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Treatment of acutely sick, frail elderly patients in a geriatric evaluation and management unit

Results from a prospective randomised trial

Doctoral thesis
for the degree of doctor medicinae

Trondheim, March 2006

Norwegian University of
Science and Technology
Faculty of Medicine
Department of Neuroscience and
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NTNU
Norwegian University of Science and Technology

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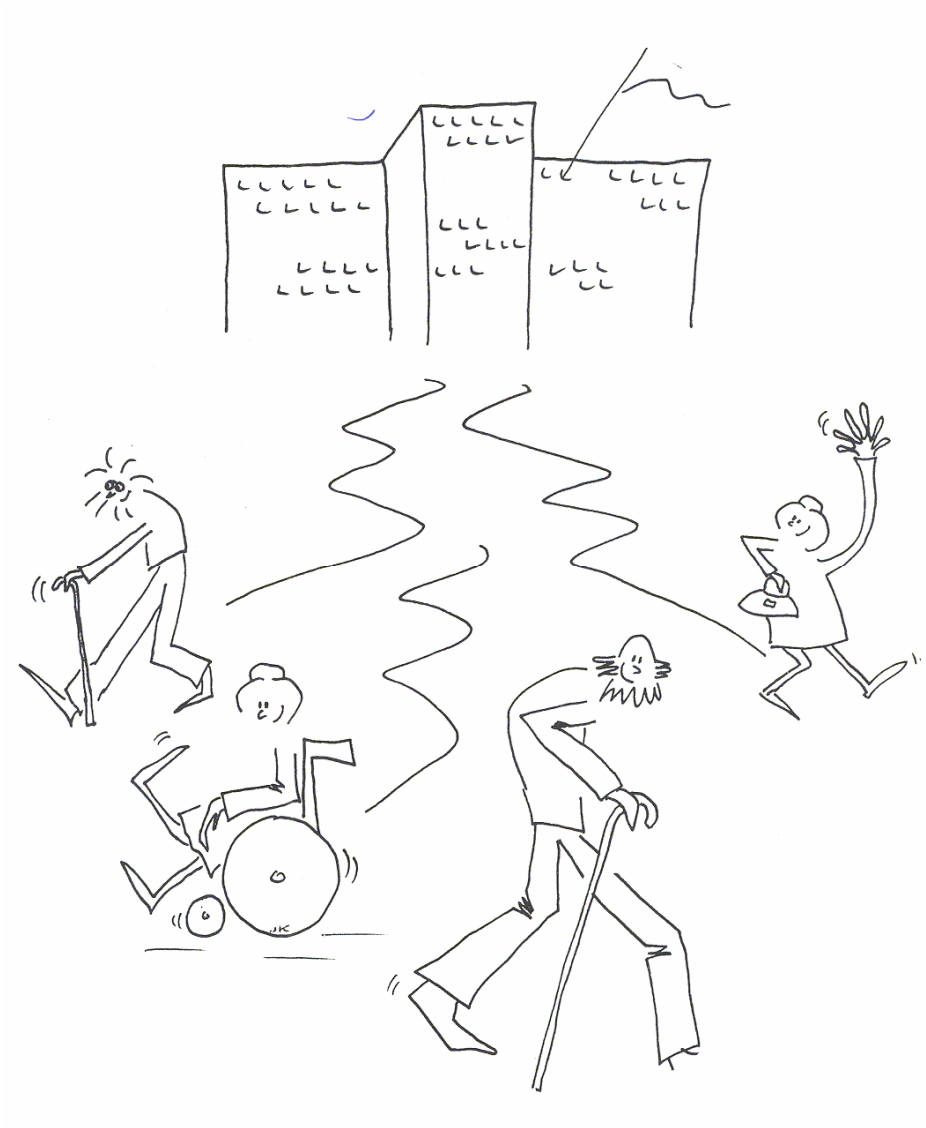
ISBN 82-471-7816-8 (printed ver.)
ISBN 82-471-7814-1 (electronic ver.)
ISSN 1503-8181

Doctoral Theses at NTNU, 2006:36

Printed by Tapir Uttrykk



I enjoy talking with very old people.
They have gone before us on a road by which we, too,
may have to travel,
and I think we do well to learn from them what it is like.

Socrates, in Plato's The Republic

Summary

Aims: The major aims of the present work were to investigate the impact of treatment in a geriatric evaluation and management unit (GEMU) as compared to the general medical wards (MW) with respect to mortality, place of care delivery, function, morale and drug prescription.

Background: Previous research has shown that hospitalised elderly patients may experience underdiagnosis and misdiagnosis, increased risk of iatrogenic conditions, and functional decline during the hospital stay. Documentation of treatment effects in acutely sick, frail elderly patients in GEMUs is scarce.

Methods: Acutely sick, frail patients aged 75 years or older were included. These had been admitted to different sections of the Department of Internal Medicine as emergencies. The patients were randomly assigned either to treatment in the GEMU (n = 127) or to continued treatment in the section where they were already staying, defined as MW (n = 127). The following inclusion criteria were used to target frail patients: chronic disability, acute impairment of single activity of daily living (ADL), mild/moderate dementia, confusion, depression, imbalance/dizziness, falls, impaired mobility, urinary incontinence, malnutrition, polypharmacy, vision or hearing impairment, social problems or prolonged bedrest. In the GEMU interdisciplinary assessment of all relevant disorders, prevention of complications and iatrogenic conditions, early mobilisation, rehabilitation and discharge planning were emphasised. The control group received treatment as usual from the Department of Internal Medicine. After discharge neither group received specific follow-up.

Findings: Mortality in the GEMU and MW groups was 12 % and 27 % respectively at three months ($p = 0.004$), 16 % and 29 % at six months ($p = 0.02$), and 28 % and 34 % ($p = 0.06$) at 12 months. The hazard ratio (HR) was 0.39 (95% CI 0.21 - 0.72) at three months. Heart disease was the major cause of death in both groups at both three and 12 months. At 12 months deaths from infections (mainly pneumonia) were more frequent in the GEMU group than in the MW group ($p = 0.04$). Length of hospital stay was longer in the GEMU than in the MW. There was no difference regarding place of care delivery in the two groups after discharge from hospital during six months of follow-up. Of all subjects recruited to the study, more GEMU than MW patients were still living in

their own homes at three and six months. The HR of living at home versus living in nursing homes or having died, was 2.1 (95% CI 1.3 - 3.4) after three months, and 1.6 (95% CI 1.1 - 2.5) after six months. Treatment in the GEMU had no measurable effect on physical function, cognition, symptoms of depression or morale during 12 months of follow- up as compared to treatment in the MW. If the dead were included in the analysis at the highest ADL dependency level, there was better function in the GEMU group at three months. The median number of scheduled drugs withdrawn and started per patient was higher in the GEMU than in the MW. Drugs with anticholinergic effects, cardiovascular drugs, particularly digitalis glycosides, and antipsychotic drugs, were withdrawn more often, while antidepressants and oestriol were started more often in the GEMU than in the MW. Fewer GEMU than MW patients had potential drug-drug interactions at discharge.

Conclusion: Treatment in the GEMU considerably reduced mortality as compared to treatment in the MW. Except for a longer duration of hospital stay in the GEMU group, there were no group differences regarding place of care delivery, function or morale among the survivors. If the dead were included in the analyses, patients treated in the GEMU had increased possibilities of living in their own homes during six months of follow-up and better function at three months. Drug treatment seemed to be more appropriate in the GEMU than in the MW.

Acknowledgements

The Norwegian Ministry of Health and Social Affairs gave financial support for the establishment of the geriatric evaluation and management unit (GEMU). The Research Council of Norway and the Norwegian University of Science and Technology have paid for me as a research fellow.

First, I would like to thank the patients and their caregivers who participated in this trial. They have made an important contribution to research within in geriatrics.

A number of persons have contributed to the completion of this thesis. Without Olav Sletvold and Ellen-Sofie Opdahl Mo there would be no thesis! Olav Sletvold was the project leader. He had the idea of the study, planned and designed it, and was responsible for building up the GEMU. In addition, he organised the study, performed study related assessments, assessed and treated patients in the GEMU. As my mentor for almost 12 years he has been introducing me into the exciting world of geriatric medicine and research. His never-ending enthusiasm, knowledge and humanity towards both patients and employees have been impressive.

Ellen-Sofie Opdahl Mo was involved in the planning of the study and participated in building up the GEMU. She was responsible for recruitment of patients into the study, data monitoring, and supervision of the staff at the GEMU during the study. Her small blue books containing records on every study patient have been valuable afterwards.

My co-mentors Stein Kaasa and Peter Fayers were introduced into this study while I was sweating over the data files. Peter Fayers has in addition to linguistic support, given me excellent supervision within the fields of statistics, research methods and presentation of data. Stein Kaasa has been giving me excellent scientific support by pointing me in the right direction through difficult, but necessary questions, especially when preparing the manuscripts.

Most of the time my work was carried out at the Unit of Applied Clinical Research that offered excellent working facilities with many nice colleagues. I would like to thank my friend and co-author Marit Slaaen Jordhøy who has been giving me a lot of support and help during all these years, co-author Turi Saltnes for her for pleasant collaboration and her assistance in the work with the data files and analyses of data on place of care delivery; Finn Guttvik, Karin Tulluan, and Gunn-Heidi Tobekk for their assistance whenever I needed it.

I would like to thank professor Jørund Straand for his contribution in planning the data collection on drug profile in the study population; the two medical students Tom Borza and Hilde Rygh Hjorthen for making the recording and coding of the information on drugs; and my co-authors Olav Spigset and Sabine Ruths who helped me creating a paper of all variables collected on drug prescription.

The study intervention and study related assessments were performed by the staff at the GEMU, and I will like to thank all who were employed at the GEMU during the study period for their enthusiasm, willingness and competence. Especially I would like to thank Brit Mæhlen for organising questionnaires and taking care of all data-files, and Kari Klevset Sneen who was the nurses' head in the GEMU during the study period. I would also like to thank the leadership of the Department of Internal Medicine who made the performance of this study possible.

Line Oldervoll and Jorunn Helbostad have given me kind support during the final parts of this work.

I would also like to thank my very good friend Anne Kvikstad and her husband Anders Todal Jenssen for all support during these years! My neighbour Gunlaug Solbakk and my sister Trude have been of great help during busy periods.

At last I would like to thank my two children Ingrid and Jens Christian for being the great pleasure of my life!

List of papers

The thesis is based on the following publications, which are referred to in the text by Roman numerals I – IV

I. Ingvild Saltvedt, Ellen-Sofie Opdahl Mo, Peter Fayers, Stein Kaasa, Olav Sletvold. Reduced Mortality in Treating Acutely Sick, Frail Elderly Patients in a Geriatric Evaluation and Management Unit. A Prospective Randomized Trial. J Am Geriatr Soc 50: 792-798, 2002.

II. Ingvild Saltvedt, Turi Saltnes, Ellen-Sofie Opdahl Mo, Peter Fayers, Stein Kaasa, Olav Sletvold. Acute geriatric intervention increases the number of patients able to live at home. A prospective randomized study. Aging Clin Exp Res 16: 300-306, 2004.

III. Ingvild Saltvedt, Marit Jordhøy, Ellen-Sofie Opdahl Mo, Peter Fayers, Stein Kaasa, Olav Sletvold. Randomised trial of in-hospital geriatric intervention: Impact on function and morale. Submitted for publication.

IV. Ingvild Saltvedt, Olav Spigset, Sabine Ruths, Peter Fayers, Stein Kaasa, Olav Sletvold. Patterns of drug prescription in a geriatric evaluation and management unit as compared with the general medical wards. A randomised study. Eur J Clin Pharmacol 61: 921-8, 2005.

Abbreviations

ACE	Acute Care for Elders
ADL	Activities of Daily Living
ADR	Adverse Drug Reaction
ATC	Anatomical Therapeutic Chemical classification
C	Control group
CGA	Comprehensive Geriatric Assessment
CI	Confidence Interval
DDI	Drug-drug interaction
DIM	Department of Internal Medicine
GDS	Geriatric Depression Scale
GEMU	Geriatric Evaluation and Management Unit
GP	General Practitioner
HR	Hazard Ratio
I	Intervention group
IADL	Instrumental Activities of Daily Living
iqr	Interquartile range
LOS	Length Of Stay
MW	General Medical Wards
MMSE	Mini Mental Status Examination
MADRS	Montgomery and Åsberg's Depression Rating Scale
OR	Odds Ratio
PGCMS	Philadelphia Geriatric Centre Morale Scale
RAI	Residential Assessment Instrument
RCT	Randomised Clinical Trial
SF-36	Short-form measure of generic health status
SD	Standard Deviation
UK	United Kingdom

1.0 Introduction

1.1 General aspects

In all parts of the world, the industrialised countries in particular, the population is growing older (Butler, 1997; Carpenter, 2005). The over-65s account of the populations is expected to increase considerably during the next decades (Figure 1) (Waaler, 1999; Ellis and Langhorne, 2004). In Norway 14% of the population was 67 years or older in 2004. This is expected to increase to about 19 - 22% in 2050. The number of persons over 67 years will double during this period, especially the number of persons over 90 years will increase (Figure 2) (Waaler, 1999; Statistisk sentralbyrå, 2005).

Longitudinal studies from industrialised countries indicate that elderly preserve health and function better now than they did 30 years ago (Manton *et al.*, 1997; Andrews, 2001; Cutler, 2001; Freedman *et al.*, 2002; Fries, 2002). Nevertheless, the number of elderly patients with chronic disorders is expected to increase. This is related to higher prevalence of chronic disorders among elderly as well as improved medical treatment that has reduced mortality of patients with disorders like heart failure and cancer (Khaw, 1997; Waaler, 1999; Mor, 2005).

