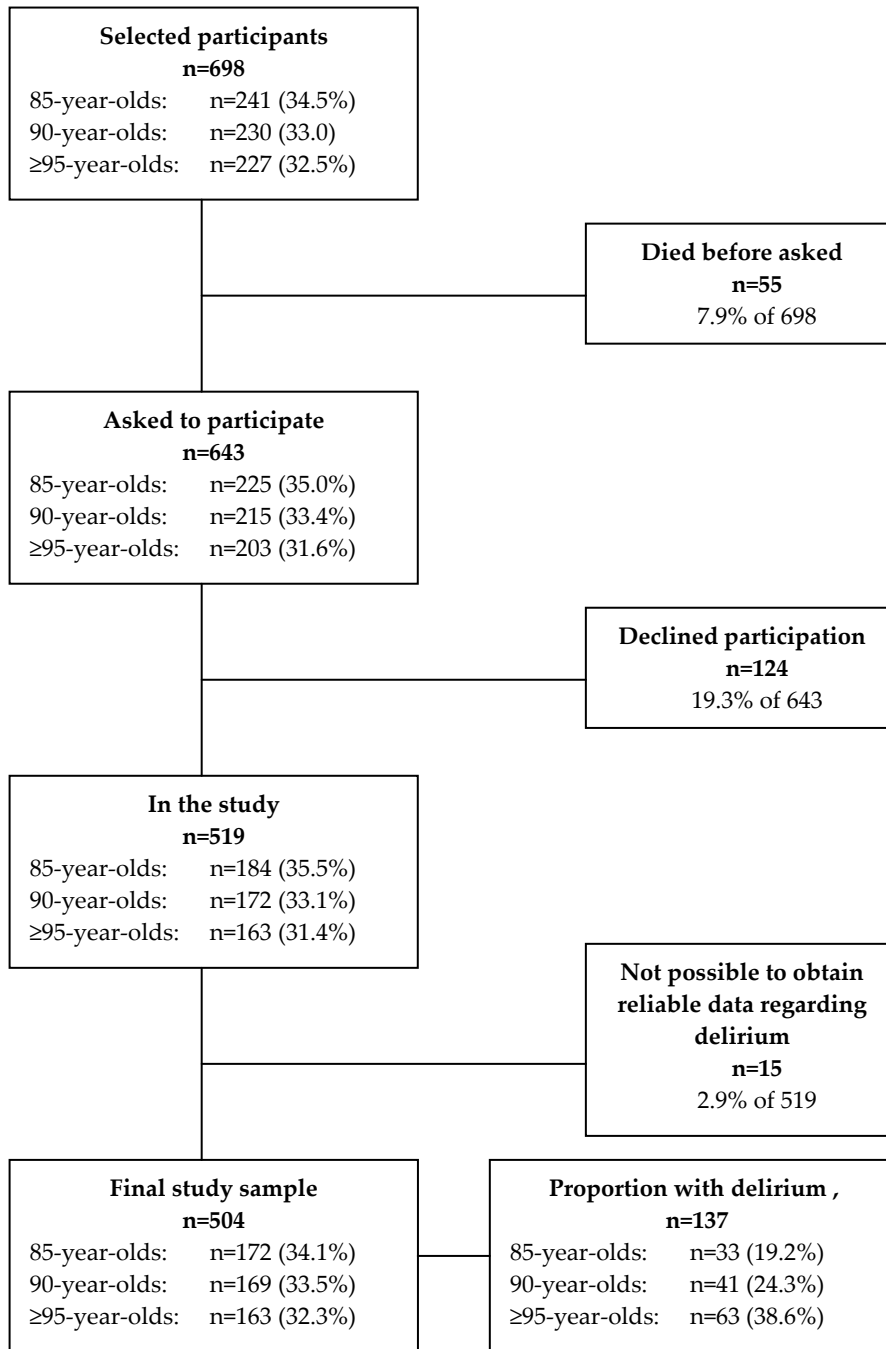


FIGURE 2. Flow chart for Paper II



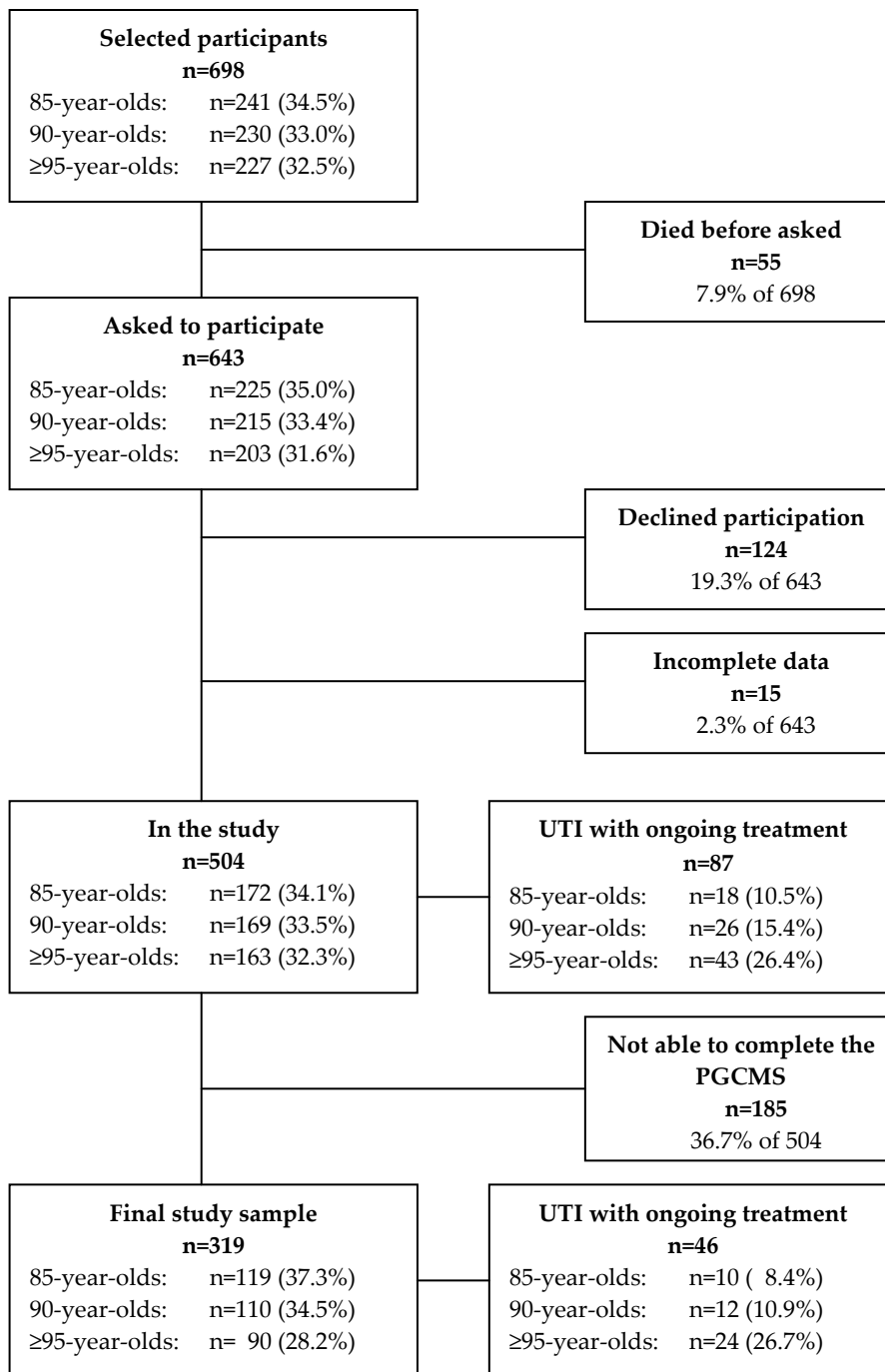
Paper III

In Paper III, 698 women were selected for participation. Four-hundred and twenty-seven women were from Umeå and five rural municipalities in the county of Västerbotten in Sweden and 271 were from Finland, from the data collection during 2005-2007. Fifty-five died before they could be asked, thus 643 were asked to participate. One hundred and twenty-four out of 643 women (19%) declined participation, in 15 cases it was incomplete data and another 185 were unable to answer the PGCMS questions. Those who declined participation or were unable to answer the questions did not differ from the remaining sample regarding the prevalence of UTI but they were older and a larger proportion suffered from dementia. The study sample comprised 319 women, 49% of those asked to participate (Figure 3).

Sociodemographics

Information concerning living circumstances, such as civil status, classified as single or not single, whether the participants lived alone, classified as living with someone or living alone and whether they lived in an institution, classified as yes or no, were collected.

FIGURE 3. Flow chart for Paper III



Physical and psychological assessments (Papers I-III)**Activities of Daily Living**

Independence in activities in daily living was assessed using the ADL Staircase (including the KATZ Index of ADL) which measures both Instrumental ADL (I-ADL) and Personal ADL (P-ADL) ^{132, 133}. I-ADL includes cleaning, shopping, transportation and cooking and P-ADL includes bathing, dressing, toileting, transferring, continence and eating. In this study, only the P-ADL measurement was used. In addition, the Barthel ADL Index was used, with a maximum score of 20 indicating independence in all personal ADL activities ¹³⁴. In addition, one question was asked if they went outside independently.

Cognition

The Mini-Mental State Examination (MMSE) was used to assess cognitive function ¹³⁵. The MMSE consists of sections including orientation, registration, attention, calculation, recall, language and copying. The scale has a maximum score of 30 with a score of 23 or below indicating impaired cognitive function. The Organic Brain Syndrome (OBS) scale ¹³⁶ was used to determine a person's awareness and orientation and to differentiate between delirium, dementia, depression and other mental disorders. The scale consists of two parts: the disorientation subscale and the confusion subscale. The disorientation part was not used in the present study since MMSE yields similar information. The confusion subscale is an observation scale covering 39 clinical features. It describes the participant's emotional reactions, suspiciousness, delusions, hallucinations, language and speech disturbances, neurological symptoms, spatial disorientation, impaired recognition, physical disability and various kinds of time-related variations and fluctuations in the clinical state. This subscale is based on observations of the participants and interviews with caregivers and next of kin. The original OBS scale has been evaluated and compared with other assessment scales and is judged as a concurrent valid instrument ¹³⁶. In comparisons with the Confusion Assessment Method (CAM), 100% conformity concerning the diagnosis of delirium has been shown ^{94, 137}. The OBS scale was used to screen for delirium during the past month.

Depression

Depressive symptoms were screened for using the Geriatric Depression Scale, 15 item version (GDS-15) ¹³⁸. The GDS-15 has a maximal score of 15 and has yes/no questions. Scores between five and nine indicate mild depression and a score of ten or more indicates moderate to severe depression. In addition, depression was rated using the Montgomery-

Åsberg Depression Rating Scale (MADRS) ¹³⁹ but only when the investigator was a physician or a medical student trained in its use. The rating for the MADRS is based on a clinical interview including 10 symptoms of depression. Depression was also registered if the participant had a depression diagnosis documented in their medical records with ongoing treatment.

Falls

The participants were asked if they had sustained any falls during the preceding year, classified as yes or no.

Hearing and vision

Vision was rated as unimpaired if the participant could read a word printed in five mm capital letters at reading distance, with or without glasses. Hearing was rated as unimpaired if the participant could hear a normal speaking voice from a distance of one meter, with or without a hearing aid.

Morale

Morale was assessed using the Swedish version of the 17-item British English version of the Philadelphia Geriatric Center Morale Scale (PGCMS) ^{123, 140}. The scores range from 17 to 0, where scores of 17-13 indicate high morale, 12-10 middle range and 9-0 low morale. The PGCMS is also comparatively easy to use in people with mild to moderate cognitive impairment since the questions are in a yes/no format ^{123, 131}. In this study, the scale was interviewer administered.

Nutrition

Nutritional status was assessed using the Mini Nutritional Assessment scale (MNA), a screening instrument for assessment of nutritional status which is valid for the very old ^{141, 142}. The MNA scale consists of two parts, a screening part which is a short form with a maximum score of 14 (used in Paper IV), where a score of 12 or more indicates normal nutrition status. The next part of the MNA has a maximum score of 16. When the screening part is included, the complete version of the MNA has a maximum score of 30 ¹⁴³. A MNA maximum score of 30 indicates very good nutritional status; scores of between 23.5 and 17 indicate a risk of malnutrition and those below 17 indicate the presence of malnutrition ¹⁴¹. In Papers I-III both parts of the MNA scale were used.

Weight and height were assessed using a digital bathroom scale and a tape measure and

Body Mass index (BMI) was calculated (kg/m²).

Diagnoses and prescribed drugs

Information about diagnoses and prescribed drugs was collected from participants, caregivers and/or next of kin, and from medical records at the hospital, general practitioners and/or at the institutional care facility.

Dementia, depression and delirium

Dementia was diagnosed if the participant had had a previous diagnosis of dementia according to their medical records and/or assessments performed during the home visit. Dementia diagnoses were divided into Alzheimer's disease, multi-infarct dementia (MID) and/or other dementia diseases.

Delirium was diagnosed if the participant had had episodes of delirium during the preceding month, based on assessment using the OBS scale and MMSE and interviews with relatives and caregivers, as well as delirium documented in the medical records.

Depression was diagnosed based on information about diagnosis and ongoing treatment with antidepressants from medical records and/or using assessments from the home visit such as the GDS-15, the MADRS and the OBS scale. A specialist in geriatric medicine evaluated all data after the study was finished. Based on information from the interviews, medical records and on test results on the MMSE assessment and the OBS scale, a dementia, depression or delirium diagnosis was confirmed. The DSM IV criteria for dementia, depression and delirium disorders were used⁹⁵.

Inflammatory rheumatic disease and vertebral fracture

Inflammatory rheumatic disease and vertebral fracture were diagnosed based on information from the participants and from medical records at the hospital, general practitioners and/or the institutional care facility.

Definition of urinary tract infection

UTI was diagnosed if the person had a documented symptomatic UTI, with either short or long-term ongoing treatment with antibiotics, or symptoms and laboratory tests that were judged to indicate a UTI by the responsible physician or the assessor. Medical records from the general practitioner, the hospitals in the catchment area or records from the caring institutions were also investigated to evaluate and validate the UTI diagnosis. The UTI diagnosis in the medical records was based on urinary tests in combination with symptoms that were judged to be associated with UTI by the responsible physician. In addition, the results from all urinary cultures registered at the regional bacteriological laboratory were reviewed. This means that the UTI diagnoses were registered if the participants had symptoms or signs of UTI when they were assessed or had had a recent diagnosis of UTI with or without ongoing treatment, but also if they had had a UTI during the preceding year and the preceding 5 years.

The qualitative study

Participants (Paper IV)

The study was performed at a primary healthcare centre in western Sweden which all the participants had visited but where they had met different physicians. Purposive sampling was used to recruit the respondents in order to achieve variety regarding age. The inclusion criteria were that participants were females, aged 65 years and older, who had had at least two diagnosed UTIs in the preceding year and were recruited according to diagnosis statistics from the primary healthcare centre medical records. Women who fulfilled the criteria were asked to participate and letters were sent to them during spring 2008, describing the purpose of the study and asking them for their written consent. Women with a diagnosed dementia disease were excluded from the study. Forty-six women, who met the criteria, were asked to participate and 20 agreed to do so. Their age distribution was the same as for those who refused to participate. Table 3 shows the background characteristics of the participants. Ages varied between 67 and 96 years (median 79 years).

Table 3. Characteristics of participants in Paper IV

	Total (n=20)
	n
Living alone	12
Living in an institution	4
Living with partner	8
Depression	5
Diabetes	7
Ongoing urinary tract infection	0
Stroke	1
Urinary incontinence	15
Oestrogen (local oestrogen)	12
	Median (range)
Age	79 (67-96)
Barthel ADL Index (0-20)	17 (7-20)
GDS-15 (0-15)	2 (0-12)
MMSE (0-30)	26 (20-30)
MNA (0-14)	13 (12-14)
PGCMS (0-17)	12 (0-17)
Number of UTIs in the preceding year	3 (2-8)
Number of drugs	8 (1-19)

Procedure (Paper IV)

First the participants received a letter describing the purpose of the study, the voluntary nature of participation and asking them for their written consent; this information was reiterated before they were interviewed. The interviews were semi-structured and the interview guide was constructed collaboratively by all four authors, influenced by clinical experience and previous studies^{50, 70}. The question domains covered their UTI symptoms and how UTI influenced their daily life, social contacts, hobbies, sexual activities, sleep and appetite and how they experienced the care received. All the interviews opened with the same question; "How do you feel about your health in connection with UTI?" The interviews were carried out by the first author (IE) during the period September 2008-February 2009. All but two interviews were carried out in the homes of the participants. The other two were carried out at the primary healthcare centre, in accordance with the participants' wishes. The interviews lasted approximately 30-60 minutes. Data concerning background characteristics, medical history and assessment

METHODS

scales were collected before the interview started and from the medical records after the home visit. The medical conditions asked about were those known, from previous research, to be relevant for UTI problems⁶⁸. The medical history also included a question about whether or not they received oestrogen treatment. Reliable and well-known assessment scales were used, for example: independence in Activities of Daily Living (ADL) was evaluated using the Barthel Index with a maximum score of 20 indicating independence in all personal ADL activities¹³⁴. Nutritional status was assessed using the short form of the Mini Nutritional Assessment (MNA) with a maximum score of 14, where a score of 12 or more indicates normal nutritional status¹⁴³. Morale or psychological wellbeing was assessed using the Philadelphia Geriatric Center Morale Scale (PGCMS)¹⁴⁰. Depressive symptoms were screened for using the Geriatric Depression Scale-15 (GDS-15)¹³⁸. The Mini Mental State Examination (MMSE) was used to assess the participant's cognitive function¹³⁵.