Hospital admissions for emergencies have continued to increase year by year and is expected to increase even more with the largest increase among the elderly (Ellis and Langhorne, 2004; Jørgenvåg, 2005). In 2003 the 5% of the Norwegian population over 80 years caused 21% of all emergency admissions to somatic hospitals (Jørgenvåg, 2005). The number of early readmissions is also increasing, especially among those over 80 years (Jørgenvåg, 2005).

Hospitalised elderly are characterised by atypical symptom presentation, multi-morbidity and impaired cognitive and physical function (Levkoff *et al.*, 1988; Jarrett *et al.*, 1995; Waaler, 1999; Grimley Evans, 2000; Rø, 2000). During hospital stays they are at high risk of deconditioning and increased functional impairment, having

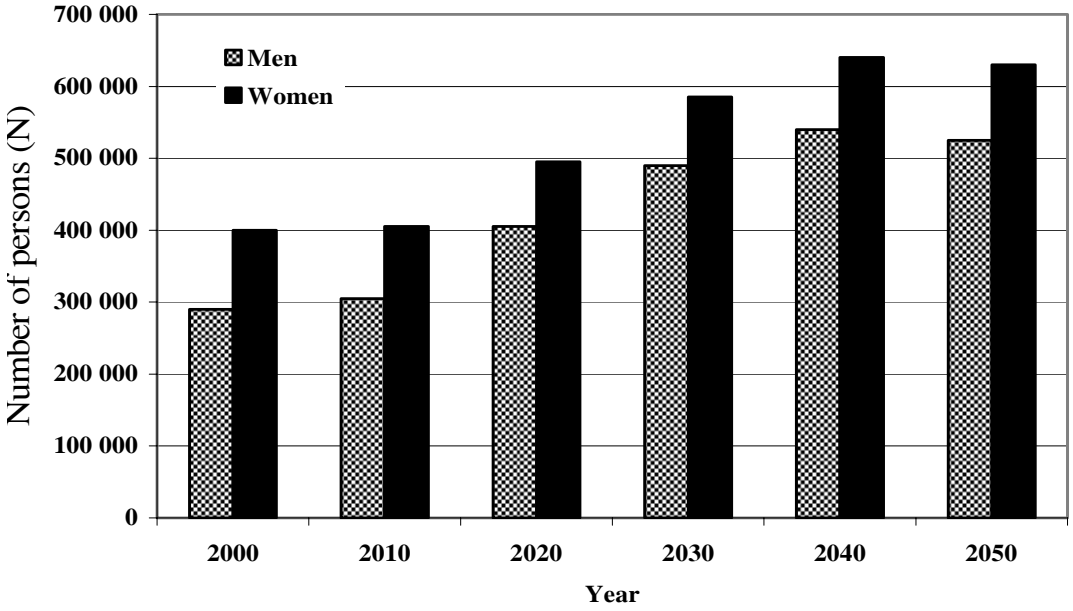


Figure 1. Number of persons over 65 years in Norway from 2000 to 2050 (Waaler, 1999)

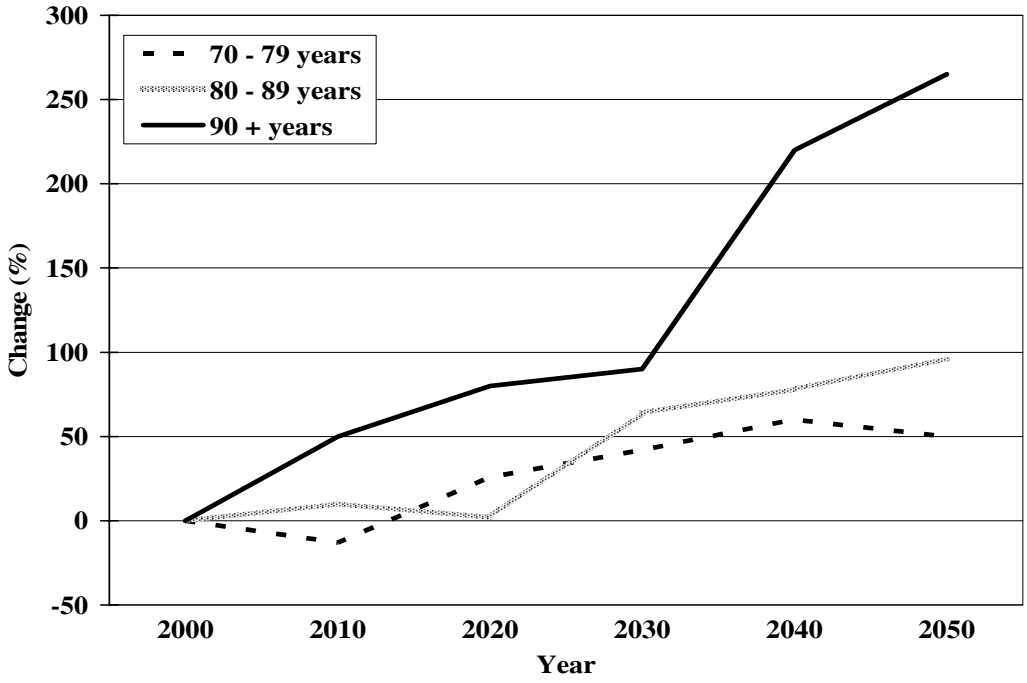


Figure 2. Expected change in the population over 70 years (%) (Waaler, 1999).

Both figures are reprinted with permission from the Norwegian Ministry of Health and Social Affairs (Waaler 1999).

increased risk of adverse hospital outcomes such as increased length of stay (LOS), nursing home placement and death (Gillick *et al.*, 1982; Harper and Lyles, 1988; Hoenig and Rubenstein, 1991; Creditor, 1993; Sager *et al.*, 1996; Fortinsky *et al.*, 1999). Iatrogenic complications and adverse drug events are common (Gorbien *et al.*, 1992; Lefevre *et al.*, 1992; Ebbesen *et al.*, 2001), but seem at least to be partly preventable (Leape *et al.*, 1991; Rothschild *et al.*, 2000).

1.2 Comprehensive geriatric assessment (CGA)

The basic principles of geriatric medicine were created in UK by Marjory Warren (1897-1960) who during the 1930s was in charge of a large chronic disease hospital filled with bedfast, neglected elderly patients. Marjory Warren introduced one of the cornerstones in modern geriatric medicine, the comprehensive geriatric assessment (CGA). Her approach towards these patients included individual assessment of needs, treatment matching these needs, improved environment for patients and staff, active rehabilitation and increased attention to these patients. This attitude soon showed to be beneficial in that many of the patients got out of bed, and some could even be discharged home (Grimley Evans, 1997).

CGA has become a fundamental component of geriatric care due to the complexity of the frail elderly patients who requires a multidimensional approach to obtain optimal diagnoses and treatment plans (Rubenstein *et al.*, 1991). CGA is a systematic, multidimensional diagnostic process focusing on evaluation of a frail elderly person's medical, psychosocial and functional capabilities and limitations in order to develop a coordinated and integrated plan for treatment and long-term follow-up, including appropriate rehabilitation (Rubenstein *et al.*, 1991; Rubenstein *et al.*, 1995; Elon *et al.*, 2000; Sletvold *et al*., 1996; Ellis and Langhorne, 2004). The goal of the CGA is accurate multidimensional diagnoses in order to improve care outcomes and quality of life for frail elderly (Rubenstein *et al.*, 1991). CGA has a number of major measurable dimensions, usually grouped into: physical health, functional status, psychological health and socio-/environmental parameters (Rubenstein, 1995).

1.3 In-hospital geriatric treatment

In general two models of in-hospital geriatric intervention have been described for high risk elderly patients: 1) A multidisciplinary geriatric consultation team that makes a systematic assessment of the patients and recommends a plan of treatment (Ellis and Langhorne, 2004). 2) Treatment of patients in geriatric evaluation and management units (GEMUs). A GEMU is a ward admitting frail elderly in-patients for a process of systematic multidisciplinary assessment, review and therapy (Ellis and Langhorne, 2004). GEMUs have been crucial in developing basic concepts of CGA. During the last ten years another kind of in-hospital wards has been introduced, the Acute Care for Elders units (ACE) (Palmer *et al.*, 1998). These are units designed to prevent functional decline in hospitalised elderly in general. The ACE model is characterised by prepared environment, patient centred care by primary nurse, interdisciplinary team rounds and medical care reviews. Later in this thesis ACE and GEMU studies will both be referred to as GEMU studies.

Early uncontrolled studies on the effectiveness of in-hospital geriatric assessment and treatment were performed on both interdisciplinary teams and treatment in GEMUs. Many of them showed beneficial effects of the treatment in terms of improved diagnostic accuracy (Rubenstein *et al.*, 1981; Applegate *et al.*, 1983; Rubenstein *et al.*, 1987), reduced discharge to nursing homes (Sloane, 1980; Applegate *et al.*, 1983; Lefton *et al.*, 1983), improved functional status (Rubenstein *et al.*, 1981; Applegate *et al.*, 1983; Rubenstein *et al.*, 1987), improved cognition (Applegate *et al.*, 1983), and reduced medication (Rubenstein *et al.*, 1981; Rubenstein *et al.*, 1987).

Randomised clinical studies (RCTs) on the effect of geriatric consultation teams have shown conflicting results, but generally no or small effects have been found (Stuck *et al.*, 1993; Naughton *et al.*, 1994; Reuben *et al.*, 1995).

Before the present study was performed a meta-analysis of the effectiveness of treatment in GEMUs as compared to usual care was published (Stuck *et al.*, 1993). Six studies of treatment in GEMUs were included in the analyses (Teasdale *et al.*, 1983; Rubenstein *et al.*, 1984; Gilchrist *et al.*, 1988; Applegate *et al.*, 1990; Powell and

Montgomery, 1990; Harris *et al.*, 1991). Only one of these concerned acute medical diseases (Harris *et al.*, 1991), and one has only been published as an abstract (Powell and Montgomery, 1990). Four were rehabilitation studies of which only two were RCTs including general high risk elderly patients (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990), one was done in an orthogeriatric unit (Gilchrist *et al.*, 1988) and one did not use a randomised design (Teasdale *et al.*, 1983). In the meta-analysis it was concluded that treatment in GEMUs reduced six-month mortality (OR 0.65, 95% CI 0.46 - 0.91). Further it increased the chance of living at home versus being dead or in nursing homes at six months (OR 1.8, 95% CI 1.28 - 2.53) and 12 months (OR 1.68, 95% CI 1.17 - 2.41). In addition, it was concluded that treatment in GEMUs improved physical function at six and 12 months and cognitive function at six months. The magnitude of these effects was not specified.

As mentioned above only three single randomised clinical studies on treatment in GEMUs had been published when the present study was planned (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Harris *et al.*, 1991). Later results from four studies have been published (Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000; Cohen *et al.*, 2002) (Table 1), one of them being a multi-centre study (Cohen *et al.*, 2002).

Rubenstein, Applegate and Cohen performed studies in a subacute setting; they included patients who had been stabilised after admission for acute disorders (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002). Patients in these studies were also targeted for frailty, and those who were too healthy or too ill were excluded. The study of Harris, Landefeld, Asplund, and Counsell were all performed in acute care settings recruiting patients with non-elective admissions, excluding those in need of any kind of specialised treatment (Harris *et al.*, 1991; Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000).

In most of these studies the intervention is briefly described with few details. All studies performed CGA and rehabilitation, and they had multidisciplinary teams that in most cases were staffed with a geriatrician, trained nurses, physiotherapists, occupational

Table 1. Randomised clinical studies comparing treatment in GEMUs with conventional hospital treatment.

Trial	Patients	Patient characteristics	GEMU	Results
Rubenstein *et al.*, 1984 Veteran administration hospital, USA	Sub-acutely sick, frail patients ≥ 65 years hospitalised > 7 days in medical and surgical wards with functional problems that interfered with discharge to home. Excluded patients were medically unstable, too sick, too healthy or nursing home patients.< 10% of those screened were eligible. I: n= 63, C: n=60	Mean age (I/C) 79/77 years Sex (% male) (I/C) 95/97 6-month mortality (C) 26% 1-year mortality (C) 48%	Multidisciplinary team* with regular meetings and goal setting. CGA and outpatient follow-up.	During one year of follow up GEMU patients had reduced mortality (24% versus 48%), were less likely to be discharged to or to have spent any time in nursing homes, reduced readmissions to hospital, improved function and morale. LOS (mean) (I/C) 55/44 days.
Applegate *et al.*, 1990 Community rehabilitation hospital, USA	Sub-acutely ill, frail patients ≥ 65 years referred to geriatric clinic after acute medical or surgical illness with potentially reversible functional impairment and risk of nursing home placement. Excluded patients were medically unstable, too sick, too healthy or nursing home patients. 56% screened eligible. I: n=78 C: n=77	Mean age (I/C) 79/78 years Sex (% male) (I/C) 21/26 1-year mortality (C) 25%	Multidisciplinary team* with regular meetings and goal setting. CGA.	During 6 months of follow-up GEMU patients had improved ADL, were more often residing in the community, had less nursing home stays. 6-month mortality was (%) (I/C) 10 / 21 (p=0.08). LOS (mean) (I/C) 24/18 days.
Cohen *et al.*, 2002 11 Veterans Affairs hospitals, USA	Sub-acutely ill, frail patients ≥ 65 admitted to medical and surgical wards. Excluded patients who were medically unstable, too sick or too healthy and nursing home patients. 3% of those screened were eligible. Multicentre, two by two factorial design. GEMU and geriatric follow-up (n=346); GEMU and usual follow- up (n=348); usual in-hospital care and geriatric follow-up (n=346); usual in-hospital care and usual follow up (n=348).	Mean age (I/C) 74/74 years Sex (% male) 98% (whole study population) 1 year mortality 21% (C)	Multidisciplinary team* with regular meetings and goal setting. CGA.	At discharge GEMU patients had greater improvements in scores of SF-36 (4 of 8 subscales), ADL and physical performance. At 1 year patients with geriatric follow-up had better scores on the SF-36 mental health subscale. LOS (mean) (I/C) 35/28 days.