Ethics

Studies I-III were approved by the Regional Ethical Review Board in Umeå (§05-063M) and the Ethics Committee of Vaasa Central Hospital (05-87) and Study IV was approved by the Regional Ethical Review Board in Umeå (§08-052M) and conforms to the principles outlined in the Helsinki Declaration (2008).

Analysis

Statistical methods - Quantitative analysis

Quantitative analysis were performed using the Statistical Package for the Social Sciences (SPSS®), version 11.5 and the Predictive Analytics Software (PASW®), version 18, (both from SPSS Inc., Chicago, Illinois). Univariate analyses were made using the Pearson chi-square test and Student's t-test (Papers I-III) and Pearson's correlation analyses were used for associations between continuous variables (Paper III). In Paper I, a multivariate logistic model was constructed, based on an a priori hypothesis concerning potential risk factors for UTI and variables with an association ($p \leq 0.15$) with UTI in the preceding year were included in the model. In Paper II, multivariate logistic regression models were constructed based on an a priori hypothesis concerning potential risk factors such as acute medical conditions (e.g. infections) and diseases known to precipitate delirium or to reduce the brain reserve capacity. Variables with an association ($p \leq 0.15$) with delirium were included in the model. In Paper III, a multivariate linear regression model was constructed, based on an a priori hypothesis that morale could be

influenced by medical conditions such as infections, diabetes, stroke, depression, Parkinson's disease and heart failure. Variables with an association ($p \leq 0.15$) with low PGCMS scores were included in the model. In Paper I variables with a statistically significant association with UTI in the preceding year and in Paper II, variables with a statistically significant association with delirium, were included in the final multivariate logistic regression models in order to find factors that were independently associated with UTI (Paper I) and delirium (Paper II) respectively. In Paper III variables showing statistically significant associations with low PGCMS scores were included in the final multivariate linear regression models to find independent diagnoses associated with PGCMS scores. A p-value of <0.05 was considered statistically significant in all statistical analyses.

Qualitative content analysis

The qualitative data were analyzed using a qualitative content analysis method influenced by Graneheim & Lundman¹⁴⁴. Content analysis can have either a quantitative or a qualitative approach. A qualitative content analysis is a systematic method used to describe or illuminate a phenomena, identify latent as well as manifest content and focuses on differences and similarities in the text¹⁴⁴. The interviews were tape-recorded and were transcribed verbatim by the first author. To provide further information, both the researcher's and the participant's comments and intonation were indicated. Initially, the text was read through several times by the first author (IE) to gain an overall view of the contents. In the second step of the analysis, words, expressions and sentences (meaning units) that reflected to the purpose of the study were identified; the remainder of the text was not included in the analysis. In the third step, the meaning units were condensed and labelled with a code. Finally, in the fourth step the codes were sorted into six sub-themes and two main themes based on differences and similarities. The two main themes, including the sub-themes, are expressions of the participants' subjective meaningful content. The themes and sub-themes constitute the results of the study and quotations from the interviews are used to illustrate these themes. To achieve trustworthiness for the study, all the authors were involved in the data analysis. All the authors read the interview texts but the codes were sorted and themes and sub-themes were derived by two of the authors independently.

RESULTS

Paper I

Paper I included 395 women of whom 117 (29.6%) were diagnosed as having suffered from at least one UTI during the preceding year and 233 (60%) had had at least one diagnosed UTI during the preceding 5 years. Fifty-three out of 395 (13.4%) received ongoing treatment, including short-and long-term treatment with antibiotics as well as treatment with methenamine, for a diagnosed UTI when they were assessed. One quarter of the 85-year-olds, 29.6% of the 90-year old and 34.4% of the >95-year old had had at least one diagnosed UTI the preceding year.

Among the diagnoses, vertebral fractures, dementia, multi-infarct dementia (not Alzheimer's disease), inflammatory rheumatic disease, stroke (during the past 5 years) and heart failure were associated with UTI during the previous year among old women in this study. Women with UTI also suffered more often from constipation and urinary incontinence. In addition UTI was associated with delirium during the preceding month and ongoing treatment with estrogens. A history of falls during the previous year was more common among women with UTI and UTI was also more common among participants living in institutional care facilities. Not able to go outside independently and dependence in toileting, according to the Katz Index, were also significantly more common among women who had suffered a UTI in the previous year. Only three women had or had had an IUC. A larger proportion of the Finnish women than the Swedish women suffered from UTI. Women with a UTI during the previous year had poorer ADL function according to the Barthel Index, poorer cognition according to the MMSE and poorer nutrition measured using the MNA (Table 4).

RESULTS

Table 4. Characteristics of women (n=395) in Paper I with and without urinary tract infection in the preceding year

	UTI (n=117)		NO UTI (n=278)		P-value
	n	%	n	%	
<i>Demographic and social factors</i>					
Civil status (single) (n=115/274)	109	94.8	249	90.9	0.194
Institutional care (n=117/269)	72	61.5	119	44.2	0.002
Living in Finland	65	55.6	112	40.3	0.005
Living in Umeå	52	44.4	166	59.7	
Women 85 years old (n=132)	33	25.0	99	75.0	0.254
Women 90 years old (n=135)	40	29.6	95	70.4	
Women ≥95 years old (n=128)	44	34.4	84	65.6	
<i>Medical factors</i>					
Constipation current	62	53.0	108	38.8	0.010
Dementia	73	62.4	123	44.2	0.001
Alzheimer's disease	37	31.6	67	24.1	0.121
Multi-infarct dementia	25	21.4	27	9.7	0.002
Delirium previous month	44	37.6	69	24.8	0.010
Depression	53	45.3	102	36.7	0.110
Diabetes	19	16.2	41	14.7	0.706
Heart failure (n=117/277)	49	41.9	90	32.5	0.075
Hip fractures	14	12.0	28	10.1	0.577
Indwelling urinary catheter	3	2.6	4	1.4	0.439
Rheumatic disease current	18	15.4	21	7.6	0.017
Urinary incontinence current	67	57.3	81	29.1	<0.001
Vertebral fractures in the previous five years	15	12.8	14	5.0	0.007
<i>Functional factors</i>					
Fall/falls in preceding year (n=93/231)	61	65.6	105	45.4	0.001
Not going outside independently (n=110/243)	75	68.2	119	49.0	0.001
Not independent in toileting ^a (n=115/258)	57	49.6	76	29.4	<0.001
<i>Medications</i>					
Estrogen (n=117/277) (systemic and local)	29	24.8	34	12.3	0.002
	Mean±SD		Mean±SD		
Barthel's ADL index	11.8±7.0		15.0±6.6		<0.001
BMI	25.3±4.3		25.2±4.8		0.859
MMSE	15.6±9.4		19.7±8.3		<0.001
MNA	20.1±4.9		22.5±4.3		<0.001

^a According to KATZ ADL staircase

RESULTS

Multivariate logistic regression analyses resulted in the model shown in Table 5. Vertebral fractures (OR=3.2), urinary incontinence (OR=2.8), inflammatory rheumatic disease (OR=2.8) and multi-infarct dementia (OR=2.4) were the factors which, in the final regression model, remained independently associated with UTI during the preceding year.

Table 5. Multivariate logistic regression model of factors associated with urinary tract infection the preceding year in Paper I

	N=395		
	OR	95 % CI	P-value
Vertebral fractures	3.2	1.4-7.1	0.005
Urinary Incontinence	2.8	1.8-4.5	<0.001
Rheumatic disease	2.8	1.4-5.7	0.004
Multi-infarct dementia	2.4	1.3-4.5	0.007

χ^2 for the model = 45.57, p-value: <0.001, $R^2=0.155$

Association between predicted probabilities and observed responses:

Concordant: 73.9%

Paper II

The mean age of the 504 women included in Paper II was 90.6 years (SD±4.7) and 87 (17.3%) were diagnosed as having a UTI with or without ongoing treatment when they were assessed, and almost half of them, 39 women (44.8%), were diagnosed as delirious or having had episodes of delirium during the preceding month.

One-hundred and thirty-seven (27.2%) of the 504 women were delirious or had had episodes of delirium during the preceding month and 39 (28.5%) of them were diagnosed as having a UTI (Table 6). Of the 39 women with delirium and UTI, 22 received ongoing treatment for UTI and in 17 cases, the assessor who made the home-visit, found documentation in the records and/or received information from the staff (responsible nurse) indicating the presence of a UTI. In 15 of the 39 cases documentation of laboratory tests, such as urinary cultures, was found. The documentation included both symptoms and laboratory tests. In two cases it was documented that the physician might have interpreted the delirium as a symptom of the infection. In 10 of the 39 cases with delirium and UTI it was documented that the participants had been delirious in association with a previous infection and that the delirium had resolved after treatment of that infection.

RESULTS

Of the 85-year-old women, 33/172 (19.2%) were delirious, 41/169 (24.3%) of the 90-year old and 63/163 (38.6%) of the ≥ 95 -year-old women (Figure 2). The characteristics of the women with delirium compared to those without are presented in Table 6.

Table 6. Characteristics of women (n=504) in Paper II with and without delirium

	Delirium (n=137)		No delirium (n=367)		P-value	Total sample (n=504)	
	n	%	n	%		n	%
<i>Demographic and social factors</i>							
Institutional care	115	83.9	123	33.5	<0.001	238	47.2
<i>Medical factors</i>							
Angina pectoris	69	50.4	136	37.1	0.007	205	40.7
Constipation current	85	62.0	130	35.4	<0.001	215	42.7
Dementia	121	88.3	113	30.8	<0.001	234	46.4
Alzheimer disease	66	48.2	61	16.6	<0.001	127	25.2
Multi-infarct dementia	39	28.5	29	7.9	<0.001	68	13.5
Depression	79	57.7	112	30.5	<0.001	191	37.9
Heart failure (n=136/367)	65	47.8	101	27.5	<0.001	166	33.0
Hypertension	68	49.6	252	68.7	<0.001	320	63.5
Indwelling urinary catheter	6	4.4	3	0.8	0.015	9	1.8
Stroke	4	2.9	4	1.1	0.144	8	1.6
Urinary tract infection	39	28.5	48	13.1	<0.001	87	17.3
<i>Functional factors</i>							
Not eating independently ^a (n=132/333)	25	18.9	27	8.1	0.001	52	11.2
Not independent in toileting ^a (n=132/333)	88	66.7	66	19.8	<0.001	154	33.1
Not transfer independent ^a (n=132/333)	65	49.2	55	16.5	<0.001	120	25.8
Not going outside independently (n=119/316)	101	84.9	119	37.6	<0.001	220	50.6
	Mean\pmSD		Mean\pmSD			Mean\pmSD	
Age	91.9 \pm 4.7		90.1 \pm 4.6		<0.001	90.6 \pm 4.7	
GDS-15 (n=67/266)	4.5 \pm 2.7		3.5 \pm 2.6		0.005	3.7 \pm 2.6	
MNA (n=122/283)	19.0 \pm 3.9		23.3 \pm 4.4		<0.001	22.0 \pm 4.7	
MMSE (n=118/314)	12.3 \pm 7.9		21.1 \pm 7.7		<0.001	18.7 \pm 8.6	
PGCM (n=62/257)	10.5 \pm 3.2		12.0 \pm 3.1		0.001	11.7 \pm 3.2	

^a According to KATZ

RESULTS

Delirium among old women was significantly associated with angina pectoris, dementia, heart failure, hypertension and UTI. Women with delirium also suffered more often from constipation. Delirium was more common among those living in institutional care facilities than in those living in ordinary housing.

Women with delirium had poorer ADL function according to the KATZ ADL Index. These women also had poorer cognition according to the MMSE and poorer nutritional status measured using the MNA. Women with delirium had significantly higher GDS-15 and lower PGCMS scores, indicating both more depressive symptoms and poorer psychological wellbeing (Table 6).

Regression analyses resulted in the model shown in Table 7. Alzheimer's disease (OR= 5.8), multi-infarct dementia (OR=5.4), depression (OR=3.1), heart failure (OR=2.3) and urinary tract infection (OR=1.9) were the factors which, in the final regression model, remained independently associated with delirium.

Table 7. Multivariate logistic regression model of factors associated with delirium in Paper II

	N=503		
	OR	95 % CI	P-value
Alzheimer disease	5.8	3.5-9.5	<0.001
Depression	3.1	2.0-5.0	<0.001
Heart failure	2.3	1.4-3.7	0.001
Multi-infarct dementia	5.4	3.0-9.8	<0.001
Urinary tract infection	1.9	1.1-3.3	0.025

χ^2 for the model = 133.2, p-value: <0.001, R²=0.233

Association between predicted probabilities and observed responses:

Concordant: 73%

Paper III

In Paper III, the study comprised 319 women, 46 (14.4%) of whom were diagnosed as suffering from a UTI with or without ongoing treatment when they were assessed. Of these 46 women with a UTI, 10/119 (8.4%) were 85 years old, 12/110 (10.9%) were 90 years old and 24/90 (26.7%) were ≥ 95 years old (Figure 3). Almost two thirds of these 46 women had had two or more UTIs in the preceding year, documented in the medical records.

Of the 46 women with a UTI, 31 were receiving ongoing treatment for UTI and in 15 cases, the assessor who made the home-visit, found documentation in the records and/or received information from the staff (responsible nurse) indicating the presence of a UTI. In 12 of the 46 cases documentation of laboratory tests such as urinary cultures were found. The documentation included symptoms and laboratory tests.

Reduced morale according to the PGCMS was associated with the diagnoses of depression, dementia, constipation, heart failure, stroke, impaired vision and UTI (Table 8).

RESULTS

Table 8. The total PGCMS scores in Paper III for women (n=319) with and without specific characteristics

	Yes (n)	PGCMS Mean±SD	No (n)	PGCMS Mean±SD	P-value
<i>Social factors</i>					
Living alone	276	11.5±3.2	43	12.6±3.0	0.048
In institutional care	113	10.8±3.5	206	12.1±2.9	0.001
<i>Medical factors</i>					
Constipation	125	10.8±3.2	194	12.2±3.1	<0.001
Dementia	102	10.9±3.2	217	12.0±3.2	0.003
Depression	122	9.5±3.2	197	13.0±2.4	<0.001
Diabetes	49	11.9±3.2	270	11.6±3.2	0.538
Heart failure	105	11.1±3.3	214	11.9±3.1	0.028
Hip fractures	35	11.3±3.4	284	11.7±3.2	0.502
Indwelling urinary catheter	6	8.2±4.4	313	11.7±3.2	0.007
Impaired hearing (n=315)	54	11.1±3.7	261	11.8±3.1	0.182
Impaired vision (n=318)	55	10.4±3.0	263	11.9±3.2	0.002
Malignancies	25	11.0±3.5	294	11.7±3.2	0.286
Rheumatic disease	35	11.4±2.7	284	11.7±3.3	0.576
Stroke in the preceding five years	30	9.7±3.6	289	11.9±3.1	<0.001
Urinary incontinence	98	11.2±3.0	221	11.9±3.3	0.066
Urinary tract infection - current	46	10.4±3.6	273	11.9±3.1	0.003
<i>Functional factors</i>					
Not eating independently ^a (n=318)	8	9.1±4.0	310	11.7±3.2	0.024
Not going outside independently (n=316)	113	10.7±3.2	203	12.2±3.0	<0.001
Not independent in toileting ^a (n=318)	53	10.1±3.5	265	12.0±3.1	<0.001
Not transfers independent ^a (n=318)	41	10.4±3.4	277	11.8±3.2	0.008

^a According to KATZ ADL Index

RESULTS

Women with a UTI had a mean score on the PGCMS of 10.4±3.6 versus 11.9±3.1 ($p=0.003$) for those without UTI. Living conditions, e.g. being in institutional care or living alone, were also associated with reduced morale. The participants who were dependent in eating, transfer, toileting, according to the KATZ Index of ADL, and going outside and had an indwelling urinary catheter also scored lower on the PGCMS (Table 8). The low PGCMS scores correlated significantly with high age, large number of drugs and low scores on Barthel's ADL index and the MMSE and high scores on the GDS (Table 9).

Table 9. Correlations between PGCMS and continuous predictor variables among the women (n=319) in Paper III

Predictor variables	Mean±SD	Range	Correlation with PGCMS	P-value
Age	90.1±4.6	84-104	-0.142	0.011
Barthel's ADL index	16.9±4.7	0-20	0.235	<0.001
Body Mass Index	25.6±4.4	14.5-40	-0.014	0.812
Geriatric Depression Scale-15	3.6±2.5	0-11	-0.674	<0.001
Mini Mental State Examination	22.1±5.6	5-30	0.205	<0.001
Number of drugs	7.0±4.0	0-19	-0.211	<0.001

The final regression model showed that low PGCMS scores were associated with depression ($\beta = -3.31$, $p < 0.001$), urinary tract infection ($\beta = -1.07$, $p = 0.014$) and constipation ($\beta = -0.74$, $p = 0.018$). Among these old women, the regression model explained 31% of the variations in the PGCMS score (Table 10). Diagnoses such as urinary incontinence, heart failure, dementia and stroke did not qualify for inclusion in the final multivariate linear regression model.

Table 10. Multivariate linear regression model of medical diagnoses associated with the total PGCMS scores (n=318) in Paper III

	β	95% CI	P-value
Depression	-3.31	2.70-3.93	<0.001
Urinary tract infection with or without ongoing treatment	-1.07	0.22-1.91	0.014
Constipation	-0.74	0.13-1.36	0.018

P-value: <0.001, $R^2 = 0.309$, Adjusted $R^2 = 0.303$

Paper IV

Themes and sub-themes

The analysis revealed two main themes and six sub-themes (Figure 4). The main themes are *Being in a state of manageable suffering* and *Being dependent on alleviation*, which indicate that suffering is the meaning of older women's experiences of repeated UTI. The sub-themes are illustrated by quotations from the interviews.