Harris *et al.*, 1991 Australia	Acutely ill patients ≥ 70 years admitted to medical department. Excluded patients hospitalised last 7 years and nursing home residents. Percentage eligible or included of all admitted not given. I: n=97 C: n=170	Mean age (I/C) 79/78 Sex (% male) (I/C) 35/41 1-year mortality (C) 29%	Multidisciplinary team* CGA.	No difference in survival, health care utilisation, ADL, mental health. LOS (mean) (I/C) 10/10 days
Landefeld *et al.*, 1995 Teaching hospital, USA	Acutely ill patients ≥ 70 years admitted for general medical care. Excluded if specialised treatment needed. 46% screened were eligible. I: n=327 C: n=324	Mean age (I/C) 80/80 Sex (% male) (I/C) 32/35 3-month mortality (C) 13%	ACE with specially designed environment and nursing protocols. Multidisciplinary team* with regular meetings and goal setting. CGA.	GEMU group at discharge: Improved ADL, improved general health status, reduced number of patients discharged to long-term care institutions. At 3 months: No difference in ADL, fewer GEMU patients lived in long-term care institutions. LOS (mean) (I/C) 7/8 days
Asplund *et al.*, 2000 University hospital, Sweden	Acutely ill patients ≥70 years admitted for general medical care. Excluded: need of specialised treatment in other ward. 37% of ≥ 70 years admitted were included. I: n=190 C: n=223	Mean age (I/C) 81/81 Sex (% male) (I/C) 58/63 3-month mortality 8%	Multidisciplinary team* with regular meetings and goal setting. CGA.	No difference in survival, ADL, function, well-being, nursing home stays. LOS (mean) (I/C) 5.9/ 7.3 days (p=0.002).
Counsell *et al.*, 2000, community teaching hospital, USA	Acutely ill patients ≥ 70 years admitted to medicine or family practice service. Nursing home patients excluded. Proportion of admissions that were eligible was not given, 23% of those eligible were randomised. I: n=767 C: n=764	Mean age (I/C) 80/79 Sex (% male) (I/C) 40/39 1 year mortality 30%	ACE with specially designed environment and nursing protocols. Multidisciplinary team* with regular meetings and goal setting. CGA.	No difference in ADL between the groups. The composite outcome of ADL decline and nursing home placement less frequent in the GEMU group. The process of care and provider satisfaction was better in the GEMU group. LOS (mean) (I/C) 6/6 days

I= Intervention group, C= Control group, CGA= Comprehensive Geriatric Assessment, ADL= Activities of Daily Living, GEMU= Geriatric Evaluation and Management Unit, ACE= Acute Care for Elderly unit (Palmer *et al.*, 1998), LOS= Length Of Stay. Multidisciplinary teams: All teams had specialised nurses, physiotherapists, occupational therapists and a geriatrician. All, except one (Asplund *et al.*, 2000) had social workers. All except two (Harris *et al.*, 1991; Counsell *et al.*, 2000) had dietetics employed. Clinical pharmacist, speech and language therapist, audiologist, dentist and psychologist were employed in two studies (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990).

therapists, dietetics, and social workers (Table 1). In most studies the teams had regular meetings with goal setting at least once a week. Two of the studies described that implementation of nursing protocols was emphasised (Landefeld *et al.*, 1995; Counsell *et al.*, 2000). In the studies of Rubenstein and Cohen an outpatient geriatric follow-up was given after discharge from hospital (Rubenstein *et al.*, 1984; Cohen *et al.*, 2002). Only in the study of Cohen a two by two factorial study design made it possible to distinguish between effects of CGA offered in the GEMU and that offered after discharge.

In four of the studies function was improved in the intervention group as compared to the control group (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Landefeld *et al.*, 1995; Cohen *et al.*, 2002). Discharges to nursing homes were reduced in two studies (Rubenstein *et al.*, 1984; Landefeld *et al.*, 1995), and the number of nursing home days during one year of follow-up was reduced in two of the studies (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990). Two studies improved morale or health related quality of life (Rubenstein *et al.*, 1984; Cohen *et al.*, 2002). Only one study demonstrated statistically significant reduced mortality (Rubenstein *et al.*, 1984), while another had a 50% reduction in mortality without achieving statistical significance (Applegate *et al.*, 1990). One study found reduced number of readmissions to hospital (Rubenstein *et al.*, 1984), and one reduced LOS (Asplund *et al.*, 2000). Improved process of care and provider satisfaction in the intervention group, was shown in the study of Counsell (Counsell *et al.*, 2000).

1.4 Separate components of CGA

CGA is directed towards prevalent and frequently overlooked conditions in frail elderly. The components most commonly included in the CGA are physical function, medication, nutrition, pain, urinary incontinence, constipation, vision and hearing, cognition, depression, socio-environmental factors and discharge planning (Rubenstein *et al.*, 1995; Elon *et al.*, 2000).

Assessment of physical function often includes ADL, IADL and mobility (Pearson, 2000). Deterioration in ADL often accompanies illness in frail elderly (Harper and

Lyles, 1988). Assessment of ADL has been shown to give clinical important information beyond that provided by laboratory data and comorbidity indexes (Covinsky *et al.*, 1997). Patients with impairments in ADL before hospitalisation have increased risk of further loss of function during the hospital stay (McVey *et al.*, 1989; Sager *et al.*, 1996; Fortinsky *et al.*, 1999). Further, impairments in ADL is predictive for increased LOS, increased risk of hospital complications, readmissions, nursing home placement and mortality (Donaldson *et al.*, 1980; Becker *et al.*, 1987; Narain *et al.*, 1988; Rowland *et al.*, 1990; Mayer Oakes *et al.*, 1991; Covinsky *et al.*, 1997; Ponzetto *et al.*, 2003; Rozzini *et al.*, 2005). All RCTs on treatment in GEMUs that targeted frail elderly have used impaired ADL as one of their inclusion criteria (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002). Four RCTs on efficacy of treatment in GEMUs and the metaanalyses of Stuck showed improvement in ADL by treating patients in GEMUs (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Stuck *et al.*, 1993; Landefeld *et al.*, 1995; Cohen *et al.*, 2002).

Impaired mobility is a risk factor for falls which is common among hospitalised elderly (Evans *et al.*, 2001). Assessments and interventions to prevent falls have been shown to be efficient among those living in the community (Gillespie *et al.*, 2003) and in nursing homes (Becker *et al.*, 2003). There are also a few studies showing beneficial effects of interventions on falls within hospitals (Evans *et al.*, 2001; Haines *et al.*, 2004), but further research is needed (Gillespie, 2004). Two GEMU studies showed that CGA improved mobility (Counsell *et al.*, 2000; Cohen *et al.*, 2002), but none of these used falls as an endpoint.

Hospitalised frail elderly patients often suffer from cognitive impairment, mostly due to delirium, dementia or delirium on dementia. In the study of Rø on hospitalised patients 75 years or older, 41% had one or more symptoms of impaired cognition (Rø, 2000). The occurrence rate of delirium among hospitalised elderly in other studies has varied between 14 - 56%. Delirium is related to several adverse outcomes like increased LOS, poor functional status, increased risk of nursing home placement and death (Cole and Primeau, 1993; McCusker *et al.*, 2001; Inouye, 2004). It is frequently overlooked by doctors and nurses, if not systematically screened for (Laurila *et al.*, 2004). Research

has shown that the implementation of a systematic program to identify and prevent delirium may be efficient (Inouye *et al.*, 1999; Anderson, 2005), while evidence for efficient treatment strategies is still lacking (Britton and Russell, 2004). No single RCT of treatment in GEMUs has shown effect on cognition, while in the metaanalysis of Stuck treatment in GEMUs was shown to improve cognitive function at six months (Stuck *et al.*, 1993).

About 5-10% of elderly outpatients have depression (Alexopoulos *et al.*, 2002), and the prevalence seem to be higher for patients who are referred to hospitals (Ames and Tuckwell, 1994). Depression is frequently overlooked in the elderly (Meldon *et al.*, 1997). Depression has negative impact on patients' quality of life and increase suicidal risk. Both milder depressive symptoms and symptoms fulfilling the diagnostic criteria for depression may increase disability (Covinsky *et al.*, 1997; Lyness *et al.*, 1999; Alexopoulos *et al.*, 2002). Adequate pharmacological and non-pharmacological treatment can be efficient, and may improve both symptoms of depression and function (Borson *et al.*, 1992; Bartels *et al.*, 2002). In the study of Counsell depression was recognised more often in the GEMU as compared to usual care (Counsell *et al.*, 2000). In the study of Landefeld depression scores was lower at discharge in the intervention group (Landefeld *et al.*, 1995).

Although assessment of nutrition is one component of CGA, none of the RCTs have reported outcomes related to nutrition. Malnutrition is common among frail elderly (Pirlich and Lochs, 2001), and is associated with decreased immune function, pressure ulcers, frailty, hip fractures, increased LOS and increased mortality (Morley, 2003). Risk factors for malnutrition in the elderly are somatic disorders, dental problems, immobility, drugs, dementia, depression, social isolation, and problems preparing food (Pirlich and Lochs, 2001). Most causes are reversible and treatment has to be directed towards the underlying factors (Morley, 2003). Treatment with nutritional supplements has been shown to produce a small but consistent weight gain in older people (Milne *et al.*, 2005), and vitamin D supplementation has been shown to have positive impact on neuromuscular function and incidence of falls (Venning, 2005). Furthermore, social

support enhanced food intake in both home-dwelling and nursing home patients (Simmons *et al.*, 2001; Suda *et al.*, 2001).

One of the goals of CGA is to improve patients' quality of life. General well-being has been an endpoint in two studies (Rubenstein *et al.*, 1984; Asplund *et al.*, 2000). One of these found that GEMU treatment had beneficial effects (Rubenstein *et al.*, 1984). The study of Cohen was the only study measuring health related quality of life (SF-36) (Cohen *et al.*, 2002). Improvements in the four subscales measuring physical function, bodily pain, energy and general health were observed at discharge. With reference to other studies it was concluded that the magnitude of these changes were clinically and socially meaningful. The finding of improved score on bodily pain is important, as pain has been shown to be prevalent among frail elderly and is associated with impaired mood, depression, impairments in ADL, and decreased activity involvement (Won *et al.*, 1999; Onder *et al.*, 2005). Under-treatment of pain has been shown to be common, especially among the oldest and those with dementia (Landi *et al.*, 2001).

Urinary incontinence has been identified as a problem in 24 -33% of all medial in-patients over 75 years (Ouslander J.G., 2000; Rø, 2000). This problem is often experienced as embarrassing and may have adverse effects on physical health, social life, mood and quality of life. In addition it is costly. The pathogenesis for urinary incontinence among elders is often multifactorial. Important risk factors are cognitive impairment, mobility problems, disorders in the lower urinary tract, increased urinary production (drugs, diabetes) and adverse drug reactions (Ouslander J.G., 2000). The identification of potentially reversible factors is important. Behavioural, pharmacologic and surgical interventions may help. None of the RCTs on treatment in GEMUs have focused on urinary incontinence.

There is little research on how the structure and organisation of GEMUs should be. In general, a broad approach towards the elderly patients seems to be sensible. Therefore the GEMU staff should represent a multidisciplinary team. Furthermore the environment has to be designed and organised for an elderly population, and findings of CGA should lead to the implementation of coordinated plans for the management of

individual patients. Studies focusing on single elements of structure and organisation are generally lacking, except for the study of Counsell (Counsell *et al.*, 2000) where the process of care and provider satisfaction was better in the GEMU as compared to conventional care.

The methods for assessment vary, but often one or more sets of instruments to assess functional, psychological and social status are employed (Rubenstein *et al.*, 1991). Use of assessment scales has been recommended in daily practice. They are more sensitive than clinical judgement in detecting moderate impairments, valuable in individual care planning, and improve quality of care. In addition, they give important information about progress in hospitalised patients, and enlighten research (Pinholt *et al.*, 1987; Schroll, 1997; Phillips *et al.*, 1997; Poulsen *et al.*, 2005).

Discharge planning has been described as a key element in all RCTs on treatment in GEMUs, but none of them were designed to evaluate the effectiveness of discharge planning. Two systematic reviews on this topic have excluded GEMU studies (Parker *et al.*, 2002; Shepperd *et al.*, 2004). The reviewers conclude that there are generally few studies on discharge planning, and most of those which exist are from USA. Most studies have excluded patients being cognitively impaired. Endpoints studied were mortality, LOS and readmissions to hospital, while patient and caregiver satisfaction, physical or cognitive function or quality of life have not been assessed. The reviews concluded that comprehensive discharge planning can have beneficial effects on subsequent readmission rates, especially if intervention is given both at the hospital and in the patients' homes.

The intervention performed in the GEMU has often been characterised as a "black box" intervention, meaning that we do not know which elements are important or efficient. As shown above we definitely have some evidence that can shed a little light into this black box. There is extensive research going on within most of the areas described above.

1.5 Drugs

There is little evidence about the effect of drug treatment in frail elderly patients because they are often excluded from clinical trials (Le Quintrec *et al.*, 2005; McMurdo *et al.*, 2005). Nevertheless, the prevalence of chronic disorders is high in the elderly, and they are often using many different drugs concurrently (Beers *et al.*, 2000). The intention of pharmacotherapy is to improve health, function and quality of life in addition to prevention of diseases. But, drug treatment in these patients may be a complex issue due to diminished physiologic reserves and age-related changes in pharmacokinetics and pharmacodynamics (Meyer, 2000). Adverse drug reactions (ADRs) are common among frail elderly with high comorbidity, those who are using many different drugs, or specific types of drugs (Carbonin *et al.*, 1991; Hanlon *et al.*, 2003; Ruths *et al.*, 2003). Many admissions to hospital are related to ADRs, of which some may even be fatal (Lazarou *et al.*, 1998; Ebbesen *et al.*, 2001; Onder *et al.*, 2002; Pirmohamed *et al.,* 2004). There are several reasons for ADRs, such as overuse of drugs, inappropriate use, or poor adherence to treatment recommendations (Kelly and Chamber, 2000; Ahmed *et al.*, 2002; Hanlon *et al.*, 2003; Onder *et al.*, 2003; Hanlon *et al.*, 2004; Hajjar *et al.*, 2005). Frail elderly patients are also at increased risk of ADRs related to withdrawal of drugs, either due to physiological reactions (for example of benzodiazepines or beta-blockers) or due to exacerbation of an underlying disease (for example increased heart failure when withdrawing diuretics) (Kennedy *et al.*, 2000; Petrovic *et al.*, 2002; Hanlon *et al.*, 2003; Ruths *et al.*, 2004). Another problem with drug treatment that frequently occurs among elderly patients is therapeutic failure leading to lack of disease control and subsequent hospital admissions (Hanlon *et al.*, 2003). In addition to non-adherence, this may be related to underuse of medications that has been shown to be a problem in the elderly for example during treatment of heart failure (Gattis *et al.*, 1998; Ruths *et al.*, 2000).

Treatment in GEMUs has been shown to reduce polypharmacy (Rubenstein *et al.*, 1984; Owens *et al.*, 1990; Kruse *et al.*, 1991), the frequency of adverse drug reactions (Carbonin *et al.*, 1991), prescription of inappropriate and unnecessary drugs (Owens *et*

al., 1990; Carbonin *et al.*, 1991; Counsell *et al.*, 2000; Schmader *et al.*, 2004) and underuse of drugs (Schmader *et al.*, 2004).

2.0 Aims

The aim of this thesis is to compare the effect of treating patients in a Geriatric Evaluation and Management Unit (GEMU) with care delivered at other sections in a Department of Internal Medicine (DIM), defined as general Medical Wards (MW).

More specific the purposes are to assess the effect on

- Mortality
- Place of care delivery after inclusion
- Function and morale
- Drug prescription

3.0 Material and methods

3.1 Local background for the study

The trial on which this thesis is based, was performed at the University Hospital of Trondheim that serve not only as the regional hospital for Central Norway, but also as the local hospital for about 200 000 inhabitants in the county of Sør-Trøndelag, Norway.

For many years there had been a problem that many patients defined ready for discharge, actually could not be discharged due to lack of nursing home beds in the municipality of Trondheim. Generally, these were elderly patients admitted to hospital due to acute disorders, but characterised by several comorbidities as well as physical and cognitive impairments. Before 1994 there was no specialist service for geriatric patients, neither in-hospital nor community-based.

In 1993, aiming for better collaboration on geriatric patients across administrative sectors, the hospital and the municipality applied for funding of a GEMU. The Norwegian Ministry of Health and Social Affairs gave support for the establishment and scientific evaluation of such a unit. Another important promoter of the study was the experience from a RCT on the efficacy of treatment in a Stroke Unit that had been performed at the Department of Internal Medicine (DIM) a few years earlier (Indredavik *et al.*, 1991).

A nine-bed GEMU was established in April 1994. The GEMU was a section of the DIM that already had eight different sections within other branch specialties of internal medicine and a total of 190 beds. Over 90% of all admissions were emergencies. The period from April to October 1994 was a run-in period in the GEMU with focus on training of employees and establishing routines for assessment and treatment.

3.2 Conventional (control) care

In the present study general medical wards (MW) have been defined as all wards in the DIM except the GEMU. Conventional (control) care is defined as treatment given in the MW. The care at the DIM was given according to the general protocol for the DIM and guidelines within internal medicine. Except for the GEMU and Stroke Unit, there was no dedicated program at the hospital focusing on the handling of frail elderly patients with high degree of comorbidity.

In the MW residents and specialists in internal medicine and different branch specialties were responsible for the medical treatment provided together with nurses and enrolled nurses (Table 2). Doctors and nurses had meetings concerning all patients of the ward every morning. Physiotherapy and occupational therapy were normally given when prescribed by the doctor, each occupational therapist and physiotherapist was serving several wards. In most cases the cooperation between physiotherapists, occupational therapists and the rest of the staff in the MW was not systematically organised. When the MW patients were referred for consultation by the geriatrician, this was performed according to general routines of the GEMU. Home care nurses were telephoned to discuss arrangements after discharge only if the hospital staff found it necessary.

The DIM had educational programs for residents who were specialising within internal medicine and in branch specialties of internal medicine including geriatrics.

3.3 The geriatric evaluation and management unit (GEMU)

3.3.1 Organisation

The physical environment in the GEMU was comparable to that in other medical wards, apart from an additional combined dining/activity-room. As far as possible an "enriched" environment was created to enlighten the patients' orientation (Inouye, 2004). This included visible calendars and clocks in all rooms, naming plates and signs on the doors, sufficient lightening, and access to necessary aids (including hearing aids) and to news (television, newspapers, and magazines).

Table 2. Comparison of staff and patient approach between the GEMU and the MW.

GEMU (9 beds)	**MW**
Staff	
Some nurses with formal training in geriatric nursing*	Same number of nurses as the GEMU
Enrolled nurses	Enrolled nurses
One geriatrician*	Branch specialists of internal medicine
One (sometime two) residents*	One resident per 5-10 beds
Two occupational therapists*	½ occupational therapist per 180 beds
One physiotherapist*	Five physiotherapist serving about180 beds
Intervention	**Conventional care**
Medical treatment according to general guidelines	Medical treatment according to general guidelines
Interdisciplinary assessment	Assessment mainly by doctors and nurses
Management of all relevant disorders	Mainly management of diseases precipitating the emergency admission
Screening	
Orthostatic hypotension	
Drug regimen	
Malnutrition	
Urinary incontinence	
Constipation	
Function (cognition, ADL, IADL)	
Gait, balance and mobility	
Depression	
Vision and hearing	
Social problems/ caregiver burden	
Prevention of iatrogenic conditions and complications	
Early mobilisation and rehabilitation	
Discharge planning	
Visit in patients' homes if indicated	

*Also performing study related assessments in both groups during index stay and follow-up. GEMU= Geriatric Evaluation and Management Unit, MW= General Medical Wards, ADL= Activities of Daily Living, IADL= Instrumental Activities of Daily Living.

The number of nurses and enrolled nurses employed in the GEMU was comparable to that in MW, some of those employed in the GEMU had formal training in geriatric nursing. In addition, the GEMU had two occupational therapists and one physiotherapist. One geriatrician and one (occasionally two) residents were responsible for the medical treatment in the GEMU (Table 2). During nights, week-ends and holidays residents working at the DIM were responsible for the medical service of the GEMU patients. When needed, other specialists, a social worker or dentist was consulted.

An interdisciplinary approach was employed with close collaboration between all disciplines involved. The nurses and doctors had formal meetings discussing all patients every morning. Interdisciplinary team meetings were arranged twice a week to report assessments, set goals, discuss problems and plan discharge. There were also frequent informal meetings where specific tasks were discussed.

Patient and family involvement was encouraged. Both patients and caregivers got information regularly during the whole stay in the GEMU and at discharge. As soon as possible after admission Home services were called by a nurse to get further information about patients' background and living conditions. Before discharge meetings were arranged for the majority of the patients to discuss necessary arrangements after discharge. In most cases the patient, caregivers, a representative from the Home services and GEMU staff participated.

The collaboration with the general practitioners (GPs) was deficient. Initially a letter was sent to the GPs informing that their patients were admitted to the GEMU, and with an invitation to contact the GEMU to discuss further treatment. As there was hardly any response, this system was discontinued after three to four months. In some cases the doctors of the GEMU called the GPs to discuss specific patients who needed specific medical follow-up by their GPs after discharge.

The GEMU had a multidisciplinary educational program 45 minutes per week consisting of lectures on central issues within geriatric medicine for all members of the staff. In addition, the doctors had an educational program 45 minutes every morning within geriatrics and internal medicine.

3.3.2 Assessment and treatment

The treatment in the GEMU consisted of both CGA and conventional medical treatment focusing on both the acute medical problems that precipitated the hospital admission and other relevant illnesses i.e. medical conditions that seemed to affect the patients' (or caregivers') function or quality of life (Sletvold *et al*., 1996).

The medical history of the patients was obtained through previous medical records and interviews with patients and caregivers. In addition to a medical history concerning acute and chronic illnesses, patients, caregivers and Home services were questioned regarding the social situation, physical and cognitive function, drug regimens, nutrition, urinary incontinence, constipation and depression before admission to hospital.

A thorough clinical work-up and inspection of the skin, neurological examination, assessment of vision and hearing and digital examination of rectum was performed in all patients. Body mass index was calculated; blood pressure was measured with the patient supine, sitting and standing after two minutes. Physical function including gait and balance, ADL and instrumental ADL (IADL) was evaluated. The GEMU staff performed observations of the patients with respect to physical function, ADL, eating habits, elimination, cognition, mood and behaviour. Patients having problems related to their urinary bladder were always examined for residual urine. Standard study related assessments with respect to ADL, IADL, cognition and symptoms of depression were also used in the clinical evaluation of each patient. Drug regimens were continuously evaluated with respect to side-effects, efficacy, appropriateness, doses, interactions and compliance.

Further examinations and medical management were performed if appropriate according to general guidelines within geriatric medicine and internal medicine and in concordance with the patients' (and caregivers') wishes.

For all patients prevention of iatrogenic conditions and complications including further functional loss were considered important. Early mobilisation and encouragement to participate in ADL and communal meals were instituted to prevent functional decline. When necessary, relevant rehabilitation measures were initiated in the GEMU. In general the rehabilitation aimed at improving ADL, walking on level surface and in stairs, and improvement of muscle strength and balance. In addition, adaptation and adjustments of necessary aids were important. Individual rehabilitation plans were made for each patient to restore function and ensure continuity of treatment. These plans were implemented by the physiotherapists, nurses and enrolled nurses to ensure mobilisation throughout the day and also during holidays. If further rehabilitation was indicated and the patients' seemed to benefit from the rehabilitation in the GEMU, they were referred to specialist rehabilitation facilities after discharge.

Discharge planning started as early as possible, and discharge destination was discussed in the first interdisciplinary meeting. Decision on discharge destination was based upon the assessments in the GEMU, reports from the Home services, and the patients' and caregivers' wishes. If the patients were to be discharged home, necessary aids, environmental adjustments and assistance were discussed. When necessary, nurses or occupational therapists arranged visits to the patients' homes to evaluate their capability to live at home, and whether technical arrangements, aids or assistance from the Home services were required.

3.4 Patient care during follow-up

After discharge from the hospital the responsibility for follow-up was transferred to the primary health care system and none of the groups received systematic follow-up from the hospital. Responsible for the nursing care in the community health care system in Trondheim at the time of this study were the Home services which mainly employed

nurses, enrolled nurses and nursing assistants, but also physiotherapists and occupational therapists. The nursing care could be organised in the patients' own homes or in nursing homes. Representatives from the Home services decided which patients needed to stay in nursing homes for both the GEMU and MW groups. The GPs were responsible for the medical treatment for home-dwelling patients in both groups, while nursing home doctors were responsible for nursing home patients.

3.5 Study design

3.5.1 Patient selection

Patients were enrolled between October 31, 1994 and November 13, 1995.

For practical reasons (geographical distances from the hospital when performing follow-up assessments and collaboration with only one municipality) only patients admitted as emergencies to the DIM from the municipality of Trondheim were screened for enrolment into the study. If more patients were eligible for the study, priority was put on those who had been admitted most recently. Patients planned to be discharged within three days were not included.

The intention was to target frail patients who were neither too sick nor too healthy, as these were thought to benefit the most from the intervention in the GEMU. As a measure of frailty Winograd's targeting criteria were applied. Eligible patients had to meet at least one of the following targeting criteria: acute impairment of single ADL, imbalance/dizziness, impaired mobility, chronic disability, prolonged bedrest, falls, confusion, depression, mild/moderate dementia, weight loss, malnutrition, vision or hearing impairment, urinary incontinence, social/family problems or polypharmacy (Winograd *et al.*, 1991). Previously independent patients who seemed to recover on a traditional medical treatment, were not included. Excluded were also patients who were staying in nursing homes, those who had known severe dementia with need of supervision or help 24 hours a day, and patients who had known terminal illness with life expectancy less than six months, including known cancer with metastases (Table 3).

Some patients were of course in need of specific treatment offered by the section to which they were already admitted. Therefore, the doctor on the ward had to approve before patients could be included. Patients with acute stroke were only included if the Stroke Unit was full and the patients had problems additional to their stroke making them eligible for the study.

Table 3. Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
I. 75 years or older	I. Too healthy: Previously independent, no need for geriatric assessment
II. Admitted as emergency	II. Too sick – at least one of the following: Nursing home patient
III. Living in Trondheim	Severe dementia [3]
IV. Frail - at least one of the following: Acute impairment of single ADL	Terminal illness
Imbalance or dizziness	Cancer with metastases
Impaired mobility	III. Discharge planned within 3 days
Chronic disability	IV. Need treatment in another ward than GEMU
Weight loss	V. Acute stroke, possibility for transfer to the Stroke unit
Falls during the last 3 months	
Confusion during hospital stay	
Severe vision or hearing impairment	
Depression	
Malnutrition[1]	
Mild or moderate dementia	
Urinary incontinence [2]	
Social or family problems	
Polypharmacy (≥ 5 drugs per day)	
Prolonged bedrest	

[1] malnutrition with weight loss, s-albumin < 35 g/l, change in appetite or low body weight, [2] urinary incontinence developed during the last week, [3] need of care night and day GEMU= Geriatric Evaluation and Management Unit, ADL= Activity of Daily Living.