Figure 4. Overview of results in Paper IV

Theme	Sub-theme
Being in a state of manageable suffering	Experiencing physical inconveniences Experiencing psychological inconveniences Struggling to deal with the illness Being restricted in daily life
Being dependent on alleviation	Access to relief Receiving inadequate care

Being in a state of manageable suffering

The theme *Being in a state of manageable suffering* was developed from four underlying sub-themes: experiencing physical inconveniences; experiencing psychological inconveniences; struggling to deal with the illness; and being restricted in daily life.

Experiencing physical inconveniences

The women's experiences were that their general health was affected when they suffered from UTI and said that they felt bad all over: "*Awful, not good at all, not a single part of my body feels well.*" They expressed a wide range of physical inconveniences, some of them typical symptoms of UTI such as a burning sensation, an urgent-need to pass water often and pain in relation to passing urine. But they also expressed other atypical symptoms such as dizziness and pain in the hands: "*It can start with it aching and tingling in my hands.*" Moreover, they described inconveniences such as coldness, reduced appetite, sleeping disturbances, fever and increased thirst.

Experiencing psychological inconveniences

When the women suffered from UTI they thought that their mood was affected and they felt depressed and dejected, some said it was a misery: *"I usually say it's a misery because that is really what it is."* They expressed feelings of discomfort and of getting angry more easily, of being more sensitive and generally less joyful. They also said that they often felt unclean and unhygienic and were always worried about smelling bad which made them feel anxious, as described by one woman: *"I feel influenced to the max because I feel unhygienic and that I smell bad, and yes, of course it affects me psychologically."*

Struggling to deal with the illness

The women said that it felt like constantly waiting to get better and waiting for the UTI to disappear but also as if one were constantly on one's guard: *"I am really tied to these problems, at least I used to be, and when I had had the medicine the only thing I could focus on was when I would get better."* One strategy for dealing with the illness was that they avoided leaving their homes while they were experiencing the physical and psychological inconveniences: *"I try to stay still and rest a lot and I usually don't want to go outside"*. Other strategies described were thinking about visiting the toilet regularly, resting a lot, not bathing and avoiding getting cold: *"If you are going somewhere you always have to think about where the toilet is."*

Being restricted in daily life

The women said that they were restricted in daily life in many different ways and to a greater or lesser extent. They avoided contacts with other people, with their friends as well as their children: *"It affects everything, I can't even manage calling my own children or my friends"*. Their social life in general was affected because they were unable to see their friends as they felt that they were a burden to other people but also that they could not manage physical activities or hobbies. They also said that sexual activities were affected when they had a UTI because they had less sexual desire, partly for fear that they would have a urine leakage and smell bad: *"You don't want to have sexual intercourse when you feel sick and are in pain and also risk needing to use the toilet. Besides, it feels unhygienic."* The women frequently suffered from urinary incontinence and some of them thought that a UTI exacerbated this condition: *"My problems with urinary incontinence get worse in connection with UTI because then it is more difficult to hold my urine."* Always being afraid of urine leakage and of smelling bad can also be regarded as a restriction in their daily life.

Being dependent on alleviation

The theme *Being dependent on alleviation* was developed from two underlying sub-themes; access to relief and receiving inadequate care.

Access to relief

Access to relief was described in terms of getting care quickly and it being easily accessible but also receiving caring treatment from nurses and physicians: *"I can't complain about the care, they probably did what they could and when I called them I always got an appointment at once."* These women stated that it was important for the caregivers to take their inconveniences seriously and it was important to obtain the correct medicine: *"The care has been good, I have got treatment when I have called them but it is hard when the treatment doesn't help."* They said that having a UTI was difficult but if they received the correct medical treatment quickly they often felt well fairly rapidly.

Receiving inadequate care

Receiving inadequate care was described in terms of not getting the correct medical treatment and insufficient information concerning the treatment and preventative measures. They also described a lack of follow-up and of investigation into their inconveniences: *"I never had my inconveniences investigated and in my opinion I think that it is quite bad because I have had these infections for so many years."* Some of them had also experienced that when they contacted the healthcare centre they felt that their inconveniences were treated nonchalantly, as was described by one woman: *"You often meet male physicians or female younger physicians who have probably never had these problems themselves and I think that it might be difficult to put yourself in the situation and understand how tough and hard it can be."*

DISCUSSION

Main findings

The prevalence of UTI is high among very old women and the risk of UTI increases with age. Almost one-third of the women aged 85+ years had suffered from at least one UTI the previous year and two thirds during the previous five years. UTI was more common in women aged 95 years or older than in those who were 85 years old. About 34% of the >95-year-olds had had at least one diagnosed UTI the preceding year compared with 25% of the 85-year-olds. Although it is often difficult to diagnose UTI among the oldest women the prevalence of diagnosed UTI is still high in this sample of very old women.

It was found that UTI during the preceding year was independently associated with vertebral fractures, urinary incontinence, inflammatory rheumatic disease and multi-infarct dementia. Previously well-known risk factors for UTI such as diabetes, malnutrition and cortisone treatment did not remain in the final regression model. These findings may suggest that the associated factors we found could be consequences of UTI rather than risk factors and raises the suspicion that UTI could have serious medical health effects in very old women. Almost half of all women with a diagnosed UTI, with or without ongoing treatment, were delirious or had had episodes of delirium during the past month. These findings support the suspicion that UTI may be a common cause of delirium.

In addition to serious health effects, these women with UTI also assessed their morale or subjective wellbeing as rather poor. UTI was together with depression and constipation independently associated with poor subjective wellbeing. The interviews with the old women who had suffered repeated UTI the last year confirmed the effect as a generally poor state of health, physically, psychologically and socially.

This thesis shows, both quantitatively and qualitatively, that UTI causes great suffering in many old and very old women.

The prevalence of urinary tract infection

The present study shows a high prevalence of symptomatic, diagnosed UTI among old women and the findings are in line with previous international studies^{30, 33, 88, 145}. Previous studies report a prevalence of UTI of between 25-50% among women aged 65 to 95 years^{31, 88, 145, 146} but no studies have been found where the oldest women in particular have been studied.

The difficulty in diagnosing UTI increases with age, as is supported by previous studies^{30, 39, 52, 147}, because among the old atypical symptoms, such as frequent urination and UI are more common but also because of a higher

prevalence of comorbidities^{30, 39}. Old women may also present with psychological symptom such as irritability, tiredness and delirium in connection to UTI^{45, 49, 50}. UTI might go undetected in many old women for a variety of other reasons. In addition people with dementia may have difficulties reporting symptoms which may also result in an underestimation of the prevalence of UTI. Aging results in elevated pain thresholds and reduces the intensity of the inflammatory reaction. Another explanation for why these very old women do not have the same local symptoms may be that they use analgesic and anti-inflammatory drugs to a greater extent which could mask the symptoms. More than half of the participants in the GERDA study (men and women) were treated with such drugs¹⁴⁸.

Asymptomatic bacteriuria is a common finding among very old women and distinguishing asymptomatic bacteriuria from UTI can be complex, especially if the old women present with impaired cognition or if they have difficulty explaining their symptoms^{30, 67, 149}. It can also be difficult to distinguish between asymptomatic bacteriuria and UTI if they have other concurrent comorbidities and especially if they do not present with typical local urinary tract symptoms⁶⁷. Some of the very old women in the present study could potentially have had asymptomatic bacteriuria but still been diagnosed as having UTI. One possible explanation for this could be that if bacteria were found in the urine in a delirious old woman and it might have been interpreted as the presence of a UTI. This was the case, however, in only two of the 39 cases with delirium and UTI. In this study, UTI was diagnosed if the person had a documented symptomatic UTI, with short-or long-term ongoing treatment with antibiotics and the symptoms and laboratory tests that were judged to indicate a UTI by the responsible physician or the assessor. In addition, the results from all urinary cultures registered at the regional bacteriological laboratory were reviewed. This was, however, no help in distinguishing between ASB and UTI so even if some of these very old women had positive cultures they might not have shown symptoms of their UTI.

Urinary tract infection and associated factors

In the present study, UTI was associated with vertebral fractures in the previous five years, which was in line with a previous study that showed an association in postmenopausal women between UTI and fractures⁷⁹. One possible explanation for this is that the reduced level of oestrogen in postmenopausal women increases the risk of contracting both fractures and urinary tract disorders, such as UTI. UTI was also associated with falling in the univariate analyses but did not remain in the final regression model. Falling might at least partly explain the association between UTI and fractures. Very old women with UTI might run an increased risk of suffering

from tiredness, delirium, fatigue and poor general condition which could increase their risk of falling ^{10, 47}. The risk of fractures is also associated with osteoporosis ¹⁵⁰. Osteoporosis is associated with oestrogen reduction at menopause but also with increased production of pro-inflammatory cytokines ¹⁵¹. These pro-inflammatory cytokines are important regulators of bone resorption and may play a central role in age- and oestrogen-deficiency-related bone loss. Thus UTI might increase the production of inflammatory cytokines that may cause bone resorption ¹⁵².