3.5.2 Randomisation procedure

During the study period one experienced study nurse was assigned to organise the study and recruit patients. She was responsible for screening and randomisation of 90% of the patients. During her holidays, the project leader screened and randomised the remaining 10%. Suitable patients were screened when there was a free bed in the GEMU. Randomisation was executed after patients had given their informed consent. If the patient was cognitively impaired a caregiver gave consent.

To ensure allocation concealment (Altman and Schulz, 2001), an independent research office used permuted block randomisation with unknown and varied block size to produce allocations that were kept in sealed, serially numbered opaque envelopes. Block sizes varied randomly between 4 and 10. All envelopes were opened in sequence after the patients had given their consent, with at least one independent witness present (usually a nurse on the ward where the patient stayed). Both the research nurse and the witness signed the result of the randomisation.

During the study period 1426 patients 75 years or older from Trondheim were admitted as emergencies to the DIM, of these 254 patients (18%) were recruited and randomly allocated, 127 to the GEMU and 127 to continued treatment in the MW. Five patients refused to participate in the study. Patients allocated to the GEMU were transferred from the MW on the day of inclusion (Figure 3).

3.6 Outcomes

3.6.1 Baseline characteristics

Baseline characteristics of the patients were collected before randomisation by interviewing nurses at the wards where the patients were first admitted, and through interviews with the patients and their caregivers.

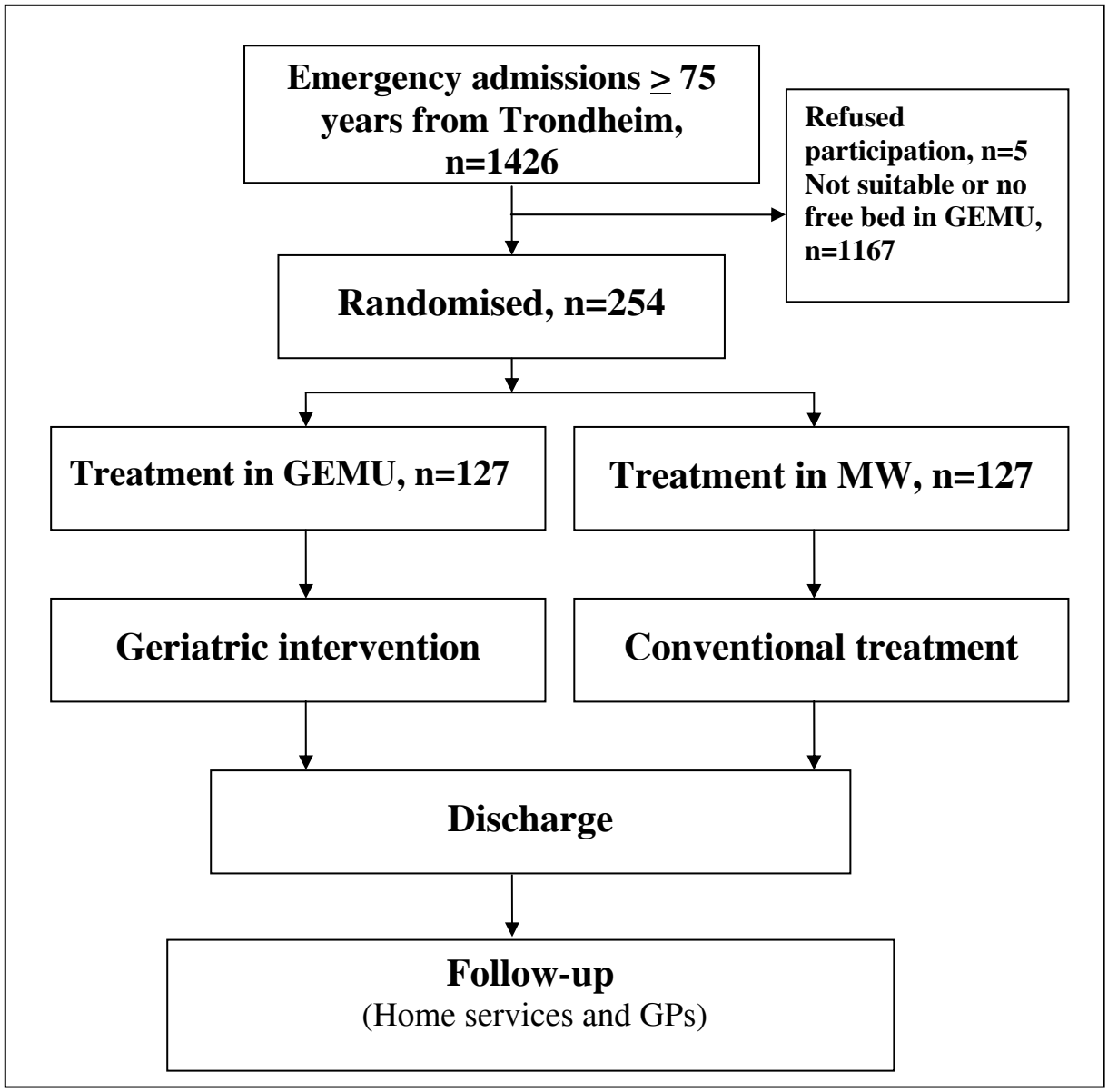


Figure 3. Flow of the study.

GEMU= Geriatric Evaluation and Management Unit, MW= General Medical Wards. GP= General Practitioners.

3.6.2 Mortality

Mortality during one year of follow-up was chosen as the primary endpoint of the present study. Information on mortality and causes of death were obtained from the official death certificates that were linked to the computerised system of the hospital.

3.6.3 Place of care delivery after inclusion

Place of care delivery included the following endpoints: LOS, time to and number of readmissions to hospital and/or admission to nursing homes, proportion of observed time spent in nursing homes, hospital and at home. Information was partly obtained from the medical records at the hospital (computerised system), from interviews with the patients and caregivers and from the records of the Home services and the nursing homes. These registrations were completed two years after the study was finalised.

Originally the plan was to analyse these endpoints for one year of follow up, but due to inferior data quality, only results for six months of follow-up were published. Inferior data quality was related to patients who were lost to follow-up, records in the municipality being insufficient because a new computerised system had been established shortly before study start, and patients and/or caregivers who did not remember details on stays in nursing homes.

3.6.4 Function and morale

To assess function and morale, assessment scales that had been used by others and were recommended by the British Geriatric Society were used (Dickinson, 1992). As measures of physical function Barthel Index (Mahoney and Barthel, 1965) and Lawton's IADL instrument were chosen (Lawton and Brody, 1969). Barthel Index has become widely adopted in clinical research as a measure of ADL. This is an ordinal scale comprising ten ADLs: feeding, bowel and bladder continence, personal toilet, dressing, toilet use, transfer from bed to chair, walking on level surface, going up/down stairs and bathing. In this study a widely used modification of the index that includes a revised score range of 0 – 20 was used (Collin *et al.*, 1988). The IADL instrument

comprised eight activities: ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for medications and ability to handle finances (Lawton and Brody, 1969).

Cognitive function was assessed by Mini Mental Status Examination (MMSE) (Folstein *et al.*, 1975). Montgomery and Åsberg's Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) was used as screening for symptoms of depression. To evaluate morale the Philadelphia Geriatric Center Morale Scale (PGCMS) was used (Lawton, 1975; Morris and Sherwood, 1975).

The selection of patients, getting the patients' and caregivers' consents and randomisation was to be organised during a few hours in the morning. Only one study nurse was employed, while several patients had to be screened; up to six were included during one day. When the study was designed the intention was that Barthel Index, MMSE and MADRS would be baseline characteristics of the patients, i.e. they should be assessed before the randomisation of patients. Due to the logistic challenges described above, and that the exact methods were not formally specified in the protocol Barthel Index, MMSE and MADRS were all performed *after* the randomisation and transfer of the intervention patients from the general ward to the GEMU.

The assessment of Barthel Index during the hospital stay was performed by the occupational therapists and physiotherapist employed in the GEMU (three different persons) both for GEMU and MW patients. Assessments in the MW were based upon self-report; if the patient was cognitively impaired a nurse was asked. In the GEMU the assessments were performance-based. The MW patients had priority because they were frequently discharged without any notice. The mean time from inclusion to assessment was 1.7 days in the MW and 3.5 days in the GEMU. Median Barthel Index scores were 15 (iqr 11; 19) for GEMU and 14 (iqr 9; 18) for MW patients ($p = 0.03$).

The MMSE was mainly assessed by the resident(s) in the GEMU group, and by the geriatrician in the MW group. In the MW, assessments were done bedside, often in a corridor or four-bed room, while in the GEMU the assessment were performed in a

quiet room. It also turned out that the method for asking and scoring had been somewhat different. The mean time from inclusion to assessments was 0.9 days in the MW and 1.8 days in the GEMU. The median MMSE score was 25 (iqr 20; 28) in the GEMU and 22 (iqr 17; 28) in the MW ($p = 0.05$).

Because assessments had been performed after the randomisation, with different methods and timing, Barthel Index and MMSE were disregarded as baseline characteristics. However, ADL and cognition are important prognostic factors for survival (Campbell *et al.*, 2004). Therefore they were analysed in a Cox model as covariates in the survival analyses. When these two covariates were included in the analyses, the three-month survival was still statistically significant better in the GEMU group, but the p-value changed from $p = 0.004$ to $p = 0.05$.

The follow up assessments on MMSE, Barthel Index, IADL, MADRS and PGCMS were performed as interviews three, six and 12 months after discharge from the index stay by different employees of the GEMU staff. If the patients were not able to answer, proxies were interviewed on Barthel Index and IADL. These interviews were performed either at the hospital's outpatient clinic or in the patients' homes.

3.6.5 Drug prescription

Drug prescription was registered as scheduled drugs used at the time of inclusion and at discharge. The selected endpoints were: number of drugs withdrawn and started, number of drugs used per patient, polypharmacy (i.e. five or more drugs used concurrently), drug-drug interactions and use of inappropriate drugs. There was a special attention towards cardiovascular and psychotropic drugs during the stay in the GEMU, and these drugs were explored in detail. Use of drugs was registered by two research assistants after the study was finalised. Data were transferred from the medical charts to a registration form and classified according to the Anatomical Chemical Classification (ATC) (World Health Organisation and Collaboration Center for Drugs Statistics Methodology, 1998). Before starting the analyses the data quality was checked in 100 patients and found to be correct in over 90%.

Table 4. Time of assessments and completeness of data from GEMU (n=127) and MW (n=127) patients.

Time	Outcomes	GEMU	MW
		n	n
Inclusion	Baseline characteristics, drugs	127	127
Discharge	Diagnoses, discharge destination, LOS, drugs	127	127
3 months	Mortality, causes of death	127	127
	Time in nursing homes	116	109
	Living location	126	123
	Place of care delivery	126	125
	Barthel Index, IADL, MMSE, MADRS*	89	68
	PGCMS	74	60
6 months	Mortality	127	127
	Time in nursing homes	116	109
	Living location	126	123
	Place of care delivery	126	125
	Barthel Index, IADL, MMSE, MADRS*	79	63
	PGCMS	76	62
12 months	Mortality, causes of death	127	127
	Barthel Index, IADL, MMSE, MADRS*	71	61
	PGCMS	67	51

*Compliance for MMSE, IADL and MADRS approximately as for Barthel Index.
LOS= Length Of Stay, IADL= Instrumental Activity of Daily Living, MMSE= Mini Mental Status Examination, MADRS= Montgomery and Åsberg's Depression Rating Scale, PGCMS= Philadelphia Geriatric Center Morale Scale.

3.7 Statistical methods

3.7.1 Sample size estimations

An estimate of possible effect size was based upon literature review. Donaldson conducted a study of mortality in relation to age and functional capacity, and found a one-year mortality among patients in acute and geriatric beds of about 40% if they had considerably reduced ADL-scores, and about 30% in patients with moderately reduced ADL-scores (Donaldson *et al.*, 1980). In the study of Rubenstein a 50% reduction of one-year mortality was achieved (Rubenstein *et al.*, 1984). Based on these studies the sample size was estimated (Pocock, 1983). If one-year mortality was 30% in the MW patients, to detect a 50% reduction to 15% in the GEMU, with $\alpha = 0.05$ and power 80%, 113 patients would be required in each group. For an estimated mortality reduction from 40% to 20% the sample size would be less. Thus it was decided to recruit patients over a one-year period with at least 113 in each group.

3.7.2 Statistical analyses

The statistical methods are described in each of the four papers. General considerations when performing the analyses were that t-test were used for data that were normally distributed, Mann-Whitney U-test was used for data that was not normally distributed and for ordinal scales. Chi-square test was used to test group differences for categorical data. For survival analyses and for analyses of time to event (for example time to first nursing home admission) Kaplan-Meier plots and log-rank tests were used. Cox proportional hazards analyses were used to estimate hazard ratio (HR). A p-value of less than 0.05 was used as indication of statistical significance in paper I - III. In paper IV multiple comparisons were performed, therefore a p-value of less than 0.01 was used. For statistical analyses SPSS for Windows was employed.

3.7.3 Missing values

The number of patients registered with complete data varied for the different outcome measures as shown in Table 4. Data that could be registered directly from the medical records of the hospital were complete, while data based upon interviews or assessments

during follow-up and records in the municipality were not. More details are described in each of the papers. To avoid bias and in concordance with general recommendations it was decided that data could be used for analyses if available for more than 80% of the patients at risk (Schulz and Grimes, 2002).

Missing data for Barthel Index, IADL, MMSE, MADRS, PGCMS were due to missing forms or missing items. Forms were missing because patients died, withdrew their consent, were lost to follow-up or were too ill. Missing items were due to medical conditions that made the complete test impossible, because the patients did not understand, or were not able to answer single questions.

The patients who withdrew or were lost to follow up in the two groups did not differ with respect to age, gender, living location after three months, or one-year survival.

According to the literature different methods has been used to handle missing values in the present study (Curran *et al.*, 1998; Fayers *et al.*, 1998; Schulz and Grimes, 2002). Among these were treating the scale as missing, imputation of the mean of the items that were available, imputation of the most likely value, and for missing forms by imputing different combinations of worst case, best case, the mean for the study population and the last value carried forward and sensitivity analyses. The conclusions were not affected by the specific method chosen.

3.8 Ethical considerations

Participation in the trial was voluntary and in accordance with the Helsinki Declaration. The Regional Ethics Committee approved the protocol.

Written informed consent was obtained before inclusion in the study. If the patients were not able to write, an oral consent was accepted. Many of the patients asked to participate were cognitively impaired and not capable of giving their informed consent. Therefore a caregiver was asked to give consent on behalf the patients, a method that is frequently used, but nevertheless not without ethical scruples.

Because the study population was elderly patients frequently suffering from cognitive impairment and sensory losses, the written informed consent was formulated with fonts that were possible to read and with a limited amount of text. After the study was finalised it was discovered that due to inferior quality of data it would be necessary to collect information from health registers in the municipality of Trondheim. This was not mentioned in the informed consent. With permission from the Norwegian Data Inspectorate and the Norwegian Board of Health these data were collected after the patients or their caregivers had given their passive informed consent (three patients did not give their consent).

A few times, study-related screening by MADRS in the MW group revealed severe depressions, sometimes with suicidal thoughts. This was then reported to the physician responsible for the patients immediately. While performing assessments in the MW group it was sometimes observed that treatment offered in the MW was not optimal. As a general rule the responsible physician could refer the patient for a geriatric consultation when needed.

3.9 Financial support

The GEMU was established and run during the study period through support from the Norwegian Ministry of Health and Social Affairs. The Research Council of Norway and Norwegian University of Science and Technology (NTNU) paid fellowship for the author.

Table 5. Baseline characteristics

	GEMU (n=127)	MW (n=127)
Age - mean ± SD	81.8 ± 4.8	82.4 ± 5.2
Female - no. (%)	81 (64)	84 (66)
Widowed / living alone - no. (%)	93 (73)	85 (67)
Residence at time of inclusion – no. (%)		
Private home	115 (91)	110 (87)
Sheltered housing	12 (9)	17 (13)
Days in hospital before inclusion – median (iqr)	2 (1 - 5)	3 (1 - 6)
Targeting criteria[1] – no. (%)		
Acute impairment of single ADL	111 (87)	109 (86)
Imbalance or dizziness	110 (87)	108 (85)
Impaired mobility	54 (43)	59 (47)
Chronic disability	52 (41)	58 (46)
Weight loss	31 (24)	20 (16)
Falls during the last 3 months	30 (24)	32 (25)
Confusion	24 (19)	31 (24)
Vision or hearing impairment	22 (17)	28 (22)
Depression	21 (17)	24 (19)
Malnutrition	15 (12)	13 (10)
Mild or moderate dementia	14 (11)	18 (14)
Urinary incontinence	12 (9)	11 (9)
Social or family problems	10 (8)	7 (6)
Polypharmacy (≥ 5 drugs per day)	5 (4)	5 (4)
Prolonged bedrest	3 (2)	3 (2)
No. of targeting criteria per patient – median (iqr)	4 (3 - 5)	4 (3 - 5)

Table 5. Baseline characteristics (cont.)

	GEMU (n=127)		MW (n=127)	
Previous diagnoses[2] – no. (%)				
Heart disease	46	(36)	58	(46)
Infectious disease	30	(24)	21	(17)
Gastrointestinal disorder	27	(21)	22	(17)
Cerebrovascular disease	24	(19)	17	(13)
Endocrine disease	20	(16)	16	(13)
Airway disease	18	(14)	9	(7)
Cancer	15	(12)	12	(9)
Other	41	(32)	44	(35)
No. of drugs used continuously per patient - median (range)	4	(0-11)	4	(0-11)
No. of patients (%) using drugs continuously with effect on				
Gastrointestinal system and diabetes (ATC class A)	57	(45)	65	(51)
Blood and blood building organs (ATC class B)	68	(54)	68	(54)
Cardiovascular system (ATC class C)[3]	80	(63)	97	(77)
Urogenital system, sex hormones (ATC class G)	8	(6)	8	(6)
Endocrine system (ATC class H)	17	(13)	15	(12)
Systemic infections (ATC class J)	32	(25)	40	(31)
Muscle and skeletal system (ATC class M)	8	(6)	16	(13)
Central nervous system (ATC class N)	39	(31)	32	(25)
Respiratory system (ATC class R)	21	(17)	21	(17)

[1] Winograd's targeting criteria (Winograd *et al.*, 1991), [2]diagnoses at earlier admissions to the University Hospital of Trondheim, [3]p = 0.02, else there were no statistically significant differences. GEMU = Geriatric Evaluation and Management Unit, MW = General Medical Wards, SD = standard deviation, iqr = interquartile range, ADL = Activity of Daily Living, ATC = Anatomical Therapeutic Chemical classification (World Health Organisation and Collaboration Center for Drugs Statistics Methodology, 1998).

4.0 Summary of papers

4.1 Paper I

Reduced mortality in treating acutely sick, frail elderly patients in a geriatric evaluation and management unit. A prospective randomized trial.

This paper presents mortality and causes of death in the two groups.

Of 127 patients included in each of the groups, 8 (6%) GEMU and 17 (13%) MW patients died during the initial hospital stay (p = 0.002). At three months, mortality was 15 (12%) and 34 (27%) in the GEMU and MW groups respectively (p = 0.004), at six months 20 (16%) and 37 (29%) (p = 0.02), and at 12 months 35 (28%) and 43 (34%) (p = 0.06). The reduction in mortality was greatest during the initial three-month period with a hazard ratio (HR) 0.39 (95% CI 0.21 – 0.72). Adjustment for age, history of heart disease, duration of stay in hospital before inclusion in the study, number of targeting criteria and gender in a Cox Proportional Hazard's Model, did not have any impact on HR during the first three months.

For both groups the mortality was highest initially. This was related to the acute disorders that precipitated the hospital admission, and then it stabilised after 2-3 months. The curves came together at 18 months. The median survival was two years in both groups.

Heart disease was the major cause of death in both groups at three and 12 months. At 12 months deaths from infections (mainly pneumonia) were more frequent in the GEMU group than in the MW group (p = 0.04).

We concluded that patients treated in the GEMU had a considerable reduction in mortality as compared to those treated in the MW. This difference was explained by

higher competence and better organisation of the treatment of acutely sick, frail elderly patients in the GEMU as compared to the MW.

4.2 Paper II

Acute geriatric intervention increases the number of patients able to live at home. A prospective randomized study.

When designing the present study it was hypothesised that the intervention would reduce readmissions to hospital and need of nursing home placement for GEMU patients. The aim of the present paper was to compare place of care delivery during six months of follow-up in the GEMU and the MW group.

The mean number of days spent in hospital before entering the study was 3.8 (SD 3.7) in the GEMU and 4.6 (SD 4.3) in the MW ($p = 0.09$). The total LOS had a median of 19 days (iqr 13; 30) in the GEMU group and 13 days (iqr 7; 18) in the MW group ($p < 0.001$). The difference in LOS was related to a "delay" during the first five days after the patients had been transferred to the GEMU.

There were no statistically significant differences in discharge destination in the two groups. After the index stay 73% of the GEMU and MW patients were discharged home, 13% of the GEMU and 14% of the MW patients to nursing homes, the rest to rehabilitation institutions or other hospital departments. At three months 91% of the GEMU and 88% of the MW patients were living at home. At six months 86% in both groups lived at home.

Of all patients recruited to the study, 101 (80%) GEMU and 79 (64%) MW patients were living at home at three months ($p = 0.005$), and at six months the numbers were 91 (72%) and 74 (60%) ($p = 0.04$). The HR of living at home versus living in nursing homes or having died, was 2.1 (95% CI 1.3 - 3.4) after three months, and 1.6 (95% CI 1.1 - 2.5) after six months.

After the index stay, there was no statistically significant differences in readmissions, time to nursing home placement, proportion of observed time spent in hospital and nursing homes, percentage of patients with transitory or permanent nursing home placement, number of days spent in nursing homes and percentage of patients receiving assistance from the community nurses. 35% of the GEMU and 31% of the MW patients were not admitted to any kind of institutions during six months of follow up.

The main conclusion was that an increased number of GEMU patients were able to live in their own homes in contrast to being dead or living in nursing homes during six months of follow-up, an effect that was mainly related to the considerably reduced mortality in the GEMU group. Patients treated in the GEMU had increased LOS.

4.3 Paper III

Randomised trial of in-hospital geriatric intervention: Impact on function and morale.

The aim the present article was to describe the impact of treatment in the GEMU as compared to MW on ADL, IADL, cognitive function, symptoms of depression and general well-being during one year of follow-up.

Barthel Index and the Lawton instrumental IADL scale were used to assess physical function, MMSE to assess cognition, MADRS to screen for symptoms of depression and PGCMS to assess general well-being.

The mean scores for MMSE, PGCMS, Barthel Index and IADL did not differ during follow up, indicating that cognitive function, general well-being, ability to perform ADL and IADL were similar in the two groups. There was no difference in number of patients with symptoms of depression.

If the dead were given a Barthel Index score of zero and included in the analysis, there was better function in the GEMU group at three months ($p = 0.03$).

In conclusion, there was no significant difference in ADL, IADL, cognition, symptoms of depression or general well-being between those who survived after GEMU and MW treatment respectively. A significant reduction in mortality may theoretically lead to decreased function and general well-being among the survivors in the GEMU group if life was prolonged in those who were at the highest risk of death and morbidity. Hence, the findings of no difference between the GEMU and MW survivors were regarded as positive.

4.4 Paper IV

Patterns of drug prescription in a geriatric evaluation and management unit as compared with the general medical wards. A randomised study.

The aim of this paper was to study if patients treated in the GEMU had a more appropriate drug profile than patients treated in the MW. The analyses were based upon prespecified hypotheses. Due to multiple comparisons a p-value < 0.01 was regarded as statistically significant.

There were no statistically significant differences in the median number of drugs used per patient, or in the number of patients with polypharmacy (defined as using 5 or more drugs concurrently), neither at inclusion nor at discharge. More scheduled drugs were withdrawn per patient from inclusion to discharge in the GEMU ($p = 0.005$). There was also a trend for more drugs being started in the GEMU than in the MW ($p = 0.03$). At discharge fewer GEMU patients had potential drug-drug interactions (DDIs) ($p = 0.009$). There was a trend for more MW patients using anticholinergic drugs at discharge ($p = 0.03$), more drugs with anticholinergic effects were withdrawn in the GEMU than in the MW ($p = 0.003$).

There were 60 withdrawals of cardiovascular drugs in the GEMU as compared to 13 in the MW ($p < 0.001$). Digitalis glycosides were withdrawn in 14 (12%) GEMU patients and none of the MW patients ($p < 0.001$). There were 33 withdrawals of psychotropic drugs in the GEMU as compared to nine in the MW ($p = 0.009$). On the other hand 35 prescriptions of psychotropic drugs were started in the GEMU as compared to 16 in the MW ($p = 0.02$). In the GEMU 14 antipsychotic prescriptions were withdrawn as compared to two in the MW ($p = 0.009$). Treatment with antidepressants was started in 20 GEMU patients and in two MW patients ($p < 0.001$). At discharge more GEMU patients used drugs with effect on the uro-genital system/sex hormones than in the MW ($p = 0.001$). This was related to treatment with oestriol which was started in 15 GEMU patients as compared to one MW patient ($p = 0.001$), and was used by 25% of the female GEMU patients and 4% of the female MW patients at discharge ($p < 0.001$).

We concluded that there were distinct differences in prescribing patterns between the GEMU and MW. Based upon literature review and clinical recommendations, the patterns of prescribing in the GEMU seemed to be more appropriate than in the MW.

5.0 Discussion

This thesis presents the first study to show that treatment of acutely sick, frail elderly patients in a GEMU may significantly reduce mortality and improve the chance of living in own home versus being dead or living in nursing homes as compared to traditional treatment in MW. There was no difference in care delivery after the hospital stay or in function and morale during follow-up, which was also considered a positive finding because prolonged survival among frail elderly patients might theoretically result in poorer average function and morale. Patterns of drug prescribing in the GEMU seemed to be more appropriate than in the MW.

5.1 Comparison with other studies

5.1.1 Setting

To our knowledge a total of eight RCTs assessing treatment of hospitalised high-risk elderly patients in GEMUs have been published (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Harris *et al.*, 1991; Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000; Cohen *et al.*, 2002; Saltvedt *et al.*, 2002) (Table 1). In addition to our study there was one RCT from Sweden (Asplund *et al.*, 2000), and none from other parts of Europe. Five RCTs were performed in USA where the health care system is quite different from ours, making comparisons difficult regarding characteristics of patients referred to the hospitals, use of long-term beds and management of patients.

In general, the studies can either be categorised into those treating patients with acute disorders that are not stabilised (Harris *et al.*, 1991; Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000) or those treating patients in the subacute stage of the disease (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002). The setting in our study was mixed, where 60% of the patients were included within three days, while 18% were included one week or more after admission.

5.1.2 Patient recruitment

In our study and the three studies performed in subacute settings (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002) patients were targeted for frailty before inclusion. However, criteria for frailty varied between the studies. Patients who were too healthy, nursing home patients, patients with severe dementia and patients with terminal illnesses were excluded in all studies. Rubenstein aimed at including patients having "problems that interfered with discharge home" (Rubenstein *et al.*, 1984). In the study of Applegate patients having reversible functional impairment defined as not being able to perform one or more ADL were included (Applegate *et al.*, 1990). The targeting criteria used by Cohen were overlapping with those in our study, including patients with falls/mobility problems, nutritional problems, cognitive impairment, depression, urinary incontinence, prolonged bedrest, and problems in performing one or more ADLs (Cohen *et al.*, 2002). In these studies patients were recruited from different populations. The percentage of those screened or admitted to hospital that were eligible or included to the study varied considerably (Table 1).