One of the factors that were most strongly associated with UTI in the final regression model was UI, which is supported by several previous studies among postmenopausal women ^{31, 70, 85}. UI is very common among old women and the prevalence increases with age ^{85, 86} which is also true of UTI. Previous studies have shown a prevalence of UI of between 15->50% among community-dwelling old women and at least 50% among those living in residential care ^{69, 86-88}. UI has been found to be associated with factors such as diabetes ⁶⁹, falls and dementia ⁸⁵. Some of these factors have been found to be associated with UTI in the present study. The strong relationship may indicate that these old women could have a defect causing both UTI and UI. Furthermore, it is rather unclear from previous research whether UI is a risk factor for UTI or how these two conditions are associated with each other ^{31, 68-70}. As both UTI and UI have similar symptoms it may be difficult to distinguish between them, especially in old women with impaired cognition or those who have difficulties explaining their symptoms. In some cases UI may be a symptom of UTI but it is perhaps not obvious that UI causes UTI. Likewise, no studies have been found that support the view that UTI causes UI, but some patients in the qualitative study felt that their incontinence problems got worse when they also had a UTI. Other studies have suggested that UI has to be regarded as a symptom rather than a disease and that UI is not a normal consequence of aging ^{66, 87}. Unfortunately, the old women themselves, often regarded UI as an unavoidable consequence of aging and so often too do healthcare professionals ^{69, 86}. Many old women with UI only receive diapers which, it has been suggested, increase the risk of UTI ⁷⁴. This result, that many old women with UI not receiving adequate treatment of its underlying causes, may negatively affect their wellbeing, both physically and psychologically. Reduced oestrogen levels, however, is a common denominator for both UI and UTI and it has been suggested is involved in both of these conditions ^{66, 79}.

This study showed that UTI in the preceding year was associated with inflammatory rheumatic disease. In previous studies, musculoskeletal complaints in females have been found to be associated with UTI but this was among women younger than those in the present study ^{153, 154}. The relationship between UTI and inflammatory rheumatic diseases still seems

to be rather unclear. With regard to rheumatoid arthritis (RA), one hypothesis that has been suggested is that UTI caused by *Proteus Mirabilis* is involved in the onset of RA ^{155, 156}. Another study, which found that RA patients more frequently had *Proteus Mirabilis* in the urine than control patients, supports to this hypothesis that RA may have developed as a result of a subclinical UTI caused by *Proteus* ¹⁵⁷. Many of the old women with inflammatory rheumatic diseases are treated with corticosteroids, a fact which must be taken into consideration. If an infection occurs, the immune system will release cytokines into the circulation which in turn sends further signals to the brain for activation ¹⁵⁸. This cytokine response results in a negative feedback which suppresses inflammatory events that could potentially trigger autoimmune disease. Glucocorticoids play a central role in the regulation of the immune response and are expected to result in dysregulation of the immune response which may enhance the susceptibility to develop infection or an inflammatory disease ¹⁵⁸. Although we controlled for corticosteroid treatment, it was not related to UTI either in the univariate analyses or in the multivariate analysis. Therefore, it might be the underlying disease that is most relevant and might increase the risk of infection or that the UTI might be etologically related to the inflammatory disease. Further research exploring the association between UTI and inflammatory diseases is urgently needed.

A previous study found that subclinical UTI was common among patients with acute coronary syndromes (ACS) and hypothesised that an underlying infection might precipitate ACS via activation of systemic inflammation ¹⁵⁹. An activation of a cytokine cascade occurs in connection with UTI, and this may induce systemic inflammation ¹⁵⁹. Infectious agents are considered to initiate or exacerbate a chronic vascular or systematic inflammatory process ¹⁶⁰ which could possibly explain the connection between inflammatory rheumatic disease and UTI and ACS ¹⁶¹. In previous research, both RA and polymyalgia rheumatica have been reported to be associated with cardiovascular diseases ^{161, 162}. There is strong evidence for an association between oral infections and cardiovascular diseases including both myocardial infarction and stroke ^{163, 164}.

Dementia has been found to be associated with UTI in earlier studies ^{46, 165, 166}, but in the current study, only multi-infarct dementia was associated with UTI. The association with MID but not Alzheimer's disease, indicates that the association could be mediated through vascular pathology. Inflammatory mediators, including inflammatory cytokines, have been found to be involved in the pathogenesis of various types of dementia but different inflammatory cytokines are regulated up and down in MID patients compared to Alzheimer patients, showing that in MID patients the peripheral cytokine system is more widely affected ¹⁶⁷.

Inflammation and infections have been discussed as important risk factors for ischemic stroke ¹⁶⁸. Atherosclerosis is considered to be a chronic inflammatory vascular condition that contributes to a large proportion of all stroke cases and infectious diseases are believed to contribute to its pathophysiology ¹⁶⁸. Interleukins may contribute to the inflammatory process in blood vessels, which in turn increases the risk of thrombosis formation ¹⁵⁹. Periodontal infection is also associated with atherosclerosis and is regarded as a risk factor both for stroke ^{168, 169} and for cardiovascular disease ¹⁷⁰. Periodontal infections are often caused by gram-negative bacteria and it has been shown that patients with periodontitis have elevated markers of systemic inflammation, such as increased levels of interleukins ¹⁷¹. However, the exact mechanisms by which local inflammatory conditions may contribute to systemic inflammation are not fully understood ¹⁷¹. Acute infections, mainly respiratory tract infections and UTIs, and chronic infections, such as periodontitis, are considered risk factors for stroke ¹⁷². These infections are commonly caused by gram-negative bacteria and could therefore explain why some infections might lead to an increased risk of stroke and probably also vascular dementia. Since chronic and acute infections are treatable conditions it might be possible to prevent stroke and vascular dementia.

UTIs are more common among women than among men which may partly explain why women are more susceptible to osteoporosis, MID and autoimmune diseases such as rheumatic diseases. This could be a possible explanation but further research is obviously important within this area.

Urinary tract infection and delirium

Almost one-fifth of the participants in the present study had a diagnosed UTI with or without ongoing treatment and almost half of those with a UTI were delirious or had had episodes of delirium during the preceding month. More than a quarter of the women with delirium had a UTI, with or without ongoing treatment. Delirium was independently associated with Alzheimer's disease, MID, depression, heart failure and UTI in the final multivariate regression model. Previous studies have shown that chronic diseases such as dementia, heart failure and depression seem to increase the risk of developing delirium in old persons ^{99, 101, 102}.

It can be difficult to differentiate dementia from delirium, although they are distinct clinical syndromes they have shared pathogenic mechanisms and symptoms ¹⁰⁹. Systemic inflammation, which is present in many conditions, is known to precipitate cognitive changes in older persons. Delirium and dementia are examples of such a decline in cognition and are associated with acute and chronic inflammatory states ¹⁰⁹. Cytokines are important mediators of the immune response and play a significant role in the pathogenesis of both dementia and delirium ^{108, 109}. The role of the

inflammatory molecules in the pathological process is not fully understood but in Alzheimer's dementia, neuroinflammatory mediators, such as cytokines, are upregulated in areas of the brain ^{107, 109}. Chronic inflammation is also thought to play a role in the pathogenesis of vascular dementia, such as MID, but it seems that the peripheral cytokine system is more widely affected in connection with MID ^{109, 167}. Delirium seems to increase the risk of developing dementia ^{102, 173, 174} and the above association could be the common denominator that explains why patients with delirium are of increased risk of developing dementia.

In these old women, delirium was associated with depression and it seems that old people with depression are more vulnerable, which might increase their risk of developing delirium. Both delirium and depression are common conditions in very old people and several studies have suggested that inflammatory mediators, such as cytokines are also involved in pathogenesis of depression ^{107, 118, 120, 175}. Depression is also associated with hypercortisolism which might impair the immune system and increase the risk of contracting infections and one hypothesis is that increased immune cytokines may contribute to glucocorticoid resistance in major depression ¹²⁰. The interpretation in another study was that immune activation is a reflection of the unspecific stress perceived by patients due to an acute illness ¹¹⁸.

If chronic conditions such as dementia, heart failure and depression are considered to predispose people to delirium, acute states such as UTI seem rather to precipitate delirium, especially in frail, old women with reduced reserve capacity. In the present study almost half of the old women with UTI were delirious or had had episodes of delirium during the preceding month and more than a quarter of the delirious old women suffered from a UTI. This finding is in line with previous studies which have shown that infections, such as UTI, are common among frail, old people ³⁰ especially among those with delirium ⁴⁵. One possible explanation for the relation between UTI and delirium could be the activation of the cytokine system which is central in the pathogenesis of both UTI and in many cases of delirium. It seems that different kinds of inflammatory cytokines may also be involved in the development of UTI in old women ^{29, 72} and in persons with delirium, as they contribute to a cascade of events, such as synthesis of interleukins ^{176, 177}. Although systemic inflammation and increased cytokine levels seem to be present in both delirium and acute illness, such as UTI, aging alone can also cause an increase in cytokine production ¹⁰⁹.

A large proportion of very old women with ongoing UTI suffered from delirium, which might indicate that UTI is a common cause of delirium. As both delirium and UTI can be prevented it is important to identify and be aware of associated risk factors so as to target more effective interventions

for the benefit of these old women who are at great risk of contracting a UTI as well as delirium.

Urinary tract infection and morale or subjective wellbeing

In the present study, a diagnosed UTI, with or without ongoing treatment, was associated with a significantly lower PGCMS score; apart from UTI, depression and constipation were the diagnoses independently associated with low morale in the regression model. These findings are strengthened by those from the present qualitative study which indicates that older women suffer when they contract repeated UTIs. These women described suffering in terms of a generally affected state of health, physically, psychologically and socially.

In one of the quantitative studies it was unexpected that diagnoses such as malignancies, rheumatic disease and diabetes were not associated with low morale in the multivariate analysis. Diagnoses such as stroke, dementia and heart failure were associated with low morale in the univariate analysis but these did not remain as significant in the final regression model. Previous studies has also found these diagnoses to be associated with low morale ^{125, 126}. One possible explanation for our result could be that many of these old women suffer from multiple diseases. A combination of co-morbid diseases and an age-related reduced immune system might make the aged brain more vulnerable to the systemic effects of an infection, such as UTI. Thus, in frail old women a UTI might have a more serious impact on morale than in younger and healthier women. Another possible explanations might be that these women felt ill as a result of the medical treatment itself or because the treatment did not have the expected effect on the UTI. The women in the qualitative study also describe suffering in terms of being dependent on alleviation and not receiving adequate care. It was important for them to get care quickly and receive the correct medical treatment. Even if they experienced the symptoms of UTI as very difficult initially, they said that if they received the correct medical treatment quickly they often felt well fairly rapidly. These findings are supported by a previous qualitative study among women aged 21-64 years ¹⁷⁸. They also described experiences such as being treated nonchalantly by the caregivers and not having the underlying causes of their inconveniences investigated. One possible reason why these women felt that they had sometimes been neglected might be that the caregivers did not always regard an uncomplicated complaint in old women as particularly important. The study by Leydon et al revealed that some of the participants were ashamed for their UTI ¹⁷⁸. They expressed that their UTI should be regarded as a result of their poor hygiene and this deterred them from speaking to others, including their general practitioner, about their problems. Such experiences were not found in the present qualitative interview study among older women.

In contrast to previous studies UI was not associated with low morale in the regression model. Previous studies have found that old women suffering from UI often have a lower quality of life ^{179, 180}. In the present study UTI in very old women seems to be more important for morale than UI. However, it is important to be aware that the symptoms of UI and UTI are similar and possibly making it difficult to separate them ³⁰. Among the women in the present qualitative study, UI was common and they thought that contracting a UTI aggravated it. They also described how they felt unhygienic, that they always had to be near a toilet and for much of the time they were afraid of urine leakage. Since both UI and UTI are very common among old women it is important to be aware of the extent to which their wellbeing is affected by such conditions. Thus it is sometimes possible to deal with UI problems by treating the UTI.

The women in the present qualitative study described a wide range of physical and psychological inconveniences and a general effect on health in association with UTI. They described physical inconveniences such as frequency and urgency, which can be regarded as typical symptoms of UTI, but they also described symptoms such as dizziness, pain in the hands and a general feeling of all-over illness. This has partly been described in previous research ⁵⁰ but to our knowledge, it has not been explored qualitatively earlier with the focus on this age group of old and very old women. Malterud & Baerheim reported similar descriptions of general symptoms ⁵⁰. Such findings might help healthcare professionals to listen to the patient more carefully which might enhance competence in the diagnosis and management of a symptom-based condition such as UTI. Psychological suffering was described in terms of feelings of depression, dejection, discomfort and an increased sensitivity in the present study. Those inconveniences contributed to their feeling that their daily life was affected and their social life was experienced as a suffering. These findings are in line with previous research but those studies were performed among younger women ^{44, 181}. In the study by Malterud & Baerheim the participants described symptoms such as irritability which the authors suggest is a normal psychological reaction to pain and distress ⁵⁰. The authors also speculate that an infected bladder mucosa might trigger responses in more generalised systems of the body ⁵⁰.

The participants in the present qualitative study described strategies for dealing with the illness such as avoiding leaving their homes while they were experiencing the physical and psychological inconveniences. This means that they might also be restricted in their daily life, as revealed by many of these old women in the interviews. They described it in terms of avoiding contact with other people, friends as well as relatives, when suffering from a UTI. To our knowledge, no other study describes similar findings among old women. However, some studies have reported that the

symptoms of the UTI experienced might affect daily activities and social functioning among younger women aged 18-64 years ^{44, 181}.

These old women also reported that sexual activities were affected when they had a UTI. They felt that they felt unhygienic, were afraid of urine leakage or that they were in too much pain to engage in sexual activities. These findings are partly in line with a previous study where women aged 18-55 years reported that they were in too much pain to engage in sexual activities or they were concerned that sexual activities would worsen their condition ⁴⁴. No studies have been found, however, dealing with how UTI affects sexual activities in this old age group.

The findings from the quantitative and the qualitative studies respectively corroborate the view that UTI, among old and very old women, is associated with low morale or subjective wellbeing and also seems to impact significantly on them, physically, psychologically and socially.

Depression

Not a particularly unexpected finding in the quantitative study was that depression was associated with low morale in both the univariate analysis and in the regression model. These findings are in line with previous research among very old people ^{6, 126}. Depression among very old women is common but it often remains undiagnosed and untreated and influences their morale. Although depression and low morale are closely related they cannot be considered as synonymous. Those who are depressed can still have high morale and those with low morale are not always depressed ¹²⁶. There was a strong correlation between PGCMS and GDS score, $r=-0.674$, but the scales measure different aspects of the person's well- or ill-being and using both scales is therefore worthwhile. High scores on the GDS are probably a better predictor of low morale than low PGCMS scores are of depression ^{126, 182}.

The findings in this thesis suggest that UTI in very old women is associated with delirium. Delirium in an old person might cause suffering which in turn might lead to the development of depression or at least depressive symptoms. It is suggested that the activation of the immune system and cytokines are involved in delirium, depression and UTI, which might explain the relationship between them.

Treatment of urinary tract infection

The guidelines for treatment of UTI in Sweden suggest that UTI is harmless in women and about 30% become free of symptoms without treatment in a week ¹⁸³. The interpretation of this may be that UTI does not always need to be treated, but these guidelines are not specifically based on very old women. These recommendations should perhaps be viewed with caution.

One may not be able to treat frail, old women in the same way as healthier, younger women because their morale or subjective wellbeing is much affected by UTI and they experience UTI as a source of great suffering. According to the guidelines, further investigation, such as a gynaecological examination, should be carried out in old women if the UTI is recurrent. This seems to be important also in very old women to be able to detect treatable conditions that contribute to the frequent UTIs.

Ethical considerations

Ethical approval was obtained for the data collections in the Umeå85+/GERDA studies and for the qualitative interview study. The participants were asked, both in writing and orally, if they were willing to participate in the study and they were informed that they could end their participation whenever they wanted without giving any reason. Informed consent was given by the participants themselves and in cases of impaired cognition also by their next of kin. The investigators, who were all medical professionals and experienced in working with old people, tried during the home visits to create an atmosphere in which the participant felt comfortable. Furthermore, it was important for the investigator to be sensitive to how the participant experienced the home visit and be prepared to interrupt it if necessary. The aim was that no home visit would be longer than two hours, in order to not tire the participant. This was not always possible because of the comprehensiveness of the data collection, so if necessary, an additional home visit was made to complete the data collection. The investigator had to be vigilant in discerning any discomfort shown by the individual and prepared to stop the data collection. It is especially important to be sensitive when old people with dementia disorders are interviewed because of the difficulties in communicating, however, those with dementia might be more severely affected by UTI and it would be unethical not to include them. People with dementia often suffer from UTI which often in turn complicates their condition through causing delirium and falls ⁴⁷. People with dementia need to be included in the guidelines concerning prevention, detection and treatment of UTI.

Methodological considerations

Papers I-III

The Umeå85+/GERDA study is a cross-sectional, longitudinal, population-based study including a relatively large number of very old individuals living both in the community and in institutions. One strength of this type of study is that the number of participants is large and the sample is representative which increases its external validity. Another strength was

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that the home visits were performed by investigators who had received training in the examination procedure and assessment scales and all of the assessments, scales and questions were interview administrated and conducted in the same order. All investigators had medical education and were experienced in working with old people. However, in a cross-sectional study one cannot determine any causalities. On the basis of these results it is not possible to know whether UTI causes vertebral fractures, UI, inflammatory rheumatic disease, MID or delirium or how such diagnoses are associated with UTI.