A comorbidity index (Knaus *et al.*, 1985; Charlson *et al.*, 1987) or at least the relevant diagnoses at inclusion should have been registered at baseline in our study for the comparability of our study population with those studied by others. Nevertheless, a rough estimate of the case-mix can be obtained by comparing the mortality (Table 1). The study of Rubenstein (Rubenstein *et al.*, 1984) had the highest one-year mortality with 48% in the control group as compared to 34% in our study. At six months the mortality in the control group was 25% in the study of Rubenstein and 29% in ours. In the studies of Applegate, Harris, Counsell and Cohen the control group had a one-year mortality between 30%, and 21% (Applegate *et al.*, 1990; Harris *et al.*, 1991; Counsell *et al.*, 2000; Cohen *et al.*, 2002). In the study of Landefeld and Asplund three-month mortality was 13% and 8% respectively (Landefeld *et al.*, 1995; Asplund *et al.*, 2000), as compared with 27% in our study. The differences in mortality in these studies indicate a considerable variability of case-mix. Except for Rubenstein's study that had lower six-month, but higher one-year mortality, our study had higher mortality at three, six and 12 months than the other studies. It is therefore reasonable to believe that our study population was sicker than in the other studies.

Two of the studies on efficacy of treatment in GEMUs were performed in US Veteran Administration hospitals, nearly all participants being male (Rubenstein *et al.*, 1984; Cohen *et al.*, 2002). The other studies, including ours, had a majority of female patients. We recruited patients of 75 years or older, while the three studies performed in a subacute setting recruited patients of 65 years or older (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002). Those in acute care settings recruited patients of 70 years or older (Harris *et al.*, 1991; Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000). The highest mean age at inclusion was found in our study with 82 years, while the study of Cohen had the lowest mean age of 74 years (Cohen *et al.*, 2002).

5.1.3 Patient treatment

The medical treatment programs in the GEMUs seemed to be organised differently. In Norway geriatric medicine is a branch specialty of internal medicine, while in USA and Sweden it is an independent speciality. In our study the geriatricians were responsible both for the acute medical treatment and for the geriatric assessment and management. In the study of Asplund the internists were responsible for the acute medical treatment in both the intervention and control groups, while the geriatrician was responsible for the CGA (Asplund *et al.*, 2000). In the studies of Landefeld and Counsell attending and resident physicians provided treatment to both groups; in addition the GEMUs had geriatricians employed (Landefeld *et al.*, 1995; Counsell *et al.*, 2000). The geriatricians in these studies reviewed patients' medications and procedures, had responsibility for practice guidelines, made informal recommendations to attending and resident physicians and were consultants to the multidisciplinary team (Palmer *et al.*, 1998). In the study of Applegate medical treatment was performed either by doctors in the GEMU or by the referring physician (Applegate *et al.*, 1990).

5.1.4 Results

As in our study Rubenstein showed reduced mortality during follow-up (Rubenstein *et al.*, 1984), but the survival curves were completely different in the two studies.

Rubenstein found a difference in survival that was emerging after two months and lasting for two years, while in our study the effect was highest initially, and then diminished. There is no single explanation for the improved initial survival in the GEMU group in our study. However, further analyses have shown no differences in survival in the GEMU and MW groups for those who had stayed in the DIM more than seven days before inclusion into the study. The combination of targeting frail patients with acute illness and the geriatricians being responsible for the acute medical treatment may partially explain this result.

Some other studies have shown improved performance in ADL (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Landefeld *et al.*, 1995; Cohen *et al.*, 2002), reduced utilisation of nursing home beds (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Landefeld *et al.*, 1995), and improved morale (Rubenstein *et al.*, 1984) or quality of life (Cohen *et al.*, 2002). Lack of baseline registrations and the follow-up assessments being performed long time after the intervention, as well as significant differences in mortality, will altogether complicate the interpretation of the results in our study.

Although the use of composite outcomes may be regarded as controversial, the dead have been included in the analyses of living location (paper II) and function (paper III) (Montori *et al.*, 2005). There are mainly two reasons for this: 1) The need of implementing the differences in mortality found in the GEMU and the MW groups in the analyses. 2) Living at home was used as an endpoint in the meta-analyses of Stuck often being used as a reference publication (Stuck *et al.*, 1993). The interpretation of the composite outcomes is complicated by a considerable difference in mortality between the two groups. Nevertheless, the overall treatment effect seems to be positive because more patients were able to live at home in contrast to being dead or in nursing homes, and more GEMU patients were independent in ADL in contrast to being dependent or dead.

The only study showing reduced LOS in the GEMU as compared to the DIM was performed by Asplund (Asplund *et al.*, 2000). In our study the mean LOS in the GEMU was longer than in the MW (21 versus 12 days). The three studies performed in

subacute settings all had longer LOS in the intervention group than in the control group, and their LOS is even longer than in our study (Rubenstein *et al.*, 1984; Applegate *et al.*, 1990; Cohen *et al.*, 2002). In the four studies recruiting acutely sick patients, the LOS was ten days or shorter in both the intervention and the control groups (Harris *et al.*, 1991; Landefeld *et al.*, 1995; Asplund *et al.*, 2000; Counsell *et al.*, 2000). In our study the GEMU staff did not focus explicitly on shortening the LOS per se. Rather delivering high-quality health care was the ultimate goal. As shown in paper II the increased LOS was partly related to a delay associated with transfer of patients to the GEMU and the fact that the staff of the GEMU performed study-related assessments. Later the LOS in the GEMU has been shortened to about mean 14 days, which is still longer than in the acute care studies.

However, performing CGA, discharge planning and starting rehabilitation is all time-consuming. It is also recommended that drug prescribing in elderly should "start low and go slow", which in many cases mean that time until disorders are successfully treated will be prolonged. In addition, it is well known that many patients experience decline in function related to hospitalisation for acute disorders and therefore need time and help to recover (Fortinsky *et al.*, 1999).

The survival curves in both groups in our study showed high mortality during the first two to three months, then it stabilised. In addition, we found that two thirds of the patients in both groups had been readmitted to the hospital or admitted to nursing homes during six months of follow-up. Therefore it can be concluded that those discharged from hospital in this study were still highly unstable and vulnerable. The most logical approach would therefore be to 1) Establish optimal post-discharge follow-up. 2) Focus on shortening down LOS (Young and Philip, 2000).

Pharmacotherapy has not commonly been used as an endpoint in most RCTs of treatment in GEMUs, although there are a few exceptions (Rubenstein *et al.*, 1984; Counsell *et al.*, 2000; Schmader *et al.*, 2004). In our study we found distinct differences in prescribing between the GEMU and MW. We have hypothesised that the differences may be of clinical importance, but we do not have data to confirm these hypotheses. In

general, drug prescribing in the elderly is challenging due to both the complexity of the patients as well as the lack of evidence on drug treatment in this patient population (Wyller, 2003). Further research is needed to achieve guidelines that can improve medical treatment of frail elderly.

5.2 Internal validity

Internal validity of a trial implies that the differences observed between the intervention and control groups may be attributed to the treatment under investigation and not random errors (Juni *et al.*, 2001). Internal validity is threatened by bias that fall into four categories: Selection bias (comparability of the groups), performance bias (unequal provision of care apart from treatment under evaluation), detection bias (biased assessment of outcomes) and attrition bias (deviations from the protocol and loss to follow-up) (Juni *et al.*, 2001). Although the major strengths of our study are its originality and randomised design, similar to others we experienced that performing research on frail elderly patients may be challenging (Berkman *et al.*, 2001; Zermansky, 2005), and of course this study has limitations.

5.2.1 Comparability of the groups

The randomisation procedure was carefully planned before the study started and has also been carefully evaluated afterwards. Although computer generated randomisation would have been chosen today, the method used in our study was established practice at the time of study planning. The method used was satisfactory regarding the sequence generation, allocation concealment and implementation. The aim of randomisation is the creation of groups that are comparable for any known or unknown potential confounding factor. When randomisation is effective, baseline prognostic factors should be distributed equally (Altman and Dore, 1990).

In the present study there were no statistically significant differences in baseline characteristics and previous diagnoses, except for fewer GEMU than MW patients using drugs for cardiovascular disease at inclusion (Table 5). There were also fewer GEMU

than MW patients with cardiovascular diagnoses from previous stays in the hospital (not statistically significant). These differences could theoretically be of prognostic importance. However, there was no difference in number of patients with cardiovascular diagnoses at discharge.

Because Barthel Index and MMSE are important prognostic factors for mortality, they were planned to be baseline characteristics (Campbell *et al.*, 2004). The assessments performed during the index stay revealed statistical significantly lower scores for MMSE and Barthel Index in the MW group than in the GEMU group. However, as described in the methods section, both the methods, timing and setting for these assessments were systematically different in the two groups. It is therefore reasonable to believe that differences in MMSE and Barthel Index were biased by the design of the study.

Roberts and Torgerson have claimed that baseline tests of imbalance are inappropriate unless the investigators suspects that there are problems with the randomisation (Roberts and Torgerson, 1999), which we do not think is the case in this study. Hence, it should not be necessary to adjust the analysis for differences in baseline values. However, although randomisation is properly performed, sometimes imbalance can occur by chance (Altman and Dore, 1991). Because all differences go in disfavour of the MW group which could theoretically explain the differences found in mortality, regression analyses have been done where previous cardiovascular disorder or use of cardiovascular drugs were imputed as controlling variables. However, this did not affect the results of the survival analyses. After imputation of MMSE and Barthel Index scores in the Cox regression model, there was still a significant reduction in three-month mortality in the GEMU group, confirming the validity of our results.

5.2.2 Outcomes

In general, assessments of frail elderly patients will be complicated by slow communication due to hearing loss or cognitive impairment, and it will be more time-consuming than for younger patients. Many patients get easily exhausted and some may

even be embarrassed by for example questions assessing cognition or quality of life. Therefore the test batteries chosen and the order of testing should take these aspects into consideration (Kane, 2000). It is a growing interest towards use of specific and subjective assessments instruments for elderly patients that are shorter and can be used both for patient and proxy ratings (Kaasa and Loge, 2004).

Assessment instruments should also fulfill certain properties. 1) They should be valid, i.e. measure what they purports to measure. 2) They should be reliable, i.e. give similar results for different observers and when measurements are repeated (Bland and Altman, 2002). 3) They should be able to detect changes over time (responsiveness). Instruments used for screening of certain conditions should also have high sensitivity i.e. be able to detect a condition when it is there, and they should have high specificity i.e. be able to correctly state that the condition is absent (Kane, 2000).

Group assignment in this study was not, and could not, be blinded for patients and caregivers. Information about the project was given in a neutral way and participants were not informed about expectations for outcomes (Schulz *et al.*, 2002). However, the assessors should have been a few persons not involved in the management of the patients and blinded for the outcomes, which was not the case.

Outcomes evaluated were chosen according to the aims of the study and on the basis of findings from other studies. Mortality is easy to count and to compare between settings. From a clinical perspective reduced mortality per se is not the main goal in the treatment of frail elderly patients, but it may reflect the quality of medical treatment. For sample size estimations at the time of study planning it seemed to be the only possible endpoint for which some reliable data existed (Donaldson *et al.*, 1980; Booth *et al.*, 1983).

Place of care delivery is an indirect measure of the patients' function and health status and is important both from the patients' and health care managers' perspective. The intention of this study was to study place of care delivery during 12 months of follow-up. We succeeded in collecting data for six months of follow-up, while the data

collected for the last period were disregarded due to inferior quality. Although the data published have satisfactory quality, an underestimation of short term stays in nursing homes may have occurred.

The main goal of comprehensive geriatric assessment is to achieve the patients' best possible health, highest level of function and quality of life (Elon *et al.*, 2000). Therefore, function and quality of life were adequate endpoints. As the patient group studied was very heterogeneous, generic measures were chosen instead of condition specific instruments. Assessment scales that had been used in other studies and were recommended by the British Geriatric Society were applied (Dickinson, 1992).

Physical function was assessed by the use of Barthel Index and Lawtons IADL scales (Mahoney and Barthel, 1965; Lawton and Brody, 1969). In Barthel Index some items on mobility are incorporated (moving from wheelchair to bed, walking on level surface, climbing stairs). Further assessment of mobility would have been relevant because patients with mobility problems were targeted for the study, and the intervention in the GEMU had focus on physical training (Pearson, 2000).

Barthel Index was developed as a measure of disability in patients with neuromuscular and musculoskeletal conditions receiving inpatient rehabilitation (Mahoney and Barthel, 1965). It is simple to administer and easy to score for trained assessors (Pearson, 2000). It has been criticised because it has ´floor´ and ´ceiling´ effects and might be insensitive to changes over time (Bowling, 2001; Pearson, 2000). The instrument is designed for observation, while in our study both observation, patient and proxy interviews were used (Ranhoff and Laake, 1993). Collin has shown that interviews with nurses or relatives are as reliable as observations (Collin *et al.*, 1988). Others have shown that self-report is less valid in the very old patients, those with cognitive impairment and those with recent changes in ADL (Sager *et al.*, 1992; Sinoff and Ore, 1997). The reliability has been well documented for stroke patients (Bowling, 2001). There are few studies on reliability in frail elderly patients in general. In a systematic review Sainsbury concluded that further studies are justified to investigate reliability for older people in general (Sainsbury *et al.*, 2005). The factor structure of the scale is uni-

dimensional in stroke patients while two dimensions have been found among geriatric patients (Laake *et al.*, 1995).

Lawtons IADL scale (Lawton and Brody, 1969) was originally designed to be used as a guide to determine the most appropriate living arrangement for elderly persons. It measures three areas: household chores, mobility related activities and cognitive activities. Loss in one or more IADLs has been shown to be a potential marker of frailty (Nourhashemi *et al.*, 2001), and IADL is frequently used as a measure of function in studies with elderly people. Gender and cultural biases have been found. The Lawton IADL scale has been criticised because there are inconsistencies in scoring of single items in the instrument. Although it has been widely recommended for use, there have been few reports on reliability and validity for use of this questionnaire among frail elderly patients (Pearson, 2000).

Cognitive impairment was assessed by MMSE that is probably the most widely used screening test for cognitive impairment. It is quick and simple to use, and test-retest and inter-rater reliability has been shown to be satisfactory (Langley, 2000; Burns *et al.*, 2004). A cut-off of 23 points is frequently chosen because of optimised sensitivity and preserved moderate to high specificity for screening of dementia. Strict cut-off values have utility for research, but not for clinical purposes. MMSE has higher sensitivity for demented patients than for patients with lower levels of cognitive dysfunction (Langley, 2000). Although MMSE is widely used in studies as a screening instrument for both dementia and delirium (Hjermstad *et al.*, 2004), it is best validated for dementia (Smith *et al.*, 1995). When working with hospitalised elderly patients it is important to differentiate between dementia and delirium, and today additional instruments for screening of delirium could have been chosen, for example the Confusional Assessment Methods (CAM) (Laurila *et al.*, 2002; Inouye, 2004;).

Symptoms of depression were assessed by MADRS (Montgomery and Asberg, 1979). This scale has been demonstrated to be a sensitive measure of change when studying treatment for depression, and the reliability and validity has been shown to be satisfactory (Burns *et al.*, 2004). MADRS have been recommended for use among

geriatric patients in the Nordic countries (Sletvold *et al.*, 1996). However, during the last years the Geriatric Depression Scale (GDS) has been recommended for use among geriatric patients who are not or moderately cognitively impaired (Yesavage *et al.*, 1982; Watson and Pignone, 2003). Shortened versions of GDS has been evaluated and found to be reliable and valid, and it seems that the five items version can now recommended for clinical use and research (Almeida and Almeida, 1999; Hoyl *et al.*, 1999).

Quality of life was assessed by the PGCMS (Lawton, 1975; Morris and Sherwood, 1975), which is actually measuring morale. Although the PGCMS has been widely recommended for use in geriatric populations (Dickinson, 1992), intact cognition is required to answer many of its items. The trend within clinical research is to measure health related quality of life that would be most influenced by health and health care interventions (Kaasa and Loge, 2002), and an instrument such as SF-36 (Ware, Jr. and Sherbourne, 1992) might have been suitable to measure the effect of the intervention given in the GEMU.

5.2.3 Performance

All patients randomised to the GEMU group were treated in the GEMU during the initial stay. If they were readmitted to the hospital during the period of follow-up, they were treated in the MW. None of the patients randomised to the MW were treated in the GEMU neither during the initial hospital stay nor during the period of follow-up.

To evaluate the effect of the intervention it would be optimal if the patients in the MW were not seen by the staff in the GEMU. On the other hand, it was unethical to resist any evaluation of these patients. Therefore, in concordance with general recommendations (Feussner *et al.*, 1991), study patients could be referred to consultation by a geriatrician if the doctor responsible for the patient found it indicated, either during the index stay or later. These patients got the same type of consultation and advice as patients not included in the study.

During standardised follow-up assessments patients occasionally presented clinical problems. These were then described in a letter to the GP who was responsible for follow-up. For ethical reasons clinical problems that could be characterised as emergencies were initially handled by the GEMU physician, until someone else could take responsibility.

The impact of these factors on the results of the study is unknown. RCTs on consultation teams in hospital have shown little or no effects on the outcomes relevant for the present study (Stuck *et al.*, 1993; Naughton *et al.*, 1994; Reuben *et al.*, 1995). In our study, single patients were seen by the geriatrician and not by a team. We hardly think this influenced the results.

5.2.4 Attrition

The compliance was over 80% for all assessments, except for the PGCMS for which it was somewhat lower. We considered this to be satisfactory, because low attrition is a well-known problem when studying a group of patients who are sick and disabled (Jordhoy *et al*., 1999). As described in the method chapter, different methods were used to handle missing values. We concluded that only extreme differences between those who were lost to follow-up in the two groups would have had impact on the results of the study. As patients who withdrew or were lost to follow up in the two groups did not differ with respect to age, gender, living location after three months, or one-year survival, there is no reason to believe that the reduced compliance had substantial impact on the results.

When recruiting patients for the study there was one violation of the protocol: A few times there were no eligible patients 75 years or older. Being part of a busy department the GEMU was not allowed to keep beds free to wait for study patients. Therefore, five patients between 72 and 74 were included (two in the GEMU and three in the MW group). Apart from age these patients met the inclusion criteria of the study. Analyses have been performed both with these included or excluded which made no differences.

5.3 External validity

External validity (generalisability) of the trial is the extent to which results of trials provide a correct basis for generalisation to other circumstances (Juni *et al.*, 2001). As this was a single centre study the external validity may be difficult to interpret.

The study was meant to be "naturalistic" i.e. patients included should as far as possible reflect sick, frail elderly patients that are frequently admitted to hospital. Therefore the inclusion criteria were broad. Of all emergency admissions among patients 75 years or more with living location in Trondheim, 18% were included. In addition to the formal exclusion criteria (Table 3) patients were not included if there was no free bed in the GEMU. In addition, the Stroke Unit at the DIM had an ongoing trial (Indredavik *et al.*, 2000). Therefore stroke patients were only included if they would not receive treatment in the Stroke Unit and had problems additional to their stroke. The exclusion of patients due to lack of beds could hardly have any impact on the generalisability. However, the results of this study are not applicable for acute stroke patients.

Unfortunately we did not screen all patients admitted to the DIM and therefore do not know the exact proportion of patients who would have been eligible (Moher *et al.*, 2001). After the study was finalised the prevalence of "geriatric" patients in the DIM was studied through a one-day prevalence study (criteria used were largely overlapping with those used in the present study). It was estimated that about 30% of patients of 75 years or older staying at the DIM were in need of treatment at the GEMU. In 1998 a similar national one-day prevalence study of patients over 75 years at 59 Norwegian medical departments was performed (Rø, 2000). It was shown that of 4234 patients, 1781 (42%) were 75 years or older. These patients were characterised by many relevant diagnoses concurrently. In addition, a considerable proportion had impaired cognitive and/or physical function. In the study of Rø it seemed to be differences in case-mix when comparing the larger hospitals with established geriatric services and hospitals without such services (mostly smaller hospitals) (Rø, 2000). It was concluded that the larger hospitals had sicker patients than the smaller hospitals, although the number of patients treated for terminal illness was higher in the smaller hospitals. The need of geriatric treatment for the patients was defined by each department, which estimated

that 21 % of all patients would profit from geriatric treatment. The proportion was 30% in hospitals that had established geriatric services. Reuben found that 35 % of the hospitalised patients over 65 years would be appropriate for comprehensive geriatric assessment (Reuben *et al.*, 1992). Based upon these results we have concluded that probably about 30% of all patients over 75 years admitted to the DIM at our hospital and other larger hospitals would benefit from treatment in a GEMU.

The MW patients in this study were treated in highly specialised sections at the DIM of a university hospital. Regarding generalisability we do not know if the quality of care for frail elderly patients differs between highly specialised university hospitals and smaller hospitals, not so specialised.

CGA is kind of "black box" treatment. Although there is evidence that assessment and treatment of many of its components are efficient, other factors such as competence of the staff, physical environment, traditions within different hospitals or countries, may influence the outcomes measured. Our GEMU was localised within a medical department with mostly non-elective admissions and patients with acute medical illnesses. Acute medical treatment was an important part of the intervention and had priority, CGA was performed when the patients were medically stabilised. The role of the geriatricians seem to have been somewhat different in some of the other studies. It is impossible to answer the question on whether "our " type of intervention can be implemented into GEMUs that are not part of internal medicine.

5.4 Are the results still relevant?

Geriatric medicine had been introduced as a GEMU at the University hospital of Trondheim shortly before the study took place, and the study was initiated because it was important to assess efficacy of treatment in the GEMU. With hindsight it is obvious that today the treatment offered in the GEMU is better and more developed than it was during the study period. It is reasonable to believe that certain conditions such as silent delirium and mild dementia may have been underdiagnosed, and also that the function of the interdisciplinary team sometimes might have been suboptimal. Based upon the

experiences that the patients often were unstable after discharge, we have recently established a team for transitional care that focus on the first four weeks after discharge from hospital. In general, the attitude towards frail elderly patients in our hospital seems to have improved today as compared to 10 years ago. It is also fair to say that due to continuous educational programs both for doctors and nurses on treatment of frail elderly patients, the competence in handling conditions like delirium is probably better now.

Although recent studies show that older patients are getting better treatment for common diseases there is still evidence that care offered to elderly patients is less than optimal for general medical conditions, and even more so for geriatric giants (Reuben *et al.*, 2003; Wenger *et al.*, 2003). The case-mix and targeting of patients obviously are important predictors of treatment effects. It should be noted that no RCT except ours has shown reduced mortality by treating geriatric patients with acute conditions in a GEMU. Possible explanations for the positive results in our study may be linked to: 1) The geriatrician had responsibility both for the acute medial treatment and for the CGA. 2) The patients were older and sicker and also characterised by increased frailty as compared to the other studies. Therefore, due to demographic and epidemiological trends, our findings may become even more relevant in the future indicating a need of transferring geriatric competence into the acute medical care for the elderly.

Focus on specific competence and organisation may also explain some of the beneficial effects shown in our study. In our hospital three other studies have been performed that have shown beneficial effects of improving competence and organisation in the care of previously neglected groups of patients. A cluster randomised study showed that a palliative care intervention enabled more patients with advanced cancer to die at home as compared to traditional care (Jordhoy *et al.*, 2000). Two RCTs on treatment of patients with acute stroke have shown that treatment in a Stroke Unit was beneficial as compared to traditional treatment in the DIM and that an extended stroke unit service with early supported discharge improved functional outcome and reduced the length of hospital stay compared to traditional stroke unit care (Indredavik *et al.*, 1991; Indredavik *et al.*, 2000). This also is in accordance with results from other studies

showing that only treatment in specially organised wards has beneficial effects on outcomes (Stuck *et al.*, 1993; Langhorne *et al.*, 2005), while consultation by specialised teams has no effects. It is therefore reasonable to believe that CGA can best be performed in special settings like the GEMU, supporting the findings in our study.

6.0 Conclusion

- Mortality in the GEMU and MW groups respectively was 12% and 27% at three months (p = 0.004), 16% and 29% (p = 0.02) at six months, and 28% and 34% (p = 0.06) at 12 months. The HR for the difference in mortality was 0.39 (95% CI 0.21 – 0.72) at three months. Heart disease was the major cause of death in both groups at both three and 12 months. At 12 months deaths from infections (mainly pneumonia) were more frequent in the GEMU group.
- The LOS in the GEMU was longer than in the MW. There was no difference in place of care delivery in the two groups after discharge from hospital during six months of follow-up. Of all subjects recruited to the study, more GEMU than MW patients were still living in their own homes at three and six months, an effect that was mainly related to considerably reduced mortality in the GEMU group. It was concluded that there was an overall positive effect of treating acutely sick, frail elderly in a GEMU.
- Treatment in the GEMU had no measurable effect on ADL, IADL, cognitive function, symptoms of depression or morale during 12 months of follow- up. If the dead were included in the analyses at the highest ADL dependency level, there was better function in the GEMU group at three months. Taken the previously shown mortality reduction into consideration, an additional effect on function was less likely and the overall treatment effect was considered to be positive.
- The median number of scheduled drugs withdrawn per patient was higher in the GEMU than in the MW. Drugs with anticholinergic effects, cardiovascular drugs, particularly digitalis glycosides, and antipsychotic drugs were withdrawn more often in the GEMU. There was a trend for more scheduled drugs being started in the GEMU than in the MW. In particular antidepressants and oestriol were started more often. Fewer GEMU than MW patients had potential drug-drug interactions at discharge. The number of patients with polypharmacy did not differ significantly between the GEMU and MW. It was concluded that drug treatment in the GEMU seemed to be more appropriate than in the MW.

- The survival curves in both groups show increased mortality during two to three months after inclusion in the study. Two thirds of the patients in both groups had been admitted to nursing homes or readmitted to hospital during six months of follow-up. In can therefore be concluded that these high risk patients in the future would need further attention.
- This trial is one of relatively few in this area probably because such studies are difficult to conduct. It may serve as an example of the complexity of carrying out an adequate trial on geriatric management. It exemplifies the importance of performing rigorous checks that the randomisation has been effective. Ideally, assessors should be blinded to the allocation, and it is essential that the randomised groups are managed and assessed in an identical manner. The protocol should be explicit about the time of assessment and standardisation of methods.

7.0 Areas for future research

There is a major need for scientifically rigorous RCTs to demonstrate convincingly the benefits of different geriatric management policies in general. Geriatric research should be performed in acute care settings, on home-dwelling elderly and nursing home residents. Research on how to organise post discharge follow-up to make sure that patients are not falling between the cracks will also be important.

To be able to target the right intervention to the right patient and streamline the CGA process, further research is needed to find valid tools to predict the prognosis of geriatric patients. Still much is unknown about both the process of care including staffing, environmental issues, discharge planning and single components of CGA and their impact on the patients' function and quality of life. Studies involving the patients' and caregivers' preferences are also lacking. Frail elderly patients have been excluded from clinical trials of drug treatment, thus further research is needed to investigate strategies for optimal drug treatment in such patients.

Making RCTs on very old patients with many chronic disorders are challenging. Alternative methods should therefore be considered in addition to RCTs, using quality indicators or establishing high-quality databases with equal datasets within and across countries. The Resident Assessment Instrument (RAI) is an example of a dataset that has been recommended for use among geriatric patients (Phillips *et al.*, 1997). Such databases may improve possibilities for assessing case-mix, care plans, outcome measures and quality measures.

8.0 References

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