UTI was diagnosed if the person had a documented symptomatic UTI, with either short-or long-term ongoing treatment with antibiotics, or symptoms and laboratory tests that were judged to indicate the presence of a UTI by the responsible physician or the assessor. Medical records from the general practitioner, the hospitals in the catchment area or records from the care institutions were also investigated to evaluate and validate the UTI diagnosis. The UTI diagnosis in the medical records was based on urinary tests in combination with symptoms that were judged to be associated with UTI by the responsible physician. In addition, the results from all urinary cultures registered at the regional bacteriological laboratory were reviewed. This means that UTI diagnoses were registered if the participants had symptoms or signs of UTI when they were assessed or had received a recent diagnosis of UTI, with or without ongoing treatment, but also if they had had a UTI during the preceding year and the preceding 5 years, documented in the medical records or when they were assessed during the home visit in the Umeå 85+/GERDA project five years earlier. However, it is a weakness that no urinary tests or urine cultures were taken in these women in conjunction with the home visits. The optimal situation would have been if a urinary test had been taken in all the women in connection with the home visit. However, despite the high prevalence of UTI among these very old women, the data in the study probably represent a significant underestimation of the clinical problem since only UTIs diagnosed and documented in the records were registered.

Regarding the association between UTI and delirium, it was a limitation that there were no comprehensive somatic examinations made in connection with the patient's delirious state. Furthermore, delirium was registered if the participant had had episodes of delirium during the preceding month. We are, therefore, unable to be sure that they were delirious before the UTI diagnosis or if they had any other medical complications that may have contributed to their delirium. The physician might have interpreted the delirium as a symptom of UTI and thus interpreted the UTI as a result of the delirium, but this was only documented in two of the 39 cases with delirium and an ongoing UTI, with or without ongoing treatment. Another limitation was that there were no assessments for delirium before and after the UTI

treatment. From a methodological point of view, a randomized, placebo, controlled intervention study would have been preferable. In addition, a large proportion of the participants with delirium were unable to complete the PGCMS and thus the result may underestimate the impact of an UTI with an associated delirium on morale or subjective wellbeing.

The PGCMS scale was used to assess the participants' morale or subjective wellbeing. This scale is described as an appropriate instrument for measuring morale or subjective wellbeing among very old people^{123, 131}. Its strength lies in that it was developed for use in older people, is easily self- or interviewer-administered and is also applicable to participants with mild and moderate cognitive impairment since the 17 questions can be answered with only yes or no^{123, 131, 140}. The scoring of the PGCMS has an acceptable level of reliability, validity and a high internal consistency¹²³. However, one limitation is that in the oldest age group several women could not complete the PGCMS due to severe cognitive impairment. Additionally, no urinary tests were taken in conjunction with the home visits when the PGCMS was administered which makes it impossible to evaluate whether the participants with UTI and ongoing treatment had responded to the treatment.

There may possibly be instruments other than the PGCMS which are more suitable for measuring morale or subjective wellbeing. A previous study reported that there is a lack of appropriate health-related quality-of-life instruments for use in individuals with UTI¹⁸⁴. The study suggests that disease-specific questionnaires would provide a more accurate measure of the disease impact on health-related quality of life as for e.g. in connection with UTI¹⁸⁴.

Paper IV

The study population comprised only 20 women and a larger sample size might have been preferable to get a broader perception of the meaning of suffering from UTI. Nevertheless, this study population consisted of a specific sample of women. These 20 women were selected since they had had at least two UTIs in the preceding year. None of the interviewed women had an ongoing UTI which might have limited the variation of the experienced suffering. As this was a qualitative study, the results cannot be generalized to all women suffering from UTI, but the results were supported by our previous quantitative study of low morale among very old women with a diagnosed UTI, with or without ongoing treatment. The findings could, however, be applied to comparable situations in new contexts and provide new perspectives on old women's experiences of living with UTI. The results should also be understood in relation to the author's

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preunderstanding but such preunderstanding is an important part of the qualitative content analysis method.

The interviews were of different lengths, as some were more verbal than others. In some cases this could be because the women did not feel that their health was affected by UTI. The interviews still seemed to provide rich material. However, there were women in the qualitative study who did not report any effects of repeated UTIs, e.g. socially. In addition, 26 women declined to participate and some of them explained that they did not find UTI especially bothersome when they explained why they did not want to participate in the interview.

During the analysis, the author's tried to always stay close to the text in order to strengthen the credibility of the findings. Representative quotations from the text are presented to make a distinction between sub-themes and themes and to enhance the trustworthiness of the study all the authors were involved in the data analysis. All the authors read the interview texts but codes were sorted and themes and sub-themes were derived by two of the authors separately (IE, LF). Any text which was not relevant to the aim of the study was not included in the analysis.

Clinical implications

The findings in this thesis show that UTI is common among old and very old women and seems to be a serious health problem for many of them. Among the very old women UTI was associated with conditions such as vertebral fractures, UI, inflammatory rheumatic disease, MID and delirium. If these associations are valid one should assess old women with these conditions for an underlying UTI. If these associations indicate an etiological relation, prevention, detection and treatment of UTI is important. This means that UTI in old women can not be regarded as a trivial condition.

It seems that UTI among old and very old women has a serious impact on their morale or subjective wellbeing. Therefore, the problem these women experience should be taken more seriously. Knowledge about how UTI affects the health of old women can help nurses in developing strategies to support these women in order to alleviate unnecessary suffering. An awareness of the connection between UTI and UI is similarly essential if the women's needs are to be met and they are to be helped to gain better control of the inconveniences.

This thesis contributes knowledge concerning how, among old and very old women, UTI might be associated with other conditions and how UTI affects old women's morale and subjective wellbeing, all of which caregivers should be aware of. Assessment scales, such as the PGCMS, can be useful in these old women for detecting poor morale or poor subjective wellbeing.

The guidelines for treatment of UTI in Sweden cannot be regarded as based specifically on old and very old women, who are often frail and suffer from several co-morbid conditions. There may be reason to question these guidelines in this population. Among these old and very old women a comprehensive geriatric assessment is necessary to find the underlying causes for each individual. Likewise, the selection of antibiotics and the duration of treatment should be considered in each case and the result of the treatment should be evaluated.

Because UTI among old and very old women seems to have such serious consequences we must become better at preventing and detecting it. Regarding the detection of UTI, one must consider that these old women do not always present with symptoms typical of UTI as in younger women. It may also be that they take drugs that mask the symptoms and/or have a cognitive impairment that makes them unable to express their symptoms. Various ways of preventing repeated UTIs are described in previous research but no consensus has yet been reached. Local oestrogen therapy, long-term treatment with metenaminhippurat and cranberry drinks are examples of suggested preventive measures. Since UTI causes much suffering for so many old women, there should be more focus on secondary prevention, which should include assessment of the underlying causes of UTI. Treatment of predisposing factors such as malnutrition, UI and urinary

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retention should be implemented. When old women turn to the healthcare system with repeated UTI, the standard care should always include an examination of underlying causes; it should be mandatory and the focus should be on secondary prevention.

Implications for future research

Further research is needed among old and very old women with UTI since it seems to be a major health problem that causes them much suffering. Studies designed as interventions are important in this context if UTI is to be reduced or prevented, which could in turn reduce physical, psychological and social suffering.

The associations between UTI and conditions such as delirium, falls, malnutrition and UI should also be considered since it is possible to prevent these.

It is not possible to be certain about the meaning of the associations between UTI and vertebral fractures, inflammatory rheumatic disease, MID and delirium and maybe the study should be repeated to see if the same results emerge. If they do an intervention study can be planned based on these possible associations. In addition, to ensure the correct diagnosis of UTI, there should be a urinary culture for all women taken in connection with the data collection.

Advice often given to this group of patients, but for which the evidence is contradictory, concerns urinating frequently enough to empty the bladder, hygiene and drinking cranberry juice. There is probably a need to establish more consensus about this which should lead to intervention studies being conducted to measure the effects of such advice.

More qualitative research in this area is needed also including women with ongoing UTI at least in this age group of old and very old women. Perhaps a larger number of interviews should be carried out, perhaps with other types of questions and different qualitative method, such as a hermeneutic approach, used to analyse the data to gain a deeper understanding of the problem of living with repeated UTIs. More qualitative research is needed also among younger women and among men and a longitudinal qualitative study would be preferable to follow both female and male patients during a longer period and perhaps during periods when they suffer from a UTI.

Since there is a high incidence of UTI among very old women combined with an increasing older population, there is a great need for further research such as randomized interventions studies.

CONCLUSIONS

This thesis indicates that UTI is common among old and very old women and that it is a serious health problem. The strongest factors associated with UTI during the preceding year were vertebral fractures, urinary incontinence, inflammatory rheumatic disease and multi-infarct dementia. UTI seems to be associated with delirium and to have a significant impact on old and very old women's morale or subjective wellbeing and those affected suffer both physically and psychologically and their social life might be limited.

Thus healthcare professionals must improve their knowledge of UTI, change their attitude towards it and improve both treatment and primary and secondary prevention of UTI among old and very old women.

Since there is a high prevalence of UTI among old women combined with an increasing older population there is a great need for further knowledge about this area and also a great need for intervention studies.

To prevent, detect and treat UTI among very old women, the connection between the associated factors and UTI should be explored further. More attention has to be given to old and very old women with UTI and it has to be prevented, detected and treated if these women are to have a good old age.

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